Compilation of Research Papers presented by Madhavbaug Team
at various national and international research platforms

From the desk of Dr. Rohit Madhav Sane

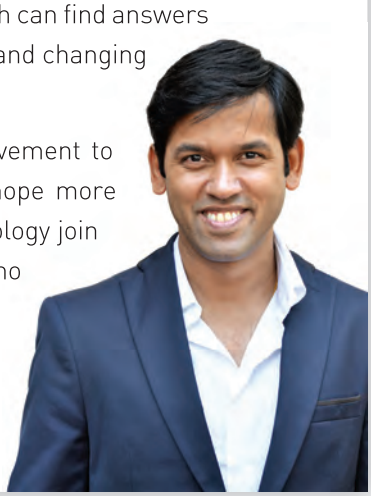
- CEO, Madhavbaug

Publishing this book is a proud moment for the whole Madhavbaug family whose years of effort in Ayurveda based research has been instrumental in bringing this book to life. I would like to congratulate the entire research team, doctors, management team and patients without whose belief this would not have been possible.

According to a report by the World Economic Forum and the Harvard School of Public Health published in 2011, NCD's will cost the world USD 47 trillion over the next 20 years. Cardiovascular disease along with diabetes, hypertension and obesity contribute to a large part of this. The existing medical systems worldwide are not fully equipped to meet this burden and Ayurvedic treatments will play a major role in fighting this disease burden.

Ayurveda is a science of life with a holistic approach to health and personalized medicine. It is one of the oldest medical systems, which comprises thousands of medical concepts and hypothesis. Interestingly, Ayurveda has ability to treat many chronic diseases such as cancer, diabetes, arthritis, and asthma, which are untreatable in modern medicine. Unfortunately, due to lack of scientific validation in various concepts, this precious gift from our ancestors is trailing. Like any other line of treatment, Ayurveda in its current form, will require heavy investment of time, intelligence and financial resources in research to prove the efficacy and safety of its treatments for not just patients but the global healthcare community. Research plays an important role in discovering new treatments, and making sure that we use existing treatments in the best possible ways. Research can find answers to things that are unknown, filling gaps in knowledge and changing the way that healthcare professionals work.

Through this book we are happy to pioneer this movement to reduce this disease burden through Ayurveda and hope more Ayurveda practitioners in the field of preventive cardiology join us. Our doors are always open to support anyone who requires any help with their research.



Madhavbaug™

From the desk of Dr. Rahul Mandole

- HOD of Research Dpt., Madhavbaug

Research should be a process that converts data into information, information into knowledge and knowledge into wisdom. This is like transforming milk into ghee. It should be more balanced, comprehensive and equally emphasizing in the literary field and experimental and clinical research.

Evidence based clinical cardiology with Ayurveda is the first step towards making Ayurveda first line treatment option. This compilation of research articles will provide you evidences that will make you start believe in our own ancient healthcare system.

This research compilation is a cluster of clinical cardiology related research article who talk about efficacy of Ayurveda based intervention in chronic heart diseases and risk factors like chronic heart failure, Ischemic heart diseases, hypertension, diabetes and obesity.

First time in a history of Indian medicines, modern parameters like VO2peak, Duke Treadmill score, ejection fraction were studied to understand efficacy of Ayurveda in treating chronic heart diseases which will surely help you to change the prospective to see towards Ayurveda.

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Sampurna Hriday Shuddhikaran: an interventional health model to improve quality of life in chronic heart failure.

Rohit Sane, Milind Hanchate
Madbavbaug cardiac Rehabilitation center, Raigad, india

Background: Heart disease is a worldwide problem affecting people in all communities. The burden of cardiovascular disease in India is immense. India will bear 60*» of the world's heart disease burden in the next two years and the average age of patients with heart disease is lower among Indian people who belong to the economically productive group, it Is not only the lack of resources but also the inability to continue with the costly treatment that further adds to the woes of the patients. Ayurveda has not only proved beneficial in chronic heart failure but also has helped to improve the quality of life of such patients.

The objectives of this study were :
(1) to study the exercise tolerance capacity of the chronic heart failure patient and
(2) to study the effect of the Sampurna Hriday Shuddhikaran (SHS) model in improving the exercise tolerance capacity of chronic heart failure patients.

Methods: Novel Ayurveda-based Madhavbaug Ayurvedic Cardiac Rehabilitation Centre (MCRC) protocol that combines a four-pronged intervention of Snehan (oil massage to reduce vascular tone), Swedan and Hrid Dhara (thermal therapy to reduce salt and water retention), and Basti (rectal herbs to increase cardiac contractility) was used in each patient who received twice daily sessions of 90 min each for six consecutive days. Symptomatic patients (age 17-80 years) with congestive heart failure (grade 1-3 of New York Heart Association classification), of either sex, with an ejection fraction more than 25% and who provided written informed consent were included in study. Patients with a history of myocardial infarction in the previous 2 weeks, uncontrollable hypertension (systolic blood pressure $\geq$180 mm Hg and diastolic blood pressure $\geq$11O mm Hg), severe hepatic/renal insufficiency, or pregnancy or lactating were excluded. Evaluation parameters used were exercise tolerance capacity (measured by the standard 6-min walk test [6MWT] and improvement in stress test [ST]), improvement in grade of symptoms (GOS), improvement in maximum oxygen uptake (V02 max), and improvement in metabolic equivalents (METs) taken on day 1 (preintervention) and on day 6 (postintervention).

Findings: A total of 200 patients were evaluated. Mean age = 55±9 years; mean BMI = 24.5±3 kg/m^2; pre-existing diabetes mellitus on treatment = 40%; and past history of coronary angiography or bypass = 7%. The mean improvement in exercise tolerance as measured by 6MWT and ST postintervention was 70.6 min 6 min and 132.1±85.4 s in 9 min (p=003), respectively. The corresponding improvement in V02 max and METs was 3.1±3.44 L/min and 2.23±1.9 METs. Patient symptoms also improved. Vital parameters were stable. No significant adverse events were seen in any patient.

Interpretation: Sampurna Hriday Shuddhikaran using a novel MCRC protocol was effective In improving the exercise tolerance and oxygen uptake in symptomatic chronic heart failure patients, and this improvement was Independent of age, sex, and body-mass index. Further studies are required to confirm these results on a large sample size.

Conflicts of interest: The authors have declared no conflicts.

The Lancet / JACC 1st Asia Pacific Cardiovascular Summit

Sampurna Hriday Shuddhikaran: An Interventional Health Model to Improve Quality of Life in Chronic Heart Failure

- Rohit Madhav Sane and Milind Sudhakar Hanchate
Madhavbaug Cardiac Rehabilitation Center, Raigad, India

Abstract: Background: Heart disease is a worldwide problem affecting people in all communities. The burden of cardiovascular disease in India is immense. India will bear 60% of the world's heart disease burden in the next two years. Average age of heart patients is lower among Indian people who belong to the economically productive group. It is not only the lack of resources but also the inability to continue with the costly treatment that further adds to the woes of the patients. Method: Present investigations has been carried out in 200 chronic heart failure patients (Mean age = 55±9 years) using novel approach of Sampurna Hriday Shuddhikaran (SHS), an interventional health model. Preintervention & post interventional cardiac effort tolerance measured and compared. Results: Mean post intervention improvement in exercise tolerance measured by 6MWT (6 Minute walk test) in meters and ST (stress test) in seconds was 70.6 m in 6 min and 132.1±85.4 s in 9 min (p = 0.03), respectively. The corresponding improvement in VO2 max and METs was 3.1±3.44 L/min and 2.23±1.9 METs. Conclusion: Sampurna Hridhay Shudhikaran (SHS) model is very much effective in improving the exercise tolerance of Chronic Heart Failure patients and this improvement is independent of Age, Sex and BMI of the study participants.

Key words: Sampurna Hridaya Shuddhikaran (SHS), Exercise Tolerance (ET), Chronic Heart Failure (CHF).

1. Introduction

Throughout the developed world, heart disease is worldwide problem affecting people in all communities. A recent study mentioned that India will bear 60 percent of the world's heart disease burden in the next two years [1]. In India prevalence of heart disease is reported to be 2.3 times higher in the urban population as compared to rural population. The causes and magnitude may vary with geographical location and socioeconomic status. To a great extent, the disease is lifestyle-related, and results from a kapha-provoking sedentary lifestyle, coupled with excess consumption of fatty foods, especially trans-fats, and insufficient intake of fruits and vegetables. Pitta factors such as stress and overwork are also known to play a major role.

"Metabolic syndrome", as it is currently described, is the precursor to heat disease [3]. Consisting of abdominal obesity, elevated serum cholesterol and triglycerides, elevated blood pressure, insulin resistance and a prothrombotic state (sticky blood that clots too easily), metabolic syndrome could more accurately be called kapha syndrome. So whatever may be the cause patients ultimately lands up in chronic heart failure. Chronic Heart Failure (CHF) is a condition in which the heart's function as a pump to deliver oxygen rich blood to the body is inadequate to meet the body's needs. CHF due to systolic or diastolic dysfunction resulting from ischemic heart disease, Myocardial Infarction (MI) leads to reduced Cardiac Output (CO). This generates neurohumoral responses resulting in activation of sympathetic system and secretion of ADH (Anti-diuretic hormone), BNP (Brain Natueretic Peptide) and. Renin angiotensin system stimulation. Consequently the blood volume increases due to salt and water retention and vasoconstriction increasing the peripheral resistance.

Average age of patients with heart disease is lower among Indian people who belong to the economically productive group. It is not only the lack of resources but also the inability to continue with the costly treatment that further adds to the woes of the patients.

At present there is no economical treatment available for cardiac failures. A comprehensive herbal therapy named Sampurna Hriday Shudhikaran (SHS) was planned to reverse the effect of above pathophysiology.

Its use as a complementary therapeutic regimen under medical supervision is appropriate and could be worth considering. The present investigations have been carried out in 200 chronic heart patients including male and females. A novel herbal procedure Sampurna Hriday Shuddhikaran (SHS) is used for the management of them. The results suggest that SHS is very effective low cost intervention in improving the exercise tolerance of heart in Chronic Heart Failure; however this improvement was independent of age, sex and Body Mass Index (BMI).

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Sampurna Hriday Shuddhikaran: An Interventional Health Model to Improve Quality of Life in Chronic Heart Failure

2. Patients and Methods

Pre diagnosed 200 patients Mean age = 55±9 years of chronic heart failure were selected for the present investigation. Symptomatic patients (age 17–80 years) with congestive heart failure (grade 1–3 of New York Heart Association classification), of either sex, with an ejection fraction more than 25% and who provided written informed consent were included in study.

Patients with a history of myocardial infarction in the previous 2 weeks, uncontrollable hypertension (systolic blood pressure 180 mm Hg and diastolic blood pressure 110 mm Hg), severe hepatic/renal insufficiency, or pregnancy or lactating were excluded.

A centre-based cohort study was conducted in "Madhavbaug Ayurvedic Cardiac Rehabilitation Center", about 100 kilometres from Mumbai city (India). The protocol used in the present investigation was approved by the Institutional Ethical Committee of Madhavbaug. Preintervention clinical status of these patients was assessed by using six-minute walk test (SMWT in meters) and Stress test (ST in second) to evaluate the exercise tolerance capacity, improvement in grade of symptoms (GOS), improvement in maximum oxygen uptake (VO2 max), and metabolic equivalents (METs) taken on day 1. The initial readings were noted down. All the 200 subjects were then given two setting of the study procedure-Sampurna Hriday Shuddhikaran (SHS) every day. Heart rate and blood pressure was monitored every day before and after procedure. On the sixth day after completing the study procedure, Six minute walk test and stress test was repeated in all subjects to record exercise tolerance capacity after intervention. All activities were performed by skilled operators and evaluated by two experienced observers blinded to each other's interpretation.

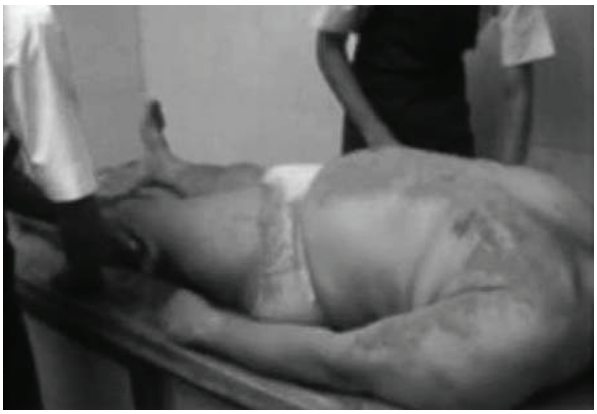
For exercise and stress Test, the modified Madhavbaug Cardiac Rehabilitation Centre (MCRC) Protocol was used — Total Duration 9 minutes, Speed: 1.6 Km/hr for first minute then speed increased every minute by 1 Km/hr till 5th minute, then speed was kept constant till 9 th minute. Inclination was kept constant of 2 degree till 4th minute then increase 2 degree every minute in 9 minutes.

Sampurna Hriday Shuddhikaran (SHS), A Herbal therapeutic procedure consist of four stages (Figd. 1–4) and takes 90 minutes. Procedure is carried out twice in a day for all consecutive six days by trained & skilled staff.

The steps are as follows:

Snehan Swedan Hrid Dhara Basti

Snehan: consist of seasame (Til) oil centripetal massage in strokes directed towards the heart, seasame oil is known antioxidant. Procedure helps in increasing venous return.



Swedan: is thermal therapy to reduce salt and water retention through profuse seating. Here patients lie down in a closed wooden box with his neck outside and medicated steam is passed inside the box.

Hrid dhara: is a procedure where in warm herbal decoction is concentrated drop by drop constantly from certain hight, which helps to reduce spasm of intercostal muscles and improves local blood supply by vasodilatation.

Basti: here enema is given with Terminalia arjuna decoction. T. arjuna is a herbal medicine which helps in increasing force of contraction of heart muscles.
Seasame oil and Terminalia arjuna bark herbal decoction was used for the treatment and was administered to the patients by rectal route, i.e., as a enema.

For decoction, 5 gm of dried bark powder of T. Arjuna, 80 ml of saline water was added and the mixture was boiled till 1/4 of water remains giving rise to 20 ml used single dose. For Enema, 25 gm of powder in 400 ml water was boiled to evaporate water upto 100 ml.
Pre and Post intervention exercise tolerance data was assessed and compared, SPSS version 16:00 was used for data analysis. Statistical tools like Mean, SD, Pairedt' test, Pearson correlation coefficient was used.

3. Results

Table 1 Shows Improvement in 6 minute walking test, stress test, METS and VO2 max.

Table 1 - 6 minute walking test, stress test, METS and VO2 max.

Improvement	Mean	N	Std. Deviation
Six Minute Walk (in meters)	70.6	200	73.27
Stress test result (in seconds)	132.10	200	85.72
Metabolic Equivalents	2.114	200	1.9
VO2 Max (Liters/Min)	3.10	200	3.4

4. Discussion

A total of 200 patients were evaluated. Mean age = 55±9 years; mean BMI = 24.5±3 kg/m2; pre-existing diabetes mellitus on treatment = 40%; and past history of coronary angiography or bypass = 7%.
The mean improvement in exercise tolerance as measured by 6MWT and ST postintervention was 70.6 m in 6 min and 132.1±85.4 s in 9 min (p = 0.03), respectively. The corresponding improvement in VO2 max and METs was 3.1±3.44 L/min and 2.23±1.9 METs. Patient symptoms also improved. Vital parameters were stable. No significant adverse events were seen in any patient.
The relation between gender and improvement in mean of 6 MWT (P = 0.26), ST (P = 0.56) and METS (0.58) was not statistically significant. Similarly the correlation between Age and improvement in Mean 6MWT (r = 0.03), ST (r = 0.03), a (0.07) was not statistically significant. The correlation between BMI and improvement in Mean 6MWT (r = 0.1), ST (r = 0.01) and METS (r = 0.1) was also not statistically significant.
It is well studied that exercise training and daily physical activities are essential for improving a cardiac patient physical fitness. Supervised cardiac exercise for 3 to 6 month generally is supported to increase patient peak of oxygen uptake by 11%to 36% with greatest improvement in most de-conditioned individuals [4, 5].
In the present investigation we propose that the SHS herbal treatment model with modified fitness training may help in oxygen uptake and reduced sub-maximal heart rate, systolic blood pressure and RPP. However, the detailed biophysical and biochemical mechanisms yet to be identify. Another study mentions that cardiac effort tolerance improved by 121 seconds measured by stress test with bruce protocol after one month of PTCA [6].
In present study after SHS therapy with MCRC protocol on stress test gives improvement in cardiac effort tolerance of 132.1 seconds on sixth day.
From above discussion we can conclude that Sampurna Hridhay Shudhikaran (SHS) model is very much effective in improving the exercise tolerance of Chronic Heart Failure patients and this improvement is independent of Age, Sex and BMI of the study participants.

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Improving the quality of life of chronic heart failure patients : Role of 'Sampurna Hridaya Shodhikaran'- An Ayurveda based Intervention model

A NOVEL AYURVEDIC APPROACH FOR MANAGEMENT OF CHRONIC HEART FAILURES.

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ABSTRACT: Ayurved, a traditional Indian medicine remains the most ancient yet living traditions. There has been increased global interest in traditional medicine. It has proved to be effective in most of the heart diseases and can be a total cure for chronic heart failure. The present investigations has been carried out in 120 (male- 84,female- 36) chronic heart failure patients using novel approach of ayurved based model i.e *Sampurna Hriday Suddhikaran* (a compete heart cleaning). The results shows that there is improvement in the 6 Minute walk test (MWT, r=0.74), Stress Test (ST, r=0.85) and METS (r=0.73) after intervention. However, it indicates a highly significant ($p<0.001$).
*Corresponding author

Key words, Sampurna Hriday Suddhikaran (SHS), Chronic heart failure (CHD).

INTRODUCTION:

Throughout the developed world, heart disease is worldwide problem affecting people in all communities. A recent study mentioned that India will bear 60 percent of the world's heart disease burden in the next two years[1]. In India prevalence of heart disease is reported to be 2.3 times higher in the urban population as compared to rural population[2]. The causes and magnitude may vary with geographical location and socioeconomic status. To a great extent, the disease is lifestyle-related, and results from a kapha-provoking sedentary lifestyle, coupled with excess consumption of fatty foods, especially trans-fats, and insufficient intake of fruits and vegetables. Pitta factors such as stress and overwork are also known to play a major role. "Metabolic syndrome", as it is currently described, is the precursor to heat disease[3]. Consisting of abdominal obesity, elevated serum cholesterol and triglycerides, elevated blood pressure, insulin resistance and a prothrombotic state (sticky blood that clots too easily), metabolic syndrome could more accurately be called kapha syndrome.

At present there is no economical treatment available for cardiac failures. However, the ayurved may provide beneficial and promising treatment for cardiac failures/hypertension.

The ayurvedic treatment referred as the use of herbal preparations, diet, meditations, yoga, pranayam etc. There is no any promising report that shows the ayurvedic is effective treatment for chronic heart diseases of any cardiac ailments. Many herbs used by Ayurvedic practitioners show promise and could appropriate for larger randomized trials. *Yoga* and *Pranayam* an integral part of Ayurveda, has been shown to be useful to patients with heart disease and hypertension. Both reduces anxiety, promotes well-being, and improves quality of life. Its safety profile is excellent. Its use as a complementary therapeutic regimen under medical supervision is appropriate and could be worth considering.

The present investigations have been carried out in 128 chronic heart patients including male and females. A novel ayurvedic approach Sampurna Hriday Suddhikaran (SHS) is used for the management of them. The results suggest that SHS is very effective low cost intervention in improving the exercise tolerance of heart in Chronic Heart Failure; however this improvement was independent of age, sex and Body Mass Index (BMI).

MATERIALS AND METHODS:

Pre diagnosed 128 (male- 84, female,36) patients of chronic heart failure were selected for the present investigation. The left ventricular ejection fraction was 30% and the mean age of the patient was 51.17 (SD= 10.73). As per WHO guidelines, the informed consent was given to patient.

The exclusion criteria was - age more than 80 years, severe heart failure (NYHA grade IV) , history of myocardial infarction in last 2 weeks severe joint disability which limits activity , hepatic or renal insufficiency (serum creatinine 2.5 mg/dL), Pregnancy or lactation , patients with the presence of specific medical disorders which require immediate treatment (e.g. fractures, infectious diseases, etc.)

A centre-based cohort study was conducted in 'Madhavbaug Ayurvedic Cardiac Rehabilitation Center', about 100 kilometres from Mumbai city (India). The protocol used in the present investigation was approved by the Institutional Ethical Committee of Madhavbaug. Pre-intervention, clinical status of these patients was assessed by using six-minute walk test (SMWT in meters) and Stress test (ST in second) to evaluate the exercise tolerance capacity. The initial readings were noted down. All the 128 subjects were then given two setting of the study procedure- *Sampurna Hriday Shuddhikaran* (SHS) every day. Heart rate and blood pressure was monitored every day before and after procedure. On the seventh day after completing the sixth sitting of study procedure, Six minute walk test and stress test was repeated in all subjects to record exercise tolerance capacity after intervention. All activities were performed by skilled operators and evaluated by two experienced observers blinded to each other's interpretation

For exercise and stress Test, the modified Madhavbaug Cardiac Rehabilitation Center (MCRC) Protocol was used- *Total Duration* 9 minutes, *Speed***:** 1.6 Km/ hr for first minute then speed increased every minute by 1 Km/hr till 5th minute, then speed was kept constant till 9th minute. *Inclination* **was** kept constant of 2 degree till 4th minute then increase 2 degree every minute in 9 minutes.

Sampurna Hriday Shuddhikaran (SHS)*, a* Ayurvedic therapeutic procedure consist of four stages (fig. 1-4) and takes one hour & thirty minutes. Procedure is carried out twice in a day for all consecutive six days by trained & skilled staff. The steps are as follows.

Snehan → Swedan → Hrid Dhara → Basti

The initial stage consist of seasame (*Til)* oil centripetal massage in strokes directed towards the heart, seasame oil is known antioxidant and helps in cholesterol lowering and controls blood pressure. Final stages consist of treatment with *Terminalia arjuna* decoction. *T. arjuna* is a herbal medicine which helps in curing cardiac diseases.

Seasame oil and *Terminalia arjuna* bark herbal decoction was used for the treatment and was administered to the patients by rectal route i.e. as a enema.

For decoction, 5 gm of dried bark powder of *T. Arjuna,* 80 ml of saline water was added and the mixture was boiled till 1/4th of water remains giving rise to 20 ml used single dose.

For Enema, 25 gm of powder in 400 ml water was boiled to evaporate water upto 100 ml. Pre and Post intervention exercise tolerance data was assessed and compared, SPSS version 16:00 was used for data analysis. Statistical tools like Mean, SD, Paired't' test, Pearson correlation coefficient was used.

Fig 1. *Snehan*

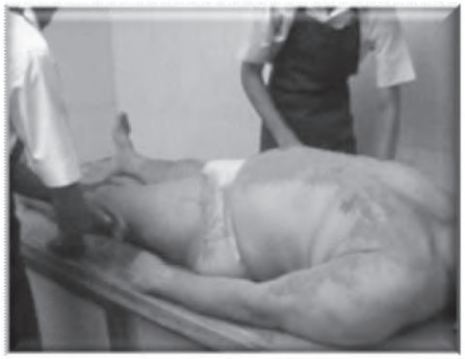

Fig. 2, Swedan

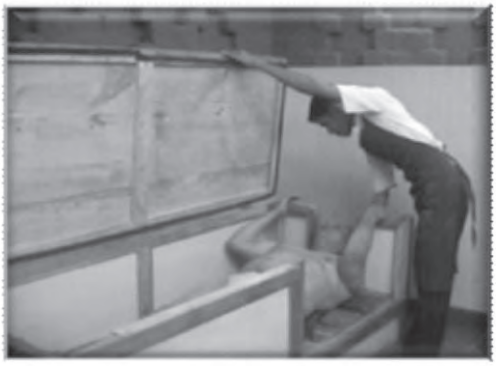

Fig.3. ***Hrid Dhara***

Fig.4. ***Bast***

RESULT AND DISCUSSION:

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Six minute walk (in meters) test before intervention	454.71	120	106.695	11.505
	Six minute walk (in meters) test after intervention	531.40	120	88.479	9.541
Pair 2	Stress test result (in seconds) before intervention	376.59	120	174.022	18.765
	Stress test result (in seconds) after intervention	503.66	120	153.803	16.585
Pair 3	Metabolic Equaivalents Before Intervention	6.0937	120	2.21726	.24946
	Metabolic Equaivalents Before Intervention	8.3937	120	1.74057	.19583

Table: Shows improvement in six MWT (Mtrs), Stress Test (Second) and METS.

Out of total 120 study participants, 84 (69.8%) were Male and 36 (30.2%) were Female. Mean age (in years) of the participants was 51.17 (SD=10.73). Mean BMI (Kg/M^2) of the participants was 24 (SD=3.5).

Pre intervention, Mean 6 Minute Walk Test (6MWT) in meters, Stress Test (ST) in seconds and Metabolic Equivalents (METS) was 454.71 (SD=106.7), 376.6 (SD=174.02) and 6.1 (SD=2.2) respectively.

Post intervention, the mean of 6 Minute Walk Test (6MWT) in meters, Stress Test (ST) in seconds and Metabolic Equivalents (METS) was 531.4 (SD=88.5), 503.7 (SD=153.8) and 8.4 (SD=1.7) respectively. Study result shows that the improvement in the results of 6 MWT (r=0.74), ST(r=0.85) and METS (r=0.73) after intervention. It was Highly Significant ($p<0.001$).

The relation between Sex and improvement in mean of 6 MWT (P=0.26), ST (P=0.56) and METS (0.58 was not statistically significant. Similarly the correlation between Age and improvement in Mean 6MWT (r=0.03), ST (r=0.03) and METS (0.07) was not statistically significant. The correlation between BMI and improvement in Mean 6MWT (r=0.1), ST (r=0.01) and METS (r=0.1) was also not statistically significant.

It is well studied that exercise training and daily

physical activities are essential for improving a cardiac patient physical fitness. Supervised rehabilitive exercise for 3 to 6 month generally is supported to increase patient peak of oxygen uptake by 11%to 36% with greatest improvement in most de-conditioned individuals [4,5]. Improved physical fitness is associated with reduction in sub-maximal heart rate, systolic blood pressure, and heart rate pressure product (RPP), thereby decrease myocardial oxygen requirements during moderate to vigorous activities of daily living. In the present investigation we propose that the SHS Ayurvedic model with modified fitness training may help in oxygen uptake and reduced sub-maximal heart rate, systolic blood pressure and RPP. However, the detailed biophysical and biochemical mechanisms yet to be identify.

CONCLUSION :

Sampurna Hridhay Shudhikaran (SHS) model is very much effective in improving the exercise tolerance of Chronic Heart Failure patients and this improvement is independent of Age, Sex and BMI of the study participants.

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Effect of the Sampurna Hriday Shuddhikaran (SHS) Model in Heart Failure Patients in India: A Prospective Study

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[2]Research Department, Madhavbaug Cardiac Rehabilitation Center, Raigad, India.

Authors' contributions

This work was carried out in collaboration between both the authors. Author RS reviewed the protocol & literature of the study. Author MH designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Both the authors wrote & approved final manuscript for publication.

Research Article

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ABSTRACT

Background and Objectives: Chronic heart failure (CHF) is an increasingly widespread, costly and deadly disease, frequently named as an epidemic of the 21st century. Herbal treatments may provide promising & beneficial treatment for heart failure. But unfortunately there is no promising report that shows herbal treatment is effective treatment for chronic heart failure. In that context we planned present study. The objective of the study was to evaluate the effect of the herbal procedure Sampurna Hriday Shuddhikaran (SHS) model in improving the left ventricular (LV) structure & function and exercise tolerance capacity in patients with heart failure.
Methods: 133 patients (107 male & 26 Female) were selected for study. A prospective interventional study with novel noninvasive intervention SHS consist of the 4 pronged interventions of Snehan, Swedan, Hrid Dhara and Basti was used in each patient who received twice daily sessions of 90 mins each for 6 consecutive days. Preintervention 2 D echo & 6 minute walk test in meters were done on first day of admission. Postintervention 2 D echo & 6 MWT were done after 30 days and 6 days respectively.
Results: Preintervention mean Ejection fractions was 39 ±, 14.6 & after intervention ejection fraction was 45 ±13.6. This difference was found to be highly significant ($p<0.001$). Preintervention Interventricular septum (IVS) was 9.2 ±2.8 & Post intervention

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IVS was 9.7 ±3 ($p<0.05$). Preintervention mean of 6 MWT in meters was 395 ±93.3 & after intervention 510 ±123.3 found to be highly significant ($p<0.001$).
Conclusion: Herbal treatment procedure SHS is associated with improvements in ejection fraction, myocardial thickness and exercise tolerance.

Keywords: Heart failure; herbal procedure; sampurna hriday shuddhikaran; 6 minute walk test; echocardiography; ejection fraction; interventricular septum.

1. BACKGROUND & OBJECTIVES

The definition of heart failure has been variable but as per American Heart Association (AHA) guidelines, HF is a complex clinical syndrome that can result from any structural or functional cardiac disorder which impairs the ability of the ventricle to fill with or eject blood. In 2000, there were an estimated 30 million people with coronary heart disease (CHD) alone in India, or a nearly 3% prevalence [1,2]. The annual incidence of HF for patients with CHD ranges from 0.4% to 2.3% per year [3,4], suggesting that 120 000–690 000 Indians could develop symptomatic HF due to CHD every year leading to disability adjusted life years (DALYs) [5,6,7].

Important social determinants of health such as poverty, lack of empowerment, and healthcare inequalities impede these efforts and are likely to exacerbate the burden of HF in India & globally [8].

Herbal treatment may provide promising & beneficial treatment for heart failure [9]. But unfortunately there is no promising report that shows herbal treatment is effective treatment for chronic heart failure. Reviewing the clinical researches in herbal treatment is found intertwined with huge difficulties primarily because of unavailability of qualitative research works which are published and accessible [10]. In that context we planned to study the effect of the herbal procedure Sampurna Hriday Shuddhikaran (SHS) model in improving the exercise tolerance capacity of chronic heart failure patients.

The objective of the study was to evaluate the effect of the Sampurna Hriday Shuddhikaran (SHS) model in improving the left ventricular (LV) structure, function and exercise tolerance capacity in patients with heart failure.

2. METHODS

The study was a prospective interventional study. All patients provided written informed consent and the study was approved by the Institutional ethical committee on medical research ethics. Patients were recruited as inpatients by a single centre at Madhavbaug hospital. Symptomatic patients (age 33–80 yrs) with CHF (Grade 2-3 of NYHA classification), of either gender, with ejection fraction more than 25%. were included in study. Patients with history of Myocardial infarction in last 2 weeks, uncontrollable hypertension (SBP ≥180 & DBP ≥110 mmHg), severe hepatic/renal insufficiency, pregnancy/lactating were excluded. The patients was kept in hospital for 6 days after which he gets discharged.

Expert persons performing 2 D echo & 6 MWT were blinded & following protocol was followed for study participants:

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0 Day - Admission and 2 D echo testing & 6 Minute walk test measured in meters.
0 to 6th day - Two sessions of SHS were performed everyday for 6 consecutive days.
6th day – 6 Minute walk test & discharge.
30th day- 2 D echo testing.

2.1 Intervention

A single session of novel noninvasive interventional herbal procedure, Sampurna Hriday Shuddhikaran (SHS) is of 90 minutes duration. Two sessions of SHS were performed everyday for 6 consecutive days to treat CHF patients. There was no other intervention received by patients during their hospital stay of 6 days.

SHS consists of the 4 pronged interventions in following order.

1. SNEHAN: A til oil centripetal massage in strokes directed toward the heart from periphery. 2. SWEDAN: Patient lies in a closed wooden chamber with head remains outside the chamber. An herbal moist steam bath to the whole body below the neck, using about 50 g of *Terminalia arjuna* bark. This procedure leads to profuse body sweating. 3. HRID DHARA: Patients chest is packed with dough. Warm herbal decoction of 50 g of *T. arjuna* bark is made to concentrate on the precordial area. 4. BASTI: An herbal enema given very slowly using decoction of 10 g of *T. arjuna* bark. The decoction was prepared in 1000 ml of water that was boiled until the water evaporated to 100 ml. This was administered rectally.

2.1.1 Clinical assessment

2.1.1.1 D Echocardiogram

The aims of the echocardiography examination were to evaluate the effect of SHS on interventricular septum and EF. 2 D echo parameters were measured by M-mode as per guidelines of American Society of Echocardiography (ASE) using standard protocol based on apical two and four chamber views [11,12]. Parameters measured were ejection fraction in % & thickness of interventricular septum in mm. 2 D echo testing was done first on day 1 on admission & second was done after 30days by same qualified person.

2.1.1.2 Exercise tolerance capacity [as measured by standard 6 minute walk test (6MWT)

The 6MWT has been used in many studies to assess the effect of therapeutic interventions in patients with heart failure [13,14,15,16]. After 6 min had elapsed, patients were instructed to stop walking, and the total distance walked was measured. The test was supervised by a physical therapist who encouraged the patients in a standardized fashion at regular intervals. A baseline 6MWT was performed on the first day of admission before treatment and on the 6th day on which patients get discharged after treatment. Patients were called after 30 days for 2 D echo testing.

2.1.1.3 Statistical analysis

Data were entered on and analyzed using the SPSS-16.0 statistical package. Change in six minute walking distance and 2 D echo parameter were normally distributed and analyzed using two sample Student's paired *t* test. Post study statistical power of the test was found to be 96.38%.

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3. RESULTS

Out of total 133 majority of the study subjects were in age group between 53 to 62 years of age(34.6%) followed by 63 to 72 years.(30.8%). Mean age of the study participant was 58.38±1.03. 107 (80.5%) were male while 26(19.5%) were female (Table 1).

Table 1. Sociodemographic characteristics of study sample by age & sex

Characteristics	Number of participants
Age in years	N=133
33—42	11(8.3)
43—52	25(18.8)
53—62	46(34.6)
63—72	41(30.8)
73—82	10(7.5)
Sex	
Male	107(80.5)
Female	26(19.5)

Figures in parenthesis indicate percentage.
Mean age: 58.38± (SD 1.03)

50.4% was found to be normal BMI (18.5—24.99 kg/m2) & 44.4% was overweight (BMI > 25 kg/m2). The Mean BMI (kg/m2) was 24.52± 3.89 (Table 2).

Table 2. Body mass index (BMI) of study participants

BMI (kg/m2)	**No**
< 18.5	7(5.3)
18.5—24.99	67(50.4)
25 & above	59(44.4)

Figures in parenthesis indicate percentage.
Mean BMI =24.52 ± 3.89.

Preintervention mean Ejection fractions (%) was 39.4± 14.6 & after intervention mean EF (%) was 45.9 ± 13.6. It was found to highly significant (P<0.001). Preintervention IVS (in mm) 9.28 ± 2.8 and Post intervention IVS 9.73 ± 3 (P=0.05) (Table 3).

Preintervention mean of 6 MWT in meters was 395.47 ± 93.3 & after intervention mean of 6 MWT in meters was 510.27 ± 123.3. It was found to be highly significant (P <0.001).

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Table 3. Pre & post intervention 2 D Echo & 6 MWT findings in study participants

Pair	Row no.	Variables	N	Mean	SD	SE	P value
Pair 1	1	EF (before intervention)	133	39.43	14.69	1.27	<0.001
	2	EF (After intervention)	133	45.98	13.69	1.18	HS
Pair 2	3	IVS before intervention	133	9.28	2.83	0.244	<0.05
	4	IVS after intervention	133	9.73	3.08	0.267	S
Pair 3	5	Six minute walk test (in meters) before intervention	133	395.47	93.37	10.78	<0.001 HS
	6	Six minute walk test (in meters) After intervention	133	510.27	123.44	14.25	

Rows 1,3,5 represents before intervention values & Rows 2,4,6 represents after intervention values. HS: highly significant; S: significant

4. DISCUSSION

The most important result of this study is that 6 days of SHS intervention showed a significant improvement in echocardiography parameters as well as exercise tolerance in 133 patients with heart failure. Because all of the patients were studied echocardiographically, the relationship between outcomes and LV structure and function was confirmed.

SHS improves hemodynamic conditions as ejection fraction (EF) increases after 6 days of Intervention by 6.5 % (39 ±, 14.6 & 45 ± 13.6). This difference was found highly significant ($p< 0.001$). Also thickness of interventricular septum was improved significantly from 9.2 mm to 9.7mm.

Comparison of the preintervention & postintervention in study participants at day 1 & day 6 showed an increase in mean 6 MWT of 115 meters (395 ± 93.3 vs. 510 ± 123.3 $P<0.001$) Our outcomes were consistent with previous research studies involving outpatient intervention programs designed to increase the functional capacity [17].

However, one observational study similar to ours study found equal improvements between individuals with and without left ventricular dysfunction in the six-minute walk distance and quality of life scores [18]. Evaluation & management of heart failure using oral drug therapy was also seen in some studies [19,20,21]

Lower levels of functional capacity (a distance <300 m during 6MWT) have proven to be predictive of mortality (total or cardiovascular) and morbidity (hospitalization for worsening heart failure) both in patients with with mild-moderate [22,23,24] and advanced heart failure [25,26]. In the SOLVD study, total mortality was 10.23% in subjects with a 6MWT<300 m and 2.99% in subjects with a 6MWT≥450 m [27].

The improvement in echocardiographic & exercise tolerance findings in the current study is associated with SHS intervention in heart failure patients.

Such studies are necessary and serve as an important indication that individuals with CHF can safely benefit from cardiac rehabilitation programming while learning lifestyle modifications that may improve overall health. Although there may never be complete restoration of pre-disease physical functioning levels in individuals with CHF, these initial

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increases, if sustained, may be meaningful in terms of the quality of a potentially prolonged life span.

4.1 Limitation of Study

A limitation of this study is the lack of a control group for comparison to treatment withheld and long term follow up parameters is difficult & needs patients cooperation.

5. CONCLUSIONS

Herbal treatment procedure SHS is associated with improvements in ejection fraction, myocardial thickness and effort tolerance capacity in patients with heart failure in just 6 days. The study results further illustrate the usefulness of monitoring structural changes in the left ventricle as a guide to long-term efficacy in heart failure treatment.

CONSENT

All authors declare that 'written informed consent was obtained from the patients for publication of this research work.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the Institutional ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

ACKNOWLEDGEMENTS

We are grateful to all the participants who gave their time, support and enthusiasms in making this study a success.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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IMPROVE-MENT IN EXERCISE TOLERNCE CAPACITY OF HEART
REDUCTION IN ONGOING ISCHEMIA
REDUCTION IN FUTURE CARDIAC EVENTS
Rohit Sane

Rohit Sane et al., J Clin Exp Cardiolog 2015, 6:4
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April 27-29, 2015 Philadelphia, USA

Evaluation of the efficacy of the Ischemia Reversal Program (IRP) as add on therapy to conventional treatment in patients with Stable Ischemic Heart Disease (IHD)

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Introduction: CVD (Cardiovascular diseases) affects Indians with greater frequency and at a younger age than counterparts in developed countries, as well as many other developing countries. , CVD manifests here almost 10 year earlier on an average than other countries in the world, resulting in substantial number of deaths in working age group.4 This calls for the need to develop effective and economical treatment measures to address the issue. In classical Ayurvedic texts there is mention of various therapeutic procedures which can be adopted for improving the functional capacity and quality of life in patients with cardiovascular diseases.

The present study has been planned to evaluate the efficacy of IRP (Ischemia reversal program), a combination of Snehana (Oleation), Swedana (fomentation) and Basti (medicated enema) on improving the functional capacity and quality of life in patients with Ischemic heart disease (IHD).

Materials and Methods: Inclusion and Exclusion criteria: Patients of either sex, between 25 to 65 years of age with clinical diagnosis of Stab and time of onset of ischemia with stress test by M. Bruce protocol in between 60 to 600 seconds, significant occlusion in branches of coronary artery seen in CAG report were recruited in the study. Pregnant or lactating females or females planning to become pregnant during the course of the study, those with acute heart failure, acute decompensated heart failure attack within last 3 months were excluded from the study. Patients who were not on stable dose of standard treatment of chronic heart failure since last 3 months and needed upward dose titration, patients with uncontrolled hypertension (Systolic blood pressure (SBP) more than 150 and Diastolic blood pressure (DBP) more than 90) &Blood sugar level (fasting below 60 and Post Prandial above 250) and patients with anemia (Haemoglobin less than 10gm%) were also excluded from the study.

Ischemia Reversal Program (IRP): The IRP therapy consists of three steps:

a) Snehana (Oleation) which involves oil massage with Sesame oil. The procedure was carried out for 20 minutes with 15 to 30 strokes, followed by Swedana (fomentation).

b) The Swedana was done by asking the patient to lay down in supine position in a wooden box with his/her neck outside the box for 15-20 minutes or till the patient was able to tolerate the procedure.

c) Further Basti (per rectal drug administration) of100 ml decoction of medicated herbs (Tribulus terristris, Curcuma longa, Phyllanthus emblica) was administered to the patient by the rectal route.

Dose and Duration of treatment:

a) The IRP therapy was administered as 1 therapy daily for 7 Days i.e. 7 IRP therapies & 23 days of follow up. The therapy was administered at 10 am in the morning, maintaining a gap of at least 24 hours in between two therapies.

Methods of Evaluation: The detail history of the patient along with demographic information such as age and sex of the patient was recorded on Day 1. Further the patients were classified based on the cardiac functional capacity as per NYHA (New York Heart Association) classification before and after treatment. The stress test was conducted on Day 1, Day 7 and day 30 to evaluate the effect of IRP on the stress test duration, metabolic equivalents (METs) and Time of onset of ischemia. The patients were also assessed for improvement in the symptoms of IHD and overall health, any other associated complaints and requirement of concomitant drug usage before and after the study.

Results: The IRP therapy was administered to 29 patients, of whom 26 were male and 3 were female. The mean age of the patients recruited in the study was 58.93 Â± 7.61 years. At the baseline the average weight of the patients was 73.03 Â± 14.20 Kg which was decreased to 70.84 Â± 13.46 Kg at the end of IRP therapy (Day7). Mean time of onset of Ischemia at day 1 was 562.13 sec which was improved to 733.35 sec hence time to onset of ischemia was improved by 171.22 sec ($p<0.05$) at end of day 30.

CONCLUSION: Ischemia Reversal Program (IRP) when administered as add on therapy to conventional treatment may improve blood supply to myocardium & reduced symptoms of angina to improve quality of life in patients with stable Ischemic Heart Disease (IHD).

Biography

Rohit Sane, Pioneer of Ayurvedic non- invasive cardiology in India with those 200+ Ayurvedic physicians team treated more than 20,000 CHD patients.

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WORLD HEART FEDERATION
Madhavbaug
Functional Capacity is an Independent Predictor of Mortality in Heart Failure Patients with Low Ejection Fraction
1) ROHIT M. SANE, Clinical Cardiology, Madhavbaug, Mumbai, India
2) RAHUL S. MANDOLE, R & D, Madhavbaug, Thane
Introduction: Abnormal six-minute walk test (6MWT) findings which indicates decreased functional capacity is considered as predictor of increased cardiovascular risk and mortality. However, the importance of this variable as predictor of mortality in heart failure (HF) patients with low ejection fraction (EF) is not well established.
functional capacity measured through 6MWT findings (expressed as the distance walked in meters) to determine its prognostic importance during 1 year of follow-up. Of 128 patients, 50 (39%) died during follow-up; all reported deaths were found to be as cardiac related.
128 Patients Prognostic Factors associated with 1 year Survival of Chronic Heart Failure Patients
>400m Survived
<355m Died
28.7 Survived
26.62 Died
290gm Survived
290gm Died
6 Minutes Walk Test
Ejection Fraction
LV Mass

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A Retrospective cohort to study the mortality and survival rate amongst Chronic Heart Failure (CHF) patients after Ayurvedic Sampurna Hruday Shudhikaran (SHS) therapy

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Introduction: In India, by 2015, the cases of Coronary Heart Disease detected will be rising to 61,522,343 and the deaths due to Coronary Heart Dis-eases are predicted to reach 3,420,752. [1]. These figures seem to be really alarming. Cardiac diseases are seen affecting majority of population these days irrespective of age. Many modern drugs like beta blockers, inotropes, diuretics, along with upcoming interventional therapies like Cardiac resynchronization therapy (CRT), Implantable cardiac defibrillator (ICD) are currently ceasing the worsening of cardiac conditions. But these methods bring in lifetime dependency in patients, and so the affordability of treatment becomes a major concern [2]. In such scenarios, a novel Ayurvedic Non-interventional therapy Sampurna Hruday Shudhikaran therapy (SHS) of six days can be believed to bring in genuinely promising and convincing results. The present study was conducted to assess the effectiveness of SHS treatment among CHF patients after! Three years of completion of therapy.

Materials and Methods: In this retrospective cohort study, 690 patients who were admitted in Madhavbaug centres across Maharashtra during the year 2010-2011, were contacted by phone, out of which 542 patients were willingly to participate in this survey and were consented verbally. Primary data was collected using a tailored questionnaire over phone and analyzed for mortality, survival and re-hospitalization rates. Secondary data analysis was done for outcomes like 6 Minute's Walk Test (6MWT) in meters and Metabolic Equivalents (METs) done before and after the patients were treated with SHS therapy.

Results: Figure 1 explains that 72% had a remarkable improvement measured using New York Heart Association Class (NYHA). These 72.32% patients improved from NYHA Class II and III to NYHA Class I, 12.96% still possessed NYHA Class II, III and IV symptoms and 14.76% were dead.

SHS 4-step procedure: The re-hospitalization rate was 9.39% which covered elderly age group 50-59 years. The mean improvement after six days of SHS therapy was found to be 65 meters in 6MWT and 1.6 METs value.

Conclusions: SHS is a therapeutic Ayurvedic treatment consisting of four major steps of Snehan, Swedan, Hridhara, Basti followed in same order. This procedure is carried out twice on patients for six consecutive days. Highly efficacious naturally medicated oils and other formulations are used only on external basis for this treatment. This treatment has proven to reduce the drug dependency and improved quality of life amongst Chronic Cardiac Failure patients to a significant extent. The results were found positive even after three years of treatment showing the sustainability of SHS treatment.

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A Retrospective Cohort To Study The Mortality And Survival Rate in Chronic Heart Failure (CHF) Patients After Multidisciplinary Heart Failure Reversal Therapy (HFRT)

Dr. Rohit Sane, Dr. Gurudatta Amin, Dr. Rahul Mandole
Madhavbaug Multidisciplinary Cardiac Care Clinics & Hospital

Introduction

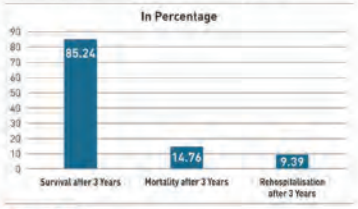
India will have nearly 61 million coronary heart disease (CHD) cases which would lead to 3.4 million of deaths by year 2015. So we thought that Heart Failure Reversal Therapy (HFRT), a Multidisciplinary non-interventional therapy, can provide convincing beneficial outcomes in long term chronic heart failure (CHF) patients. Therefore, present study was aimed to assess the effectiveness of HFRT retrospectively in CHF patients after 3 years.
HFRT consisting of four major procedures – Snehan(Centripetal Oleation), Swedan(Thermal Vasodilation), Hridhara(Herbal decoction thoracic drip), Basti(Per rectal medication).

Methods

In this retrospective cohort study, 690 patients who were admitted in Madhavbaug centres across Maharashtra during the year 2010 - 2011, were contacted by phone, out of which 542 patients were willingly to participate in this survey and were consented verbally. Primary data was collected using a tailored questionnaire over phone and analyzed for mortality, survival and re-hospitalization rates.

Results

HFRT showed remarkable improvement in study population where 72.32% patients improved from NYHA Class II and III to NYHA Class I, 12.96% still possessed NYHA Class II, III and IV symptoms and 14.76% were dead. The re-hospitalization rate was 9.39% which covered elderly age group 50-59 years.



Conclusions

This treatment has proven to reduce the drug dependency and improved quality of life in CHF patients to a significant extent. Positive cardiovascular health outcomes even after three years indicates long lasting effects of HFRT.

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Pilot Open Label Single Arm Efficacy Study of Ischemia Reversal Program as Add-on Therapy to Conventional Treatment in Patients with Stable Ischemic Heart Disease

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Abstract

Objective: There is need to develop effective and economical treatments for cardiovascular diseases (CVD) as they affect Indians with great frequency and at a young age. The present study evaluates the efficacy of an Ayurvedic therapeutic procedure, the Ischemia reversal program (IRP), on improving the functional capacity and quality of life in patients with Ischemic heart disease (IHD).

Materials and Methods: Twenty nine patients of either gender, (between 25-65 years of age) who qualified for strict inclusion criteria, were recruited in the study. The IRP therapy consisted of three steps: *Snehana*, *Swedana*, and *Basti*. The dose and duration of treatment consisted of one IRP therapy daily for seven days and follow up for 23 consecutive days. Stress test was conducted on days 1, 7 and 30 to evaluate the effect of IRP on stress test duration, metabolic equivalents (METs), and time of onset of ischemia, improvement in symptoms of IHD, overall health, and requirement of concomitant drug usage before and after the study.

Results: Mean time of onset of Ischemia in the patients improved from 562.13 sec at day 1 to 733.35 sec (improvement by 171.22 sec; $p<0.05$) at day 30. The regimen was observed to improve the quality of life of patients and blood supply to their myocardium at higher workload, as evident by reduced symptoms, improvement in overall health, and increase in their MET values. The baseline average weight of the patients decreased from 73.03 ± 14.20 Kg to 70.84 ± 13.46 Kg at the end of IRP therapy at day 7 ($p<0.001$). Moreover, Duke tread mill score, which suggests risk of mortality of the patients, was 25% before treatment, reduced to 20% post treatment on 30th day follow up.

Conclusions: Ischemia Reversal Program (IRP) when administered as add-on therapy to conventional treatment may reduce symptoms of angina to eventually improve quality of life in patients with stable Ischemic Heart Disease (IHD).

Keywords: Ischemia reversal program; *Snehana*; *Swedana*; *Basti*; Add-on therapy; Ayurveda

Introduction

Over the past few decades, there has been a rapid transition of disease burden in India. The load of communicable and non-communicable diseases (NCDs) is projected to undergo a reversal [1] by 2020 from its current widespread status since 1990. Among the NCDs, cardiovascular diseases (CVD) account for nearly 50% of all deaths [2,3]. In 2000, an estimated 29.8 million people (~ 3% of the total population of the subcontinent) were identified with Coronary heart disease (CHD) in India [3]. This escalation has been attributed to a paradigm shift in lifestyle including changes in the patients' dietary pattern and sedentary lifestyle associated with progressive economic growth and urbanization. South Asian and Asian migrants are at an unusually high risk of developing coronary artery diseases (CAD) [4]. Cardiovascular diseases (CVD) affect more number of Indians than their counterparts in developed countries, as well as in many other developing countries. In addition to high rates of mortality, CVD manifests in patients in India at a younger age (almost 10 years earlier) on an average compared to that of the rest of the world [5,6]. This puts additional burden on the country's economy and calls for a need to develop effective and economical treatment measures. Although drugs and surgery are conventional treatments for cardiovascular diseases, the traditional Indian way of healing, or Ayurveda, is both effective and economical, and is accepted globally now. In fact, a large number of people are getting relief from various diseases with the help of Ayurvedic treatments. In classic Ayurvedic texts, various therapeutic treatments have been mentioned, which can be adopted for improving the functional capacity and quality of life (QOL) in patients with CVD. However, not many studies have reported the efficacy of combination therapies for improving the QOL in patients with CHF.

The present study evaluates the efficacy of ischemia reversal program (IRP), which includes a combination of *Snehana* (oleation), *Swedana* (fomentation) and *Basti* (medicated enema) in improving the functional capacity and quality of life in patients with ischemic heart disease (IHD).

Materials and Methods

Inclusion criteria

Men and women in the age group of 25 to 65 years having clinical diagnosis of stable ischemic heart disease (IHD) were recruited for the study. The time of onset of ischemia in recruited patients, as determined by stress test using Modified Bruce protocol, spanned 60- 600 seconds and significant occlusion in branches of coronary artery was seen in their CAG reports.

Exclusion criteria

Pregnant or lactating women or women planning to get pregnant during the course of the study, patients who have had acute heart failure, or

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acute decompensated heart failure episode within last 3 months, patients not on a stable dose of standard treatment for chronic heart failure since last 3 months with the need for an upward dose titration, patients with uncontrolled hypertension (systolic blood pressure [SBP]>150 mmHg and diastolic blood pressure [DBP]>90 mmHg), patients with blood sugar level (fasting<60 and post-prandial>250), and patients with anaemia (haemoglobin<10 gm%) were excluded from the study.

Ischemia reversal program

Standard operating procedures were designed for all the procedures included in the ischemia reversal program (IRP) therapy administered to the patients. The IRP therapy consists of following three steps:

1. The treatment is initiated with *Snehana* (oleation) which involves massage with sesame oil. The massage is performed on the hands, legs, shoulders, thorax, abdomen and the back in a centripetal manner, *viz.* strokes directed towards the centre of the trunk region. The procedure is carried out for 20 minutes with 15 to 30 strokes applied on each part.
2. This is followed by *Swedana* (fomentation), when the patient lies down in a supine position in a wooden box with his/her neck outside the box (temperature range: 45°C to 55°C). This is carried out for 15 to 20 minutes or till the patient is able to tolerate the heat.
3. The final step involves *Basti,* when-per rectal drug administration of 100 ml decoction of medicated herbs (*Tribulusterristris, Curcuma longa* and *Phyllanthusemblica)* is performed on the patient.

Dose and duration of treatment

The IRP therapy was administered as one session daily for 7 days, i.e. seven IRP therapy sessions and follow-up for 23 days. The therapy was conducted at 10 am in the morning, with a gap of at least 24 hours in between two consecutive therapies.

Method of evaluation

A detailed history of the patients along with demographic information was recorded on day 1. The weight of the patients was recorded at baseline, at first follow-up, and on day 30. The patients were categorized before and after treatment, based on the cardiac functional capacity as per New York Heart Association (NYHA) classification.

A stress test was conducted on day 1, day 7, and day 30 to evaluate the effect of IRP on the stress test duration, metabolic equivalents (METs), and time of onset of ischemia.

The patients were also assessed for improvement in the symptoms of IHD, overall health, associated complaints and any requirement of concomitant drug usage before and after the study.

Results

The IRP therapy was administered to a total of 29 patients, of which 26 were men and 3 were women. The mean age of the patients recruited in the study was 58.93 ± 7.61 years.

All 29 patients showed occlusion of one or more arteries on angiography. The details of arterial occlusion analysis are mentioned in table 1.

The cardiac functional capacity as per NYHA classification was assessed before and after treatment. The number of patients classified as per NYHA showed statistically significant improvement post treatment ($p<0.05$) and are mentioned in table 2.

Stress test was conducted before and after the completion of the study to evaluate stress test duration, METs, and time of onset of ischemia (Figures 1-5) and the results are mentioned in table 3.

Occlusion of arteries on Angiography	Number of Patients
LMCA: Left Main Coronary Artery	2
OM: Marginal Branch Of Lcx	1
LAD: Left Anterior Descending CA	17
RCA: Right Coronary Artery	16
LCX: Left Circumflex CA	13

Table 1: Status of arterial occlusion

NYHA Class	Before IRP treatment	After IRP treatment
I	6	15
II	10	10
III	11	4
IV	2	0

Table 2: Cardiac functional capacity as per NYHA classification (number of patients)
Note: $p<0.05$

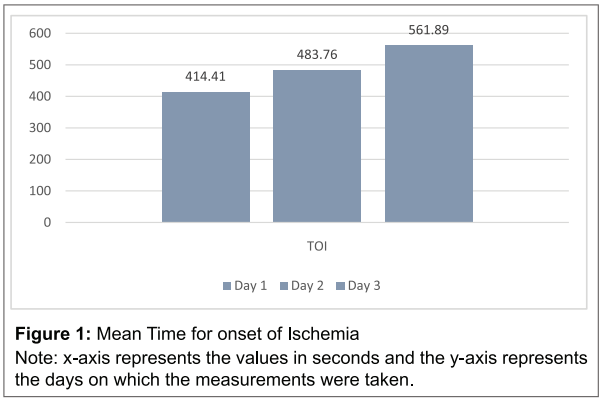

Figure 1: Mean Time for onset of Ischemia
Note: x-axis represents the values in seconds and the y-axis represents the days on which the measurements were taken.

Of the 29 patients (as represented on x-axis) who took the treatment (Figure 2), 23 patients observed increase in the time of onset of ischemia (as represented on y-axis) at day 30 compared to that on day 1. The average increase in ischemia onset value was observed to be 147.48 seconds, and the p-value for ischemia was calculated to be 0.001. Since this is a statistically significant value, impact of the treatment proves to be effective in delaying the time of onset of ischemia.

While conducting the stress test, the HR, SBP and DBP were recorded on day 1, day 7, and day 30, the details of which are mentioned in table 4.

The Heart Rate Recovery (HRR) was also recorded in patients on days 1 and 30. There was a decrease in the HRR from day 1 to day 30; however, this was not statistically significant (Figure 6) and the results are mentioned below in table 5.

The difference between the above mentioned parameters before and after exercise was calculated and analyzed. There was significant difference ($p<0.001$) in the HR before and after treatment and the average heart rate recovery timing improved by 50 seconds at day 30 and the details are mentioned in table 6.

Furthermore, the efficacy of IRP on various symptoms of IHD such as chest pain and heaviness was assessed. Effect on overall health, miscellaneous complaints apart from symptoms of IHD and/or the need for concomitant medication was also documented before and after treatment in 17 patients. There was a significant difference in occurrence chest pain and heaviness before and after treatment ($p<0.05$). In addition, there was a significant improvement in the overall health of the patients ($p<0.001$). The results have been tabulated in table 7.

Citation: Sane R, Mandole R (2016) Pilot Open Label Single Arm Efficacy Study of Ischemia Reversal Program as Add-on Therapy to Conventional Treatment in Patients with Stable Ischemic Heart Disease. J Hear Health 2(3): doi http://dx.doi.org/10.16966/2379-769X.125

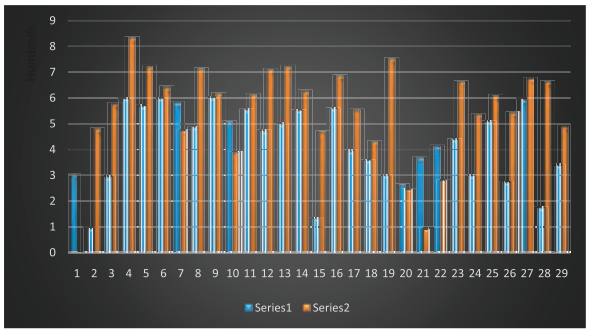

Figure 2: Graphical representation of change in time for onset of Ischemia in all subjects (Series 1=Day 1; Series 2=Day 30)

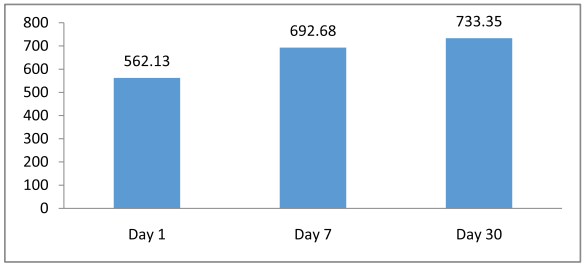

Figure 3: Mean MET Values

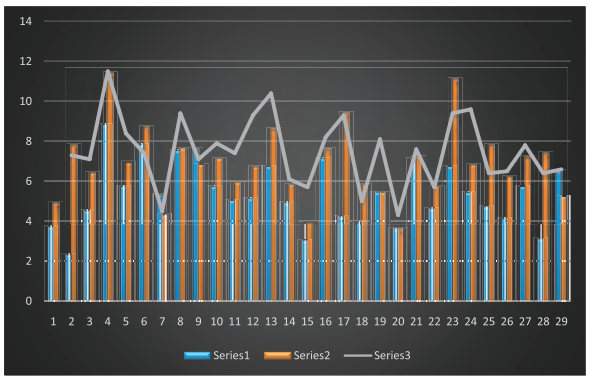

Figure 4: Graphical representation of change in MET value of all subjects (Series 1=Day 1; Series 2=Day 7; Series 3=Day 30)
(x-axis represents the patients who took the treatment; y-axis represents the MET values)

The Duke Treadmill Score (DTS) is a weighted index combining treadmill exercise time using standard Bruce protocol, maximum net ST segment deviation (depression or elevation), and exercise-induced angina. It was developed to provide accurate diagnostic and prognostic information for the evaluation of patients with suspected coronary heart disease.

Amplitude of ST segment change in V5 lead before the treatment was 1.43, which reduced considerably (>50%) to 0.7 after the treatment (Table 3). A low score proves the positive impact of treatment and thus is better at excluding IHD.

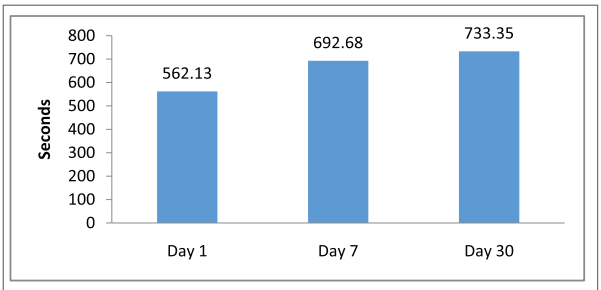

Figure 5: Stress Test Duration

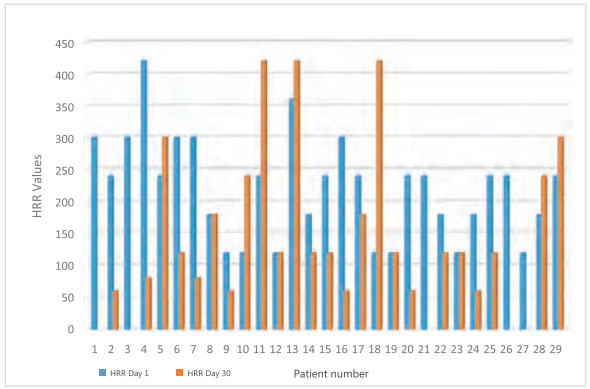

Figure 6: Graphical representation of by-subject data for Heart Rate Recovery

The baseline average weight of the patients was 73.03 ± 14.20 Kg, which decreased to 70.84 ± 13.46 Kg at the end of IRP therapy (Day 7). This difference in change in body weight was found to be statistically significant ($p<0.001$).

Discussion

In the present study we evaluated the efficacy of an Ayurvedic treatment regimen (IRP) as add on therapy to conventional treatment in patients with IHD. We observed that the regimen improves blood supply to the myocardium at higher workload, as well as quality of life as evident by reduced symptoms and change in overall health status of the patient. The underlying etiology in patients with IHD is reduced capacity of coronary artery blood (oxygen) supply to meet the myocardial oxygen demand. The determinants of myocardial oxygen demand relate to the workload on the myocardium and include heart rate, systemic systolic blood pressure, ventricular wall tension, and velocity of myocardial contractility [7].

A significant difference in HR before and after treatment might be blunt inotropic response due to antihypertensive medicine like angiotensin-converting-enzyme inhibitors (ACE), calcium channel blockers, and diuretics. Another important observation is improvement in functional capacity and QOL that have been identified as the goals of managing patients with stable IHD [7,8].

Cardiac ischemia is a result of an imbalance between myocardial oxygen supply and demand. Oxygen extraction from the blood perfusing the myocardium is very high; therefore, an increase in myocardial oxygen supply can only be met by an increase in coronary blood flow. Altered coronary reactivity (impaired dilation from endothelial dysfunction,

Days	Time to onset of ischemia (seconds)	Metabolic Equivalent values (*METs)	Stress test duration (seconds)	Amplitude of ST change (mm)	Dukes Score	5 years Risk mortality based on Duke score
Day 1	414.41 ± 149.34	5.36 ± 1.60	562.13 ± 155.56	1.5	-6	25%
Day 7	483.76 ± 174.23	6.86 ± 1.83	692.68 ± 128.60	1		
Day 30	561.89 ± 167.01	7.51 ± 1.75	733.35 ± 116.06	0.7	-1.5	20%
p-value	<0.001	<0.01	<0.001			

Table 3: Effect of IRP on parameters
*MET-Metabolic Equivalent of Task

Days	Heart Rate (/min)		Systolic Blood Pressure (SBP; mm of Hg)		Diastolic Blood Pressure (DBP; mm of Hg)	
	At rest	After exercise	At rest	After exercise	At rest	After exercise
Day 1	80 ± 12.52	126.10 ± 15.34	125.65 ± 15.16	152.27 ± 21.98	78.62 ± 8.33	83.79 ± 9.02
Day 7	74.51 ± 10.72	131.55 ± 15.99	119.10 ± 11.35	144.82 ± 19.01	73.44 ± 5.52	78.27 ± 6.58
Day 30	80.66 ± 17.52	130.18 ± 22.05	115.96 ± 18.10	145.64 ± 22.39	82.5 ± 16.91	90.71 ± 24.33

Table 4: Effect of IRP on Heart Rate, Systolic Blood Pressure and Diastolic Blood Pressure

Mean HR recovery (HRR)	
Day 1	**Day 30**
221.37 ± 78.72	171.66 ± 42.42

Table 5: Effect of IRP on Heart Rate Recovery

Days	Difference in HR (/min)	Difference in SBP (mm of Hg)	Difference in DBP (mm of Hg)
Day 1	46 (20 to 75)	24 (-40 to 70)	0 (-20 to 20)
Day 7	56 (37 to 85)	20 (0 to 60)	5 (-10 to 20)
Day 30	57 (-115 to 88)	30 (0 to 78)	5 (-10 to 50)
p value	p<0.001		

Table 6: Effect of IRP on stress test outcomes of HR, SBP and DBP

Symptoms	At baseline		After 30 days		p value
	Good/ Present	Bad/ Absent	Good/ Present	Bad/ Absent	
Chest Pain	11	6	3	14	p<0.05
Heaviness	13	4	6	11	p<0.05
Overall Health	0	17	14	3	p<0.001
Other complaints	8	9	6	11	p=0.73
Concomitant Medicines	3	14	3	14	p=1.34

Table 7: Effect of IRP on symptoms of IHD (number of patients)

heightened smooth muscle activation like spasm, etc.) at both macro- and micro-vascular levels may contribute in limiting the blood flow. Stiffness in central arteries increases in atherosclerosis and is an independent predictor of adverse coronary events [8]. Various procedures performed as a part of IRP may help to reverse the phenomena responsible for ischemia. We hypothesize that *Snehana* (centripetal oleation) can be useful in reducing sympathetic over-stimulation and improving vascular tone. This decrease in myocardial workload would thus reduce the risk of ischemia. Furthermore, *Swedana*, by inducing sweating, may cause vasodilation at the microvasculature, which in turn reduces systemic vascular resistance and the resulting afterload. The reduction in afterload decreases cardiac workload and myocardial oxygen demand, thus reducing the risk of ischemia. Finally, the 100 ml *Basti* decoction contains *Tribulusterrestris* (preclinical studies have proven it has nitric oxide mediated vasodilatory effect) [9], *Curcuma longa* (a proven anti-inflammatory herb) [10] and *Phyllanthusemblica* (animal studies have proved that *Phyllanthusemblica* can reduce oxidative stress) [11]. Besides, the *Basti* procedure may reduce oxidative stress and inflammation along with the risk of ischemia.

Evidence from INTERHEART study provides rationale for developing treatment algorithms and treatment guidelines for CHD at various levels of healthcare. As per the implications of the INTERHEART study, strategies should focus on early detection of clinical disease in patients and cost-effective secondary prevention measures to avoid complications for the management of CAD [12,13]. The IRP regime can prove to be a cost-effective measure that can be afforded by patients from lower socio-economic strata too.

Cardiovascular diseases (CVD) are the one of the primary causes of mortality in India, where, among the top five causes of death, CVDs rank first among rural as well as urban population [14]. The IRP can prove to be a major breakthrough in the management of CVDs.

Metabolic Equivalent of Task (MET) provides a convenient method to describe the functional capacity or exercise tolerance of an individual. After IRP, there was a significant improvement in the METs. This improvement was associated with significant changes in time for onset of ischemia [15].

Heart rate recovery as a prognostic marker has been validated in both asymptomatic patients and in those being evaluated for chest pain. The IRP reduces the HRR at higher workload; meanwhile, the MET value increased, although the change was not statistically significant.

In addition, Duke tread mill score, which suggests risk of average risk of mortality in all subjects was 25% before treatment, but reduced to 20% post treatment on 30th days follow up.

Our study proves the optimal efficacy of IRP; however, since this was a pilot study, the inclusion for age was over a wide range (25-65 years) to ensure maximum representation of patients. However, for future trials we intend to include larger sample size and classify the patients in 3 age groups of young, adults and aging patients versus age matched controls, with equal gender representation.

Conclusions

Ischemia Reversal Program (IRP) when administered as an add-on therapy to conventional treatment may improve blood supply to the myocardium and thus reduce symptoms of angina to significantly improve quality of life in patients with stable Ischemic Heart Disease (IHD).

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Original Article

Effect of heart failure reversal treatment as add-on therapy in patients with chronic heart failure: A randomized, open-label study☆

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ABSTRACT

Objectives: The present study was designed to evaluate effect of heart failure reversal therapy (HFRT) using herbal procedure (*panchakarma*) and allied therapies, as add-on to standard CHF treatment (SCT) in chronic heart failure (CHF) patients.
Methods: This open-label, randomized study conducted in CHF patients (aged: 25–65 years, ejection fraction: 30–65%), had 3-phases: 1-week screening, 6-week treatment (randomized [1:1] to HFRT + SCT or SCT-alone) and follow-up (12-week). Twice weekly HFRT (60–75 min) consisting of *snehana* (external oleation), *swedana* (passive heat therapy), *hrudaydhara* (concoction dripping treatment) and *basti* (enema) was administered. Primary endpoints included evaluation of change in metabolic equivalents of task (MET) and peak oxygen uptake (VO_{2peak}) from baseline, at end of 6-week treatment and follow-up at week-18 (non-parametric rank ANCOVA analysis). Safety and quality of life (QoL) was assessed.
Results: Seventy CHF patients ($n = 35$, each treatment-arm; mean [SD] age: 53.0 [8.6], 80% men) were enrolled in the study. All patients completed treatment phase. Add-on HFRT caused a significant increase in METs (least square mean difference [LSMD], 6-week: 1.536, $p = 0.0002$; 18-week: −1.254, $p = 0.0089$) and VO_{2peak} (LSMD, 6-week: −5.52, $p = 0.0002$; 18-week: −4.517, $p = 0.0089$) as compared with SCT-alone. Results were suggestive of improved functional capacity in patients with HFRT (QoL; Mean [SD] HFRT + SCT vs. SCT-alone; 6-week: −0.44 [0.34] vs. −0.06 [0.25], $p < 0.0001$ and 18-week: −0.53 [0.35] vs. −0.29 [0.26], $p = 0.0013$). Seven treatment-emergent adverse events (mild severity) were reported in HFRT-arm.
Conclusion: Findings of this study highlight therapeutic efficacy of add-on HFRT vs. SCT-alone in CHF patients. The non-invasive HFRT showed no safety concerns.
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What is already known?

- Current CHF management guidelines recommend evidence-based treatment and care-modalities. Moreover, there is an emphasis on patient rehabilitation that acknowledge the need for improvement in patient health-related outcome. Add-on therapies based on Ayurveda and/or herbal treatment are known to have the potential to address this lacunae.

What this study adds?

- Present study introduces HFRT, an add-on therapy to SCT that shows promising results for better CHF management.

☆ **Registration**: Clinical Trials Registry of India registration number: CTRI/2015/01/005384.

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Abbreviations: 2D-ECHO, two dimensional-echocardiogram; ACE, angiotensin converting enzyme; ANCOVA, analysis of covariance; ARBs, angiotensin receptor blockers; CHF, chronic heart failure; DPP, double pressure product; ECG, electrocardiography; EF, ejection fraction; FAS, Full Analysis Set; IHD, Ischemic Heart Disease; HFRT, heart failure reversal therapy; HRR, heart rate recovery; LSMD, least square mean difference; MET, metabolic equivalents of tasks; NYHA, New York Heart Association; PLBS, post lunch blood sugar; PP, Per Protocol Set; QoL, quality of life; SAS, statistical analysis system; SCT, standard CHF treatment; SD, standard deviation; SHS, sampurna hruyday shudhikaran; SS, Safety Set; TEAEs, treatment emergent adverse events; TOI, time to onset of ischemia; VO_{2peak}, peak oxygen uptake.

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1. Introduction

The management of chronic heart failure (CHF) is a topic, broadly discussed since eons, and has well-established treatment regimens emphasizing the goal of reduction in symptoms and improvement of prognosis. The worldwide growing prevalence of CHF shows an annual incidence of 0.5–1.8 million in India.[1] As a result, plethora of research is performed to identify newer therapeutic targets for better management of CHF.[2] A contemporary physician is mindful of crucial objective of maximizing function in everyday life and strives to achieve the highest level of quality of life (QoL) within the limitations imposed by the disease. Along with symptoms of CHF, an array of undesirable emotions including fear and anxiety of health status lead to deterioration in the patient's morale and a progressive decline in QoL. Despite improvement in therapeutic drugs and devices, CHF has poor prognosis. The critical therapeutic advantages are those that maintain and stabilize the patient's limited functional abilities and, also improve the comfort of the patient for remaining life-span.[3]

The standard CHF treatment (SCT) includes β-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), digoxin, anti-platelets and diuretics.[4] However, majority of CHF patients require complex management due to growing age, comorbidities, multiple medications, and depression or reduced coping skills.[5] Considering these exigencies, a search is ongoing for preferably non-invasive add-on therapies with SCT. Historical data have reported that β-blockers, ARBs have antioxidant, and/or anti-inflammatory properties, which may attribute to their therapeutic effects.[6,7] Several herbs are known to possess antioxidant, anti-inflammatory, antiplatelet or hypolipidemic properties.[8–14] It would, therefore, be interesting to explore if these herbs have an additional cardioprotective effect in CHF patients.

Ayurvedic physicians advocate use of conventional treatment in the acute disease phase and in chronic condition subsequent use of panchakarma therapy (a 5-step procedure for internal purification of the body) as an add-on, for providing maximum benefit to the patient.[15] Heart failure reversal therapy (HFRT) formerly known, sampurna hruyday shudhikaran (SHS) therapy is a combination of herbal treatment with panchakarma and allied therapies.[16–18] The techniques used in panchakarma namely snehana (massage), swedana (fomentation therapy) and basti (type of enema) are known to eliminate toxins.[15,19]

The primary objective of this randomized, open-label, comparative study was to evaluate the effect of HFRT as an add-on therapy to SCT on metabolic equivalents of tasks (METs) and peak oxygen uptake (VO_{2peak}) in CHF patients. The effect on ejection fraction (EF), time to onset of ischemia (TOI), double pressure product (DPP), heart rate recovery (HRR) and quality of life (QoL) were also evaluated.

2. Methods

2.1. Study population

Study participants included patients (both gender, aged 25–65 years) with CHF (New York Heart Association, NYHA Class I–III), history of CHF irrespective of angioplasty and coronary artery bypass graft on SCT, having MET values: 3–7 (inclusive), and EF between 30–65% (inclusive) on a standard two dimensional-Echocardiogram (2D-ECHO) test (6 months prior to screening). Additional inclusion criteria were systolic blood pressure not >150 mmHg and diastolic blood pressure not >90 mmHg, hemoglobin levels ≥10 g/dL, blood sugar level (fasting not <60 mg/dL and PLBS not >250 mg/dL).

Patients with suspected hypersensitivity to study therapy, acute heart failure, decompensated heart failure attack (last 3-months), irritable bowel syndrome, bleeding piles or fistula (grade-I or II piles), 2nd/3rd degree hemorrhoids, asthma or chronic obstructive pulmonary disease, abnormal thyroid function test, hepatic or renal insufficiency, cancer, physical disability (any form) leading to immobilization, participation in another study 30-days prior to screening were excluded. Patients not on stable dose of SCT (last 3-months), needing upward dose titration were excluded and also pregnant or lactating women.

The Independent Ethics Committee approved the protocol. The study was conducted in accordance with the ethical principles in the Declaration of Helsinki, consistent Good Clinical Practices, and applicable regulatory requirements. All patients or their legally acceptable representatives provided written informed consent to participate in the study.

2.2. Study design

Open-label, randomized study, conducted from 2014 to 2015 in outpatients at two centers (Bhaktivedanta Hospital, Mumbai and Shree Saibaba Heart Institute and Research Center, Nasik) was divided into 3-phases: screening (up to 1-week), treatment (6-week) and follow-up phase (12-week). At treatment phase, patients enrolled after screening were randomized (1:1) to either groups: (1) HFRT, twice/week plus SCT (like β-blockers, ACE inhibitors, digoxin, anti-platelets and diuretics) or (2) SCT-alone. Randomized and treated patients were evaluated at end of the treatment (6-week) and at 18-week in the follow phase (Fig. 1).

Permuted block randomization was performed to allot either treatment: HFRT + SCT or SCT-alone based on next available number as per the randomization chart.

2.3. Study therapy

The HFRT, a 4-step procedure *(snehana, swedana, hrudaydhara, basti)* requiring 65–75 min was performed after a light breakfast (Fig. 2; Supplementary material[15,19]).

2.4. Study evaluations

2.4.1. Cardiac function measures

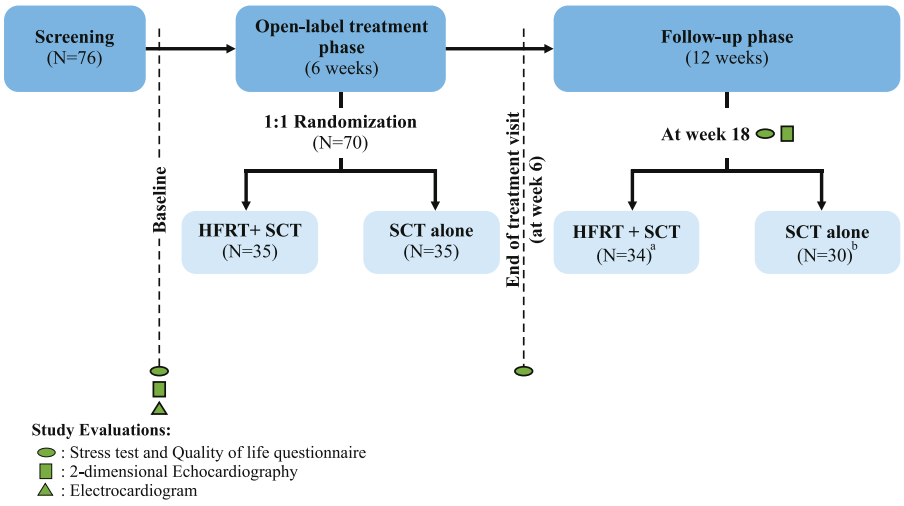
Primary endpoints were improvement in MET and VO_{2peak} as evaluated by cardiac stress test with modified Bruce protocol and 12-lead electrocardiography (ECG) at baseline, 6 and 18-week. MET is ratio of metabolic rate (the rate of energy consumption) during a specific physical activity to a reference metabolic rate (3.5 ml O_2 kg^{-1} min^{-1}). VO_{2peak} is the measurement of the volume of oxygen that the body can utilize during physical exertion (VO_{2max} = MET value × 3.6).

Secondary endpoints (monitored at 6 and 18-week) included improvement in QoL: assessed by questionnaires (adapted from validated questionnaires[20–23]), EF, improvement in TOI and DPP and HRR as assessed by monitoring heart rate.

HRR is time taken to return to normal heart rate at end of stress test. TOI (time to onset 1 mm of ST segment change in more than 2 leads) and DPP (product of maximum heart rate and systolic blood pressure) were recorded during stress test.

2.4.2. Safety and tolerability

Safety was assessed throughout the study and evaluated by frequency, severity and intensity of treatment-emergent adverse events (TEAEs), serious TEAEs, physical examinations, vital signs and laboratory tests (biochemistry, hematology, and urine analysis).



HFRT=Heart failure reversal therapy (study therapy), SCT=Standard cardiac failure treatment,
a: one patients withdrew, b: two patients withdrew, two patients were lost to follow up and one death occurred.

Fig. 1. Study design and patient flow.

Heart failure reversal therapy	Type of technique	Duration	Herbs used	Additional information
Snehana[15]	External oleation or massage	30–35 minutes	100 mL extract (processed in sesame oil): 10 gm *T. arjuna,* 5 gm *V. negundo* and 10 gm *Dashamoola*	It uses centripetal or upward strokes directed towards the heart
Swedana[15]	Passive heat therapy	10-15 minutes + 3-4 minutes of relaxation after procedure	*Dashmoola* (group of ten herbal roots) steam (temperature not > 40°C)	During the procedure, patients were asked to lie down inside a sudation box in supine position with head positioned outside
Hrudaydhara	Decoction dripping treatment (constant speed, from 7-8 cm height over the medial mediastinum region)	15 minutes	Luke-warm *dashmoola* decoction	Variation of *shirodhara* technique[19]
Basti[15]	Medicated enema	10 minutes	10 mL aqueous extract of: 1880 mg *T. arjuna*, 420 mg *B. diffusa* and 180 mg *A. calamus*	Administered per rectal solution had to remain inside the body ≥15 minutes for maximum absorption

Fig. 2. Study therapy.

2.5. Statistical methods

2.5.1. Analysis set

Analysis sets were as follows: Safety Set (SS) randomized patients who received treatment at least once; Full Analysis Set (FAS) – patients who had primary efficacy parameters assessed post-baseline; Per Protocol Set (PP) – patients who completed the study with no protocol deviations.

2.5.2. Sample size determination

The sample size ($N = 27$, each treatment group) was pre-specified to the minimal detectable differences of 1.5 in MET and 3.0 in VO_{2peak} levels (mean change from baseline) between the two treatment groups at week 12 with 80% power and a 0.05, two-sided significance level and standard deviation of 1.9 in MET and 3.8 in VO_{2peak} levels. Assuming 20% dropout rate, 35 CHF patients were required to be enrolled in each group.

2.5.3. Statistical analyses

Demographic and baseline characteristics of SS were summarized descriptively. The mean change in efficacy endpoints between groups was analyzed using non-parametric rank analysis of covariance (ANCOVA), with baseline values as covariates. Wilcoxon Rank Sum test was used to compare QoL data. Statistical analyses were performed using SAS software version 9.2 (SAS Institute Inc., USA).

3. Results

3.1. Study population

Total 70/76 screened CHF patients were enrolled and randomized in open-label treatment-phase to either groups: HFRT + SCT ($n = 35$, 50%) or SCT-alone ($n = 35$, 50%). The study population (mean [SD] age: 53.0 [8.6]) comprised of 80% men (HFRT + SCT group, $n = 27$ [77%]; SCT-alone group, $n = 29$ [83%]). The baseline

Table 1
Baseline and clinical characteristics (Safety Set).

Parameters	HFRT + SCT ($N = 35$)	SCT alone ($N = 35$)	Total ($N = 70$)
Age, years			
Mean (SD)	53.5 (8.1)	52.5 (9.1)	53.0 (8.6)
Men, *n* (%)	27 (77)	29 (83)	56 (80)
Baseline weight, (kg)			
Mean (SD)	67 (11.3)	69 (13.1)	68 (12.1)
Smoking, n (%)			
Yes	1 (3)	1 (3)	2 (3)
Tobacco consumption, n (%)			
Yes	1 (3)	1 (3)	2 (3)
Alcohol consumption, n (%)			
Yes	3 (9)	4 (11)	7 (10)
History of allergy, n (%)			
Yes	0	1 (3)	1(1)
Medical history, n (%)			
Hypertension	18 (51)	19 (54)	37 (53)
Diabetes	8 (23)	12 (34)	20 (29)
Hypercholesterolemia	2 (6)	2 (6)	4 (6)
Intervention			
PTCA	11 (31)	12 (34)	23 (33)
NYHA Class, n (%)			
I	9 (26)	5 (14)	14 (20)
II	25 (71)	30 (86)	55 (79)
III	1 (3)	0	1 (1)
Concomitant medicines, n (%)			
Anti-platelets drugs	15 (43)	17 (49)	33 (47)
NSAIDs	5 (14)	5 (14)	10 (14)
Statins	5 (14)	5 (14)	10 (14)
β-Blockers	3 (9)	3 (9)	7 (10)

HFRT, heart failure reversal therapy; NSAID, non-steroidal anti-inflammatory drug; NYHA, New York Heart Association; PTCA, percutaneous transluminal coronary angioplasty; SCT, standard chronic heart failure treatment.

demographic and clinical characteristics were comparable between the groups (Table 1).

All randomized patients completed the 6-week treatment-phase in both groups. A total of 34 (97%) patients in HFRT + SCT and 30 (86%) in SCT-alone group completed the follow-up (Fig. 1).

3.2. Efficacy measurements

Efficacy parameters were analyzed at 6 and 18-week. Patients in HFRT + SCT group showed significant improvement in MET and VO_{2peak} values from baseline, at 6-week (least square mean difference [LSMD], MET: −1.536, $p = 0.0002$; VO_{2peak}: −5.52, $p = 0.0002$) and 18-week (LSMD, MET: −1.254, $p = 0.0089$; VO_{2peak}: −4.517, $p = 0.0089$) as compared to SCT-alone group. The percent change for MET and VO_{2peak} values was higher in HFRT + SCT vs. SCT-alone group from baseline, at 6-week (MET: 45.33 vs. 15.44; VO_{2peak}: 45.34 vs. 15.49) and 18-week (MET: 51.48 vs. 26.03; VO_{2peak}: 51.49 vs. 26.03). Results obtained from PP population confirmed findings from FAS population (Table 2).

QoL improved significantly from baseline (Mean [SD] HFRT + SCT vs. SCT-alone at 6-week: −0.44 [0.34] vs. −0.06 [0.25], $p < 0.0001$ and 18-week: −0.53 [0.35] vs. −0.29 [0.26], $p = 0.0013$). At 6-week, TOI (LSMD: −97.202, $p = 0.002$) and DPP (LSMD: −2242.404, $p = 0.0116$) was improved significantly from baseline in HFRT + SCT as compared to SCT-alone group. However, the values were not statistically significant at 18-week. The EF was significantly improved from baseline, at 18-week (LSMD: −3.205, $p = <0.0001$) in patients of HFRT + SCT as compared with SCT-alone group (Table 2).

3.3. Safety and tolerability

Total 15 TEAEs in either treatment group (HFRT + SCT: $n = 7$ [20%] and SCT-alone: $n = 8$ [23%]) were reported with mild severity and resolved by end of the study. The TEAEs were mainly of cardiac or respiratory organ class. One death was reported in the SCT group during follow-phase (Table 3).

Overall, no TEAEs of abnormal laboratory results, vital signs, or ECG values were reported from baseline to follow-up.

4. Discussion

This randomized, open-label study of HFRT as add-on therapy for CHF management, yielded significant improvements in MET and VO_{2peak} values in comparison with SCT-alone, from baseline to 6-week. Interestingly, the improved status was maintained even 12-weeks after the therapy. Significant improvements in secondary endpoints, EF and QoL were also demonstrated in HFRT treated patients. Furthermore, the HFRT group showed a better safety profile vs. SCT-alone.

The CHF patients have a decreased rate of O_2 uptake compared to healthy individuals, leading to fatigue and slow recovery after exertion. Therefore improvement in VO_{2peak}; a validated indicator of O_2 uptake can help to improve CHF prognosis.[24] Consistent with our results, increased VO_{2peak} in CHF patients was noted in other studies, although the intervention was different.[25,26] Further, our observations of enhanced MET from baseline to 18-week are corroborated by another report evaluating the relationship between exercise volume and clinical events in CHF patients wherein 3–7 MET showed a clinical benefit.[27] Previous studies conducted for HFRT (or SHS) also showed improvement in MET and VO_{2peak} values.[18]

A retrospective study in coronary heart disease patients reported that 1-unit (mL/kg/min) increase in VO_{2peak} is associated with ~15% decrease in risk of death.[28] A patient's capacity for exercise as measured by VO_{2peak} was thus considered as a strong predictor of mortality. In the current study, a significant enhancement of VO_{2peak} by 45.34% at the end of HFRT therapy possibly reflects a decline in the risk of mortality in CHF patients.

The CHF patients experience a progressive decline in QoL as their ability to perform routine physical activities is compromised due to early onset of dyspnea and fatigue. Exercise training is known to substantially increase VO_{2peak} and MET and is currently recommended to improve QoL in these patients as they become more tolerant to exertion, experience less fatigue and dyspnea and become comfortable in performing routine activities.[29–31] The significantly enhanced QoL post HFRT reflected a remarkable improvement in these features, sleep pattern, memory and routine lifestyle. The 4-elements of the HFRT treatment: *Snehana, Swedana, Hrudaydhara* and *Basti* mostly act in cohesion to alleviate the detrimental effects of CHF. The improvement in QoL with HFRT treatment by 6-week was maintained till 12-weeks after treatment. In a retrospective-cohort study in CHF patients, SHS therapy caused a remarkable improvement from NYHA Class II and III to Class I in 72% patients.[18]

The TOI and DPP are associated with Ischemic Heart Disease (IHD). The HFRT was efficacious with respect to these parameters for 6-week but not in long-term. Therefore, the role of HFRT in IHD treatment requires further investigation. HRR is an effective prognosis parameter at constant workload and MET-value. In this study, workload and MET-values were variable and hence, HRR could not be a reliable measure. This explains the erratic HRR results obtained in both arms of the study.

Although this study had a small sample size, there was 100% compliance in both treatment arms and the protocol deviations

Table 2
Analysis of change from baseline in study parameters (Full Analysis Set).

Parameters	HFRT + SCT		SCT alone		LS mean change between groups[a]	95% CI	ANCOVA *p*-value	Non-parametric rank ANCOVA *p*-value
	LS mean CFB (SE)	95% CI	LS Mean CFB (SE)	95% CI				
	N = 34		*N* = 33					
Week-6								
METs	2.33 (0.27)	1.78, 2.88	0.79 (0.28)	0.23, 1.35	−1.54	−2.32, −0.75	0.0002	<0.0001
VO_{2peak}	8.38 (0.99)	6.40, 10.35	2.86 (1.00)	0.85, 4.86	−5.52	−8.34, −2.70	0.0002	0.0001
TOI	200.41 (21.09)	158.29, 242.54	103.21 (21.41)	60.45, 145.97	−97.20	−157.50, −36.90	0.002	0.0016
DPP	1977.51 (604.1)	770.68, 3184.35	−264.89 (613.24)	−1489.98, 960.20	−2242.40	−967.16, −517.65	0.0116	0.016
HRR	24.25 (16.48)	−8.67, 57.17	−24.29 (16.73)	−57.70, 9.13	−48.54	−95.46, −1.62	0.0428	0.0695
QoL	Mean (SD) −0.44 (0.34)		Mean (SD) −0.06 (0.25)				<0.001	
Parameters	LS Mean CFB (SE)	95% CI	LS Mean CFB (SE)	95% CI	LS Mean Change between groups[a]	95% CI	ANCOVA *p*-value	Non-parametric rank ANCOVA *p*-value
	N = 34		*N* = 30					
Week-18								
METs	2.63 (0.32)	2.0, 3.27	1.38 (0.34)	0.70, 2.05	−1.25	−2.18, −0.33	0.0089	0.0016
VO_{2peak}	9.48 (1.14)	7.20, 11.77	4.96 (1.22)	2.53, 7.40	−4.52	−7.86, −1.18	0.0089	0.0016
TOI	3.28 (0.48)	2.33, 4.24	0.08 (0.51)	0.94, 1.10	−3.21	−4.64, −1.77	<0.0001	<0.0001
DPP	194.68 (25.34)	144.01, 245.35	134.73 (26.98)	80.78, 188.68	−59.95	−134.08, 14.19	0.111	0.0608
HRR	2236.71 (807.92)	621.17, 3852.24	474.33 (860.49)	−1246.33, 2194.99	−1762.38	−4131.25, 606.50	0.142	0.0694
	26.87 (15.6)	−4.33, 58.07	18.55 (16.61)	−14.67, 51.77	−8.33	−53.93, 37.28	0.7164	0.984
QoL	Mean (SD) −0.53 (0.35)		Mean (SD) −0.29 (0.26)				0.013	

[a] LS Mean change between groups is calculated as SCT-alone − HFRT + SCT.
ANCOVA, analysis of covariance; CFB, change from baseline; CI, confidence interval; DPP, double pressure product; HRR, heart rate recovery; HFRT, heart failure reversal therapy; LS mean, least square mean, MET, metabolic equivalents of task; QoL, quality of life; TOI, time to ischemic onset; VO_{2peak}, peak oxygen uptake.

Table 3
Treatment-emergent adverse events (Safety Set).

	HFRT + SCT	SCT alone
	N = 35	*N* = 35
	n (%)	*n* (%)
Number of patients		
With at least one TEAE	5 (14.3)	2 (5.7)
With at least one severe TEAE	0	2 (5.7)
With at least one serious TEAE	0	2 (5.7)
TEAEs		
Lower respiratory tract infection	1 (2.9)	0
Upper respiratory tract infection	1 (2.9)	0
Pain in cubital fossa	1 (2.9)	0
Dengue fever	1 (2.9)	0
Chest pain	1 (2.9)	0
Cough	0	1 (2.9)
Hemoptysis	0	1 (2.9)
Breathlessness	0	1 (2.9)
Breathlessness secondary to cardio-myopathy with left ventricular failure	0	1 (2.9)
Dysphagia	0	1 (2.9)
Elevated hypertension	1 (2.9)	0
Vertigo	0	1 (2.9)
Weakness	1 (2.9)	0
Serious TEAE		
Death	0	1 (2.9)

HFRT, heart failure reversal therapy; SCI, standard chronic heart failure treatment; TEAE, treatment-emergent adverse event.

were minimal. Future studies involving HFRT with a larger sample-size and long-term follow-up in patients with different levels of CHF severity can shed more light on understanding this novel treatment option.

5. Conclusion

Add-on therapy with HFRT demonstrated significant therapeutic effects with improvement in METs, oxygen uptake and cardiac measures as compared with SCT-alone and no safety concerns were observed. The HFRT therapy augments the beneficial effects of SCT thereby improving the exercise tolerance, aerobic capacity, prognosis and QoL of CHF patients. Hence, the non-invasive HFRT therapy can be a viable option for planning the modus operandi for better CHF management

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Conflicts of interest

Dr. RM is an employee of Vaidya Sane Ayurved Labs Pvt. Ltd. Drs. RS, AA and AP has received honoraria from Vaidya Sane Ayurved Labs Pvt. Ltd.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ihj.2016.10.012.

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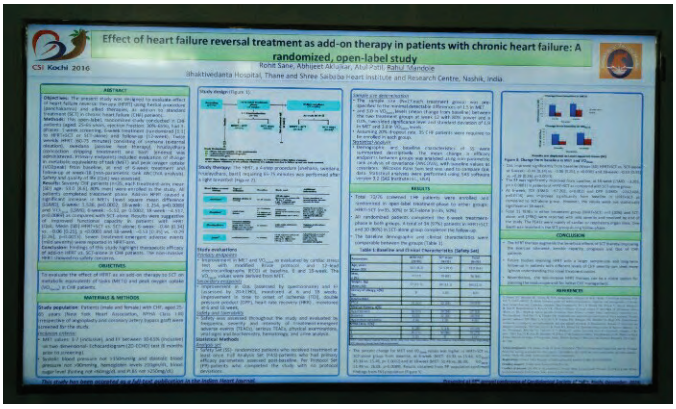
Effect of heart failure reversal treatment as add-on therapy in patients with chronic heart failure: A randomized, open-label study
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Original Research Article

The effect of a polyherbal oral formulation in the management of essential hypertension: an open label, pilot clinical study

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ABSTRACT

Background: Effective control of blood pressure in patients with hypertension decreases cardiovascular mortality. However, many hypertensives are unresponsive to standard antihypertensive treatment. Research has found anti-hypertensive potential in the Ayurvedic drugs Brahmi (*Bacopa monnieri*) and Shunthi (*Zingiber officinale*). Hence, a pilot study was conducted to evaluate the efficacy and safety of Capsule Artyl (the oral formulation of Brahmi and Shunthi) as a treatment option in hypertensive subjects.
Methods: There were 30 hypertensive subjects attending out-patient departments of clinics in Maharashtra, India were enrolled in this four-week, open label, single arm study. All subjects received capsule Artyl (500mg) twice a day orally daily. The mean systolic (SBP) and diastolic blood pressure (DBP) on days 1 and 28 of the study were compared along with the mean arterial pressure (MAP).
Results: The mean SBP was significantly lesser on day 28 (141.86±12.54mm Hg) as compared to the mean SBP recorded on day 1 (155.48±19.37mm Hg) ($p<0.001$). The mean DBP on day 28 (89.66±6.8mm Hg) was lesser than that on day 1 (90.34±7.44mm Hg) but this difference was not statistically significant ($p>0.05$). There was a significant decrease in the mean value of MAP on day 28 (107.06±7.03mm Hg) as compared to that on day 1 (112.06±10.75mm Hg) ($p<0.01$).
Conclusions: Capsule Artyl significantly decreased the BP in hypertensive patients, without any adverse effects. Controlled trials are needed to confirm the positive outcome of this promising herbal formulation in hypertensive patients.

Keywords: Capsule artyl, Essential hypertension, Systolic blood pressure

INTRODUCTION

Hypertension has become a crucial health issue to tackle worldwide not only due to its increasing prevalence but also because of the severe complications associated with it. About 10-15% of the rural and 25% of the urban population are estimated to be affected by hypertension in India. Also, Government of India has estimated that by 2020, 159.46/1000 Indians will be suffering from hypertension.[1,2] Moreover, multiple complications associated with hypertension is a cause of high mortality due to the disease. According to the World Health Organization (WHO) data released in 2014, 26% of the deaths in India are due to cardiovascular disease. Another striking data is that 29% of strokes, 21% of acute myocardial infarction and 16% of ischemic heart disease in India are all attributed to hypertension.[3]

The current management of hypertension involves lifestyle modifications along with pharmacotherapy. The pharmacological agents used for the treatment include angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), diuretics and alpha blockers. However, these agents are not enough to control the blood pressure of patients. It has been estimated that in more than two-third hypertensive patients on treatment, the blood

pressure cannot be controlled with a single pharmacological agent and they require multiple drugs.[4] A recent Indian study has revealed that the control rates of blood pressure in hypertensive cases are as low as 1/10th in rural and 1/5th in the urban population.[5] Other pitfalls of the pharmacological agents for hypertension include the plethora of adverse effects as well as the high costs associated with their use. Hence, there is a strong need to search safe and cost-effective options for the management of hypertension in India.

Ayurveda, the Indian traditional discipline of medicine, has been used by various physicians to treat multiple types of disorders. However, many of the herbal extracts have not been investigated thoroughly for their possible beneficial effects in the treatment of hypertension. Two of such herbal drugs are Brahmi (Bacopa monnieri) and Shunthi (Zingiber officinale). In Ayurveda, Brahmi is considered to be a powerful Medhya (brain tonic) and has been widely studied for its nootropic effect. However, it has also shown promise as an anti-stress as well as an anti-oxidative agent.[6] There have been very few studies which have tried to evaluate the effect of Brahmi as an anti-hypertensive agent.[7,8] Shunthi, the processed dry ginger is a popular herb used extensively in the Indian subcontinent as a food additive. The beneficial effect of Shunthi in cardiovascular disease has been known for long.[9] According to a systematic review published by the British Medical Journal, many animal studies have established the beneficial effect of Shunthi as a dietary supplement to conventional anti-hypertensive drugs. However, the same review has stated the need for more clinical studies to assess the possible effect of Shunthi in hypertensive patients.[10]

Capsule Artyl is a polyherbal Ayurvedic oral formulation which is made from the aqueous extracts of Brahmi (Bacoside 30%) and Shunthi (Gingerol 2.5%). Considering the beneficial anti-hypertensive effect of both these extracts individually, this combination looks like a promising agent that can help physicians, as well as the patients, tackle the grave problem of uncontrolled hypertension. Hence, we planned to conduct an open label pilot study to assess the efficacy and the safety of this promising herbal combination in patients suffering from essential hypertension at various health care centers in Maharashtra, India.

METHODS

This study was a four-week, open label, single arm, multicentric, pilot study which was conducted to evaluate the effect of capsule Artyl on blood pressure in hypertensive patients.

There were 30 patients belonging to the age group of 30 years to 70 years having pre-diagnosed essential hypertension with systolic blood pressure (SBP) between 140-170mm Hg were included in this study. These subjects were attending the out-patient departments (OPDs) at different Madhavbaug clinics located in various cities of Maharashtra, India. The subjects enrolled in the study had to be willing to follow the protocol strictly over the four weeks of study period. Patients who were suffering from cardiovascular co-morbidities (left ventricular hypertrophy, heart block, congestive heart failure or coronary artery disease) were excluded from the study. Patients having deranged liver function tests or renal function tests, pregnant women or women planning pregnancy in the next 6 months were also excluded from the study. If the subjects failed to adhere to the protocol or decided to drop out of the study themselves or developed some complication due to increase in SBP and diastolic blood pressure (DBP) which would have required urgent treatment, then they were to be withdrawn from the study.

The study was initiated in November 2017 and completed in February 2018. The patients were prescribed capsule Artyl 500mg, to be taken twice daily for a period of 28 days, along with the conventional treatment, if it was ongoing for the patient. All the patients were motivated to modify their lifestyle and dietary habits. The assessment of SBP and DBP was done with the help of a sphygmomanometer after enrolment of the subject in the study, which was considered the baseline or day 1 reading. The follow up reading of SBP and DBP was taken at day 7, day 14, day 21 and day 28. The weight, height, BMI and the concomitant medication data was noted down on day 1 and again on day 28. The mean arterial pressure (MAP) was also calculated for all the patients on day 1 and day 28 using the formula: 2/3rd DBP + 1/3rd SBP.

Data were analyzed using MS excel and Graphpad Instat softwares. The data were represented as mean±SD. The variables on day 1 and day 28 were compared to each other using paired student's t test. P value of less than 0.05 was considered significant for all the variables.

Table 1: Constituents of capsule Artyl.

Composition of Cap. Artyl	Percentage (%)
Brahmi (*Bacopa monnieri)*	62.5
Shunthi (*Zingiber officinale)*	34
Excipient	3.5

RESULTS

A total of 90 hypertensive patients were screened for participation in the study. Out of these 90 patients, 30 were included in the study based on the selection criteria. 29 of the 30 enrolled patients completed the full study period and the data collected from these 29 patients were analyzed at the end of the study (Figure 1). The demographic details of the patients have been mentioned in Table 2.

Many of the patients (n=11) were found to have hypertension for the first time on their visit to the Madhavbaug Clinic OPDs. These 11 patients were started on Capsule Artyl with the advice of lifestyle and dietary modifications. The remaining 18 patients were on

concomitant allopathic medications, the details of which have been mentioned in Figure 2.

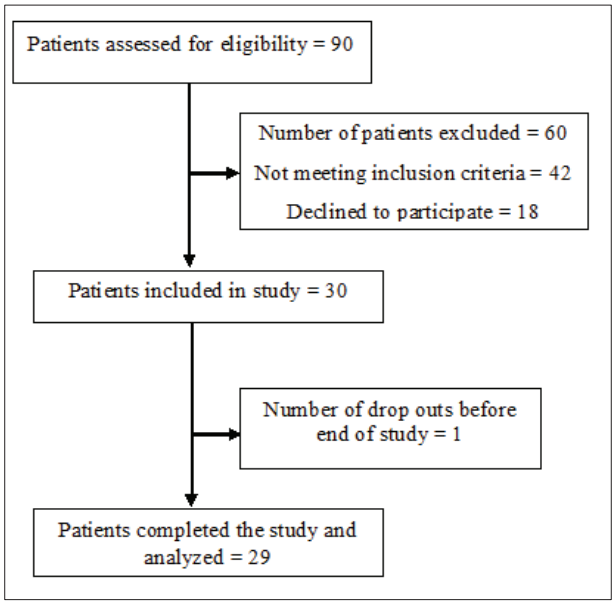


Figure 1: Patient enrolment flow chart.

Table 2: Demographic details of patients enrolled in the study (n= 29).

Mean demographic details of the study participants
Mean age of patients = 51.68±14.02 years
Mean weight of patients (Day 1) = 70.29±10.65 kilograms
Mean weight of patients (Day 28) = 70.12±10.80 kilograms
Mean BMI of patients (Day 1) = 27.08±3.21kg/m^2
Mean BMI of patients (Day 28) = 26.53±3.02kg/m^2

Table 3: Effect of artyl treatment on improvement of Systolic Blood Pressure (SBP) from baseline to day 28.

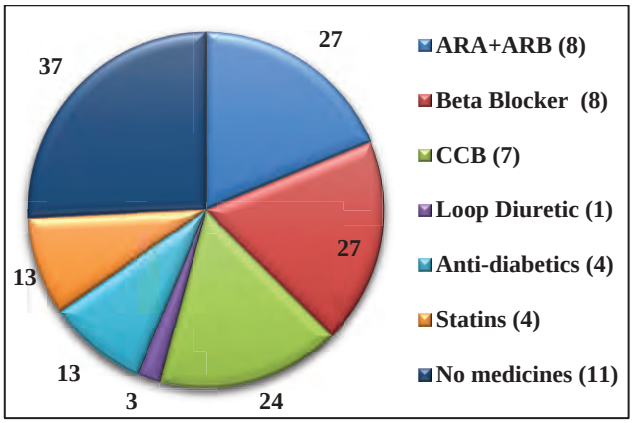
SBP	No. of patients	Baseline	Day 28	Changes	% changes
1. All					
Mean	29	155.48	141.86	13.62	8.76
Standard deviation		10.61	12.54		
P value	P <0.001				

Table 4: Effect of artyl treatment on improvement of Diastolic Blood Pressure (DBP) from baseline to day 28.

DBP	No. of patients	Baseline	Day 28	Changes	% changes
1. All					
Mean	29	90.34	89.66	0.69	0.76
Standard deviation		6.68	6.80		
P value	P >0.05				

Table 5: Effect of Artyl treatment on improvement of Mean Arterial Pressure (MAP) from baseline to day 28.

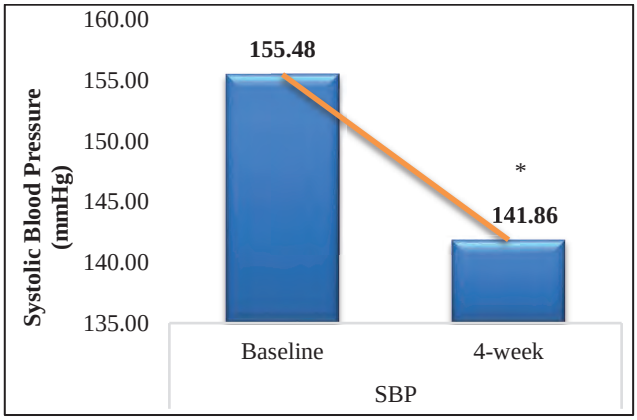
DBP	No. of patients	Baseline	Day 28	Changes	% changes
All					
Mean	29	112.06	107.06	5.00	4.46
Standard deviation		6.29	7.03		
P value	P <0.01				



ARA= Antagonist receptor blocker, ARB= Angiotensin Receptor Blockers, CCB= Calcium Channel Blockers

Figure 2: Percentage of subjects using allopathy medicines (n=29).

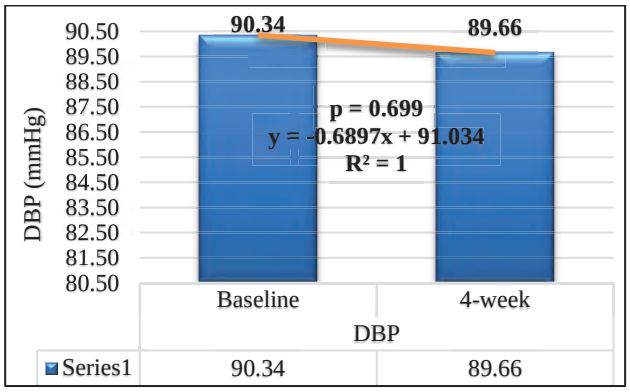
The mean SBP on day 28 was compared with that at baseline using Paired t-test; P<0.05 considered significant (Table 3). The efficacy parameters were analyzed at baseline (day 1) and on the last day of the study (day 28). It was found that the mean SBP was significantly lesser on day 28 (141.86±12.54mm Hg) as compared to the mean baseline SBP of the patients recorded on day 1 (155.48±19.37mm Hg) (p<0.001). The decrease in the mean SBP was by a margin of 8.76% (Figure 3).



Comparison of the mean values done by paired t-test.
*: p<0.05 considered a statistically significant difference

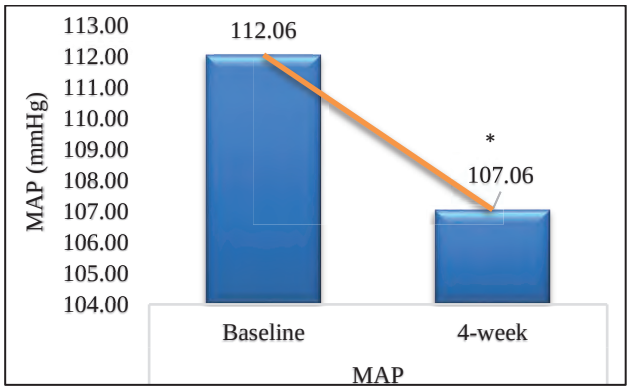
Figure 3: Comparison of mean Systolic Blood Pressure (SBP) at baseline and at 4 weeks (n=29).

The mean DBP on day 28 (89.66±6.8mm Hg) was lesser than that on day 1 (90.34±7.44mm Hg) but this difference was not statistically significant (p>0.05). The decrease in mean DBP was 0.76% (Figure 4).



Comparison of the mean values done by paired t-test.
The mean values were not found to be statistically different from each other (p>0.05)

Figure 4: Comparison of mean Diastolic Blood Pressure at baseline and at 4 weeks (n=29).



Comparison of the mean values done by paired t-test.
*: p<0.05 considered a statistically significant difference

Figure 5: Comparison of mean values of mean arterial pressure at baseline and at 4 weeks (n=29).

There was a significant decrease in the mean value of MAP on day 28 (107.06±7.03mm Hg) as compared to that on day 1 (112.06±10.75mm Hg) (p<0.01). The difference in the mean values of MAP was 4.46% (Figure 5). None of the participants in the study developed any kind of adverse event over the study period.

DISCUSSION

Hypertension is one of the most common and dangerous non-communicable disease affecting the world population. The complications associated with the disease is a grave concern, especially because of the high rates of uncontrolled BP in the patients with hypertension, despite being on the standard pharmacological treatment. An Indian study published in 2014 concluded that the control rates of blood pressure in hypertensive cases on medication are just about 10% in rural and 20% in the urban population.[5] Current drugs used for hypertension are not only associated with adverse effects but are also not cost-effective.[11] Hence, it is important to look to alternative medicine for more efficacious, safe and cost-effective options to treat hypertension. This search took us to Ayurveda, the Indian discipline of traditional medicine. Two herbal drugs, namely Brahmi (Bacopa monnieri) and Shunthi (Zingiber officinale) have been studied by researchers for their possible anti-hypertensive effect individually. However, none of them has studied a combination of these herbal medicines for the treatment of hypertension. Capsule Artyl is a herbal drug made by combining the extracts of Brahmi and Shunthi. Considering the surrounding evidence and the need for new medicines to control hypertension, we conducted this study.

On analyzing the collected data from the 29 participating hypertensive patients, we found that there was a statistically significant decrease in the mean SBP and the mean values of MAP on day 28 as compared to the baseline reading. The mean DBP was also found to be lower on day 28 as compared to the baseline reading, however this difference was not statistically significant. None of the patients on capsule Artyl showed any adverse effect in the study, and thus the formulation can be considered safe. These results were in sync with many of the studies conducted using Brahmi and Shunthi individually.

In a preclinical study conducted in Thailand, it was found that Brahmi reduces the blood pressure significantly in Wistar rats.[7] In a clinical study conducted in India, Brahmi was found to decrease SBP, DBP and MAP significantly at 4 weeks of treatment, similar to the findings in this study.[8]

Shunthi, the processed dry ginger, has shown promising results individually in various studies as an anti-hypertensive agent. In a study conducted in China, daily consumption of ginger was associated with decreased risk of hypertension in adults (OR = 0.92, CI: 0.87-0.99).[12] A clinical study conducted in hypertensive patients of Egypt showed a statistically significant decrease in SBP and DBP at the end of 4 weeks of taking ginger with the prescribed medication.[13] A systematic review on ginger published in the British Medical Journal concluded that animal studies have found ginger to have the potential to offer natural anti-hypertensive effect when taken as a supplement to conventional anti-hypertensive drugs.[10]

Preclinical studies have assessed the possible mechanism of actions behind the antihypertensive effects of Brahmi and Shunthi. The study conducted by Kamkaew et al. found that the fall in blood pressure caused by Brahmi is because of its vasodilatory effects on the resistance arteries. The researchers also found that this vasodilation is through the nitric oxide pathway. At high concentrations, Brahmi was found to decrease the contractions generated by the voltage gated calcium

channels and reduce the action of calcium release from the sarcoplasmic reticulum.[7] Brahmi has also shown anti-stress as well as anti-oxidant property, which may also play a role in its anti-hypertensive action. A pre-clinical study in Nigeria found that Shunthi (ginger) showed ACE inhibitory activity in vivo which could be the reason behind its BP lowering action.[14] A study conducted by Ghayur et al found that ginger exhibited a vasodilator action through the blockage of the voltage gated calcium channels, which may be another possible mechanism behind its anti-hypertensive action.[9]

Our study had a few limitations. It was a one arm pilot study which was done mainly as a proof of concept research with low sample size and without a control arm. Sphygmomanometer was used to assess the SBP and the DBP, which is a subjective tool to measure BP in comparison to ambulatory BP monitoring. The study duration was just 28 days, due to which long term efficacy and safety of capsule Artyl was not assessed.

CONCLUSION

Our preliminary study has found that capsule Artyl, which is a herbal drug produced by combining Brahmi and Shunthi, is successful in significantly decreasing the BP in hypertensive patients, without any adverse effects. Considering that this was a pilot one-arm study, controlled trials with larger sample size are needed to confirm the positive outcome of this promising herbal drug in hypertensive patients.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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To study the efficacy of Heart Failure Reversal Therapy (HFRT) program in elderly male patients with reduced ejection fraction

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Abstract
Background and Aims: Some authors consider heart failure (HF) to be a pandemic now, since nearly 26 million people have been affected by it, globally. Out of these, India alone has around 8-10 million patients. Heart Failure Reversal Therapy (HFRT) combines Herbal *Panchakarma* therapy with Dietary management. This study was conducted to evaluate the effect of HFRT on VO2peak, 6 Minute Walk Test (6MWT), systolic blood pressure (SBP), and diastolic blood pressure (DBP), BMI, weight, abdominal girth, and heart rate.
Setting and Design: This observational study was conducted from January 2015 to December 2017, wherein the data of elderly male patients with HF (NYHA class II and III) with reduced ejection fraction (<40%) who attended *Madhavbaug hospital, Khopoli, Maharashtra*, India were identified.
Materials and Methods: Data of patients who were administered HFRT (60-75 minutes) with minimum 7 sittings over 7 days were considered. Variables were compared between day 1, 7, 30, 60 and day 90 of HFRT.
Results: 50 elderly males with HF and EF < 40% were enrolled in the study for analysis. There was significant improvement in VO2peak, from 12.71 ± 2.47 at baseline to 14.89 ± 2.05 at day 90 ($p<0.001$). 6MWT also showed significant improvement from 339.42 ± 106.85 at day 1 to 432.4 ± 89.27 at day 90 ($p<0.001$). Also, BMI, abdominal girth, weight showed similar statistically significant improvements. Improvements in SBP, DBP and HR were not statistically significant.
Conclusion: From the findings of our study, HFRT has been found to be a potent and viable therapeutic alternative for elderly male patients with HF with reduced ejection fraction.

Keywords: heart failure reversal therapy, HFRT, Panchakarma, heart failure, blood pressure, systolic, diastolic, VO2peak, 6MWT, NYHA

1. Introduction

Reduced capacity of the heart to function optimally leading to insufficient amount of blood pumped for routine metabolic activities, resulting in increased resting pressure within the heart is known as Heart Failure (HF) [1, 2]. Some authors consider HF to be a pandemic now, since nearly 26 million people have been affected by it, globally. Out of these, India alone has around 8-10 million patients. Even the mortality rates in India due to HF are as high as 0.16 million per year [3]. In past few decades, urbanization and industrialization has boomed significantly in India, which has greatly contributed to increased sedentary lifestyle and other risk factors of HF. Due to improved healthcare, population in age group>60 years have escalated by more than 1.7 times in a short span of 20 years [4]. Since advancing age is a major risk factor for HF, it is logical to anticipate that prevalence and burden of HF in India is rising [5]. Apart from age, Hypertension (HTN) is other major risk factor for HF patient. Cases of HTN are consistently increasing with every passing year, thus increasing the likelihood of HF cases [6, 7].

A variety of drugs are available for treatment of HF, like angiotensin 2 receptor blockers (ARBs), angiotensin converting enzyme inhibitors (ACEIs), beta blockers, diuretics, anti-platelet drugs, etc [8]. Despite availability of extensive list of conventional therapeutic options, HF carries poor prognosis. HF has dual effects on patients- firstly, direct effect of its symptoms, and secondly anxiety and dread associated with these symptoms. These dual effects adversely affect quality of life of patient. Also, it has been commonly observed that adherence to conventional therapies is less than 50% in such patients, attributed to high cost of therapy, adverse effects of drugs, etc [9]. Due to these drawbacks of conventional therapies, there is need of novel therapy which will maintain and preserve optimal heart function and raise the quality of life of the patient [10].

Therapeutic benefits of conventional therapies in HF like ACEIs, ARBs, beta blockers, diuretics are due to anti-inflammatory, hypolipidemic, antiplatelet, and antioxidant actions [11]. Similar actions have been found in various herbal drugs in clinical studies [12, 13, 14]. Thus, the quest for search of novel therapeutic agent for the management of HF can end up here. *Panchakarma* and diet therapy are combined under the umbrella of Heart Failure Reversal Therapy (HFRT). *Panchakarma* in HFRT is administered via *Snehana* (External Oleation Therapy), *Swedana* (Passive Heat Treatment), *Hrudaydhara* (Decoction Drip Therapy), and *Basti* (Per Rectal administration); which are established detoxifying procedures [15, 16].

Functional working capacity is reduced in HF, as measured by maximum aerobic capacity/VO2peak [17]. This reflects in reduced quality of life [18]. Keeping this in mind, we planned an observational study, to analyze the effect of HFRT on

VO2peak in elderly male of HF with reduced ejection fraction (EF<40%). We also analyzed the effect of HFRT on SBP, DBP, HR, weight, BMI, abdominal girth.

2. Materials and methods

a. Sample Size: 50
b. Study design: Observational.
c. Duration of study: January 2015 to December 2017
d. Study Site: *Madhavbaug Hospital, Khopoli, Maharashtra, India.*
e. Inclusion Criteria: We have observed the efficacy of HFRT program in:
   1. Elderly male patients = Age ≥ 60 years
   2. Ejection fraction = ≤ 40%
   3. NHYA Grade – II and III
f. Methodology
   1. We identified the data of male patients suffering from HF (New York Heart Association, NYHA Class II–III) of age >60 years, and who had attended the out-patient departments (OPDs) at *Madhavbaug hospital* located in *Khopoli, Maharashtra, India*. The data of patients who had been administered HFRT with minimum 7 sittings over a span of 7 days were considered for the study. Cases were identified, and data was assessed from the records of *Madhavbaug Hospital in Khopoli, Maharashtra*. The selection was based upon the availability of complete relevant baseline data (day 1 of HFRT) to final day data (day 90 of HFRT) of the patients. The information about comorbidities, if any, was also noted down.
   2. The Follow-up schedule is shown in figure 1.
g. Primary End-point: VO2peak
h. Secondary End-points: Weight, BMI, Abdominal Girth, Heart Rate, SBP and DBP.

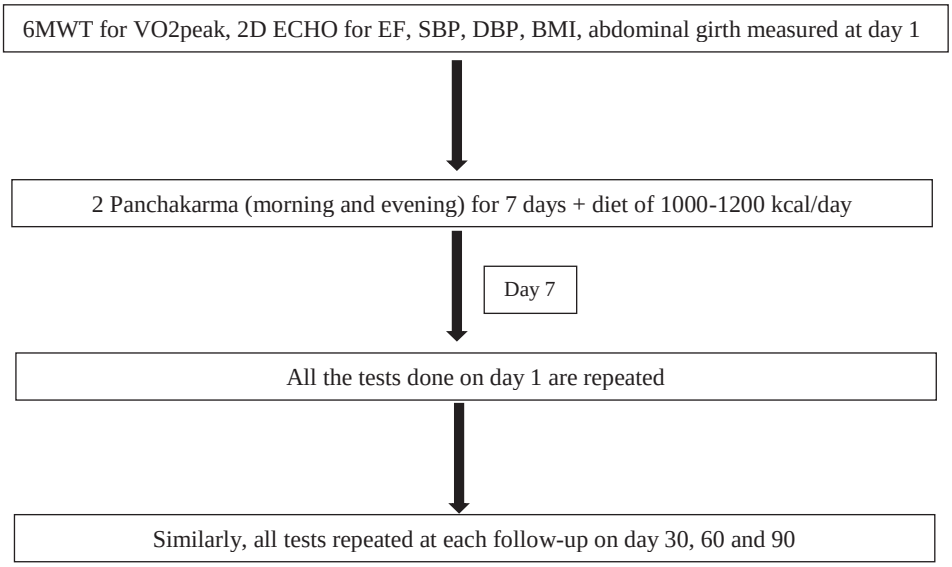

Fig 1: showing follow-up schedule.

The HFRT is a 4-step procedure, which was performed on the patients with HF after a light breakfast. One sitting of the procedure took 65-75 minutes, as described in table 1 [16, 19].

Table 1: Study Treatment: Heart Failure Reversal Therapy (HFRT)

Step of HFRT	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes directed towards heart)	10 grams *T. arjuna*, 10 grams *Dashamoola* and 5 grams *V.negundo* [100 ml extract processed in *sesame oil*]	30-35 minutes
Swedana	Passive heat therapy	*Dashmoola* (group of ten herbal roots) with steam at ≤ 40 degrees Celsius)	10-15 minutes + 3-4 minutes of relaxation after procedure
Hrudaydhara	Decoction dripping therapy from a height of 7-8 cm	Luke-warm *dashmoola* decoction	15 minutes
Basti	Drug administered per rectal, should be in body for ≥ 15 minutes for maximum absorption	1.88 grams *T. arjuna*, 0.42 grams *B. diffusa* and 0.18 grams *A. calamus* [10 ml aqueous extract]	10 minutes

On day 1 of HFRT, the patients had undergone 6MWT, VO2peak, SBP, DBP as per international recommendations [20]. These readings were considered as baseline readings. This process was repeated as per figure 1. The patients followed a diet chart/plan of 1000-1200 kcal/day.

Statistical analysis

Repeated measured ANOVA was used to test statistical significance for Primary endpoint (Improvement in VO2peak) and secondary endpoint (reduction in Weight, BMI, abdominal Girth, Heart Rate, SBP and DBP as well as

reduction in dependency of conventional medicine) for a washout period (DoA, DoD, 1st follow up, 2nd Follow up and 3rd Follow up). We used R (Version 3.5.0) software and excel to analyze the data (table 2).

Table 2: Hypothesis for ANOVA test

Null Hypothesis	**Means are equal among all 5 different time periods i.e. DOA, DOD, 1 f/u, 2 f/u & 3 f/u**
Alternative Hypothesis	Means of at least 2 groups are significantly different
Level of significance	0.05

3. Results

3.1 Study population

A total of 55 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1, day 7, day 30, 60 and Day 90) and the inclusion criteria, 50 patients were selected, and their data were considered for analysis. The baseline characteristics of these patients are shown in table 3.

Demographic characteristics of the subjects enrolled in the study was as shown in Table 2. The present involved a total of 50 HF patients. The mean age of the enrolled subjects was 67.84±5.71years. The mean ejection fraction in these patients was 30.78±5.54.

Table 3: Baseline characteristics of the study subjects (n= 30)

Variable	**Mean ± SD**
Gender (M)	50/0
Age (Years)	67.84±5.71
Height (cm)	165.45±5.93
LV Mass	241.22±61.08
EF	30.78±5.54
Past medical history Frequency (%)	
CAD	24 (48.00)
HTN	31 (62.00)
DM	21 (42.00)
IHD	33 (66.00)
MI	6 (12.00)
NYHA functional class Frequency (%)	
Class I	0 (0.00)
Class II	34 (68.00)
Class III	13 (26.00)
Class IV	1 (2.00)

Data were expressed in % and mean ± SD

The baseline characteristics of the study populations are shown in Table 3. In that 50 subjects, 24 (48%) have Coronary artery disease (CAD), 31 (62%) have Hypertension (HTN), 21 (42%) have Diabetic Mellitus (DM), 33 (66%) have ischemic heart disease (IHD), 6 (12%) have Myocardial infarction (MI). Most of the patients belongs Class II 34 (68%) and Class III 13 (26%) as per NYHA functional class. Only single respondent belongs to class IV.

Table 4: Effect of HFRT treatment on improvement of various body parameters according to overall and NYHA subjects

Variable	**Sample size**	**Mean ± SD**					**P-value**	**Conclusions from ANOVA**
		DOA	**DOD**	**1 f/u**	**2 f/u**	**3 f/u**		
VO2 Peak	50	12.71± 2.47	13.96 ± 2.12	14.65 ±2.15	14.8 ± 2.19	14.89 ± 2.05	<0.001	Statistically significant
6 MWT (Meters)	50	339.42 ±106.85	391.98 ±91.97	422 ± 93.5	428.2 ±95.08	432.4 ±89.27	<0.001	Statistically significant
Weight	50	64.82 ± 12.01	62.91 ±11.67	62.31 ±11.26	62.37 ±10.89	62.48 ±10.94	<0.001	Statistically significant
BMI	50	23.56 ± 3.92	22.85 ± 3.73	22.64 ± 3.6	22.66 ± 3.47	22.7 ± 3.47	<0.001	Statistically significant
Abdominal Girth	50	91.66 ± 10.4	89.82 ±10.19	89.16 ± 9.94	88.2 ± 9.47	89.04 ± 9.43	<0.001	Statistically significant
Heart Rate	50	76.5 ± 12.77	78.3 ± 11.42	72.94 ±13.41	74.82 ±13.18	75.54 ±11.96	0.14	Statistically insignificant
SBP	50	114.04 ± 14.57	115.2 ±14.18	112.8 ±15.52	112.32 ±12.86	115.6 ±14.02	0.49	Statistically insignificant
DBP	50	73.6±8.75	74±8.08	72.4 ± 8.47	73.32 ±10.77	72.8 ± 8.34	0.79	Statistically insignificant

Effect of HFRT treatment on improvement of body parameter is summarized in Table 4. For all 50 cases, HFRT treatment showed significant improvement in weight, BMI, Abdominal Girth, 6MWT (meters) and VO2peak. HFRT treatment wasn't statistically significant for Heart rate, SBP and DBP.

Following figure shows us a comparison of endpoint among all time periods (DoA, DoD, 1st follow up, 2nd Follow up and 3rd Follow up).

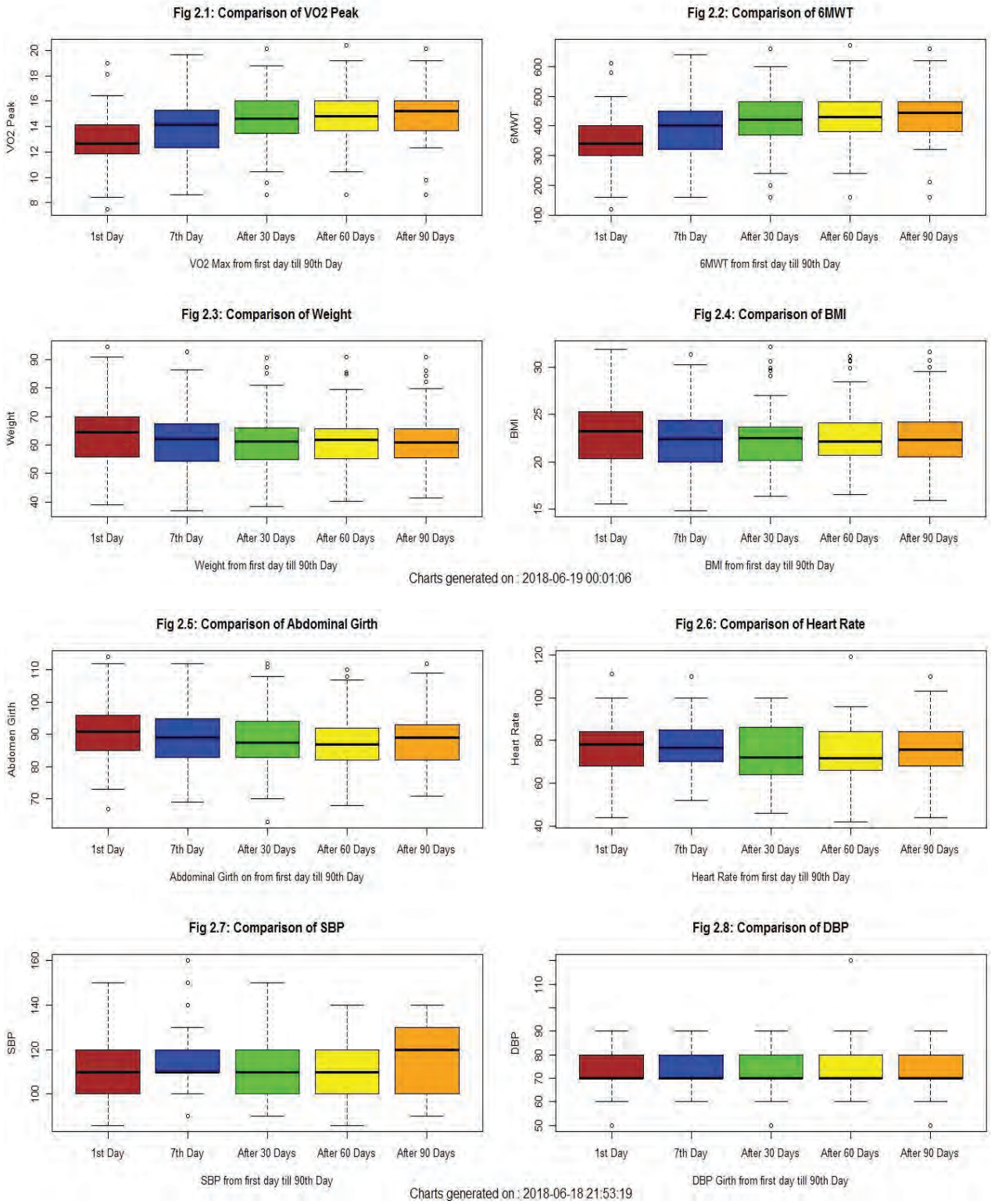

Fig 2: showing effect of HFRT on body parameters

Thus, HFRT treatment showed statistically significant results for the primary endpoint (Improvement in VO2peak) but partially significant in case of secondary endpoint (Reduction in Weight, BMI, abdominal Girth, Heart Rate, SBP and DBP). Heart rate, SBP and DBP were statistically insignificant amongst secondary endpoint.

4. Discussion

The present observational study analyzed the effect of HFRT in elderly males of HF, found that there was significant improvement in 6MWT and VO2peak from day1 to day 7 of HFRT. It was fascinating to observe that these improvements were sustained even on day 90 of follow-up. Even secondary

endpoints like BMI, weight, abdominal girth showed substantial improvement after HFRT. Oxygen uptake is drastically reduced in patients of HF due to weakened heart. This is reflected by reducing VO2peak [21]. Thus, significant improvement in VO2peak in the present study carries a favourable prognosis in patients with HF. This was corroborated by the findings of other such studies, although treatments used in those studies were different [22]. Around 14-16% reduction in risk of mortality with increase in VO2peak by 1ml/kg/min was seen in one clinical study in patients with ischemic heart disease [23]. Thus, significant improvement in VO2peak in the present study signifies favourable prognosis in patients of HF. VO2peak increased in the present study by hefty margin of around 50% from baseline to day 90 of follow-up. This indicates a reduction in death risk in patients with HF.

Despite availability of wide range of conventional allopathic drugs and extensively designed guidelines to combat the havoc of HF, morbidity and mortality of HF is rising continuously. *Panchakarma* is administered in HFRT as 4-step process, which includes *Snehana, Swedana, Hrudaydhara* and *Basti* [24]. Plausible mechanism of HFRT might be:

1. *Snehana*- calms the patient through its anxiolytic effect
2. *Swedana*- reduces preload of the heart by reducing water and sodium load
3. *Hrudaydhara*- which is a type of *Shirodhara*; it calms the patient and helps in reduction of BP
4. *Basti- Terminalia arjuna* helps in reduction of BP, thus reducing afterload of heart [*terminalia*].

We studies the effect of HFRT in elderly male of HF with reduced EF and found significant improvement in VO2peak and 6MWT at the end of 3rd follow-up visit. Since the patients had EF< 40%, stress test was contraindicated. VO2peak is reduced in patients with HF due to the reduced pumping action of heart [25]. Reduced VO2peak in HF patients clinically as diminished capacity to work/exercise [26]. VO2peak is derived from Cahalin's formula, using the results of 6MWT, as stated below [25].

Mean Peak VO ml/kg/min = 4.948 + 0.023 x Mean 6 MWD (meters)

Where: 6MWD is 6 minute walk distance measured by 6 minute walk test (6MWT).

A 6MWT result >300 meter and VO2peak >12 has been found to be associated with better survival long term, in patients with HF [27]. In the present study we found that, both 6MWT was more than 400 meters and VO2peak more than 14 points, which signifies better prognosis, thus reducing risk of mortality in patients of HF. Increased BMI, and abdominal girth are associated with increased morbidity and mortality in HF patients. Significant reduction in BMI and abdominal girth after 90th day of HFRT, indicates favorable prognosis in terms of reduction of risk of mortality in patients of HF.[28] Although, significant positive findings were obtained in the present study, further such studies need to be done on a larger scale, probably a prospective head to head comparative clinical trial, so as to generalize the findings of present study to larger population.

6. Conclusions

We observed significant improvement in VO2peak, 6MWT coupled with reduction in body weight, BMI; HFRT offers a promising candidature for consideration as potent therapeutic option for treatment of elderly males of HF with reduced EF.

7. Acknowledgments

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Efficacy of heart failure reversal treatment (HFRT) in patients with heart failure with preserved ejection fraction: An observational study

Rohit Sane and Rahul Mandole

Abstract
Objective: Heart failure has emerged as global health issue despite multiple treatment options. The present study was conducted to explore the efficacy of heart failure reversal therapy in patients with heart failure with preserved ejection fraction.
Material and Methods: An observational study was conducted in *Madhavbaug Hospital, Khopoli* from January 2015 to December 2017. All elderly male patients aged>60 years with heart failure and ejection fraction>40% were considered eligible. Patients were hospitalized and HFRT was given twice daily for seven days, following which they were discharged and advised to follow-up at 30, 60 and 90 days. The primary efficacy endpoint was improvement in maximal oxygen uptake (VO2 max) and secondary endpoints were changes in body weight, BMI, abdominal girth, heart rate, blood pressure.
Results: A total of 194 patients could complete the entire 90 day treatment and considered for analysis**.** The VO2max measured at day 90 was significantly higher compared to baseline values (26.36 ± 6.88 versus 18.37 ± 5.47, p<0.001). Such improvement was also observed in bodyweight (64.64 ± 9.22 at day 90 versus 68.69 ± 10.31 at baseline) abdominal girth (90.19 ± 8.46 versus 95.06 ± 9.34) BMI (23.76 ± 2.93 versus 25.23 ± 3.15) heart rate (76.61 ± 14.17 versus 80.66 ± 14.59) systolic BP (122.99 ± 12.56 versus 124.55 ± 15.25) and diastolic BP (78.39 ± 7.67 versus 78.15 ± 8.37) (p value <0.001 for all the secondary endpoints).
Conclusion: Our study demonstrated HFRT causes significant improvement in VO2 max in patients with HFpEF which implies better exercise tolerance. HFRT also showed improvement in weight, BMI and abdominal girth, blood pressure of the patients, which could have a positive impact on quality of life**.**

Keywords: Heart failure with preserved ejection fraction, heart failure reversal therapy, Panchakarma, maximal oxygen uptake

1. Introduction
Heart failure (HF) is a disease clinically characterized by the impaired ability of the heart to pump and/or fill with blood [1]. It is escalating in epidemic proportions and has emerged as a major global health issue, with an estimated worldwide prevalence of >37.7 million [2]. It is projected that by 2030, the number of HF patients would rise by 25 % [2]. Heart failure is associated with shorter life expectancy, increased frequency of hospitalization and poor quality of life (QOL), and is a major public health challenge even in India [3]. On the basis of ejection fraction, HF has been classified into three subtypes, namely HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF) and HF mid-range ejection fraction (HFmrEF) [4].Heart failure with preserved ejection fraction (HFpEF) is considered as a primary cause of morbidity and mortality and accounts for approximately 50% of HF cases [5]**.** In Indian context, The Trivandrum Heart Failure Registry (THFR) reported that HFpEF accounted for 25% of the total HF burden, indicating that in Indian clinical practice, HFrEF is predominantly observed [6]. A careful overview of population-based studies revealed that HFpEF is more common in elderly, with associated comorbidities, such as obesity, hypertension, coronary artery disease (CAD), chronic kidney disease, anemia, dyslipidemia, diabetes mellitus [7]. The pathophysiology of HFpEF is poorly understood, and a literature search revealed that no medication trials could demonstrate significant improvement on the primary endpoints of cardiovascular mortality and morbidity.

Consequently, there is an unmet clinical need for new strategies for improving HFpEF quality of life and outcomes.

Ayurveda is a traditional scientific medicinal system indigenous to India. *Ayurveda* means 'knowledge of life', which comprises two Sanskrit words, *Ayu* (life) and *Veda* (knowledge or science). The principal aim of *Ayurveda* is to achieve equilibrium between the physiological and structural entities, which ultimately culminates in good health. Any disparity or unevenness because of external or internal factors may lead to disease development [8]. Ayurvedic treatment aims to restore the equilibrium through the utilization of different techniques, regimens, diet as well as medicines. Ancient Ayurvedic texts mention the clinical features and treatment of heart failure indicating that the knowledge of the disease was present with the Ayurvedic physicians [9].

In our institute (Madhavbaug Hospital, Khopoli) the Ayurvedic physicians are using a multi-faceted management treatment protocol [Heart Failure Reversal Therapy (HFRT)] to treat heart failure, which includes a combination of herbal treatment with Panchakarma and allied therapies. HFRT uses various decoctions and oils and constitutes of a 4-step procedure namely: a. *Snehana* / external oleation or massage b. *Swedana* / passive heat therapy c. *Hrudaydhara* / variation of shirodhara technique and *Basti* / per rectal drug administration.

However, a literature search revealed that there is a dearth of published literature to show the efficacy of HFRT in HFpEF patients. In this backdrop, the present study was conducted to demonstrate the efficacy of HFRT on HFpEF patients. The primary efficacy endpoint was improvement in maximal oxygen uptake (VO2 max) and secondary endpoints included was reduction in Weight, BMI, Abdominal Girth, Heart Rate (HR), SBP and DBP.

2. Material and Methods:

2.1 Study setting and patient selection:

A prospective observational study was conducted in *Madhavbaug Hospital, Khopoli* for a period of two years, extending from January 2015 to December 2017 to address the study objective. All elderly male patients with age greater than sixty years with clinical evidence of heart failure (NYHA 1-IV) and ejection fraction greater than 40% were considered eligible to participate in the study.

2.2 Study procedure

Eligible patients with heart failure were hospitalized in the clinic after initial screening. On day 1 of the study, baseline clinical status of the patient was determined by measuring blood pressure, weight, BMI, Abdominal Girth, ejection fraction (as measured by 2D Echo) and Stress test. Following this, HFRT therapy is applied twice daily (morning and evening) to the patients. This pattern is followed in the next seven days during the hospitalization with a diet plan of 1000-1200 kcals. On Day 7, the same tests performed on day 1 were repeated and the patient was discharged from the hospital. At the time of discharge, patients were advised to follow-up at 30-days, 60-days and 90-days. During each follow-up visit, blood pressure, weight, BMI, abdominal Girth, ejection fraction were measured and Stress test was performed. In this context, it is prudent to share the details of HFRT procedure. The HFRT therapy is a combination of Panchakarma and allied therapies. HFRT uses various decoctions and oils and constitutes of a 4-step procedure namely:

a. *Snehana* / external oleation or massage (~30 -35 minutes): An oil-based decoction was used to administer external massage to the HF patients. This massage technique uses centripetal or upward strokes directed towards the heart.
b. *Swedana* / passive heat therapy (~10 -20 minutes): To administer this therapy HF patients were asked to lie in a supine position inside a sudation box and their head was positioned outside the box. *Dashmoola* (group of ten herbs) steam of temperature not more than 40 was then passed steadily for 10-15 minutes. After the treatment, patients were asked to relax for 3-4 minutes.
c. *Hrudaydhara* / variation of shirodhara technique (~ 15 minutes): During this technique, luke-warm *dashmoola* decoction was allowed to drip at a constant speed from a fixed height on the medial mediastinum region of the HF patients demarked by a hrudayapatra.
d. *Basti* / per rectal drug administration (~ 15 minutes): A drug was administered to HF. that remains inside the body ≥ 15 minutes for maximum absorption.

Each cycle of HFRT is about 60-75 minutes duration.. The detailed schedule of HFRT is described below in Table 1.

Table 1: Study Treatment: Heart Failure Reversal Therapy (HFRT)

Step of HFRT	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation centripetal upper strokes directed towards heart)	10 grams T. arjuna, 10 grams *Dashamoola* and 5 grams *V. negundo* [100 ml extract processed in sesame oil]	30-35 minutes
Swedana	Passive heat therapy	*Dashmoola* (group of ten herbal roots) with steam at ≤ 40 degrees Celsius)	10-15 minutes + 3-4 minutes of relaxation after procedure
Hrudaydhara	Decoction dripping therapy from a height of 7-8 cm	Luke-warm *dashmoola* decoction	15 minutes
Basti	Drug administered per rectal, should be in body for ≥ 15 minutes for maximum absorption	1.88 grams *T. arjuna*, 0.42 grams *B. diffusa* and 0.18 grams *A. calamus* [10 ml aqueous extract]	10 minutes

2.3 Statistical analysis:

Data was entered in MS excel and analyzed using R Version 3.5.0 software. The data of only those patients who could complete the entire treatment (hospitalized for 7 days and attended all follow-up visits) were considered for analysis. One way ANOVA was used to test statistical significance for changes in the primary endpoint (improvement in VO2max) and secondary endpoint (Reduction in Weight, BMI, abdominal Girth, Heart Rate, blood pressure) at all-time points, namely baseline i.e. Date of admission(DoA), date of discharge (DoD), 1st follow up, 2nd Follow up, 3rd

Follow up. A two tailed p-value<0.05 was considered to be statistically significant for all the variables.

3. Results

During the study period, a total of 575 patients were considered eligible for participation in the study. However, 194 patients could complete the entire treatment and were considered for analysis. The baseline characteristics of the study population are shown in Table 2. The medical history of the patients was also assessed for the presence of co-morbidities.It may be noted that put of 194 subjects, hypertension was the most common co-morbidity followed by ischemic heart disease, diabetes mellitus, coronary artery disease and myocardial infarction. Most of the patients were of Class II 137 (70.62%) and Class III 30 (15.46%) as per NYHA functional class. Only 3 respondents belong to class IV.

Table 2: Baseline characteristics of the study subjects (n= 194)

Variable	Mean ± SD
Gender (M)	194/0
Age (Years)	64.88±3.92
Height (cm)	164.83±6.48
Past medical history Frequency (%)	
CAD	82 (42.27)
HTN	139 (71.65)
DM	97 (50.00)
IHD	130 (67.01)
MI	19 (9.79)
NYHA functional class Frequency (%)	
Class I	17 (8.76)
Class II	137 (70.62)
Class III	30 (15.46)
Class IV	3 (1.55)

3.1 Primary endpoint

Assessment of improvement in VO2 max: The VO2 measured at day 90 was significantly higher when compared to the mean value on day 1 which was considered as the baseline value (26.36 ± 6.88 vs 18.37 ± 5.47, p<0.001) [Table 3, Figure 1.1].This signifies a positive impact of HFRT on cardiorespiratory fitness.

3.2 Secondary endpoints

a. Body weight: The body weight of the patients reduced significantly in the follow-up visits from their baseline values. The mean decrease in bodyweight measured at third follow-up was 64.64 ± 9.22 as compared to the baseline value on Day 1 i.e. day of admission (68.69 ± 10.31; p <0.001).(Table 3, Figure 1.2)

b. BMI: The mean BMI underwent significant reduction on day 90 when compared to the mean BMI recorded at the baseline (23.76 ± 2.93 vs 25.23 ± 3.15, p<0.001) [Table 3, Figure 1.3].

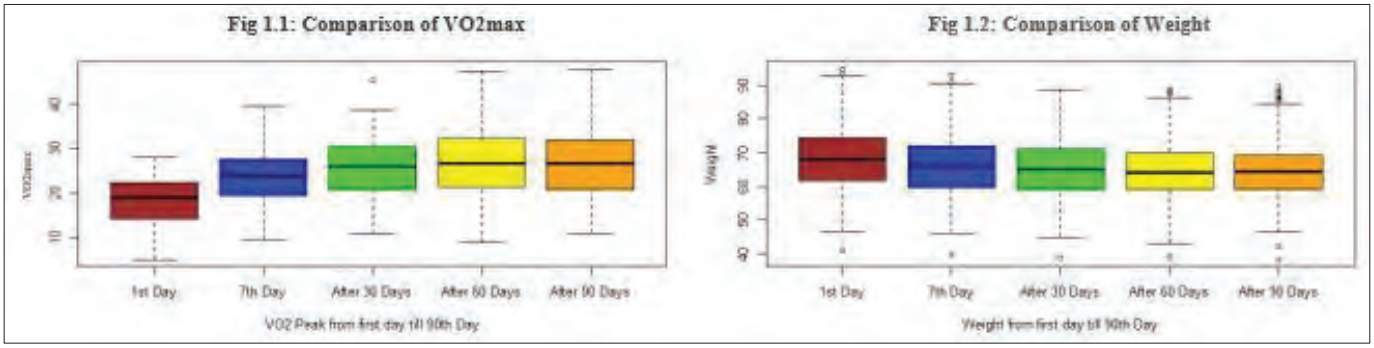
c. Abdominal girth: The abdominal girth was also significantly reduced on day 90 compared to the baseline mean abdominal girth (90.19 ± 8.46 vs 95.06 ± 9.34, p<0.001) [Table 3, Figure 1.4].

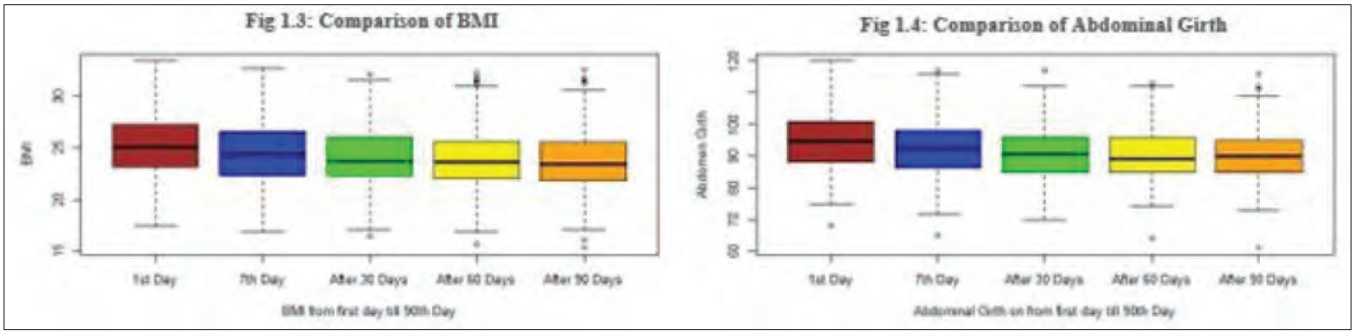
d. Hemodynamic parameter: At the third follow-up visit, there was significant reduction in the basal heart rate from baseline value (76.61 ± 14.17 versus 80.66 ± 14.59, p<0.001, Table 3, Figure 1.5).Such reduction in also noticed in SBP, DBP at third follow-up as compared to baseline (SBP 122.99 ± 12.56 versus 124.55 ± 15.25, p<0.001) and DBP (78.39 ± 7.67 versus 78.15 ± 8.37, p<0.001).(Table 3, Figure 1.6 and 1.7)

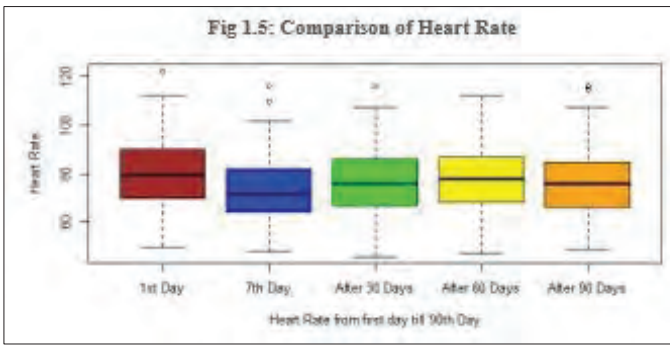
Table 3: Effect of HFRT treatment on improvement of various body parameters according to overall and NYHA subjects

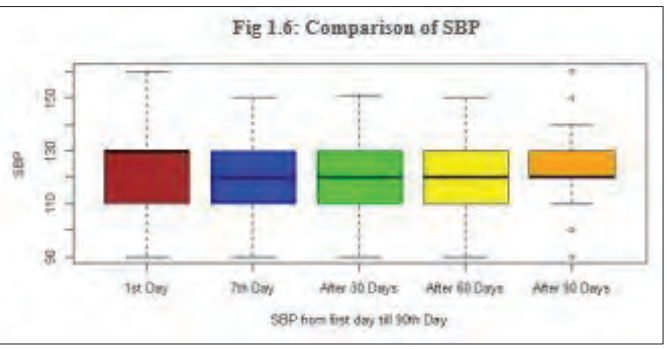
Variable	Sample size	Mean ± SD					P-value
		DOA	DOD	1 f/u	2 f/u	3 f/u	
VO2 max	194	18.37 ± 5.47	23.44 ± 6.14	25.85 ± 6.77	26.79 ± 7.24	26.36 ± 6.88	<0.001
Weight	194	68.69 ± 10.31	66.62 ± 9.98	65.57 ± 9.68	65 ± 9.52	64.64 ± 9.22	<0.001
BMI	194	25.23 ± 3.15	24.48 ± 3.08	24.09 ± 2.97	23.89 ± 2.95	23.76 ± 2.93	<0.001
Abdominal Girth	194	95.06 ± 9.34	92.89 ± 9.02	91.03 ± 8.55	90.53 ± 8.47	90.19 ± 8.46	<0.001
Heart Rate	194	80.66 ± 14.59	73.51 ± 12.88	76.62 ± 13.02	77.97 ± 13.92	76.61 ± 14.17	<0.001
SBP	194	124.55 ± 15.25	118.27 ± 12.31	120.27 ± 13.87	120.49 ± 13.02	122.99 ± 12.56	<0.001
DBP	194	78.15 ± 8.37	75.21 ± 6.99	76.53 ± 8.15	76.27 ± 7.7	78.39 ± 7.67	<0.001

Effect of HFRT treatment on improvement of body parameters is summarized in Table 2. For all 203 cases, HFRT treatment showed significant improvement in all the parameters.









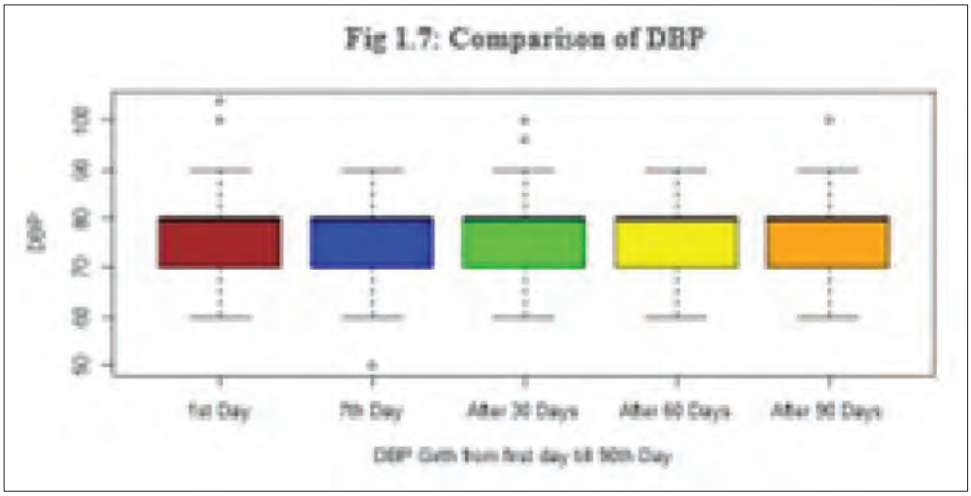


Fig 1: Comparison of study endpoint at all time period (DoA, DoD, 1st follow up, 2nd Follow up and 3rd Follow up).

4. Discussion

The global problem of heart failure is on escalation at an alarming rate worldwide as well as in India. Researchers and policymakers have repeatedly highlighted the need for new treatment options to manage heart failure, which turned our attention towards *Ayurveda*, the ancient form of alternative medicine widely used in India. Ayurvedic practitioners have been treating heart failure since ancient times.

Heart Failure Reversal Therapy (HFRT) is one such treatment used to treat heart failure in India, which includes a combination of herbal treatment with Panchakarma and allied therapies. In the present study, we have assessed the efficacy of this treatment technique on cardiovascular parameters like VO2 max, abdominal girth, BMI, blood pressure, body weight. All these parameters were significantly reduced in the patients on HFRT management, at the end of 90 days.

The primary endpoint of our study was VO2 max. Exercise intolerance constitutes one of the hallmark symptoms of heart failure. The main reason of reduced exercise capacity in HF patients is systolic and/or diastolic left ventricular dysfunction, which results in impaired hemodynamic response to exercise [11].Other pathophysiological mechanisms postulated are impaired muscle blood flow caused by increased vasoconstriction, and/or decreased local vasodilatory capacity, muscle mitochondrial dysfunction, an augmented ventilatory response to exercise, autonomic imbalance [11]. American Heart Association (AHA) in a recent statement (2016) mentioned that low levels of cardiorespiratory fitness (CRF) are associated with a high risk of cardiovascular disease (CVD) and all-cause mortality [12]. Although CRF is now recognized as an important marker of cardiovascular health, it is rarely assessed in clinical studies and practice. Researchers have opined that VO2 is a reliable indicator of the severity of heart failure and a strong predictor of the prognosis in HF patients [13]. Hence, we considered V02 max as the primary study endpoint. Our study revealed that HFRT causes a significant improvement in VO2 max from baseline value which implies better exercise tolerance of HF patients. This improvement in exercise tolerance could translate into a decrease in cardiovascular mortality, morbidly and quality of life of the patients.

Snehana is provided using *Neem* (*Azadirecta indica*) oil all over the body. Oleation is an anxiolytic procedure which decreases the sympathetic stress. The reduced sympathetic action decreases the vasoconstriction, which can be helpful to improve the hemodynamic status. *Swedana* is a process wherein patients are allowed to sleep inside a wooden box full of steam with head and neck outside the box, temperature being maintained around 40-45-degree Celsius. After 15-20 min patient is asked to come outside the box. It is hypothesized that hot fomentation, which is a relaxing process, induces sweating and decreases the excess of sodium and water which comprehensively helps to decrease fluid retention and improve hemodynamic status of HF patients. This helps in the reduction of edema in the patient thus alleviating the congestive symptoms of heart failure [10].
In *Basti*, mild purgation will occur which help in reducing the sodium retention and thus controlling the BP as evidenced in the earlier study [14]. Besides this mechanism, *Lekhana Basti* was found to have a significant effect in reducing the symptoms of *Medodushti* (dyslipidemia) and in reduction of objective parameters like weight, body mass index (BMI), body fat percentage [15].
Infact, the four basic elements of HFRT namely *Snehana*, *Swedana*, *Hrudaydhara* and *Basti* are postulated to act in synergism to alleviate the symptoms of heart failure [10]. This synergistic action ultimately resulted in the improvement of both primary and secondary endpoints.
The present study was however not free from limitations. It was single-arm study due to which the results could not be compared with the standard care. Quality of life (QoL) variables was beyond the scope of our study. Future clinical trials with large sample size are required to generate stronger evidence.

5. Conclusion

The present study demonstrated HFRT causes significant improvement in VO2 max from baseline value which implies better exercise tolerance of HF patients. This improvement in exercise tolerance could translate into a decrease in cardiovascular mortality, morbidity. HFRT also showed improvement in the metabolic parameters of weight, BMI and abdominal girth of the heart failure patients which have a positive impact on their quality of life However, multicentric clinical trials with adequate sample size could generate stronger evidence on effectiveness of HFRT in HFpEF patients.

6. Acknowledgment

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Original Research Article

Study of efficacy of ischemia reversal program (IRP) in ischemic heart disease (IHD) patients with VO2max and Duke's treadmill score

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ABSTRACT

Background: Number of people dying from IHD has increased from 0.61 million in 1990 to 1.13 million in 2010, which is a disturbing fact. According to report by World Health Organization, India would be spending a whopping 237 billion US dollars, owing to direct spending on health care and indirectly due to loss of productivity due to IHD. Ischemia Reversal Program (IRP) is a combination of *Panchakarma* and allied therapy. This study was conducted to evaluate the effect of IRP on VO2max, Duke's treadmill score, systolic blood pressure (SBP), diastolic blood pressure (DBP), and dependency on conventional therapy in IHD patients.

Methods: This observational study was conducted in January 2017, wherein the data of IHD patients (inducible ischemia on stress testing) who attended out-patient departments (OPDs) at *Madhavbaug* clinics in Maharashtra, India were identified. Data of patients who were administered IRP (60-75 minutes) with minimum 7 sittings over 90 days (±15 days) were considered. Variables were compared between day 1 and day 90 of the IRP.

Results: Out of 38 enrolled patients, 25 were males while 13 females. There was significant improvement in Duke's score with subjects at moderate (50%) and high (31.6%) risk at baseline were significantly decreased to low (52.6%) and moderate (47.4%) after the 90th day of therapy. IRP also showed significant improvement in VO2max by 9.11 (from 20.29±6.72 to 29.40±6.71; $p<0.001$), SBP by 5.78 (from 128.78±17.40 to 123±12.23, $p<0.03$), DBP by 4.76 (from 80.53±8.10 to 75.76±6.85, $p<0.005$). Dependency on concomitant medicines was reduced.

Conclusions: IRP was effective in IHD; it had dual benefits, i.e. anti-ischemic effect, as well as reducing the dependency on allopathic medicines.

Keywords: Alternative medicine, Blood pressure, Diastolic, Ischemia reversal program, IRP, Ischemic heart disease, IHD, *Panchakarma*

INTRODUCTION

Cardiovascular diseases (CVDs) comprising of coronary artery disease in the form of ischemic heart disease (IHD) have scaled the prevalence rates to the figures that signify epidemic. Around 17.5 million deaths across the globe are due to CVDs.[1] Worrisome fact is that three quarters of these deaths in developing countries alone. This is further complicated by the fact that, although the prevalence of deaths due to CVD is reducing in developed countries, it is creating a menace in developing nations like India, year after year.[2] Epidemiological transition is attributed by some authors to such increased prevalence, which comprises of urbanization, lifestyle changes, etc.[3] India is experiencing the age of obesity and inactivity, where sedentary lifestyle gives rise to diseases like lipid abnormalities, diabetes, IHD, HTN, which in turn increases morbidity and mortality in India, contributing to increased burden on healthcare and cost.[4] The Global Burden of Disease study found that in past three decades

there was doubling of morbidity and mortality due to CVD.[5] Number of people dying from IHD has increased from 0.61 millions in 1990 to 1.13 millions in 2010, which is a disturbing fact.[6] According to report by World Health Organization, India would be spending a whopping 237 billion US dollars, owing to direct spending on health care and indirectly due to loss of productivity due to IHD.[7]

IHD contributes maximum amongst deaths due to CVD in India (>80%). This mortality rate is way higher than the global average mortality rate due to IHD. In India, IHD is the culprit for 1/5th of all deaths (21%) and 1/10th of life years lost, which measures premature deaths by considering young deaths over old age.[8]

Low diagnosis rates, less adherence, reduced treatment adherence, less use of evidence based interventions are the major hurdles for optimal use of cost effective treatment on an extensive scale, in India. Poor adherence to medication, alone is the major culprit which causes increased morbidity and mortality in patients with IHD and also increases the cost of health care.[9,10] Although there are various guidelines in place to combat the menace of IHD, still its prevalence is rising. This is complicated by low adherence to medications, which is due to adverse effects to medications, increased cost, etc.[11] Hence, there is a need to explore new therapeutic option to effectively combat IHD.

Management of IHD is complex due to the role of various factors while deciding treatment plan like comorbidities, age, concomitant medication, etc. Hence, it is a vital demand of time to search for novel their alternative which will help to decrease anxiety and fear also with IHD and increase quality of life simultaneously.[12] The therapeutic role of drugs used in the treatment of IHD is due to a correction of imbalance between oxygen demand and supply to the heart, reduction in blood pressure (BP), reducing platelet aggregation, hypolipidemic action, antioxidant effect, etc.[13] Similar action has been found in numerous herbal drugs, which serve as interesting potential targets for newer therapeutic options for treatment of HTN.[14-16]

The Ayurveda practice of Medicine suggests the use of traditional drugs in the acute phase of disease, while adding "*Panchakarma*" therapy (internal body purification through multi-step process) in the chronic phase of disease. Ischemia Reversal Program (IRP) is a combination of *Panchakarma* and allied therapy. The techniques used in *Panchakarma* under this program are *Swedana* i.e. passive heat therapy, *Snehana* i.e. oleation and *Basti* i.e. per rectal drug administration. These techniques are widely recognized for their detoxification function.[17,18] It has been found in a study that IHD is associated with anxiety, depression, reduced feeling of personal strength, reduced quality of life, etc.[19] Hence, we planned an observational study to investigate the efficacy of IRP, as add-on therapy to standard anti-ischemic therapy in patients of IHD. We evaluated the effect of IRP on maximum oxygen consumption/maximum aerobic capacity measured by VO2max (V-volume, O2-oxygen, max-maximum), Duke's treadmill score, systolic (SBP) and diastolic BP (DBP), and dependency of these IHD patients on standard conventional medications.

METHODS

This was an observational study conducted between January 2017 to January 2018, wherein we identified the data of patients suffering from IHD (positive for inducible ischemia from stress test) of either gender and any age, and who had attended the out-patient departments (OPDs) at multiple *Madhavbaug* clinics located in various cities of Maharashtra, India. The data of patients who had been administered IRP with minimum 7 sittings over a span of 90 days (±15 days) were considered for the study. Cases were identified, and data were assessed from the records of *Madhavbaug* clinics in Maharashtra. The selection was based upon the availability of complete relevant baseline data (day 1 of IRP) and final day data (day 90 of IRP) of the patients.

The IRP is a 3-step procedure, which was performed on the patients of IHD after a light breakfast. One sitting of the procedure took 65-75 minutes, as described in Table 1.[18,20]

Table 1: Study treatment: Ischemia Reversal Program (IRP Kit).

Step of IRP	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes directed towards heart)	100ml [Sesame oil (80%) + Lavender oil (20%)]	30-35 minutes
Swedana	Passive heat therapy	Dashmoola (group of ten herbal roots) with steam at ≤40 degrees Celsius)	10-15 minutes + 3 - 4 minutes of relaxation after procedure
Basti	Per rectal drug administration using a rectal solution.	Luke-warm GHA decoction 100ml	15 minutes

On day 1 of IRP, the patients had undergone Duke's treadmill scoring, VO2max, SBP, DBP as per international recommendations.[25] These readings were considered as baseline readings. This process was repeated on day 90 of

the IRP to calculate % change from baseline reading. The dependency on standard medication was calculated both on day 1 and day 90 of IRP as the percentage of patients out of the total enrolled ones who required a conventional allopathic therapeutic agent during the study period of 90 days. The patients followed a diet chart/plan of 1200 calories/day.

Statistical analysis

Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the frequency form and continuous data were presented as the Mean±SD. The McNemar-Bowker test was used to assess the Duke Treadmill Score before and after 90 days of treatment. The Paired t-test was used to assess the difference between baseline values and 90th day after treatment. Box plot and histogram were used to represent the graphs

RESULTS

Study population

A total of 51 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1 and Day 90) and the inclusion criteria, 38 patients were selected, and their data were considered for analysis (Figure 1). The baseline characteristics of these patients are shown in Table 2.

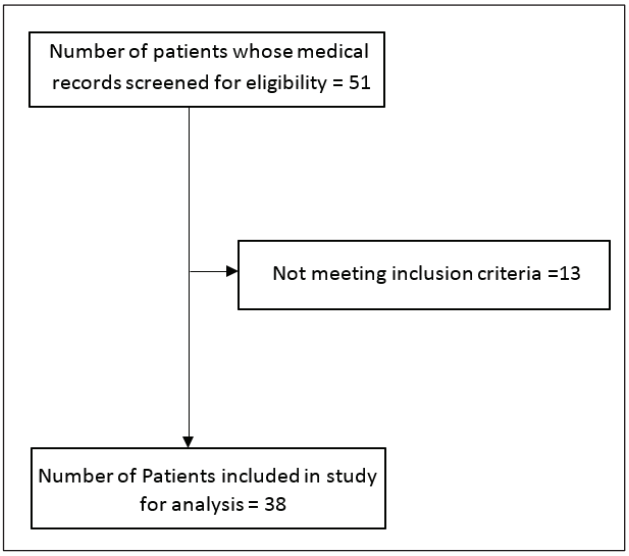

Figure 1: Patient enrolment flow chart.

Demographic characteristics of the subjects enrolled in the study was as shown in Table 2. The present involved a total of 38 IHD patients. The mean age of the enrolled subjects was 55.21±9.27 years. Nearly three-fourths of the study subjects were male (65.79%). All the patients approached *Panchakarma* unit for *Sarvanga Swedana* during the study period. Among them, nearly three-fourths 27 (71.05%) of the subjects approached *Panchakarma* unit for 7 settings.

Table 2: Baseline characteristics of the study subjects (n= 30).

Variable	N = 38
Age (years)	55.21±9.27
Gender	
Male	25 (65.79)
Female	13 (34.21)

Data were expressed in % and mean ± SD

Comparison of Duke's treadmill score baseline and after the 90 days of therapy was as shown in Table 3. At baseline, the subjects at moderate (50%) and high (31.6%) risk were significantly decreased to low (52.6%) and moderate (47.4%) after the 90th day of therapy. Overall, after 90th day, no cases of high risk were reported.

Table 3: Comparison of Duke treadmill score baseline and after 90 days of treatment (n=38).

Duke treadmill score		After 90 days			Total	p-value
		Low	Moderate	High		
Base-line (1st day)	Low	6	1	0	7 (18.4%)	0.0001
	Mod-erate	11	8	0	19 (50%)	
	High	3	9	0	12 (31.6%)	
Total		20 (53%)	18 (47.4 %)	0	38 (100%)	

* indicates high statistically significant improvement

Table 4: Comparison of clinical parameters between baseline values and 90th day.

Variable n=38	Baseline	After 90 days	Differ-ence	p value
VO2.max	20.29±6.72	29.40±6.71	-9.11026	<0.001
SBP	128.78±17.4	123±12.23	5.789474	0.03
DBP	80.53±8.10	75.76±6.85	4.76	0.005

VO2.max, Maximum amount of oxygen consumption; SBP, Systolic blood pressure; DBP, Diastolic blood pressure

Clinical parameters compared between baseline values and after the 90th day was as shown in Table 4. The maximum amount of oxygen consumption was significantly improved after 90th day of therapy (P <0.001) Figure 3. Systolic blood pressure was significantly attained near normal value after 90th day of therapy (P <0.03) Figure 4. Although, diastolic blood pressure which was normal before the therapy reduced significantly, it was within the normal range (P <0.005) Figure 5.

Allopathic medicines consumption on day 1 and after 90th day of therapy were as shown in Table 5. Most of the enrolled IHD subjects were treated with biguanides (34.21%), statins (47.37%), beta blockers (34.21%),

antiplatelets (39.47), angiotensin II receptor blockers (26.32) and nonsteroidal anti-inflammatory drugs (60.53). All the subjects who were allopathic medicines before therapy was decreased after the 90th day. However, the subjects with absence of medication history was not varied after the therapy. An illustration is given in Figure 6.

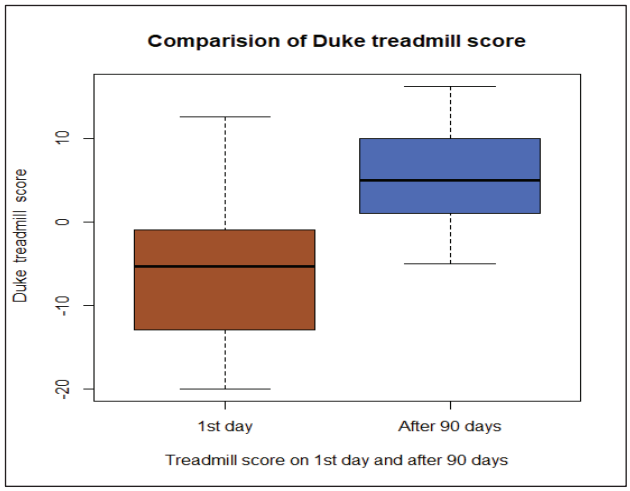

Figure 2: Comparison of Duke treadmill score baseline and after 90 days of treatment (n=38).

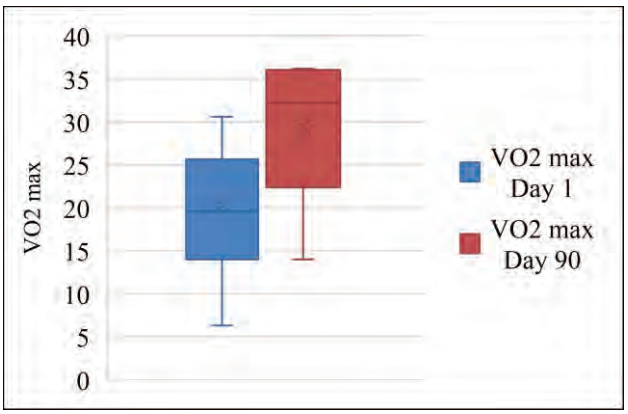

Figure 3: Comparison of clinical parameters between baseline values and 90th day.

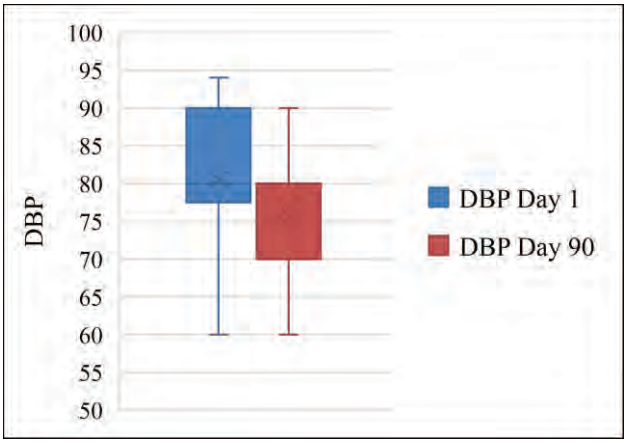

Figure 4: Comparison of SBP.

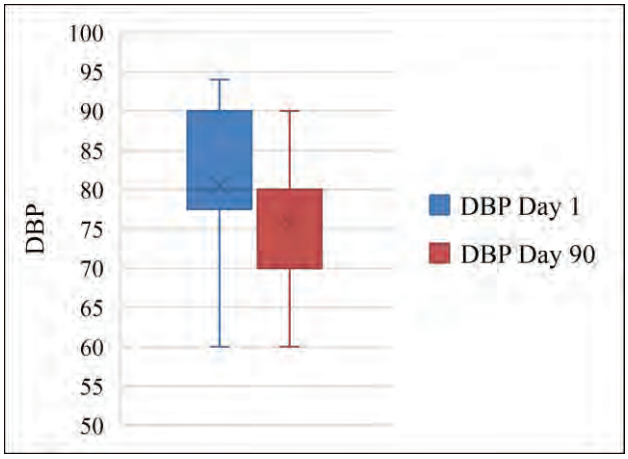

Figure 5: Comparison of DBP.

Table 5: Comparison of consumption of allopathy medicines at day 1 and after 90 days.

Medicine	Baseline	After 90 days
NSAID + antiplatelet	1 (2.63)	0 (0)
Diuretic	4 (10.53)	2 (5.26)
ACE	3 (7.89)	2 (5.26)
Statin	18 (47.37)	12 (31.58)
CCB	5 (13.16)	3 (7.89)
Beta blocker	13 (34.21)	8 (21.05)
Antiplatelet	15 (39.47)	12 (31.58)
ARB	10 (26.32)	7 (18.42)
NSAID	23 (60.53)	17 (44.74)
Sulfonylurea	7 (18.42)	5 (13.16)
Biguanide	13 (34.21)	8 (21.05)
No Medicine	3 (7.89)	3 (7.89)

CCB, Calcium channel blockers; ARB, Angiotensin II receptor blockers; NSAID, Nonsteroidal anti-inflammatory drugs

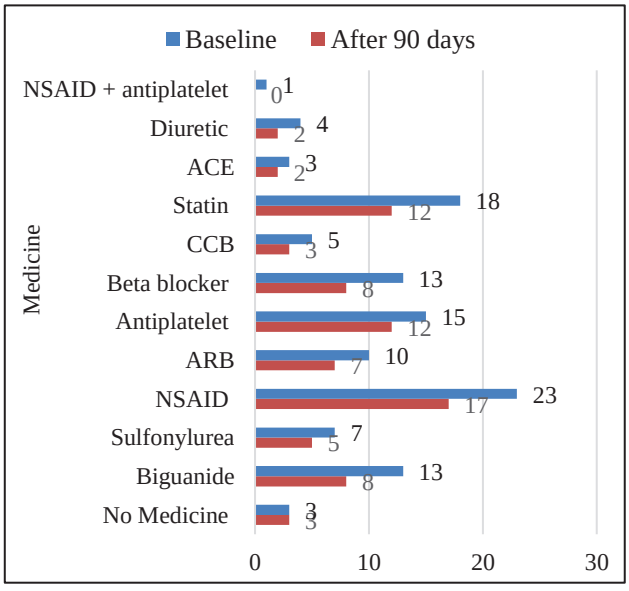

Figure 6: Comparison of consumption of allopathy medicine at 1st day and after 90 days.

DISCUSSION

Despite the availability of the plethora of the options for treatment of IHD, it is still amongst leading contributor to global morbidity and mortality rates. Thus, it is dire need of the time to look out for new therapeutic option for treatment of IHD. Traditional class of anti-ischemic drugs have therapeutic benefit in IHD by correction of imbalance between oxygen demand and supply to the heart, reduction in blood pressure (BP), reducing platelet aggregation, hypolipidemic action, antioxidant effect, etc. Similar property has been found in various herbal drugs, thus making Ayurveda a potent and viable alternative to standard therapy in the management of IHD. *Panchakarma* is administered as add on therapy for IHD management, by Ayurveda physicians.[20] IRP is a 3 step procedure consisting of *Snehana*, *Swedana*, and *Basti*. Probable mode of action of IRP is *Snehana*-anxiolytic reduces sympathetic over activity *Swedana*- reduces sodium and fluid that reduces resting preload that may help to reduce myocardial oxygen demand. Decoction of *Tribulus terristris*, *curcumin* and *Phyllanthrus embelica* can be helpful for nitric oxide liberation from endothelium. Along with it can be anti-inflammatory and antioxidant. This action may be helpful in improving coronary circulation by causing coronary vasodilation.[17,20,22-24,26] In pursuit of analyzing the efficacy of the IRP in IHD, we found that it showed significant (very high statistical significance) improvement in VO2max, Duke's treadmill score, DBP, and SBP (high statistical significance) at the 90th day of the whole procedure. SBP is one of the prognostic marker for patients of IHD. Reduction in SBP is associated with better prognosis in IHD, since it reduces afterload of the ventricles and also improves endothelial health.[27] Most importantly, we found that IRP noticeably reduced patient's dependency on standard allopathic medication at the end of 90 days of therapy.

VO2max measures the maximum oxygen hat can be utilized during exercise. IHD patient suffers from diastolic dysfunction, hence VO2max is reduced in such cases which manifests clinically as reduced exercise/work capacity.[27] Duke's treadmill score is used as diagnostic and prognostic investigation in risk patients of IHD. It is favoured more for its risk stratification role. It is calculated by the following formula:

Duke treadmill score = maximum exercise time in minutes -5×ST segment deviation in mm-4×angina index

where 0 = no angina, 1 = non-limiting angina, 2 = exercise limiting angina.

Duke's treadmill score ≥5 signifies low risk for cardiovascular complication and these people do not need coronary angiography for further evaluation. Their 4 year survival rate is almost 100 %. Duke's score <-11 denotes a high risk group and these patients need coronary angiography for further evaluation. Their 4- year survival rates are 79%. A score below +4 and -10 signify intermediate risk group. These patients require either coronary angiography or myocardial perfusion scan for evaluation, depending on patient status.[25] In our study, both VO2max and Duke's treadmill score were significant (high statistical significance) improved. Studies show that improvement in Duke's score and VO2max are associated with better prognosis in IHD patients.[25,27,28] Hence, significant reduction in VO2max and Duke's treadmill score after IRP in our study indicates favourable prognosis in cardiovascular morbidity and mortality.

In economically constraint countries like India the high dependence of IHD patients on conventional allopathic medication escalates the healthcare cost many fold. Furthermore, increased adverse effect of these drugs lead to decreased adherence, which further worsens the picture.[12] Keeping this in mind, we analyzed changes in patients' dependency on allopathic medication by IRP. There was significant reduction in dependency on almost all the class of anti-ischemic drugs, at the end of 90 days, with an increase in the number of patients who went off the allopathic drugs.

The findings of the present study can be generalized only after a comparison with the findings of other such studies with probably prospective design, larger sample size, one more arm with standard therapy alone and more follow up period. This will help in identifying long term outcomes of IRP in the management of IHD.

CONCLUSION

There was significant improvement in VO2max, Duke's treadmill score, SBP, DBP after IRP. Also, there was substantive attenuation in patient's dependency on allopathic medications. Hence, the IRP may serve as a potent and viable alternative to standard allopathic treatment of IHD.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Research Article

TO STUDY EFFICACY OF COMPREHENSIVE DIABETES CARE (CDC) MANAGEMENT PROGRAM IN TYPE II DIABETIC OBESE PATIENTS: AN OBSERVATIONAL STUDY

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ABSTRACT

Context: Diabetes mellitus (DM) contributes to a major chunk of morbidity, mortality, and healthcare cost on a global level. The prevalence of DM is rising alarmingly, worldwide and India. Comprehensive Diabetes Care (CDC) is a combination of *Panchakarma* and diet management.

Aims: This study was conducted to evaluate the effect of CDC on Glycosylated hemoglobin (HbA1c), body mass index (BMI), body weight, abdominal girth and dependency on conventional therapy in DM Patients.

Setting and Design: This observational study was conducted in July 2017, wherein the data of obese Type II DM patients (HbA1c >6.5%) who attended out-patient departments (OPDs) at *Madhavbaug* clinics in Maharashtra, India were identified.

Materials and Methods: Data of patients who were administered CDC (60-75 minutes) with minimum 6 sittings over 90 days (± 15 days) were considered. Variables were compared between day 1 and day 90 of CDC.

Results: Out of 27 patients, 22 were included for analysis, out of which 10 were males while 12 females. CDC showed significant improvement in HbA1c 1.1% (from 8.80 ± 0.93 to 6.98 ± 1.73; p<0.001), BMI by 2.66 (from 33.79 ± 3.80 to 31.13 ± 3.91, p< 0.001), weight by 6.56 kg (from 83.67 ± 11.28 to 77.11 ± 12.27, p<0.001). Abdominal girth (from 104.34 ± 9.74 to 96.97 ± 11.93; p<0.001), also showed significant reduction. Dependency on concomitant medicines was reduced, with the number of patients on no concomitant medicines increasing from 27% to 41%.

Conclusion: Comprehensive Diabetes Care Management Program found to be efficacious; by reducing HbA1c, as well as reducing dependency on allopathic medications.

KEYWORDS: Comprehensive Diabetes Care, CDC, *Panchakarma,* Glycosylated HB, HbA1C, BMI, DM, Alternative Medicine.

INTRODUCTION

Diabetes mellitus (DM) contributes to a major chunk of morbidity, mortality, and health care cost on a global level. The prevalence of DM is rising alarmingly, worldwide.[1] India is only 2nd to China, in terms of prevalence of DM, with a prevalence rate of around 10%, i.e. every 10th adult in India is suffering from DM.[2] According to WHO report, about 30 people die per 1 Lac population in India, due to diabetic complications.[3]

Conventionally DM is diagnosed based on blood glucose/sugar levels (BSL), fasting levels more than or equal to 126 mg/dl and post prandial levels more than or equal to 140 mg/dl is considered as a DM. In recent decade diagnosis is also done by measuring glycosylated hemoglobin (HbA1c), since it reflects blood sugar control over the past 2-3 months. HbA1c levels more than 6.5% is considered as DM, 5.7% to 6.4% as a borderline case/ prediabetes, and less than 5.7% as normal. Target HbA1c for treatment strategies are taken as below 6.5%.[4]

DM is dreaded due to its complications, which are short term and long term, macrovascular and microvascular. Macrovascular complications include myocardial infarction, coronary artery disease, stroke, cerebrovascular disease, peripheral vascular disease, etc. Microvascular complications include retinopathy, neuropathy, nephropathy. Out of these, cardiovascular complications are leading cause of morbidity and mortality in diabetic patients.[5] Diabetic neuropathy may manifest as foot ulcers, sexual dysfunction in young males, amputation, etc.[6,7] Amongst microvascular complications,

nephropathy is leading cause of morbidity and mortality in diabetic patients.[8] The prevalence of retinopathy in diabetics is also increasing these days.[9] It has been postulated from findings of various epidemiological studies that certain cancers are more common in diabetics like, cancers of breast, kidney, colo-rectal, bladder, etc.[10,11]

The current management plan includes lifestyle modification, including dietary modifications and physical exercise on a daily basis plus pharmacological management (oral antidiabetic drugs).

Antidiabetic drugs/oral hypoglycemic agents (OHA) should be initiated only if a lifestyle modification fails to reduce HbA1c below 6.5% after 2 months. Major class of OHAs includes Biguanides (Metformin), Thiazolidinediones (Pioglitazone), Sulphonylureas (Glimepiride), Dipeptidyl peptidase-4 (DPP-4) inhibitors like Teneligpiltin, Sodium glucose cotransporter-2 inhibitors (canagliflozin). All these drugs act either, by reducing blood glucose via increasing tissue uptake, decreasing endogenous glucose production, preventing breakdown of incretins, etc. Guidelines suggest that, if baseline HbA1c is > 9% or it remains >7.5% despite 1 OHA, then combination of 2 OHAs should be given.[12]

But, these drugs are associated with a wide variety of adverse effects like hypoglycemia (almost all classes), megaloblastic anemia (biguanides), pancreatitis, upper respiratory tract infections (gliptins), ketoacidosis, bone fractures (SGLT2 inhibitors), lipodystrophy at injection site (insulin), C cell tumour of thyroid (GLP1 agonist), etc.[13]In a multicentric study on diabetic patients, it was found that adherence of patients to antidiabetic drugs was only 58%. The investigators of the study attributed this low adherence to cost of therapy, adverse effects of medications. Also, despite numerous guidelines for DM, its prevalence is rising continuously.[14]Thus, it is the need of the hour to explore alternate forms of antidiabetic therapy, which can ameliorate the factors associated with low adherence to allopathic antidiabetic drugs.

The therapeutic benefit of allopathic antidiabetic drugs in diabetes is due to their blood glucose lowering action. Several studies have shown similar effects, with significant reduction in Glycosylated Hemoglobin (HbA1c), Fasting and Post Prandial Blood Glucose (FBG, PPBG) levels and lipids, by using herbal drugs, which serve as interesting potential targets for newer therapeutic options for treatment of DM.[15,16,17]

Panchakarma is multi-step internal purification process. *Panchkarma* therapy in Ayurveda practice is administered in chronic phase of the disease, while herbal drugs are preferred in acute phase. Comprehensive Diabetes Care (CDC) combines *Panchakarma* and diet management. Under this management program, *Panchakarma* is advocated through three techniques-

Snehana i.e. oleation, *Swedana* i.e. passive heat therapy and *Basti* i.e. per rectal drug administration. *Panchakarma* techniques are already well established in literature, as detoxifying procedures.[18,19]DM is found to be linked with depression, reduction in quality of life, etc.[20]Hence, we planned an Observational study to investigate the efficacy of the CDC, as add-on therapy to standard anti-diabetic therapy in patients with DM. We evaluated the effect of CDC on HbA1c, weight, body mass index (BMI), abdominal girth, and dependency of these diabetic patients on standard conventional oral antidiabetic medications.

Since, numerous factors play a role in causation, progression of DM, its management should be multi-pronged. Given the fact that Ayurveda may serve as potent alternative therapy, its efficacy in DM should be tested.[15,17,21] Hence, we planned this observational study to investigate the effect of the CDC, as add on therapy to standard anti-diabetic therapy in obese patients with type II diabetes mellitus. We evaluated the effect of CDC on HbA1c, body mass index (BMI), body weight, dependency on oral hypoglycemic drugs/ agents, and abdominal girth.

MATERIALS AND METHODS

This was an Observational study conducted between July 2017, wherein we identified the data of obese patients suffering from type II DM (HbA1c ≥ 6.5%, BMI ≥ 30) [4,5] of either gender and any age, and who had attended the out-patient departments (OPDs) at multiple *Madhavbaug* clinics located in various cities of Maharashtra, India. The data of patients who had been administered CDC with minimum 6 sittings over a span of 90 days (± 15 days) were considered for the study, out of which 4 sittings were done in the 1st month, and 1 sitting per month for next 2 months. These patients were maintained on a diet plan of 800-1000 calories intake per day, according to patient medical records. The diet plan consisted of low carbohydrates, moderate proteins, and low fats. Cases were identified, and data were assessed from the records of *Madhavbaug* clinics in Maharashtra. The selection was based upon the availability of complete relevant baseline data (day 1 of CDC) and final day data (day 90 of CDC) of the patients. The information about prescribed concomitant medicines, if any, was also noted down.

The CDC is a 3-step procedure which was performed on the patients of type II DM after a light

breakfast. One sitting of the procedure took 65-75 minutes, as described in table 1. [19, 22]

Table 1: Study Treatment: Comprehensive Diabetes Care (CDC)

Step of CDC	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes on the body)	100 ml *Azadirechta indica* (neem) extract processed in sesame oil	20 minutes
Swedana	Passive heat therapy to the body	*Dashmoola* (group of ten herbal roots) with steam at ≤40 degrees Celsius)	15-20 minutes + 3-4 minutes of relaxation after procedure
Basti kadha	Per-rectal drug administration should be in body for ≥ 15 minutes for maximum absorption	Mixture of 40% *Gudmaar* (*Gymnema sylvestre*), 20% *Daruharidra (Berberis aristate)* and 40% *Yashtimadhu (Glycyrrhiza glabra)*	10 minutes

On day 1 of CDC, the patients had undergone HbA1c, weight, BMI, abdominal girth measurements as per guidelines.[4] This reading was considered as baseline reading. This process was repeated on day 90 of CDC to calculate the change from baseline reading. The BMI for day 1 and day 90 of the patients was calculated by checking the weight and the height from the medical data sheets of patients and using the formula: weight in kilograms/ (height in meters)^2. The dependency on standard medication was calculated both on day 1 and day 90 of CDC as the percentage of patients out of the total enrolled ones who required a conventional allopathic therapeutic agent during the study period of 90 days.

Statistical analysis

Data were pooled and entered in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the numeric form and continuous data were presented as the Mean ± SD. The Paired t-test was used to assess the difference between baseline values and 90th day after the treatment. Box plot, histograms and scatter plot were used to represent the graphs.

RESULTS

Study population

A total of 27 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1 and Day 90) and the inclusion criteria, 22 patients were selected, and their data were considered for analysis.

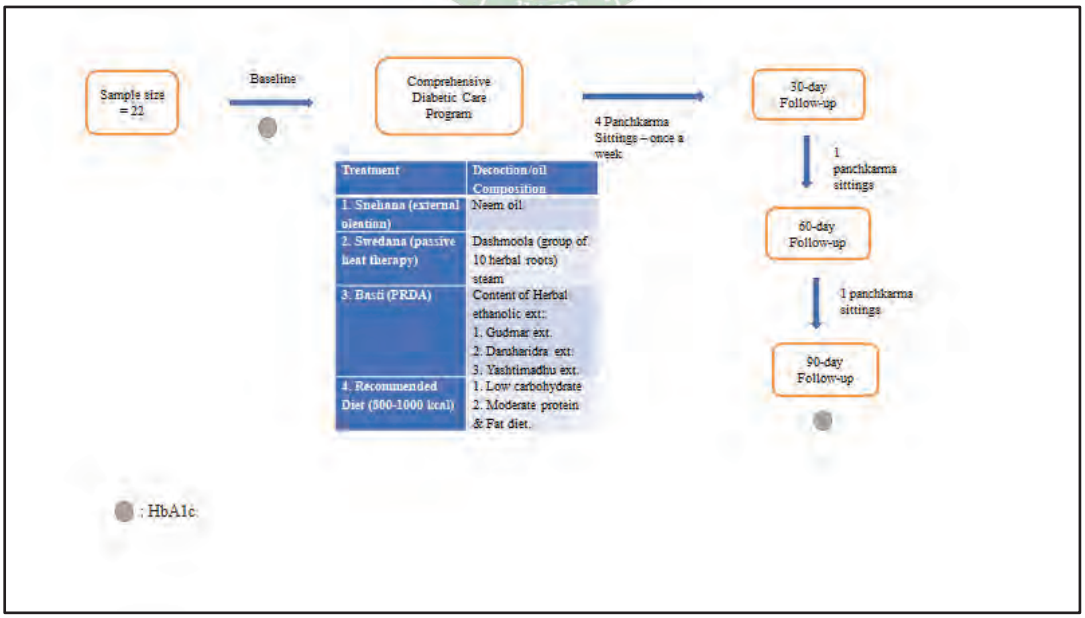


Figure 1: Treatment Plan of Comprehensive Diabetes Care Management

The study comprised of 22 type II diabetic obese patients, among them 10 (45.45 %) were men and 12 (54.55 %) were female. The mean age of the study patients was 48 ± 12.13 years. A significant improvement in weight, (77.11 ± 12.27 vs. 83.67 ± 11.28; P < 0.001), BMI (31.13 ± 3.91 vs. 33.79 ± 3.80; P < 0.001), HbA1c (6.98 ± 1.73 vs. 8.80 ± 0.93; P = 0.0002) and abdomen girth (96.97 ± 11.93 vs. 104.34 ± 9.74; P < 0.001) were observed in diabetic obese patients after the treatment (90 days) than before treatment (baseline) (Table 2; Figure 2).

Table 2: Comparison of clinical parameters between baseline values and 90th day of the treatment

Variable	Baseline (Day 1)	After 90 days	Difference	*P* value
Weight	83.67 ± 11.28	77.11 ± 12.27	6.56	<0.001
BMI	33.79 ± 3.80	31.13 ± 3.91	2.66	<0.001
HbA1c	8.80 ± 0.93	6.98 ± 1.73	1.1	0.0002
Abdomen Girth (n=19)	104.34 ± 9.74	96.97 ± 11.93	7.37	<0.001

BMI, Body Mass Index; HbA1c, Glycosylated hemoglobin

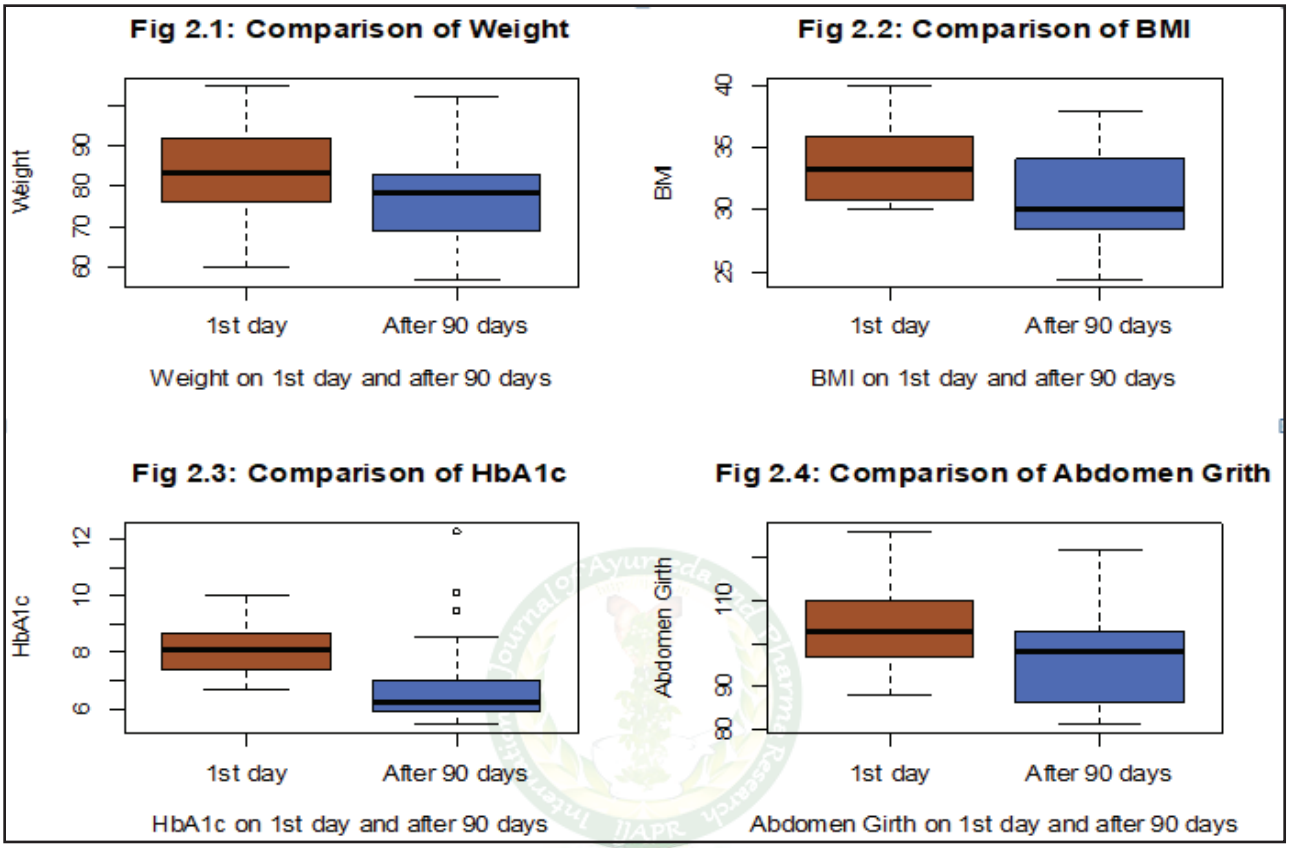


Figure 2: Comparison of clinical parameters between baseline values and 90th day (N = 22)

Most of the type II diabetic obese patients were treated with beta blockers (13.64 %), nonsteroidal anti-inflammatory drugs (13.64 %), biguanides (54.55 %) and sulfonylureas (36.36). While, the patients depending only on biguanides (36.36 %) showed marked decrease after the treatment i.e., 90 days. The patients with the absence of medication history (40.91 %) were also improved after treatment (Table 3; Figure 3).

Table 3: Consumption of allopathic medicines on days 1 and 90

Medicine	Baseline	After 90 days
Alpha-glucosidases inhibitors	1 (4.55)	1 (4.55)
DPP-4 inhibitor	3 (13.64)	1 (4.55)
Thiazolidinedione	1 (4.55)	1 (4.55)
Biguanide	12 (54.55)	8 (36.36)
Sulfonylurea	8 (36.36)	8 (36.36)
Antiplatelet	1 (4.55)	1 (4.55)
CCB	1 (4.55)	1 (4.55)
Beta blocker	3 (13.64)	3 (13.64)
ARB	2 (9.09)	1 (4.55)
Statin	1 (4.55)	1 (4.55)
NSAID	3 (13.64)	3 (13.64)
No medicine	6 (27.27)	9 (40.91)

NSAID, Nonsteroidal anti-inflammatory drugs; ARB, Angiotensin II receptor blockers; CCB, Calcium channel blockers; DPP-4 inhibitor, Dipeptidyl peptidase-4

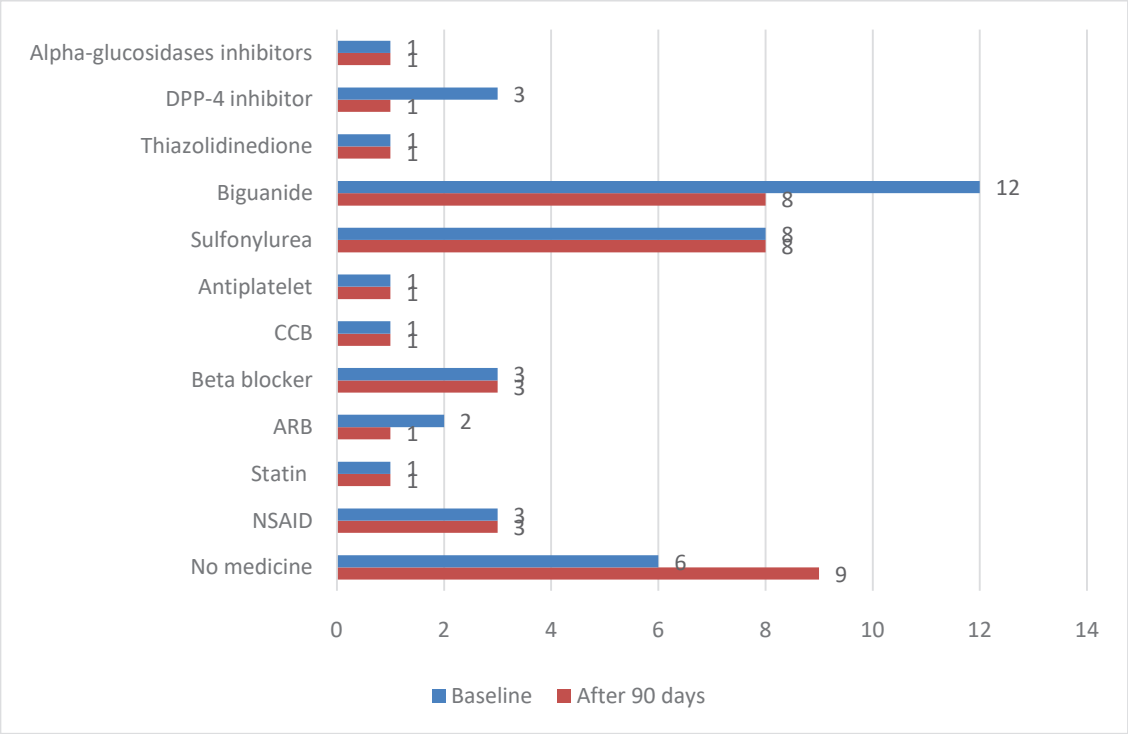


Figure 3: Consumption of allopathy medicines at days 1 and 90 days (N = 22)

NSAID, Nonsteroidal anti-inflammatory drugs; ARB, Angiotensin II receptor blockers; CCB, Calcium channel blockers; DPP-4 inhibitor,Dipeptidyl peptidase-4

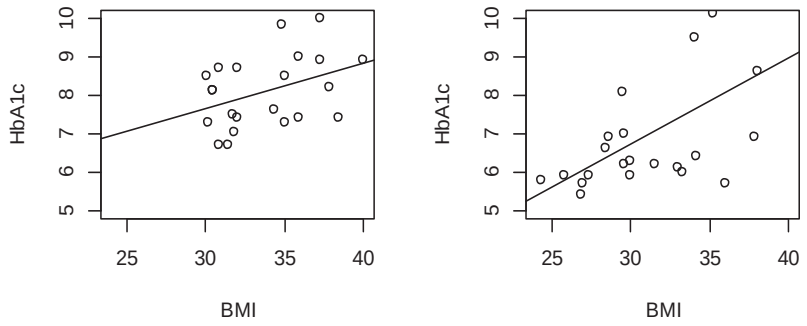
The levels of HbA1c were significantly correlated with the BMI after 90 days of treatment ($r = 0.504$; $P = 0.016$) when compared with baseline values ($r = 0.39$; $P = 0.071$). (Table 4; Figure 4).

Table 4: Correlation of BMI and abdominal girth with HbA1c at 1st day and after 90 days of treatment

Correlation between	Baseline		After 90 days	
	r	*P* value	r	*P* value
HbA1c & BMI	0.39	0.071	0.504	0.016

BMI, Body Mass Index; HbA1c, Glycosylated haemoglobin

Fig 4.1: BMI & HbA1c at 1st day **Fig 4.2: BMI & HbA1c at 90th day**



BMI, Body Mass Index; HbA1c, Glycosylated hemoglobin

Figure 4: Correlation of BMI and abdominal girth with HbA1c at 1st day and after 90 days of treatment

DISCUSSION

Although there are numerous treatment choices available for treatment of type II DM management, it is still one of the commonest culprits of morbidity and mortality globally. Thus, it is the need of the hour to explore novel therapeutic alternatives for the management of type II DM. Traditional class of antidiabetic drugs has therapeutic benefit in DM of lowering blood sugar levels. Similar property has been found in various herbal drugs, thus making Ayurveda a potent and viable alternative to standard therapy in the management of type II DM. Panchakarma is administered as add on therapy for DM management, by Ayurveda physicians.[23] CDC combines *Panchakarma* with Low carb moderate protein and low fat diet. CDC acts by reducing sympathetic stress,

reduced sympathetic action lowers hepatic glucose production, which can be helpful to reduce blood sugar levels. *Swedana* is helps by it inducing sweating and reduces excess of sodium and water, and this comprehensively helps to improve vascular health of DM patients to keep them away from probable vascular complications.[24]In pursuit of analyzing the efficacy of CDC in type II DM, we found that it showed significant (very high statistical significance) improvement in HbA1c, weight, BMI, abdominal girth at the 90th day of the whole procedure. Most importantly, we found that CDC noticeably reduced patient's dependency on standard allopathic medication at the end of 90 days, may be of therapy.

The HbA1c levels are more important in diabetic patients since it reflects the average blood sugar control over the past 1-2 months.[25] Importance of HbA1c lies in the fact that, it is an independent predictor of mortality and morbidity in patients with type II DM. This has been corroborated in a prospective study done on diabetic patients, that cardiovascular complication like stroke was significantly lower in patients with an optimal reduction in HbA1c. It was found in large study-UKPDS study on diabetic patients, that reduction in HbA1c by 1% led to reduction of heart failure, heart attack, stroke, amputation and overall morbidity and mortality in diabetic patients.[25] Hence, significant reduction in HbA1c after CDC in our study indicates favorable prognosis in DM related morbidity.

High BMI is considered to be one of the major risk factor for development of DM in normal subjects. It signifies sedentary lifestyle and obesity.[26] Also, it has been found that BMI is positively associated with type II diabetes mellitus, hypertension, cardiovascular diseases and other chronic diseases.[27] Uncontrolled DM frequently leads to the development of complications, hence various management plans across the globe have targeted sustained blood sugar control in patients with DM, to prevent the occurrence of such complications.[4] In the present study, CDC significantly reduced HbA1c, BMI, abdominal girth, body weight. Thus CDC can play significant role in preventing the development of complications in patients with DM, thereby reducing morbidity and mortality.

In developing economy like India, the dependency of diabetic patients on allopathic medicines escalates the cost of healthcare to troublesome levels. Plethora of adverse effects of these drugs complicates the scenario, furthermore.[28] Keeping this in mind, we analyzed changes in patient's dependency on allopathic medication by CDC. There was significant reduction in dependency on almost all the class of antidiabetic drugs (oral hypoglycemic agents), at the end of 90 days, with an increase in the number of patients who went off the allopathic drugs.

One limitation of the study was that, it had only one arm, thus we were not able to compare CDC findings with that of standard therapy alone. The findings of the present study can be generalized only after a comparison with the findings of other such studies with probably prospective design, larger sample size, and more follow up period. This will help in identifying long term outcomes of CDC in the management of type II DM.

CONCLUSION

There was significant improvement in HbA1c after CDC. Also, there was significant reduction in patient's dependency on allopathic medications. Significant reduction in HbA1c, coupled with reduction in BMI, body weight, abdominal girth after CDC indicates a better prognosis in patients with type II DM. Hence, CDC may serve as a potent and viable alternative to standard allopathic treatment of type II DM.

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REVIEW ARTICLE

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To Study Efficacy of Blood Pressure Management Program in Overweight to Obese Male Patients with Known History of Hypertension: A Retrospective Study

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ABSTRACT

Background and Objective: Hypertension is the leading cause of global burden of cardiovascular disease. It is an epidemic that globally affects one billion people and a common cause of death. This retrospective study was conducted in April 2017 to evaluate the effect of the Blood Pressure (BP) Management Program in overweight to obese category male hypertensive patients.

Methods: Data of 28 patients were included who had received the scheduled 6 sitting of BP management kit in a span of 90 days. In this study, the variables [mean systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), Body Mass Index (BMI) and dependency of allopathic medicines] were assessed on day 1 to day 90 of the BP management program.

Results: The mean SBP was significantly lower on day 90 (153.5 ± 9.6 mm Hg to 127.80± 10.23 mm Hg, ($p<0.001$). The mean DBP reduced significantly from day 1 (91.60 ± 9.13 mm Hg to 78.64 ± 6.92 mm Hg). The mean value of MAP was much lower on day 90 (112.21 ± 7.3 5mm Hg to 94.80 ± 7.44 mm Hg, $p<0.01$). The BMI was much lower from day 1 (27.47 ± 2.49 to 26.45 ± 2.21, $P < 0.001$). Patients dependent on allopathic medicines were lesser at 90 days.

Conclusions: The BP management program was efficacious in controlling hypertension in male patients that were overweight or obese.

KEYWORDS

Blood pressure management, Alternative medicine, Panchakarma, Ayurveda

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INTRODUCTION

According to guidelines published by the American Heart Association, the American College of Cardiology; hypertension is defined as systolic blood pressure (SBP) 130 mm Hg/diastolic blood pressure (DBP) 80 mm Hg[1], whereas according WHO it is defined as high or raised blood pressure (BP), a condition in which the blood vessels have persistently raised pressure[2]. Categories of BP are given in detail in table 1[1].

Hypertension is the leading cause of the global burden of cardiovascular disease. It is an epidemic that globally affects one billion people and a common cause of death. World health statistics 2012 state that the prevalence of hypertension was 29.2% in males and 24.8% in females[3]. Across the world, hypertension is responsible for 51% of cerebrovascular disease and 45% of ischemic heart disease deaths[3]. Recent reports suggested that nearly 1 billion adults (more than a quarter of the world's population) had hypertension in 2000, and this umber is predicted to increase to 1.56 billion by 2025[4].

In Indian population, about 33% of urban and 25% of rural Indians are hypertensive. Of these, 25% rural and 42% urban Indians are aware of their hypertensive status. Only 25% rural and 38% of the urban Indians are being treated for hypertension. One-tenth of rural and one-fifth of urban Indian hypertensive population have their BP under control[5].

Table 1 Categories of BP in adults

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	< 80 mm Hg
Hypertension			
Stage I	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

Individuals with SBP and DBP in 2 categories should be designated to the higher BP category

Uncontrolled hypertension or resistant hypertension is defined as hypertension, which will remain resistant (140/90 mm Hg or higher) although an optimal two-drug regimen which has been given adequate time to work (at least one month since last drug or dosage adjustment). It occurs in a smaller number of patients with essential hypertension. Mainly, uncontrolled hypertension is caused by inadequate therapy, patient noncompliance and inappropriate therapy[6].

Uncontrolled hypertension has become a major problem in India. High blood pressure (BP) is ranked as the third most important risk factor for attributable burden of disease in south Asia[7]. The World Health Organisation (WHO) Non-communicable disease profile for India (2014) shows that cardiovascular (CV)

disease accounts for 26% of all deaths in India. Estimates from the Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India show that by the year 2020, 159.46/1000 Indians will be hypertensive[8].

In densely populated countries like India, there are several risk factors which contribute to the prevalence of hypertension. Increasing age, unhealthy diet (especially salt intake> 5grams/day doubles the risk of hypertension), obesity, alcohol and tobacco consumption, physical inactivity and urban residence are some of the key factors out of them[8].

There are many complications which arise due to hypertension or high blood pressure, namely- Stroke, coronary heart disease, diabetes, atherosclerosis, kidney disease, eye disease, pre-eclampsia, erectile dysfunction, etc[8]. In such a difficult scenario; it is practical to focus on multiple risk factors while treating hypertension. Hence, monotherapy alone is not sufficient to treat hypertension. Many researchers are studying different Interventions along with combination therapy of multiple blood pressure lowering drugs. This is very important, and concerns should be identified while advising the appropriate dosage of combinations of anti-hypertensive therapy and adherence to the therapy. At present, management of hypertension involves lifestyle modifications along with pharmacotherapy. The classes of pharmacological agents used for the treatment of hypertension include angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), diuretics, alpha blockers, beta blockers, aldosterone antagonists, renin inhibitors, vasodilators and central-acting agents. The preferred choices for mono, dual combination and triple combination of anti-hypertensive regimens are ARBs; ARB + CCB; ARB + CCB + Diuretics, respectively[7]. However, the use of anti-hypertensives are associated with a plethora of adverse reactions which are expected to result in nonadherence to therapy, increased morbidity and mortality as well as economic consequences. These have also led to the withdrawal of some of these medicines from use. Frequent micturition, dizziness, headache, dry cough, diarrhoea, abdominal pain, weakness, insomnia are some of the adverse drug reactions[9].

Obesity is another important reason of uncontrolled hypertension or treatment-resistant or refractory hypertension[10]. If energy intake and expenditure are disproportionate, of the result is obesity. Obesity is defined as the

accumulation of ≥20% of body fat over the person's ideal body weight[11]. Worldwide, cardiovascular diseases are becoming the leading cause of mortality. Hypertension and diabetes are the chief conditions associated with obesity[12].There is growing evidence that excessive weight and central obesity are main causes of hypertension, which causes 65%-75% of the risk of essential hypertension[13]. Hence, it is important to treat obesity to achieve better control over hypertension[13]. We, at *Madhavbaug* Clinic planned a strategy to use medicinal plants to treat these co-morbidities.

In the current era of modernization and industrialization; stress has become a part of life leading to the many stress-oriented psychosomatic disorders, one of which is hypertension. In the view of these complications in the treatment of hypertension, there is a strong need for safe and cost-effective alternative methods to control hypertension. *Ayurveda* has the potential to treat stress and anxiety and promoting calm[14]. Using Ayurvedic medicines and interventions may give a strong alternate option to current allopathic medicines.

Ayurveda, the ancient Indian medical system showing presence since last 1000s of years has been used widely to treat numerous disorders. According to the *Ayurveda* principle, the blood pressure is caused by an imbalance of *Vata* and *Pitta*; hence majority treatments aim to correct this imbalance; which is the root cause of disease. *Ayurveda* treatment mainly consists of the use of different natural herbs in the form of a capsule or tea or juice or *Kadha* or tablets. In the view of this present scenario, we developed a blood pressure management program which includes use of these ancient herbs; i.e., *Nirgundi Oil, Dashmool kadha*, and *Jatamanasi kadha*.

Vitex negundo commonly known as *Nirgundi* is a plant which shows many pharmacological activities. As mentioned in *Ayurveda*; whole percolate extract of *Nirgundi* was found to contain polyphenols such as flavonoids as major constituents. These phenolic constituents possess anti-hypertensive activity[15]. The literature shows use of *Dashmool* as an agent which is used to clear the imbalance of vitiated *Vata* and *Pitta* in the body. Hence it is used as anti-hypertensive in some *Ayurveda* formulations[16]. *Jatamansi* (*Nardostachys jatamansi*) shows hypotensive activity against adrenaline induced hypertension. *N. jatamansi* is used to protect cells and tissues through its antioxidative properties[17].

Individually these herbs have shown promising results as anti-hypertensive

agents; hence in this study, their combination was used.

MATERIALS AND METHODS

From April 2017 to July 2017, 34 known hypertensive patients underwent the Blood Pressure Management program at *Madhavbaug* clinics. Out of them, 28 met inclusion criteria and were in obese to overweight category. All these patients received 6 BP management sittings over 90 days in the out-patient departments (OPDs) at *Madhavbaug* clinics.

The inclusion criteria were as follows:

- Systolic blood pressure between 140 to 170 mmHg and diastolic blood pressure between 80 to 110 mmHg.
- BMI range from Overweight to obese category (BMI 23 and Above) according Asian BMI chart.
- Only Male patient were considered for this study.

Patients were belonging to the age group of 38 years to 68 years and had pre-diagnosed uncontrolled hypertension with SBP between 140 to 170 mmHg and DBP between 80 to 110 mmHg. These patients attended the out-patient departments (OPDs) of different *Madhavbaug* Clinics located in various cities of *Maharashtra*, India. The subjects enrolled in the study were willing to follow the protocol strictly over the thirteen weeks of the study period. This study was a prospective, thirteen-week, open label, single arm, multicentric, pilot proof-of-concept study conducted to evaluate the efficacy of blood pressure management program using herbal medications such as *Nirgundi oil*, *Dashmool Kadha* and *Jatamansi Kadha* in overweight or obese patients with known history of hypertension. This program consisted of a series of procedures such as *Shehana, Swedana, Shirodhara*. Patients followed Diet chart/Plan of 1200 calories strictly.

Blood Pressure Management Kit Program

Snehana is a process wherein the body is lubricated with the help of oil, hence *Snehana* is also called as Oleation therapy. *Snehana* is a mandatory procedure before *Panchakarma*. *Sneha* meaning oil and the process which uses oil is called as *Snehana*. It is a lubrication of human body either internally or externally. Our study used *Nirgundi oil* as the lubricating oil and the type of lubrication or oleation used was external oleation. This procedure employed a specific form of massage (***Abhyanga***). It is also called as oleation. The expert therapist applied herbal *Nirgundi* (*Vitex negundo*) oil to the skin before starting the massage. This process

also improves circulation and acts like anxiolytic[18]. This massage technique uses centripetal or upward strokes directed towards the heart. The duration of this procedure was 30-35 minutes. Other details of the method are given in Table 2.

Swedana is a steam treatment employing thermal vasodilation explained in *Ayurveda* medical science. It is also called as passive heat therapy. *Sweda* word is derived from *Sanskrit* word *Swid*, meaning '*To sweat or to perspire'*. Hence, *Swedana* is the process of producing sweat with the help of steam, which is generated from medicated herbal decoctions. Our procedure employed use of *Dashmool kadha* for *Swedana* process. To administer this therapy the patients were asked to lie in a supine position inside a sudation box and their head was positioned outside the box. *Dashmoola* (group of ten herbs) steam of temperature not more than 40°C was then passed steadily for 10-15 minutes. After the treatment, patients were asked to relax for 3-4 minutes. The total duration of this procedure was 15-20 minutes. It is the process of fomentation wherein persons were advised to take a steam bath in order to produce sweating. Sweating also causes elimination of salt and water. *Ayurveda* fomentation is usually given after an oil massage. Details of the procedure are given in Table 2.

Shirodhara massage is a classic *Ayurveda* therapy, where warm herbal oil/decoction is poured on the forehead in a continuous stream. *Shirodhara* treatment is an external treatment present in *Ayurveda*. *Shirodhara* comes from two words "*Shira*" means head and "*Dhara*" means stream. It is one of the treatment used to treat stress. It also reduces the level of stress hormones such as adrenaline and noradrenaline and thus relaxes the mind[19].

Table 2 Study methodology: Blood pressure management program (HTN Kit)

Step of Method	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes directed towards heart)	100 ml Vatex oil *V.negundo* [100 ml extract processed in sesame oil]	30-35 minutes
Swedana	Passive heat therapy	*Dashmoola* (group of ten herbal roots) with steam at $\leq$ 40 degrees Celsius)	10-15 minutes + 34 minutes of relaxation after procedure
Shirodhara	Decoction dripping therapy from a height of 7-8 cm	100 ml of Luke-warm *Jatamansi* decoction	30 minutes

Shirodhara may begin with *Ayurveda* body massage or *abhyanga* after a person lies down with his/her eyes closed.

In our study, the luke-warm *Jatamansi* decoction was allowed to drip at a constant speed from a fixed height on the medial of the forehead and eyebrows. The oil was

poured continuously as a stream and in an oscillating manner. Care was taken to ensure that the oil does not enter the eyes or ears. The entire procedure took 30 to 60 minutes, depending on the condition of the patient. A therapist also gave a light head massage to the patient before or during the procedure.

The BP management program is a combination of *Panchakarma* and allied therapies. BP management programs uses various decoctions and oils and constitutes of a 3-step procedure. This blood pressure management program involved total 6 sittings of *Snehana*, *Swedana* and *Shirodhara*. In the 1st month 4 sittings once a week was performed and thereafter one sitting each month in the 2nd and 3rd month was performed, along with the conventional treatment, if it was ongoing for the patient. Table 3 provides details step wise procedure in tabular format.

Table 3 Baseline characteristics of the study participants

Variable	N = 28
Age (Years)	58.91 ± 10.75

Results are expressed in mean ± SD and N(%)

Endpoints

Primary outcome measure was reduction in SBP and secondary outcome measures were reduction in DBP, reduction in mean arterial pressure (MAP), reduction in usage of conventional medicines and reduction in BMI. SBP and DBP assessment were done with the help of a sphygmomanometer after enrolment in the study at baseline. The follow up reading of SBP and DBP was taken on day 7, day 14, day 21 and day 28, day 90. The weight, height, BMI and the concomitant medication data was noted down on day 1 and again on day 90. MAP was measured for all the patients on day 1 and day 90 using the formula: 2/3rd DBP + 1/3rd SBP.

Statistical analysis

Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the numeric form and continuous data were presented as the Mean ± SD. Comparison of all the variables was done on day 1 and day 90 were using paired t test. P value of less than 0.05 was considered as a significant for all the variables.

The paired t-test was used to assess the difference between baseline values and 90th day after treatment. Box plot and histogram were used to represent graphs.

RESULTS

A total of 34 male hypertensive patients were screened for participation in the study. Out of these 34 patients, 28 were

included in the study based on the selection criteria. Enrolled patients (28) completed the study period and the data were collected from these patients.

Figure 1 represents the number of patients screened and finally enrolled in the study. Demographic details of the patients enrolled are given in Table 4. The efficacy parameters were analyzed at baseline (day 1) and after the last day of the study (day 90). Table 5 provides detailed information on efficacy measures.

Table 4 Demographic details of patients enrolled

Variable	Value
Age (mean; SD) years	53.25 ± 15.02
Male (n)	28

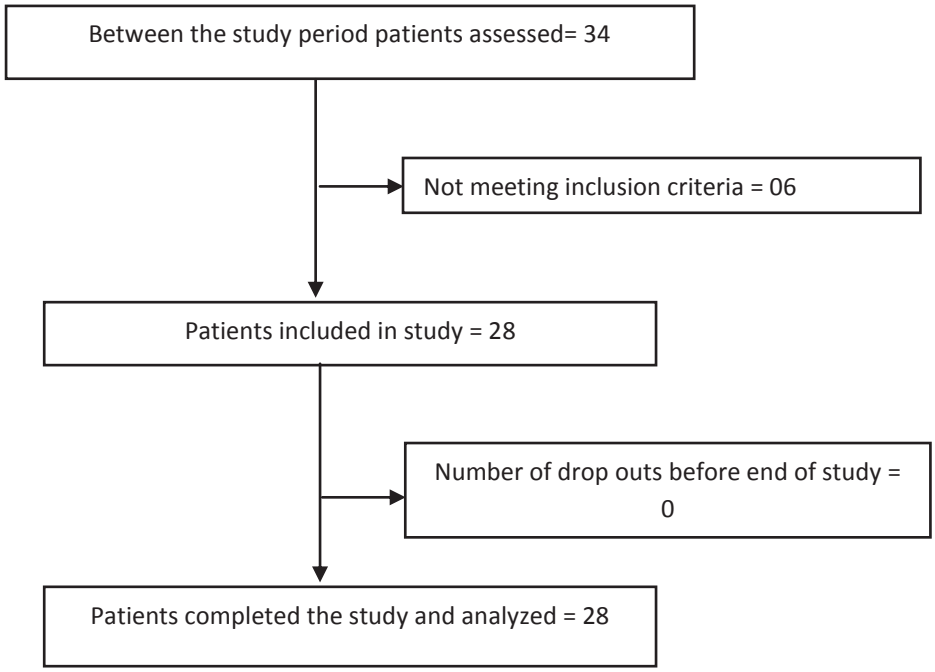

Figure 1 Patient Enrolment Flow Chart

Table 5 Comparison of clinical parameters between baseline values and 90th day

Variable (n=28)	Baseline (day 1)	After 90 days	Difference	*P-value*
BMI	27.48 ± 2.50	26.45 ± 2.21	1.13	<0.001***
SBP	153.5 ± 9.62	127.93 ± 10.23	25.57	<0.001***
DBP	91.61 ± 9.13	78.64 ± 6.93	12.96	<0.001***
MAP	112.22 ± 7.35	94.81 ± 7.45	17.41	<0.001***

****Highly significant*; *BMI, Body Mass Index; SBP, Systolic blood pressure, DBP, Diastolic blood pressure; MAP, Mean arterial pressure*

Comparison of clinical parameters between baseline values and 90th day are as shown in Table 5. The BMI ($P < 0.001$), systolic blood pressure ($P < 0.001$), diastolic blood pressure ($P < 0.001$), mean arterial pressure ($P < 0.001$) were reduced

and significantly improved after the treatment, i.e., after 90 days. Comparison of the mean values done by paired t-test.

It was found that the mean SBP was significantly lower after day 90 (127.80± 10.23 mm Hg) as compared to the baseline value on day 1 (153.5 ± 9.6 mm Hg) ($p<0.001$). The decrease in the mean SBP was shown reduction value as 25.50. This reduction shown improvement by a margin of 19.98% as given in table 5.

The mean DBP was reduced from baseline day 1 (91.60 ± 9.13 mm Hg) to the day 90 (78.64 ± 6.92 mm Hg) which shows reduction value 12.96 with % improvement 16.48 as shown in Table 5.

There was a significant decrease in the mean value of MAP on day 90 (94.80 ± 7.44 mm Hg) as compared to that on day 1 (112.21 ± 7.3 5mm Hg) ($p<0.01$). This shows reduction value as 17.41 with % improvement 18.36 as shown in Table 5.

There was a dramatic decrease in BMI as well from day 1 (27.47 ± 2.49) to day 90 (26.45 ± 2.21) $P < 0.001$; with reduction value 1.03 and percentage improvement 3.87. Details are given in Table 5.

Distribution of Allopathy medicine in 28 male patients for BP management program was seen in Table 6 below. The graphical representation of consumption of allopathic medicines on days 1 and 90 is depicted in Figure 1.

Table 6 Consumption of allopathic medicines on days 1 and 90

Medicine	Day 1	Day 90
NSAID	2 (7.14)	2 (7.14)
ARB	14 (50)	8 (28.57)
Antiplatelet	1 (3.57)	1 (3.57)
Beta blocker	10 (35.71)	5 (17.86)
CCB	9 (32.14)	4 (14.29)
Diuretic	5 (17.86)	2 (7.14)
Biguanide	0 (0)	0 (0)
Sulfonylurea	0 (0)	0 (0)
No medicine	4 (14.29)	7 (25)
NSAID + antiplatelet	1 (3.57)	1 (3.57)
Statin	2 (7.14)	1 (3.57)

NSAID, Nonsteroidal anti-inflammatory drugs; ARB, Angiotensin II receptor blockers; CCB, Calcium channel blockers

There is a significant decrease in usage of conventional allopathic medicines from baseline to the day 90. There was maximum reduction in ARB usage (from 14 at baseline to 8 at day 90) following Beta blockers and CCB usage where usage was reduced from 10 to 5 and from 9 to 4 respectively. Number of subjects that

could stop allopathic medication increased substantially from baseline to 90 days, details are given in Table 5 and 6.

No adverse events were reported during study period.

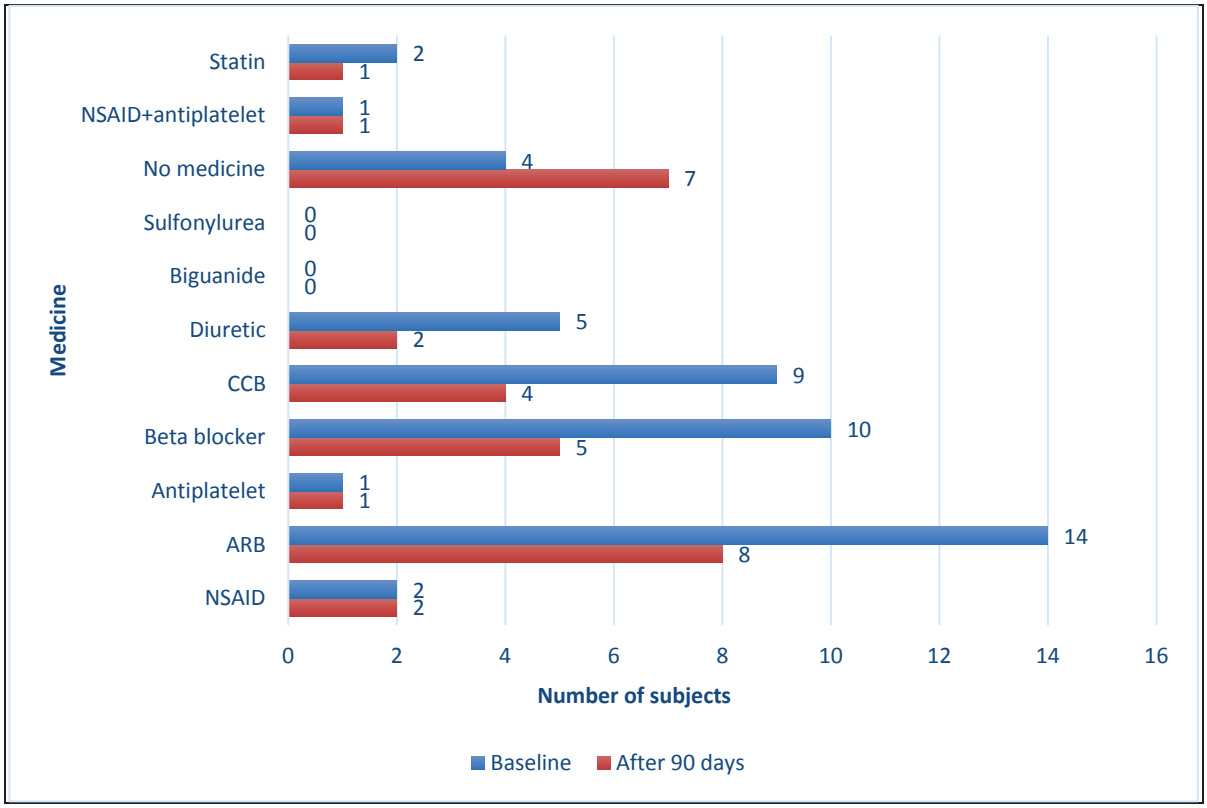

Figure 2 Consumption of allopathy medicines at days 1 and 90 days (N = 28)

DISCUSSION

Looking at global scenario; uncontrolled hypertension is major behavioral and physiological risk factor. 13% of global deaths are attributed to increased blood pressure. It is reported to be the fourth disease and cause of premature death in developed countries and the seventh in developing countries[5] whereas while looking at a national scenario; the prevalence of hypertension ranges from 2-15% in urban India whereas 2-8% in rural India[5]. Monotherapy is not sufficient to control blood pressure. Combination therapy has numerous side effects and is still unable to control high blood pressure, necessitating search of new interventions. These drawbacks of current pharmacotherapy took us to the ancient medical system of India, the *Ayurveda*.

After thorough research our team decided to use a dedicated blood pressure management program which uses herbal drugs which are without side effects and use a convenient methodology that increasing patient compliance. Our team

used *Nirgundi*, *Dashmoola* and *Jatamansi* as blood pressure lowering agents via the 3 step procedure of *Snehana*, *Swedana*, *Shirodhara*. These processes efficiently lowered blood pressure in the study population; which is confirmed in the results.

The literature has shown that these herbs *Nirgundi, Dashmoola and Jatamansi* possess anti-hypertensive activity. Whole percolate extract of *Nirgundi* (*Vitex Negundo*) contains polyphenols; this polyphenolic extract possesses excellent anti-hypertensive activity[15]. During our BP management program at *Madhavbaug* Clinic we used oil formulation of *Nirgundi* for external application in the process of *Snehana*. During this process of Massage; we used upward strokes towards Heart; which helps in improving circulation. A study conducted by Kshiteeja C *et al* demonstrates use of *Dashmool* roots as a remedy for hypertension[16]. In this study *Dashmool* was used to maintain equilibrium between *Vata* and *Pitta Dosha*. Decoction formulation was used in the study in a Saman process. We at *Madhavbaug* used *Dashmool Kadha* ; a formulation to be taken internally; during the process of swedana. Another study conducted by Rajan M *et al* also reports use of *Dashmool* for the treatment of hypertension; where it was used during shirodhara process[20]. It was used as *Dugdha Dhara* for the said purpose. Yet in another study, Nardostachys *Jatamansi* was found to be effective and safe drug having potential of anti-hypertensive activity when given along with other drugs or along with lifestyle modification[21]. In this study, its extract significantly prevented alterations in lipid profile (Cholesterol, phospholipids, fatty acids & triglycerides). We, at *Madhavbaug*, used *Jatamansi Kadha* during *Shirodhara* process which enhances anti-hypertensive activity of *Jatamansi*.

In a study conducted by Anjali C and Prakash S, the use of *Rakadabashamak Vati* is reported where the roots of the *Jatamansi* were used[22]. Another study also reports the use of *Jatamansi* where they revealed its anti-hypertensive activity by acting on adrenaline induced blood pressure in dogs. This study uses root powder obtained in a pharmacognostic way[17].

Our study showed maximum reduction in SBP as shown in Table 3 which was the primary outcome measure; following which reduction was seen in DBP and MAP. We also observed a decrease in BMI, which is one of the risk factors of hypertension. We also assessed consumption of allopathic medicines where we observed encouraging results. In

general, reduction was observed in the consumption of these medicines. Maximum reduction was seen in ARB, CCB, and ACE- inhibitor usage. The number of patients without allopathic medicine increased.

These findings from our study are encouraging yet this current study also possesses some limitations. There were only male patients enrolled as participants; hence efficacy studies in general population including female patients are recommended. Another limitation of the study was the use of only overweight or obese patients. The small study population was another limitation. Use of Sphygmomanometer is another limitation in the current era of ambulatory pressure monitoring. This was a one-arm, pilot study performed for proof of concept involving a short duration of 90 days. All these imitations create a need for larger studies with more number of patients to validate the findings from current study.

CONCLUSION

Treatment of the blood pressure management program was found to be safe; without any adverse effects, effective and cost-effective; using three herbal drugs, *Nirgundi oil*, *Dashmool kadha* and *Jatamanasi kadha*; in combination with each other for the first time and employing a unique methodology of *Snehana*, *Swedana* and *Shirodhara*. This prospective pilot study showed that this method can be used as an effective blood pressure management program in patients of India.

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EFFICACY OF HEART FAILURE REVERSAL THERAPY (HFRT) PROGRAM IN PATIENTS WITH PRESERVE EJECTION FRACTION: AN OBSERVATIONAL STUDY

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ABSTRACT

Heart failure with preserved ejection fraction (HFpEF) is a worldwide healthcare issue showing growing prevalence, with complex management algorithms. Heart failure reversal therapy (HFRT) is a combination of *Panchakarma* and allied therapies used by *Ayurveda* physicians for CHF patients. This observational study was done to evaluate HFRT in HFpEF patients. Study was conducted between January 2017 to December 2017. The data of HFpEF patients who had been administered HFRT with minimum 7 sittings over 90 days (± 15 days) were considered. VO2max, metabolic equivalent (MET), body mass index (BMI), blood pressure (BP), dependency on conventional therapy were compared on day1 and 90. 28 patients were enrolled (21 males, 7 females) with a mean age of 55.79 ± 9.83 years. On analysis, there was significant improvement in mean VO2max (18.16 ± 5.71 vs 31.85 ± 4.80 ml/kg/min, $p<0.01$) and mean MET (5.19 ± 1.63 vs 9.10 ± 1.37, $p<0.01$) of the patients on day 90, when compared to day 1. Mean BMI (27.01 ± 3.98 kg/m2 vs 25.69 ± 3.21 kg/m2 , $p<0.01$) and mean SBP (129.64 ± 15.36 vs 118.79 ± 9.69 mm Hg, $p<0.01$) were decreased after 90-day HFRT therapy. Dependency on medications was also reduced.

To conclude, HFRT is effective in managing HFpEF patients and also decreases the dependency on allopathic medications.

KEYWORDS: Heart Failure Reversal Therapy, HFRT, *Panchakarma*, Chronic Heart Failure, Preserved Ejection Fraction, *Ayurveda*, Alternative medicine

INTRODUCTION

According to the World Health Organization, cardiovascular diseases (CVDs) have become the leading cause of mortality and morbidity worldwide, and amongst all ethnic population, it is assumed that Indians are majorly affected.[1] CVD affects Indian population in their most productive midlife years and at least a decade earlier as compared with the people of European ancestry.[2] In India, 52% of CVD deaths occur prior to the age of 70 years; in Western population it is as low as 23%. There is an increase in the occurrence of CVD cases worldwide, and it shows an

annual increase rate of 0.5-1.8 million in India. Amongst the many CVDs affecting the population, chronic heart failure (CHF) is a major health concern due to the enormous number of people being affected by it. Prolonged life expectancy and progressive aging of the population have led to the rising prevalence of CHF.[3]

26 million people are estimated to be affected by CHF worldwide.[4] In India, it is estimated that 1.3 and 4.6 million people are affected by CHF, which roughly means a prevalence of 0.12–0.44 %, although this may be an underestimated number.[5] CHF is classified into two major types based on the functional status of the heart: heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF).[6] Dunlay et al. have stated that approximately 50% of patients with CHF have HFpEF.[7] The prevalence of HFpEF was greater than that of HFrEF with the former being more prevalent in women, while the latter being higher in men. HFpEF could be dominant in driving the overall CHF prevalence as the incidence of HFpEF is increasing at a higher frequency, and it is expected that by 2020, 65% of patients hospitalized for CHF will have HFpEF.[8] The condition is challenging to tackle because of multiple mechanisms being proposed which are hypothetical. Experimental models mimicking the disease are lacking and patients of HFpEF also suffer from other co-morbidities like hypertension and metabolic syndrome.[9] Campbell et al. have compared outcomes in HFpEF with patients of similar sex distribution, co-morbidity and age that were enrolled in trials of diabetes mellitus, angina pectoris, hypertension and atrial fibrillation, and concluded that patients in the HFpEF trials were at higher risk of death and at strikingly higher risk of HF hospitalizations.[10]

The standard management of CHF includes use of pharmacological agents like angiotensin receptor blockers (ARBs), beta blockers, angiotensin converting enzyme (ACE) inhibitors, antiplatelets, diuretics and vasodilators.[11] However, majority of CHF patients require elaborate management due to co-morbidities, multiple medications, growing age, reduced coping skills and depression.[12] CHF has poor prognosis despite improvement in therapeutic devices and drugs.

Considering these exigencies, there is a requirement and need for newer, cost-effective treatment modalities that will reduce the fear and anxiety of the patient and improve their quality of life. This search has brought researchers to the doorstep of alternative medicine.

Ayurvedic physicians recommend using conventional drugs in the acute disease phase while in the chronic stage of heart failure, use of *Panchakarma* therapy (a 5-step process for providing internal body purification) as an add-on for providing the best possible benefit to the patient.[12] Heart failure reversal therapy (HFRT), previously known as ***Sampurna Hruyday Shudhikaran* (SHS) therapy**, is a combination of herbal treatment with *Panchakarma* and allied therapies. The

techniques used in *Panchakarma* are[12]: *Snehana* (External oleation), *Swedana* (Passive heat therapy), *Hridaydhara* (Concoction dripping treatment) and *Basti* (per rectal drug administration), which are known to get rid of toxins from the body. However, there is a lack of evidence which supports the use of this promising treatment modality, especially in patients suffering from HFpEF. Hence, we planned a study to evaluate the efficacy of HFRT program in a CHF patient having preserved ejection fraction. The efficacy of HFRT program was evaluated by using various variables like VO2 max, metabolic equivalent (MET), systolic and diastolic blood pressure (SBP, DBP), body mass index (BMI), and reduction in concomitant medication intake.

MATERIALS AND METHODS

This was an observational study conducted between January 2017 to December 2017. We identified the data of patients who had visited the *Madhavbaug* clinics in Maharashtra, suffering from CHF but having an ejection fraction of more than 40 and the METS value of less than 8. The data of patients who had been administered HFRT with minimum 7 sittings over a span of 90 days (± 15 days) were considered for the study. Cases were identified, and data was assessed from the medical records of *Madhavbaug* clinics in Maharashtra. The selection was based upon the availability of complete relevant baseline data (day 1 of HFRT) and final day data (day 90 of HFRT) of the patients. The information about prescribed concomitant medicines or co-morbidities, if any, was also noted down.

The HFRT is a combination of *Panchakarma* and allied therapies. HFRT uses various decoctions and oils and constitutes of a 4-step procedure, as described below in table 1.

Table 1: Study Treatment: Heart Failure Reversal Therapy (HFRT)

Step of HFRT	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes directed towards heart)	10 grams T. arjuna, 10 grams *Dashamoola* and 5 grams *V.negundo* [100 ml extract processed in sesame oil]	30-35 minutes
Swedana	Passive heat therapy	*Dashmoola* (group of ten herbal roots) with steam at ≤ 40 degrees Celsius)	10-15 minutes + 3-4 minutes of relaxation after procedure
Hrudaydhara	Decoction dripping therapy from a height of 7-8 cm	Luke-warm *dashmoola* decoction	15 minutes
Basti	Medicated enema administered per-rectal, should be in body for ≥	1.88 grams *T. arjuna*, 0.42 grams *B. diffusa* and 0.18 grams *A. calamus*	10 minutes

	15 minutes for maximum absorption	[10 ml aqueous extract]	

On day 1 of HFRT, the patients underwent Cardiac stress testing by Modified Bruce Protocol.[19] Their maximum work load was evaluated in terms of metabolic equivalents (METs) which represents a modest, practical, and easily understood technique for stating the energy cost of physical activities as a multiple of the resting metabolic rate.[13] This MET was multiplied by 3.5 to give peak VO_2 max, which is nothing but the maximal aerobic capacity (MAC). This process was repeated on day 90 of HFRT to calculate VO2 max. The other baseline and day-90 data which were considered retrospectively by investigators for statistical analysis included the BMI, SBP, DBP and the conventional treatment information. The BMI for day 1 and day 90 of the patients was evaluated by checking the weight and the height from the medical data records of patients and using the formula: *weight in kilograms/(height in meters)*^{2}. Likewise, the baseline and the day 90 readings of SBP as well as the DBP were noted down from the medical records of the patients in the study. The dependency on standard medications was calculated both on day 1 as well as day 90 of HFRT, and the change in the medicine intake pattern was assessed.

Data was entered and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the numeric form and continuous data were presented as the mean ± SD. The paired t-test was used to assess the difference between baseline values and 90th day after the treatment and graphs were used to represent the assessed parameters.

RESULTS

A total of 30 patients' data was screened for inclusion in the study. However, based on the availability of complete data and the inclusion criteria, 28 patients were selected, and their data were analyzed. Figure 1 gives the screening process of patients. The majority of the enrolled patients were males (75%), with the mean age being 55.79 ± 9.83 years. The mean ejection fraction (EF) of the patients was noted (57.32 ± 8.58) which was in the normal range. Table 2 gives the baseline demographic details of the patients enrolled.

Figure 1: Patient Enrolment Flow Chart

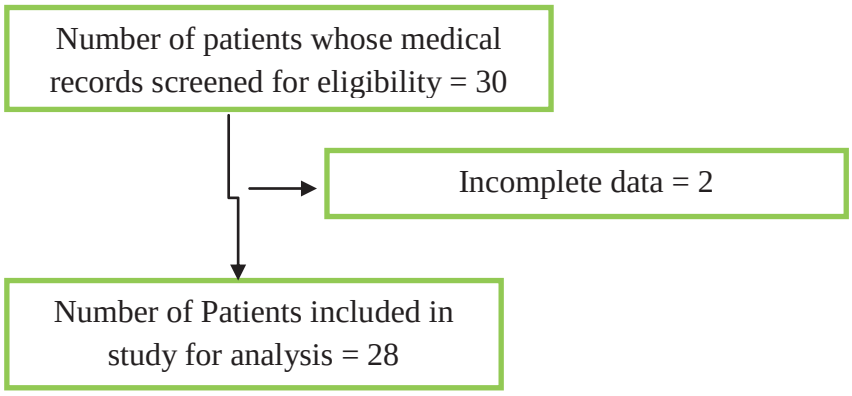


Table 2: Baseline characteristics of the study participants

Variable	N = 28
Age (years)	55.79 ± 9.83
Ejection Fraction (%)	57.32 ± 8.58
Gender	
Male	21 (75)
Female	7 (25)

Results are expressed in mean ± SD and N(%)

The VO_2 max of the patients, based on a treadmill test, was significantly increased after 90 days ($p<0.01$), with the mean difference being 13.69 ml/kg.min. (Table 3, Figure 2)

The maximum workload signified by metabolic equivalents (METS) increased significantly after day 90, as compared to mean day 1 values ($p<0.01$), with the increase being by a mean value of 3.91 units. (Table 3, Figure 3)

Figure 2: Comparison of VO2 max between baseline values and 90th day (N = 28)

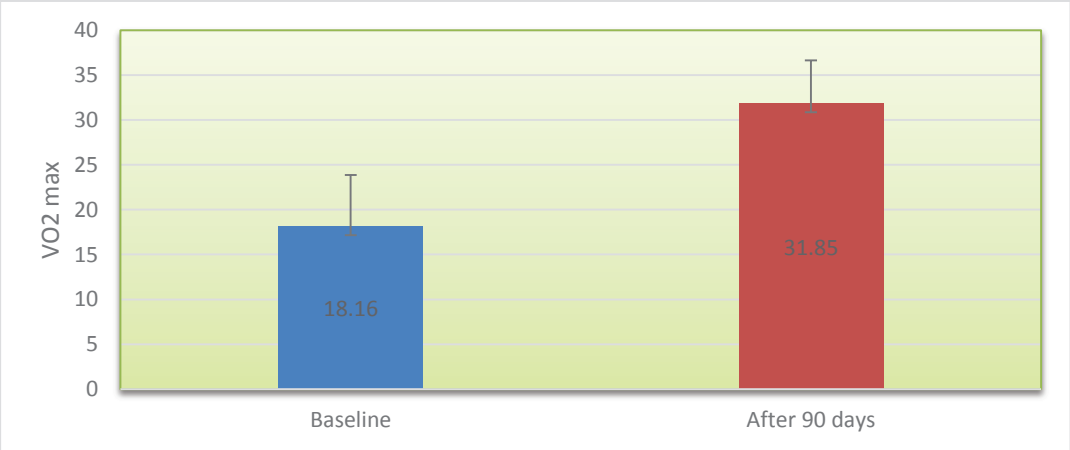
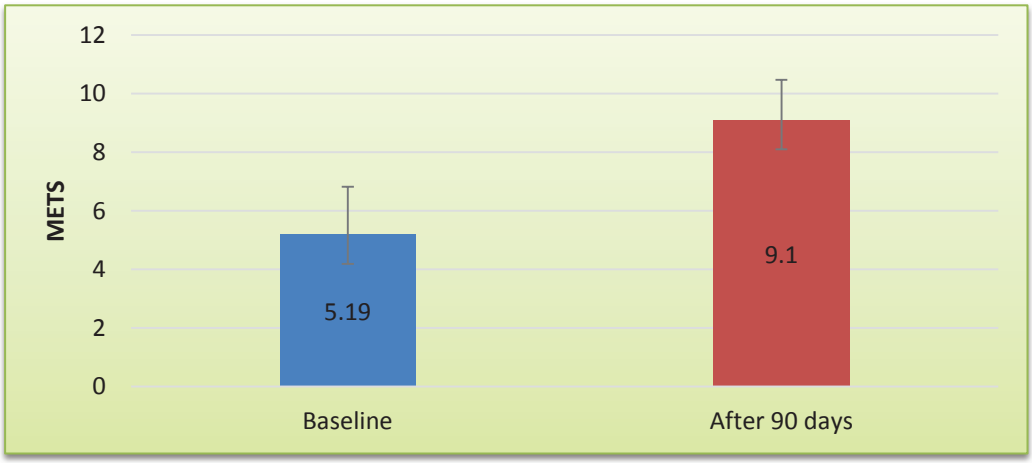
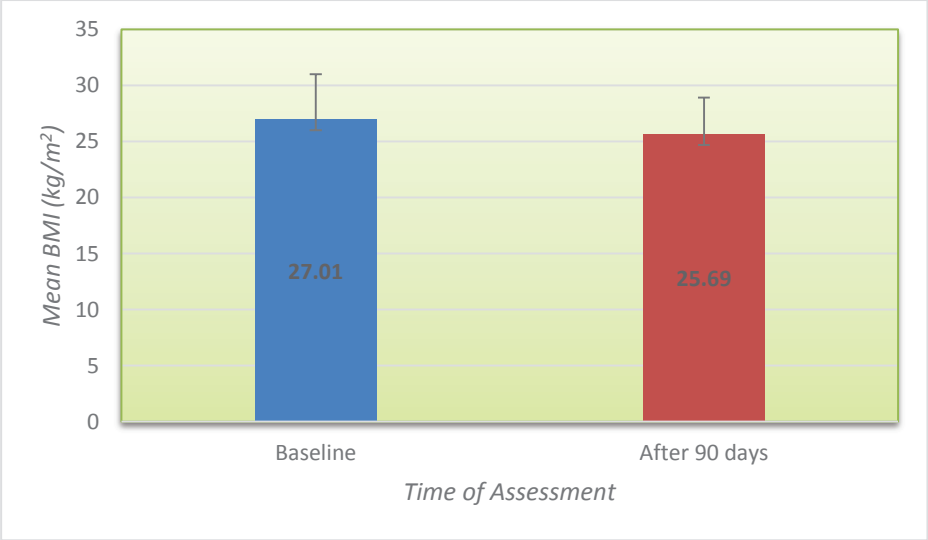


Figure 3: Comparison of METS between baseline values and 90th day (N = 28)



We noted a significant improvement in the mean BMI of the patients on day 90, when compared to that on day 1 ($p<0.01$). The decrease in the mean BMI was by a margin of 1.32 kg/m^2. (Table 3, figure 4)

Figure 4: Comparison of Body Mass Index between baseline values and 90th day (N = 28)



The mean SBP also decreased significantly on day 90 when compared to that on day 1, the mean difference being of 10.86 mm Hg ($p<0.01$). The DBP also decreased on day 90, by a mean margin of 2.21 mm Hg, but this decrease was not statistically significant ($p=0.18$). (Table 3, Figure 5)

Figure 5: Comparison of SBP, DBP between baseline values and 90th day (N = 28)

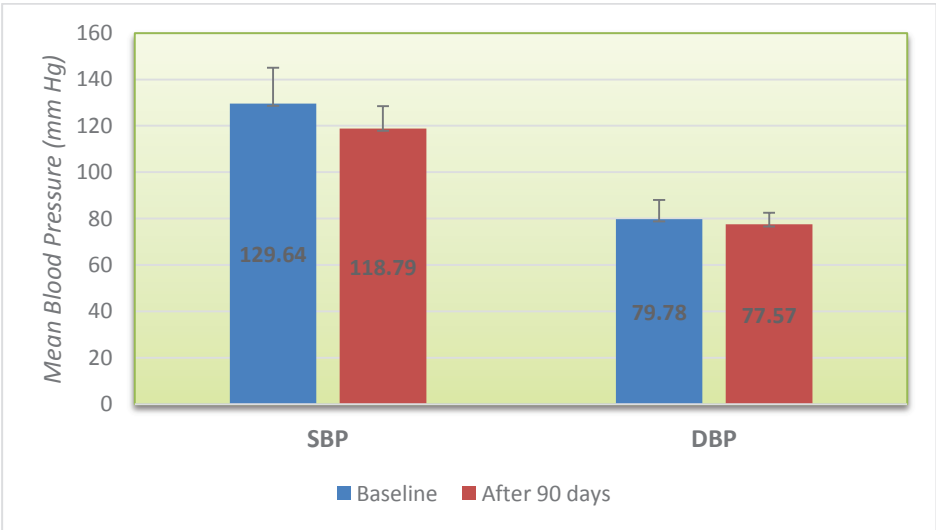


Table 3: Comparison of Clinical parameters between baseline values and 90th day of the treatment by HFRT

Variable	Baseline (Day 1)	After 90 days	Difference	p-value
VO_2 Max	18.16 ± 5.71	31.85 ± 4.80	13.69	<0.001
METs	5.19 ± 1.63	9.10 ± 1.37	3.91	<0.001
BMI	27.01 ± 3.98	25.69 ± 3.21	1.32	<0.001
SBP	129.64 ± 15.36	118.79 ± 9.69	10.86	<0.001
DBP	79.78 ± 8.24	77.57 ± 5.00	2.214	0.184

BMI, Body Mass Index; SBP, Systolic blood pressure, DBP, Diastolic blood pressure; maximal oxygen uptake; METS: Maximum Work Load

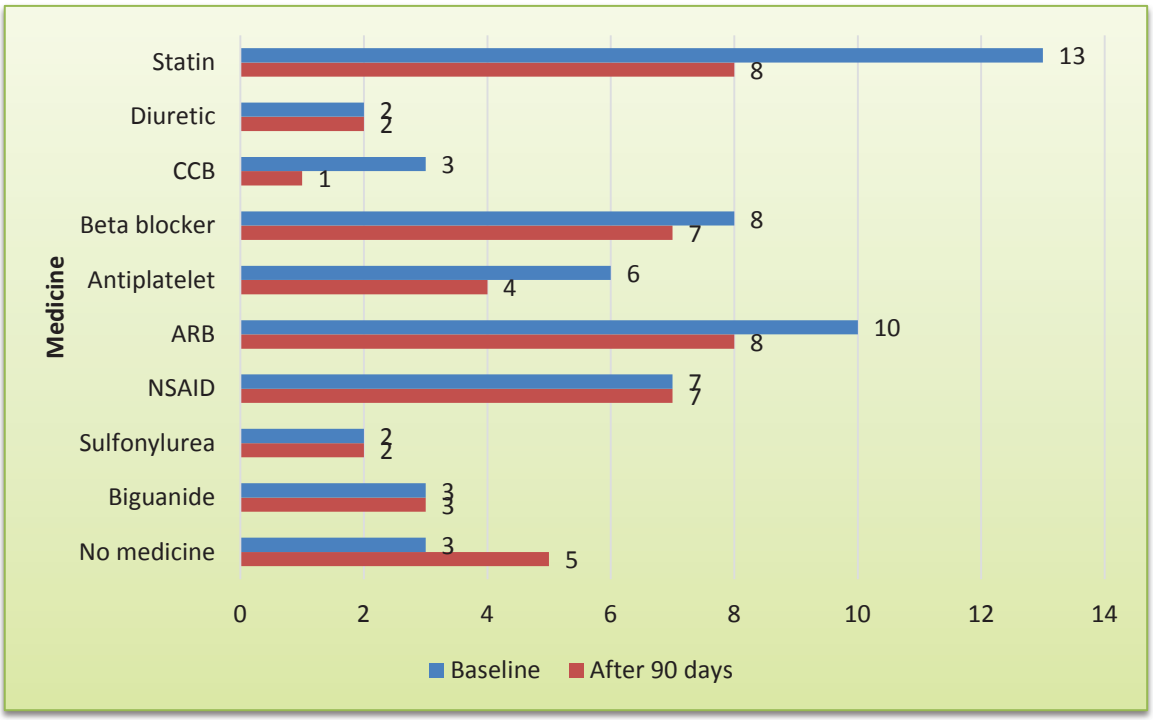
We calculated the consumption of allopathic medications on day 1 and day 90 of HFRT. Most of the participants were treated with statins (46.43 %), angiotensin II receptor blockers (35.71 %), beta blockers (28.57 %), antiplatelet agents (21.43 %) and nonsteroidal anti-inflammatory drugs (25 %). After 90 days of HFRT, the participants dependent on statins (28.57 %), calcium channel blockers (3.57 %), beta blockers (25 %), antiplatelet (14.29 %) and angiotensin II receptor blockers (28.57%) were reduced. The percentage of patients not on any conventional medication increased from 10.71% on day 1 of HFRT to 17.86% on day 90 of HFRT. Table 4 gives a tabular representation of consumption of conventional medications in our study.

Table 4: Consumption of allopathic medicines on days 1 and 90 of HFRT

Medicine	Baseline	After 90 days
Statin	13 (46.43)	8 (28.57)
Diuretic	2 (7.14)	2 (7.14)
CCB	3 (10.71)	1 (3.57)
Beta blocker	8 (28.57)	7 (25)
Antiplatelet	6 (21.43)	4 (14.29)
ARB	10 (35.71)	8 (28.57)
NSAID	7 (25)	7 (25)
Sulfonylurea	2 (7.14)	2 (7.14)
Biguanide	3 (10.71)	3 (10.71)
No medicine	3 (10.71)	5 (17.86)

NSAID: Nonsteroidal anti-inflammatory drugs; ARB: Angiotensin II receptor blockers; CCB: Calcium channel blockers

Figure 6: Consumption of allopathic medicines on days 1 and 90 of HFRT



DISCUSSION

CHF is one of the most common cause of CVD, and one of the most common causes of death worldwide. HFpEF is one of the two functional types of CHF and has overtaken the other type (HFrEF) according to multiple prevalence studies. The risk factors for HFpEF are multiple, and there is no known prevention strategy other than the management of the risk factors which include hypertension, diabetes and obesity. The prevention as well as early treatment strategies (which is early revascularization) seem to be effective in decreasing the risk and severity of acute myocardial infarction. The conventional drugs used for the management of CHF include beta blockers which have been found to have anti-oxidant and anti-inflammatory properties. Many herbal drugs have been known to have these properties and hence, *Ayurveda* seems to be a feasible alternative option for research in patients suffering from CHF. *Ayurveda* physicians utilize *Panchakarma* therapy as an add-on therapy for treatment of CHF and HFRT is a combination of *Panchakarma* with allied therapies.[14] Therefore, we evaluated the effect of HFRT in patients of CHF having preserved ejection fraction. We found that the VO2 max, which is nothing but the maximal aerobic capacity (MAC), was significantly improved after 90 days of HFRT therapy. We also found that the maximum workload, signified by metabolic equivalents (METS), augmented significantly after 90 days of HFRT. The BMI and SBP were also significantly decreased in the patients after 90-day HFRT, signalling a positive response on the risk factors of CHF, viz. obesity and hypertension. The dependency of patients on multiple concomitant medications like

statins, beta blockers and ARBs decreased significantly after HFRT, leading to less chances of adverse effects in these patients which result from polypharmacy.

Functional capacity is the ability of a person to perform his routine activities involving physical exertion. VO2max, also known as maximal aerobic capacity, signifies the maximum rate of oxygen consumption measured during incremental exercise. It is the most widely accepted marker of aerobic fitness[15] a compromise or decrease in the VO_2 max indicates a decrease in the cardiorespiratory function. In our study, the VO_2max was found to be significantly increased at the end of 90 days, thereby indicating an improvement in the patient's exercise capacity.

A metabolic equivalent (MET) is the resting metabolic rate and signifies the amount of oxygen which is consumes at rest. In exercise testing, as the exercise intensity is gradually increased, the increase in intensity from stage to stage is normally about 1 to 2 METS, or even more, in normal individuals. However, the increase is small in functionally compromised individuals, like those with CHF. It represents the energy expenditure of physical activities as a multiple of resting metabolic rate. In our study, the METs were significantly improved in the patients after 90 days of HFRT, signifying an improvement in the exercise capacity of all the patients.

BMI is considered as a crucial indicator of a sedentary lifestyle as well as impending or prevalent obesity. CHF patients having a high BMI are at greater risk of mortality.[16,17] Hypertension is a known risk factor for CHF development and modifies the prognosis. Hence, approaches have been developed to deliver sustained blood pressure control in patients suffering from HTN, to prevent CHF.[18]

Management of HFpEF is complex, and the main aim of managing this type of CHF is treatment of the various risks or aggravating factors associated with it, like obesity and HTN.[19] HFRT comprises of *Snehana* (External oleation or massage), *Swedana* (Passive heat therapy), *Hridaydhara* (Decoction dripping therapy) and *Basti* (Per rectal drug administration) which seem to act in cohesion to improve the parameters in CHF patients. In cases of heart failure, as in normal individuals, the increase in the work load proportionately increases the oxygen consumption of the left ventricle. The work of the heart though fails to rise proportionately. This leads to a disproportionate increase in aerobic energy uptake and thus, a fall in left ventricular efficiency occurs.[20] Therefore, there is a need to maintain the oxygen demand of the failing heart, especially in HFpEF where there is diastolic dysfunction and ultimate systolic function as well. It has been theorized that *Snehana* may be reducing the sympathetic activity, ultimately leading to reduction in the vascular tone and increase in the vasodilator reserve. *Swedana* leads to increase in sweating which may cause peripheral vasodilation and thus, a decrease in the systemic vascular resistance. This will cause reduction in the afterload, decrease the cardiac work load and hence, reduce myocardial oxygen demand. A rise of body temperature due to passive heating

suggestively increases the cutaneous vascular conductance which leads to an equivalent elevation in systemic conductance.[21] *Hridaydhara* will lead to relaxation of the patient both mentally and physically, which may have a beneficial effect on the BP of the patient. Research has shown that pro-inflammatory conditions may also increase the chances of causing diastolic dysfunction, as seen in HFpEF.[22] According to a research involving obese patients, *Basti* moderated immune responses by regulating pro-inflammatory cytokines, immunoglobulins and functional properties of T-cells. These changes are related to a decrease in the body weight, which is sustained even after three months of treatment[23] this finding may explain the beneficial effect of *Basti* in patients with HFpEF.

Present study has a few limitations. Study was carried over a period of 90 days, so long-term effects still need to be studied. A bigger sample size covering multiple centres will also help generate more evidence.

CONCLUSION

HFRT showed promise as a treatment modality for the management of patients of HFpEF. HFRT significantly improved VO2 max and METs along with a significant reduction in the SBP and BMI. HFRT also reduced the dependency of patients on standard concomitant medications.

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Ischemia Reversal Program (IRP) in patients suffering from Ischemic Heart Disease (IHD) with known history of Hypertension: A Retrospective Study

Ischemic Reversal Program (IRP) is designed for improving the blood flow to heart. Lack of blood supply to the heart can often cause of heart attacks and is common in people with high blood pressure. IRP aims to reduce the risk of heart attack and increase exercise tolerance levels to improve quality of life. IRP treatment is associated with significant improvement in the Duke Treadmill score and VO_2 max, thereby leading to betterment of prognosis in IHD patients. The dependency on conventional medicines was also decreased by IRP.

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Original Article

Ischemia Reversal Program (IRP) in patients suffering from Ischemic Heart Disease (IHD) with known history of Hypertension: A Retrospective Study

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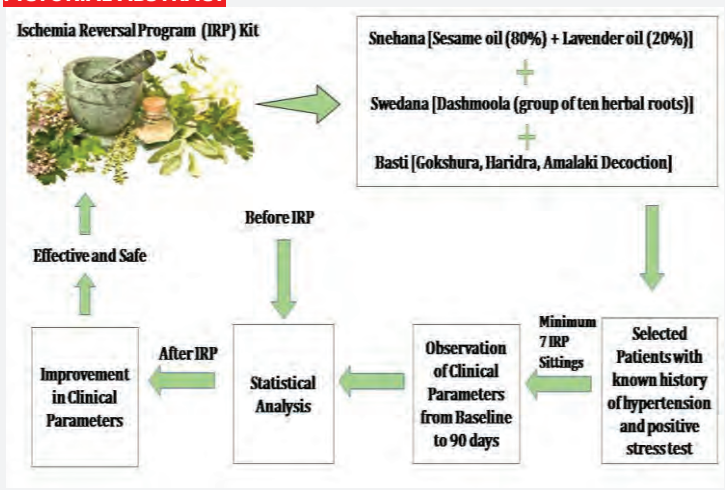
ABSTRACT

Introduction: Cardiovascular mortality has risen in the last few years and Ischemic Heart Disease (IHD) is one of the most common causes. Ischemia Reversal Program (IRP) kit uses a combination of *Snehana* (Centripetal oleation), *Swedana* (Thermal vasodilation) and *Basti* (Per rectal drug administration) for providing relief to IHD patients. This study was conducted to evaluate the efficacy of IRP in IHD patients. ***Methods***: This retrospective study included data of patients having positive inducible ischemia by stress test with known history of hypertension (HTN) and had visited the *Madhavbaug clinics*. A minimum of 7 IRP sittings were needed for inclusion. Duke Treadmill score, VO_2 max, systolic plus diastolic blood pressure (SBP, DBP) and details of conventional medications were noted on day 1 and on day 90 followed by comparison between these values. ***Results***: 19 patients having mean age 59.26 ± 8.03 years were enrolled, with 78.9% being males. On day 90, none of the patients were at high risk by Duke Treadmill Score, compared to 47.4% being at high risk on day 1 ($p<0.01$). Mean VO_2 max significantly increased on day 90 of IRP therapy ($p<0.01$) while mean SBP and DBP decreased, though not significantly ($p>0.05$). The number of subjects on allopathic medicines decreased after 90th day, as compared to day 1. ***Conclusion***: IRP treatment is associated with significant improvement in the Duke Treadmill score and VO_2 max, thereby leading to betterment of prognosis in IHD patients. The dependency on conventional medicines was also decreased by IRP.

KEYWORDS Coronary artery disease, Duke's Treadmill test, Ischemia Reversal Program, Myocardial ischemia.

PICTORIAL ABSTRACT



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1. INTRODUCTION

Cardiovascular disorders are now assumed to have become an epidemic worldwide. Although the cardiovascular mortality is reduced in developing countries, it is on a rise in developing countries like India[1]. It is estimated that 75% of cardiovascular deaths occur in developing countries like India. The main culprit for cardiovascular mortality is coronary heart disease (CHD), also known as Ischemic Heart Disease (IHD). The increase in the prevalence of IHD is attributable to various factors like urbanization, industrialization and major lifestyle changes[2]. A growing trend in cardiovascular disease related mortality has been reported from India, with 20.6% deaths in 1990, 21.4% in 1995, 24.3% in 2000, 27.5% in 2005, and 29.0% in 2013[3]. It is estimated that the prevalence of IHD in India has grown from 2% in 1960 to about 14% in 2013[4]. Another important factor, which has led to the increase in cases of IHD and other cardiovascular disorders is the presence of uncontrolled hypertension (HTN) in the population. WHO has estimated that out of the deaths occurring due to cardiovascular disease, 16% of IHD related deaths are because of HTN[5].

The current treatment algorithm for IHD and HTN comprises of lifestyle modifications and pharmacotherapy. Drugs belonging to classes of angiotensin converting enzyme (ACE) inhibitors, calcium channel blockers (CCBs), and beta blockers have been used to control both IHD and HTN. Specific treatment for IHD also includes the use of anti-platelet agents like aspirin as well as anti-dyslipidemic drugs like statins. However, despite the presence of multiple drugs in their treatment, there is an unmet need for the management of IHD and HTN, which is evident by the growing prevalence. Another drawback is the occurrence of

multiple adverse effects with the currently available allopathic drugs. Thus, there is undoubtedly a strong need to discover safer and cost-effective options for the treatment of IHD as well as HTN.

Ayurveda is the Indian traditional system of medicine, which is being used by multiple physicians to treat and manage various diseases. Panchakarma and allied therapies are used by Ayurvedic physicians to provide relief to patients suffering from numerous disorders and one such integrative way of managing IHD patients is by using Ischemia Reversal Program (IRP) Kit. This IRP kit uses a combination of *Snehana* (Centripetal oleation), *Swedana* (Thermal vasodilation) and *Basti* (Per rectal drug administration) for providing relief to IHD patients. Though, IRP is being used in practice by physicians with success, research evidences are lacking. Ayurvedic interventions have not been assessed methodically for their possible beneficial effects in the treatment of IHD. Hence, this study was planned to assess the efficacy of IRP kit in IHD patients with known history of HTN.

The functional capacity of an individual denotes his ability to perform exertional activities. IHD is associated with impaired functional capacity, indicated by a compromise in the maximum aerobic capacity (MAC), also known as VO_2 max. The cardiorespiratory fitness of an individual is denoted by VO_2 max, whose improvement is associated with better CHD outcome.[6] Hence, a study was planned to evaluate the VO_2 max and the Duke treadmill score of the patients of IHD on IRP. It was also planned to assess the effect of IRP on blood pressure (BP) and to see whether there was any decrease in the conventional medications' intake.

2. MATERIALS AND METHODS

This observational retrospective study was planned for patients between the periods March 2017 to February 2018. Data of patients having positive inducible ischemia by stress test with known history of HTN and had visited the *Madhavbaug Clinics* were considered for the study. The data of patients who had been administered the IRP kit with minimum of 7 sittings over a 90-day period was considered for the study. Cases were identified, and data were analyzed from the records of *Madhavbaug* clinics retrospectively. The selection was based upon the availability of complete relevant baseline data (day 1 of IRP) and final day data (day 90 of IRP) of the patients. The information about prescribed concomitant medicines or co-morbidities, if any, was also noted down. All the patients who received the IRP were on a standard diet of 1200 calories/day.

The IRP is a 3-step procedure, which is a combination of Panchakarma and allied therapies. IRP uses various decoctions and oils, which have been described in table 1. *Snehana* is a 30-35 minutes procedure, which involves *Lavender oil*-based decoction, to be administered by external massage to the IHD patients. This massage technique uses centripetal or upward strokes directed towards the heart. *Swedana* or passive heat therapy is a 10 -15 minutes procedure, which involves directing the IHD patients to lie in a supine position inside a sudation box, with their head positioned outside the box. *Dashamoola* (group of ten herbs) steam of temperature not more than 40 degrees is then passed steadily for 10-15 minutes. After the treatment, patients were asked to relax for 3-4 minutes. *Basti* is the procedure of per-rectal drug administration for a period of 15 minutes to the IHD patients using *Tribulus terrestris, Curcuma longa* and *Emblica officinalis* decoction.

Table 1. Study Treatment: Ischemia Reversal Program (IRP Kit)

Step of IRP	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes directed towards heart)	100 ml [*Sesame oil* (80%) + *Lavender oil* (20%)]	30-35 minutes
Swedana	Passive heat therapy	*Dashamoola* (group of ten herbal roots) with steam at ≤40 degrees Celsius)	10-15 minutes + 3 - 4 minutes of relaxation after procedure
Basti	Per rectal drug administration using a rectal solution.	Luke-warm *GHA* decoction 100 ml *Gokshura- Tribulus terrestris* Linn. *(Zygophyllaceae)* *Haridra- Curcuma longa* Linn. *(Zingiberaceae)* *Amalaki- Emblica officinalis* L.	15 minutes

Table 2. Score chart for the Duke Treadmill scores

Duke Treadmill Score and Level of Risk	
Score range	**Level of Risk**
Greater or equal to +5	Low Risk
+4 to -10	Moderate Risk
≤ - 11	High Risk

Segment deviation (depression or elevation), and exercise-induced angina. The formula used for the same is:

Duke treadmill score = maximum exercise time in minutes – 5×ST segment deviation in mm – 4×angina index, where 0 = no angina, 1 = non-limiting angina, 2 = exercise limiting angina.

A Duke Treadmill score ⩾5 indicates low risk for cardiovascular events (predicted 4-year survival was 99%). This population does not need further investigation with coronary angiography. A score ≤ -11 indicates high risk for cardiovascular events (predicted 4-year survival was 79%). These patients require further investigation with coronary angiography. A score between 4 and –10 indicates intermediate risk. Such patients may require further investigation with myocardial perfusion scanning or coronary angiography, or both, depending on the protest probability.[7] We calculated the Duke Treadmill score and classified the patients, according to the risk for cardiovascular events, on day 1 and day 90 of the study.

On day 1 of the IRP, the patients had undergone cardiac stress testing by the Modified Bruce Protocol. Their maximum work load was assessed in terms of metabolic equivalents (METs) and this was multiplied by 3.5 to give peak VO_2 max. This process was repeated on day 90 of the IRP to calculate VO_2 max.

The maximum work load was assessed in terms of metabolic equivalents (METs) and this was multiplied by 3.5 to give peak VO_2 max, which is nothing but MAC. This process was repeated on day 90 of the IRP to calculate MAC.

The other baseline and day-90 data which were considered retrospectively by investigators for the inclusion of the patients included the SBP, DBP and the conventional treatment information. The dependency on standard medication was calculated both on day 1 and day 90 of IRP as the percentage of patients out of the total enrolled ones who required a conventional allopathic therapeutic agent during the study period of 90 days.

Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the frequency form and continuous data were presented as the Mean ± SD. The McNemar-Bowker test was used to assess Duke Treadmill Score before and after 90 days of treatment. The paired t-test was used to assess the difference between baseline values and 90th day after treatment. Box plot and histogram were used to represent the graphs.

3. RESULTS AND DISCUSSION

3.1 Study population

A total of 24 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1 and Day 90), 19 patients were selected, and their data were considered for analysis (Figure 1). The baseline characteristics of these patients are shown in table 3. The mean age of the enrolled subjects was 59.26 ± 8.03 years. Nearly three-fourths of the study subjects were males (78.9 %). When the co-morbidity profile was assessed, 36.84% subjects had coronary artery disease (CAD) and 15.79% subjects had obesity. All the patients approached *Panchakarma* unit for *Swedana* during the study period.

Figure 1. Patient Enrolment Flow Chart

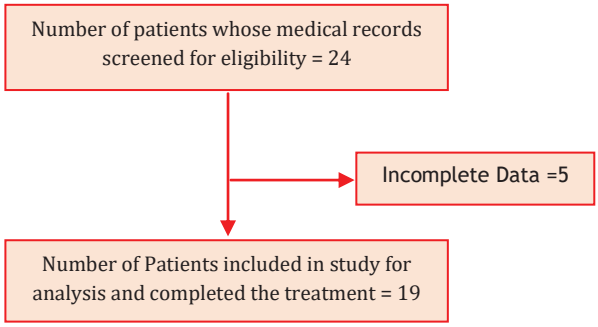


Table 3. Demographic characteristic of the study subjects (n=19)

Variable	N=19
Age	59.26 ± 8.03
Gender n (%)	
Male	15 (78.9)
Female	4 (21.1)
Past medical history n (%)	
Hypothyroidism	1 (5.26)
Obesity	3 (15.79)
Anxiety	1 (5.26)
CAD	7 (36.84)
MI	1 (5.26)
BPH	1 (5.26)

CAD, Coronary artery disease; MI, Myocardial infarction; BPH, Benign prostatic hyperplasia

Comparison of the baseline Duke Treadmill score and that after 90 days of therapy is shown in Table 4. The number of subjects having moderate (42.1 %) and high (47.4 %) risk of developing cardiovascular events at baseline were significantly decreased at day 90. There was an increase in the number of patients having low (42.1 %) and moderate (57.9%) risk after 90th day of therapy. Overall, after 90th day, no cases of high risk were reported. Figure 2 gives a graphical representation of the Duke score.

The clinical parameters were compared between baseline and 90th day values, as shown in Table 5. The maximum amount of oxygen consumption was significantly improved after the 90th day of therapy (P <0.001) [Fig 3.1]. SBP was decreased to near-normal levels after the 90th day of therapy, but it was not statistically significant (P =0.167) [Fig. 3.2]. DBP, which was normal in the patients before the therapy was initiated, was reduced after the therapy, but this reduction was not statistically significant (P=0.186) (Fig 3.3).

Table 4. Comparison of Duke Treadmill score baseline and after 90 days of treatment (n=19)

Duke treadmill score		After 90 days			Total	p-value
		Low	Moderate	High		
Baseline (1st day)	Low	2	0	0	2 (10.5%)	0.0029
	Moderate	5	3	0	8 (42.1%)	
	High	1	8	0	9 (47.4%)	
Total		8 (42.1%)	11 (57.9%)	0	19 (100%)	

Figure 2. Comparison of Duke Treadmill Score before and after treatment

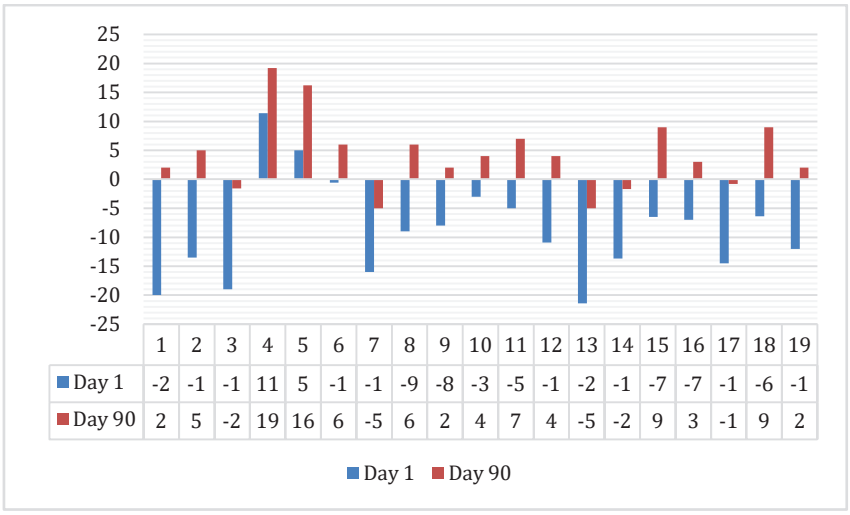
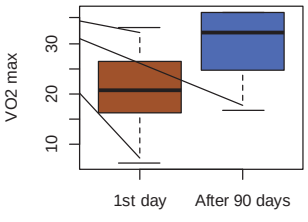


Table 5. Comparison of clinical parameters between baseline values and 90th day

Variable (n=19)	Baseline	After 90 days	Difference	p-value
VO2 max	20.74 ± 7.25	29.69 ± 6.62	-8.94	<0.001
SBP	127.68 ± 13.65	122.74 ± 11.65	4.95	0.167
DBP	78.95 ± 7.37	75.78 ± 6.92	3.16	0.186

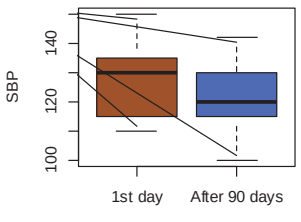
VO2 max, Maximum amount of oxygen consumption; SBP, Systolic blood pressure; DBP, Diastolic blood pressure

Figure 3. Comparison of clinical parameters between baseline and 90th day values



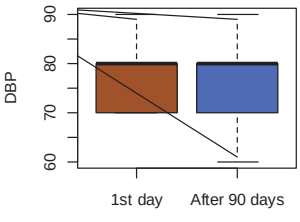
VO2 max on 1st day and after 90 days

3.1 Comparison of VO2 max



SBP on 1st day and after 90 days

3.1 Comparison of SBP



DBP on 1st day and after 90 days

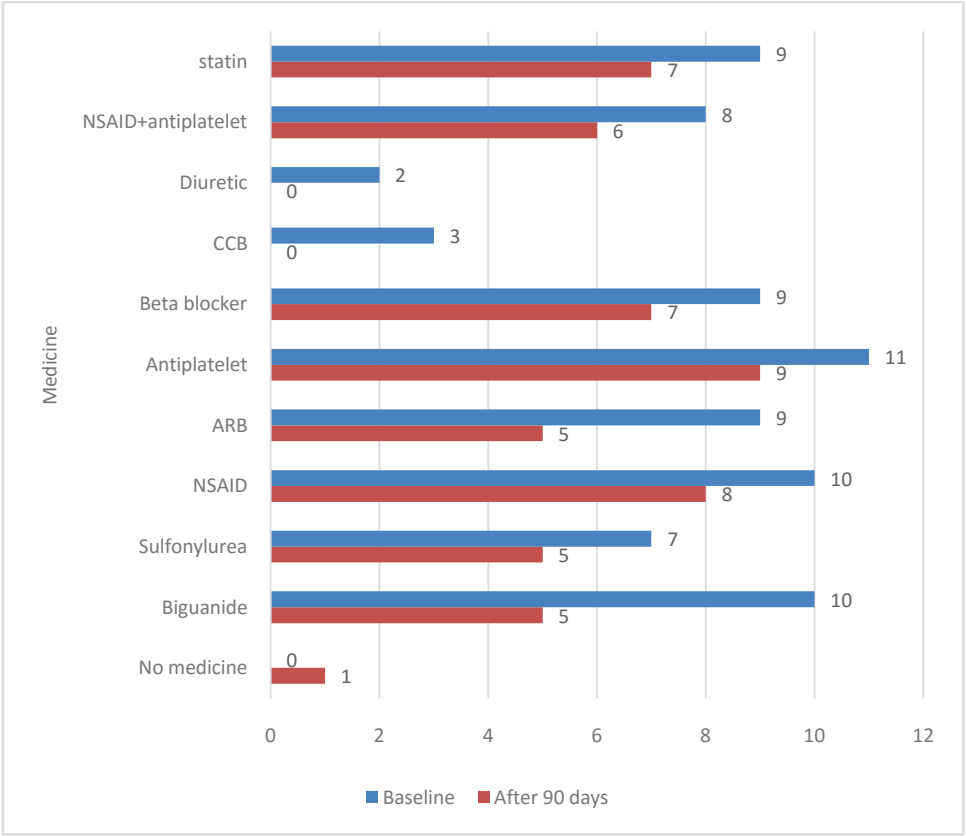
3.1 Comparison of DBP

Table 6. Consumption of allopathic medicines on day 1 and day 90 of IRP treatment

Medicine	Baseline	After 90 days
statin	9 (47.37)	7 (36.84)
NSAID+ antiplatelet	8 (42.11)	6 (31.58)
Diuretic	2 (10.53)	0 (0)
CCB	3 (15.79)	0 (0)
Beta blocker	9 (47.37)	7 (36.84)
Antiplatelet	11 (57.89)	9 (47.37)
ARB	9 (47.37)	5 (26.32)
NSAID	10 (52.63)	8 (42.11)
Sulfonylurea	7 (36.84)	5 (26.32)
Biguanide	10 (52.63)	5 (26.32)
No medicine	0 (0)	1 (5.26)

CCB, Calcium channel blockers; ARB, Angiotensin II receptor blockers; NSAID, Nonsteroidal anti-inflammatory drugs

Figure 4. Comparison of Consumption of allopathic medicines on day 1 and day 90 of IRP treatment



The consumption of allopathic medicines on day 1 and after the 90th day of therapy is tabulated in table 6. Most of the enrolled IHD subjects were on treatment of antiplatelet agents (57.89%), NSAIDs (52.63 %), beta blockers, statin and angiotensin II receptor blockers(47.37%) each. The number of subjects on allopathic medicines decreased after 90th day, as compared to the number on day 1. An illustration is given in Figure 4.

Coronary heart disease (CHD), also known as ischemic heart disease (IHD), is considered as one of the most important cause of cardiovascular mortality. Despite the presence of multiple pharmacological agents for managing IHD, there is still a growth in the prevalence of the lethal disease. HTN is known to be an important risk factor for IHD, and it is advised that IHD patients should have their BP in the normal range for better prognosis[8]. Hence, the growing prevalence of HTN is also a major contributing factor for increasing IHD cases. It is important to find novel treatment options for IHD which led us towards Ayurveda. Physicians practicing Ayurveda are using Panchakarma and allied treatment modalities for patients suffering from acute as well as chronic diseases. Hence, it was thought of testing IRP, a

novel Panchakarma technique advocated by Ayurvedic physicians for treatment of IHD, to create evidence for the same.

The Duke Treadmill was assessed to test to evaluate the effect of the IRP in patients with IHD. It was found that at baseline, 47.4% of the patients in our study were at high of cardiovascular events by the Duke score. However, at day 90 of the IRP, none of the patients were at high risk. Only 10.5% of patients were at low risk by Duke score on day 1, which increased to 42.1% after day 90 of IRP, indicating the positive response of the novel treatment modality. The Duke treadmill test has been commonly used by cardiologists worldwide for risk stratification which helps in predicting the outcome in patients suffering from CHD[9, 10]. Hence, this test was picked up as the primary variable to assess the efficacy of the IRP in IHD patients.

Functional capacity, measured by assessing the VO_2 max, is an indicator of the cardio respiratory function of an individual. A compromised VO_2 max is noted in patients suffering from cardiovascular distress, as in IHD, and the extent of decrease indicates the severity of the disease[6]. In this study, the VO_2 max was found to be significantly improved at the end of 90 days compared to the baseline, thereby indicating a betterment in the exercise capacity of the patient. The SBP and the DBP were also reduced by IRP, though the reduction in both were not statistically significant ($p>0.05$). The SBP has been found to have a correlation with aortic stiffness and endothelial dysfunction[11]. Hence, a reduced SBP may be sign of an alleviation of endothelial dysfunction.

The dependency of IHD patients on the conventional allopathic medications elevates the cost of treatment, which is an important issue in a developing country like India. Nevertheless, the exposure of patients to adverse effects of these drugs cannot be ignored. Keeping this in mind, the effect of IRP was assessed on the consumption of allopathic medicines by the patients. It was found that there was a decrease in the patients on allopathic medicines of different classes. Also, one of the patients was completely off the conventional medicines at the end of 90 days.

Cardiac ischemia occurs because of an imbalance between the myocardial demand and supply of oxygen. An increase in the coronary blood flow is the only viable option to meet this demand. If the coronary vessels are under spasm, or if these vessels have some endothelial dysfunction, then this will limit the myocardial blood flow[12]. Artery stiffness is an independent factor which can lead to coronary events. Considering the positive results of the IRP in IHD patients, it can be hypothesized that *Snehana* may be decreasing the sympathetic activity, thereby leading to decrease in the vascular tone. *Swedana* induces sweating, which may lead to peripheral vasodilation and hence, a reduction in the systemic vascular resistance. This will lead to a decrease in the afterload, thereby decreasing the cardiac workload and hence, myocardial oxygen demand. A rise of body temperature due to passive heating significantly elevates the cutaneous vascular conductance following which there is an equivalent increase in systemic conductance. A barometric homeostasis is, thus, maintained[13]. Per rectal drug administration has been associated with a reduction in the oxidative stress, which may help in reducing the myocardial ischemic damage[14]. A study comparative stated that lower part of the gastrointestinal tract is rich with parasympathetic nerves which on stimulation with per rectal drug administration (either by chemical or mechanical receptor) may cause a reduction in secretion of renin-angiotensin-aldosterone complex and may also activate the depressor area of vasomotor center which leads to vasodilatation and decrease in BP[15].

IHD is imbalance of supply versus demand of oxygen to myocardium. Endothelial dysfunction leads to atherosclerotic changes which lead to restricted coronary vasodilation due to low nitric oxide secretion. Decoction of *Tribulus territris* with *curcumin longa* and *Emblica officinalis* may have helped to reduce this endothelial dysfunction and thus, improved coronary vasodilatory reserve which might have reduced myocardial ischemia (Table 7).

This study was an observational retrospective study and thus, prospective studies can be conducted in the future to evaluate IRP in IHD patients to produce stronger evidence. The sample size was small in this study and the period of follow-up was also short. Studies with a bigger sample size and long-term follow-up in IHD patients can indicate the long-term implications of this capable treatment modality.

Table 7. Animal Studies

Herb	Action	Reference
Tribulus territris	Nitric oxide synthesizing and vasodilator	https://www.sciencedirect.com/science/article/pii/S0378874105006562
Curcumin longa	Anti-inflammatory	https://www.ncbi.nlm.nih.gov/pubmed/19594223
Emblica officinalis	Anti-Oxidant	https://www.sciencedirect.com/science/article/pii/S0378874105006057

4. CONCLUSION

Treatment with IRP is associated with an improvement in the Duke Treadmill score, thereby decreasing the risk of cardiovascular events. IRP also improves the VO2 max, thereby leading to betterment in the cardiorespiratory function. There

was a decrease in the BP by IRP, though it was not statistically significant. Future studies need to be conducted to create more evidence to support the use of the IRP in patients with IHD.

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CONFLICTS OF INTEREST None

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Efficacy of Comprehensive Diabetes Care (CDC) Management Program in Elderly Male Patients of Type II Diabetes Mellitus: A Retrospective Study

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Abstract: Globally, Diabetes mellitus (DM) prevalence has created menace, being a major culprit of increased mortality and morbidity and health care expenditures. India is the 2nd country with maximum number of diabetic patients, with an estimated prevalence of around 10%. Comprehensive Diabetes Care (CDC) is a combination of *Panchakarma* and Diet management. This study was conducted to evaluate the effect of CDC on glycosylated haemoglobin (HbA1c), body mass index (BMI), body weight, abdominal girth and dependency on conventional therapy in DM Patients. This retrospective study was conducted from July 2017 to January 2018, wherein the data of elderly male type 2 DM patients (HbA1c >6.5%) who attended *Madhavbaug clinics* in *Maharashtra*, India were identified. Data of patients who were administered CDC (60-75 minutes) with minimum 6 sittings over 90 days (± 15 days) were considered. Variables were compared between day 1 and day 90 of CDC. Out of 48 enrolled elderly male patients, 34 were included for analysis. CDC showed significant improvement in HbA1c from 8.27 ± 0.96to 7.1 ± 1.30; p=0.0001), BMI from 27.65 ± 3.20 to 25.91 ± 3.29, p< 0.0001), weight from 73.75 ± 10.76to 69.46 ± 10.39, p<0.0001). Abdominal girth (from 100.0 ± 9.08 to 95.36 ± 9.10; p<0.0001), also showed significant reduction. Dependency on concomitant medicines was reduced, with number of patients on no concomitant medicines increasing from 3% to 15%. CDC and allopathy both are found to be efficacious; but CDC acts dually, by reducing HbA1c, as well as reducing dependency on allopathic medications.

Keywords: Comprehensive Diabetes Care, CDC, Panchakarma, HbA1C, BMI, DM, Alternative Medicine

1. Introduction

Diabetes mellitus type II (DM) prevalence has reached epidemic levels in global scale. International diabetes federation quotes that number of diabetics in 2030 will rise by estimated 200 million rise in number of cases, as compared to prevalence in 2011 [1]. This is far more concerning in India, where it is estimated that around 1/10th of the population is inflicted by DM, with significantly high mortality rates [2, 3]. Historically, fasting blood sugar level >126 mg/dl and post-meal blood sugar level>140 mg/dl, which together constitute an oral glucose tolerance test is used for diagnosis of DM. Nowadays, glycosylated hemoglobin (HbA1c) is used for diagnosis of DM, as it depicts blood glucose levels over preceding 2-3 months. HbA1c levels >6.5% is diagnostic of DM, while levels less

than 6.5 but more than 5.7% are considered as prediabetics. Most of the guidelines suggest target HbA1c as ≤6.5% [4]. Plethora of complications of DM, grouped as macrovascular and microvascular, short term and long term, makes the disease more dangerous. Stroke, myocardial infarction, peripheral vascular disease are some of the macrovascular complications, while retinopathy, neuropathy and nephropathy are grouped under microvascular complications. However, major culprit for morbidity and mortality in diabetic patients is cardiovascular diseases (CVD) [5]. Foot ulcers, amputations are some of the after effects of diabetic neuropathy, while diabetic nephropathy is one of the major cause of morbidity and mortality in diabetic patients after CVD [6-9]. Diabetes is presently managed by advocating dietary corrections and regular physical exercise along with treatment with oral antidiabetic drugs/oral hypoglycemic agents (OADs). It is recommended to start OAD only when diet management and other measures are unable to bring down levels of HbA1c to < 6.5% after 2 months. The majority of the OADs act by either, reducing the intrinsic glucose production, increasing tissue uptake or increasing excretion. Sulphonylureas, thiazolidinedione, biguanides, etc. are some of the examples of conventional class of antidiabetic drugs. When 1 OAD is unable to reduce the HbA1c below 7.5% or if baseline HbA1c is too high, it is recommended to use combination of OADs from different class [10]. But, major issues faced with the use of OADs are a plethora of adverse effects which include hypoglycemia, pancreatitis, anemia, etc [11]. These adverse effects along with the increased cost of therapy has found to drastically reduce medication adherence in patients of DM [12]. Despite the availability of numerous classes of OADs and extensively laid down guidelines, number of cases of DM are consistently increasing [12]. Thus, an effective alternative therapy is needed, that will counteract these adverse effects of conventional medicines and increase patient adherence to medications for optimal outcome. OADs act by reducing blood sugar levels in the body. Various herbal drugs have shown similar effects in clinical studies, including significant reduction in HbA1c [13-15]. This makes Ayurveda a potential therapeutic alternative in patients of type 2 DM. Ayurvedic physicians advocate Panchakarma- a multi-step body detoxification process in the chronic phase of disease. *Panchakarma* and diet therapy is combined in Comprehensive Diabetes Care (CDC) Management Program. Three techniques are used in *Panchakarma* in CDC- *Snehana* i.e. oleation, *Swedana* i.e. passive heat therapy and *Basti* i.e. per rectal drug administration. *Panchakarma* is a well-known procedure for internal detoxification of the body [16-17]. Since reduction in quality of life, depression are associated with DM, we planned this retrospective study in elderly male patients of type 2 DM, to assess the efficacy of CDC on various parameters like HbA1c, BMI, reduction in body weight, abdominal girth and reduction in dependency on conventional medications after completion of CDC.

2. Subjects and Methods

2.1. Study Design

Retrospective record based study.

2.2. Study Site

Madhavbaug Clinics from all over Maharashtra

2.2.1. Study Period

July 2017 to January 2018.

2.2.2. Study Participants

Elderly male (>60 years), suffering from type 2 DM (HbA1c>6.5%),[4] who attended *Madhavbaug clinics* across *Maharashtra.*

2.2.3. Methodology

The data of patients who had been administered CDC with minimum 6 sittings over a span of 90 days (± 15 days) were considered for the study, out of which 4 sittings were done in the 1st month, and 1 sitting per month for next 2 months. These patients were maintained on a diet plan of 800-1000 calories intake per day, according to patient medical records. The diet plan consisted of low carbohydrates, moderate proteins, and low fats. Cases were identified, and data was assessed from the records of *Madhavbaug clinics* in *Maharashtra*. The selection was based upon the availability of complete relevant baseline data (day 1 of CDC) and final day data (day 90 of CDC) of the patients. The information about prescribed concomitant medicines, if any, was also noted down. On day 1 of CDC, the patients had undergone HbA1c, weight, BMI, abdominal girth measurements as per guidelines [18]. This readings were considered as baseline reading. This process was repeated on day 90 of CDC to calculate the change from baseline reading. The BMI for day 1 and day 90 of the patients was calculated by checking the weight and the height from the medical data sheets of patients and using the formula: *weight in kilograms/ (height in meters)*^{2}. The dependency on standard medication was calculated both on day 1 and day 90 of CDC as the percentage of patients out of the total enrolled ones who required a conventional allopathic therapeutic agent during the study period of 90 days.

The CDC is a 3-step procedure which was performed on the patients of type 2 DM after a light breakfast. One sitting of the procedure took 65-75 minutes, as described in table 1 [19-20].

Table 1. *Study Treatment: Comprehensive Diabetes Care (CDC).*

Step of CDC	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes on the body)	100 ml Azadirechta indica (neem) extract processed in sesame oil	25-30 minutes
Swedana	Passive heat therapy to the body	Dashmoola (group of ten herbal roots) with steam at ≤40	15-20 minutes + 3-4 minutes

Step of CDC	Type of Therapy	Herbs used for therapy	Duration of Therapy
		degrees Celsius)	of relaxation after procedure
Basti kadha	Per-rectal drug administration should be in body for ≥ 15 minutes for maximum absorption	Mixture of 40% Gudmaar (Gymnema sylvestre), 20% Daruharidra (Berberis aristate) and 40% Yashtimadhu (Glycyrrhiza glabra)	10 minutes

2.2.4. Statistical Analysis

Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyze the data. Categorical data were represented in the frequency form and continuous data were presented as the Mean ± SD. Paired t-test was used to assess the difference between baseline values and 90th day after treatment. The histogram were used to represent the graphs.

3. Results

Study population:

A total of 48 patients' data was screened for inclusion in the study. However, based on the availability of data (Day 1 and Day 90) and the inclusion criteria, 34 patients were selected, and their data was considered for analysis. The present study involved a total of 34 male patients with more than 60 years age having a diabetic history and HbA1c ≥ 6.5. The mean age of the patients was 66.32 ± 4.86 years and mean height was 163.34 ± 6.53 cm.

Clinical parameters compared between baseline values and after 90th day was as shown in Table 2. After 90 days of treatment there was significant reduction in the HbA1c (*P=0.0001; Figure 1*). There was significant reduction in weight (P<0.001; Figure 2), BMI (P<0.0001; Figure 3) and Abdomen girth (P<0.0001; Figure 4) post treatment of 90 days.

Table 2. *Comparison of clinical parameters between baseline values and 90th day.*

Variable (n=34)	Baseline	After 90 days	t statistic	p-value
HbA1c	8.27 ± 0.96	7.1 ± 1.30	4.71	0.0001
Weight (Kg)	73.75 ± 10.76	69.46 ± 10.39	10.964	<0.0001
BMI	27.65 ± 3.20	25.91 ± 3.29	7.35	<0.0001
Abdomen girth (n=25)	100.0 ± 9.08	95.36 ± 9.10	8.1	<0.0001

HbA1c; Glycated haemoglobin, BMI; Body mass index

Table 3. *Correlation of BMI and Abdomen girth with HbA1c at 1st day and after 90 days.*

Correlation between	Baseline		After 90 days	
	R	p-value	r	p-value
BMI and HbA1c	0.05	0.76	0.07	0.69
Abdomen girth and HbA1c	-0.049	0.82	0.05	0.81

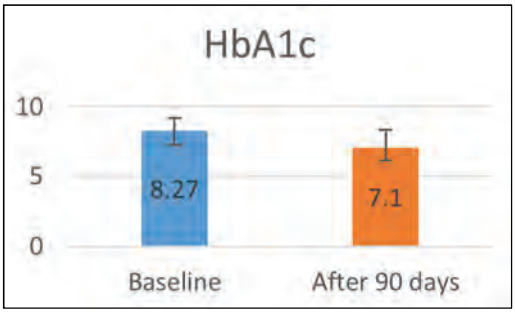

Figure 1. *Comparison of HbA1c at baseline and after 90 days.*

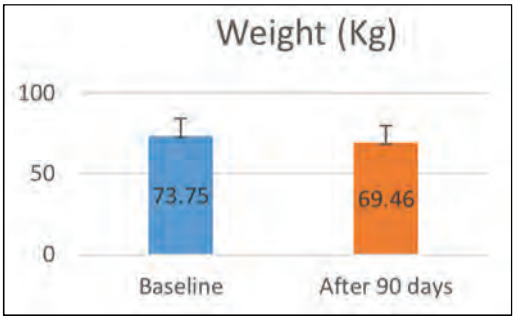

Figure 2. *Comparison of weight of the patients at baseline and after 90 days.*

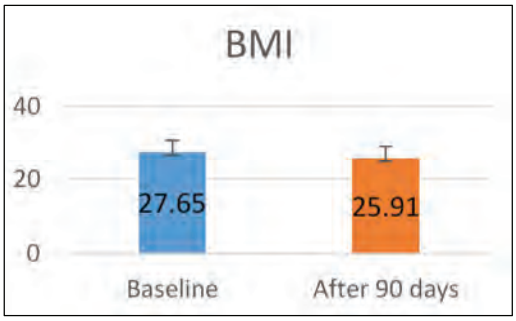

Figure 3. *Comparison of BMI of the patients at baseline and after 90 days.*

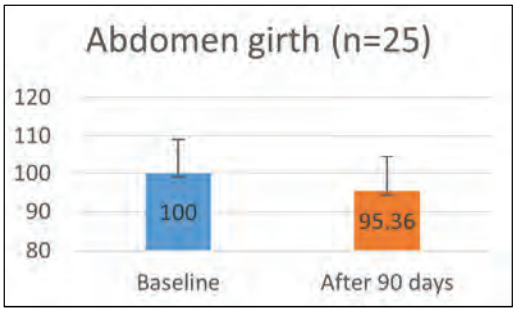

Figure 4. *Comparison of Abdomen girth of the patients at baseline and after 90 days.*

We also assessed the correlation between the BMI and HbA1c, abdominal girth and HbA1cb (table 3). There was a weak positive correlation between BMI and HbA1c (r= 0.05) on the 1st day of the treatment and it was not statistically significant (p=0.06), the same is shown in figure 5a. After 90 days of treatment we found nearly same positive relationship between BMI and HbA1c (r=0.07, p = 0.70) which is shown in figure 5b.

We found a negative relationship between HbA1c and abdomen girth (r= -0.049) on the 1st day of the treatment which was not statistically significant (p = 0.82) (figure 5c). We found a weak positive relationship between them after the treatment (r=0.051) on day 90, and it was not statistically significant (p = 0.81) (figure 5d).

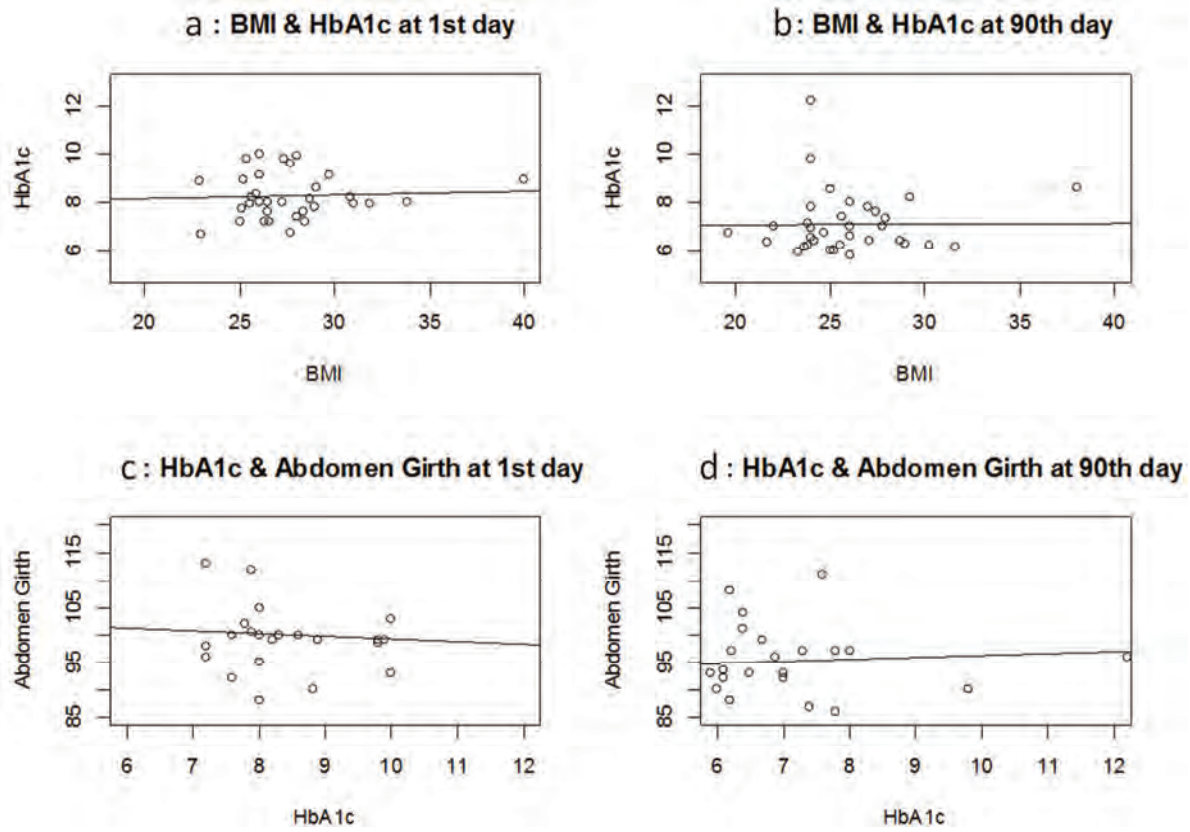

Figure 5. *Correlation between BMI and HbA1c, abdomen girth and HbA1c.*

Allopathic medicines consumption on day 1 and after the 90th day of therapy were as shown in Table 4. Most of the enrolled subjects were treated with biguanides (58.82%), sulfonylurea (38.24%), nonsteroidal anti-inflammatory drugs (35.29%), statin (29.41%). All the subjects who were allopathic medicines before therapy was decreased after 90th day. However, the subjects with nonsteroidal anti-inflammatory drugs were not varied after the therapy. An illustration is given in figure 6.

Table 4. *Consumption of allopathic medicines on day 1 and after 90 days.*

Medicine	Day 1	After 90 days
Sulfonylurea	13 (38.24)	10 (29.41)
Biguanide	20 (58.82)	13 (38.24)
Thiazolidinedione	4 (11.76)	2 (5.88)
DPP-4 inhibitor	8 (23.53)	5 (14.71)
Alpha-glucosidases inhibitors	5 (14.71)	3 (8.82)
Insulin	3 (8.82)	3 (8.82)
NSAID	12 (35.29)	12 (35.29)
Statin	10 (29.41)	6 (17.65)
ARB	8 (23.53)	6 (17.65)
Beta blocker	5 (14.71)	2 (5.88)
CCB	6 (17.65)	5 (14.71)
Antiplatelet	7 (20.59)	7 (20.59)
Nitrate	1 (2.94)	1 (2.94)
No medicine	1 (2.94)	5 (14.71)

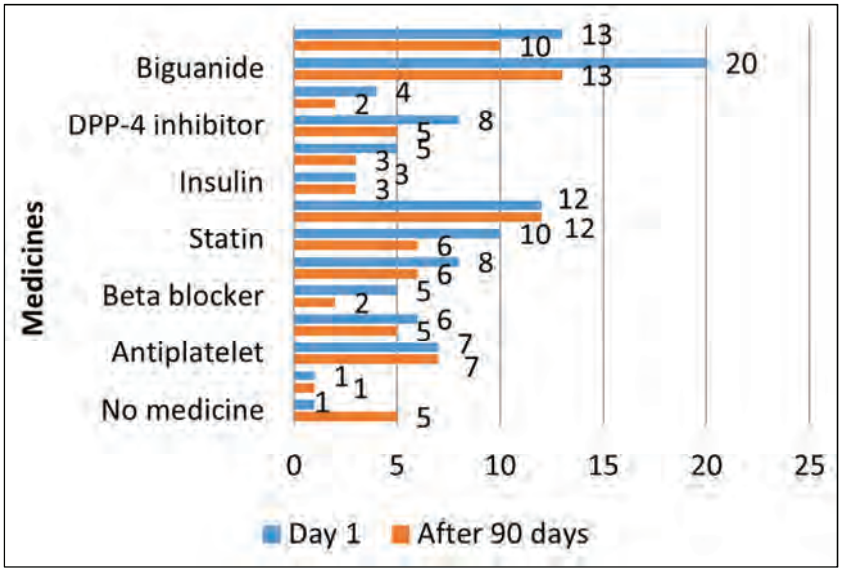

Figure 6. *Comparison of consumption of allopathy medicine at 1st day and after 90 days.*

4. Discussion

Despite the availability of a plethora of therapeutic options for treatment of type II DM, its prevalence and contribution to global morbidity and mortality remains significantly high and is increasing continuously. Therefore, alternate therapeutic option to curb the menace of DM is the urgent necessity of current time. Conventionally used allopathic medicines in the treatment of type II DM act by reducing blood sugar levels. Ayurvedic medicines serves as a potential alternate therapeutic option for management of type II DM, since many herbal drugs have been found to significantly lower blood glucose levels in clinical studies. Ayurvedic physicians administer Panchakarma to the patients of DM [16]. Panchakarma along with diet therapy consisting of low carbohydrates and fats with moderate amount of proteins is administered in CDC. Probable mechanism, by which CDC might benefit patients with type II DM are:

1. Reducing glucose production in the liver by hampering sympathetic stimulation on gluconeogenesis,
2. Reducing the shear stress of vascular endothelium by promoting water loss via sweating. This may help in reducing vascular complications significantly [16].

In the present study, the CDC was found to significantly reduce ($p<0.001$) HbA1c, BMI, body weight, abdominal girth, at the end of study period i.e. 90th day. Another crucial finding of our study was that there was significant reduction in patients' dependency on conventional allopathic antidiabetic medications at the end of the study period.

HbA1c value is one of the most crucial parameter in diabetic patients as it echoes blood sugar level control over preceding 2-3 months [4]. Another important feature of HbA1c is its prognosticator value in type 2 DM, since it has been found that morbidity and mortality is directly related to sustained increased HbA1c [21]. Thus it can be anticipated from the findings of our study that CDC carries a good prognosis in diabetic patients as it significantly reduces HbA1c. Obesity and sedentary lifestyle contribute to development of DM, which is indicated by increased BMI [22]. Apart from DM, high BMI has epidemiological linkage with many chronic diseases like HTN and other CVDs [23]. Sustained control of blood sugar levels is the utmost important factor in diabetic patients, since it has been established that poor blood sugar level control is associated with increased incidence of complications [24]. CDC can help in reducing complications of DM since it showed sustained reduction in all parameters like HbA1c, BMI, body weight, etc.

Another major issue with the use of conventional drugs is increased cost of therapy along with increased incidence of adverse effects associated with use of these drugs [25]. Hence, we assessed the effect of CDC on dependency on conventional medications. In our present study, we found that there was an overall reduction in dependency of patients on conventional medications at the end of the study period. Also, the number of patients who went off the conventional drugs increased at the end of 90th day.

In order to generalize the findings of our study to the larger population, we recommend conduction of similar studies with dual arms, to allow direct comparison with conventional therapy, prospective design, and long follow up period with larger sample size.

5. Conclusion

Major parameters of the body deranged in DM are BMI, body weight, abdominal girth all of which worsen complication rate. Although conventional correct these parameters to some extent, cost of therapy and adverse effects offset their beneficial effects and decrease patient compliance. CDC corrected all these parameters effectively and also reduced dependency on conventional drugs, all of which have positive contributory effect on enhancing patient compliance. Thus it is safe to conclude that CDC can be

considered as effective and safe therapeutic option for treatment of DM.

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Original Research Article (Clinical)

Efficacy of heart failure reversal treatment followed by 90 days follow up in chronic heart failure patients with low ejection fraction

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ABSTRACT

Background: Heart failure reversal therapy (HFRT) is designed to enhance cardiorespiratory fitness of chronic heart failure (CHF) patients.
Objectives: The present study was designed to evaluate efficacy of HFRT that uses herbal procedure (*panchakarma*) and allied therapies, in CHF patients with low ejection fraction.
Methods: This efficacy study was conducted in CHF patients (aged: 25–65 years, ejection fraction (EF) 10–30%) wherein HFRT (60–75 min) consisting of *snehana* (external oleation), *swedana* (passive heat therapy), *hrudaydhara* (concoction dripping treatment) and *basti* (enema) was administered twice daily for 7 days. During this therapy and next 30 days, patients followed the study dinarcharya and were prescribed ARJ kadha in addition to their conventional treatment. The primary endpoint of this study was evaluation of maximum aerobic capacity uptake (MAC) as assessed by 6 min walk distance (6MWD) using Cahalins equation from baseline, at the end of 7 day treatment, follow-up after 30 days and 90 days. EF was assessed by 2D Echo at baseline and after 30 days of follow-up.
Results: Fifty-two CHF patients with 10–30% EF (mean [SD] age: 58.8 [10.8], 85% men) were enrolled in the study. There was a 100% compliance to study therapy. A significant improvement was observed in MAC levels (7.11%, $p = 0.029$), at the end of 7 day therapy as compared to baseline. This improvement was maintained at two follow-up visits. Moreover ejection fraction was observed to be increased by 6.38%, $p = 0.012$ as compared to baseline at day 7 of the therapy.
Conclusion: This 90 day follow up study highlights the benefit of HFRT, as a part of maintenance treatment for CHF patients with reduced ejection fraction.
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1. Introduction

The estimate of prevalence and incidence of chronic heart failure (CHF) in India is often unreliable. However, there is a growing burden of CHF with an estimated annual incidence of 0.5–1.8 million [1]. Therefore, immense research work is performed to identify newer therapeutic targets to combat CHF, also guidelines for management of CHF are updated [2–4]. Although conventional medicinal therapy has improved over a decade, the overall survival of CHF patients may be unsatisfactory due to lowered ejection fraction or low aerobic capacity in CHF patients leading to increasing rates of mortality and morbidity. Perhaps complementary and alternative medicines can be of benefit as an adjuvant therapy for better management of CHF.

In India, Ayurveda is considered as a traditional medical system. Moreover, several studies have shown effectiveness of panchakarma therapy to treat various diseases. Panchakarma therapy is a 5-step ayurvedic procedure that is known to eliminate harmful toxins from the body thereby providing maximum health benefit to the patient [5]. Heart failure reversal therapy (HFRT) is one of its kind therapy designed to enhance cardiorespiratory fitness of CHF patients. HFRT uses techniques described in panchakarma namely *snehana* (massage), *swedana* (fomentation therapy) and *basti* (type of enema) along with *hrudayadhara* (oil dripping therapy) [5–8].

According to Ayurveda, dysfunctional *rasa dhatvagni* is a cause of *Hrudrog* (heart disease). In this study we quantify CHF patients leading to increasing rates of mortality and morbidity as maximum aerobic capacity (MAC). Present scientific study aimed to evaluate

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efficacy of HFRT as an adjuvant therapy in CHF patients with low ejection fraction.

2. Methods

2.1. Study population

Study participants included patients (both gender, aged 25–65 years) with CHF (New York Heart Association, NYHA Class I–III) and EF > 30 as measured by a two dimensional echocardiogram (2D-ECHO).

Additional inclusion criteria were blood pressure not >150/90 mmHg, hemoglobin levels ≥ 10 g/dL and blood glucose levels: fasting not <60 mg/dL and postprandial not >250 mg/dL.

Patients with suspected hypersensitivity to study therapy or unsuitable to receive study therapy (e.g. irritable bowel syndrome, bleeding piles or fistula (grade-I or II piles), 2 nd/3 rd degree hemorrhoids, asthma or chronic obstructive pulmonary disease) or patients with acute heart failure, decompensated heart failure attack (last 3-months), abnormal hepatic/renal/thyroid function test, cancer, physical disability (any form) leading to immobilization or those with participation in another study 30-days prior to screening were excluded. Cardiac patients needing upward dose titration or not on stable dose of SCT (last 3-months) were excluded and so were pregnant or lactating women.

The study was conducted in accordance with the ethical principles in the Declaration of Helsinki, consistent Good Clinical Practices. All patients provided written informed consent to participate in the study.

2.2. Study design

This study was conducted from April, 2015 to March, 2016 at Madhavbaug Hospital, Khopoli (Fig. 1).

The enrolled HF patients received HFRT, twice/day for 7 days. During this therapy and next 30 days, patients followed the study dinarcharya (Table 1) and were prescribed 10 ml of ARJ kadha, BD (decoction of *Terminalia arjuna*, *Acorus calamus* and *Boerhaavia diffusa* manufactured by Dynamic remedies) in addition to their conventional treatment.

2.3. Study therapy

The HFRT is a combination of panchakarma and allied therapies. HFRT uses various decoctions and oils (Fig. 1) and constitutes of a 4-step procedure as described below:

1. *Snehana*/external oleation or massage (~30–35 min): An oil based decoction was used to administer external massage to the HF patients. This massage technique uses centripetal or upward strokes directed towards the heart.
2. *Swedana*/passive heat therapy (~10–20 min): To administer this therapy HF patients were asked to lie in a supine position inside a sudation box and their head was positioned outside the box. Dashmoola (group of ten herbs) steam of temperature not more than 40 was then passed steadily for 10–15 min. After the treatment, patients were asked to relax for 3–4 min.
3. *Hrudaydhara*/variation of shirodhara technique (~15 min): During this technique, luke-warm dashmoola decoction was allowed to drip at a constant speed from a fixed height on the medial mediastinum region of the HF patients demarked by a hrudayapatra.
4. *Basti*/medicated enema (~15 min): A medicated enema was administered to HF using a rectal solution that remains inside the body ≥15 min for maximum absorption.

The entire HFRT treatment was performed after a light meal/breakfast and total administration duration was 65–75 min.

2.4. Study evaluations

Primary endpoint was improvement from baseline (before HFRT treatment) in MAC as assessed by 6 min walk distance (6MWD) using Cahalins equation, at the end of 7 day treatment, follow-up at 30 days and 90 days.

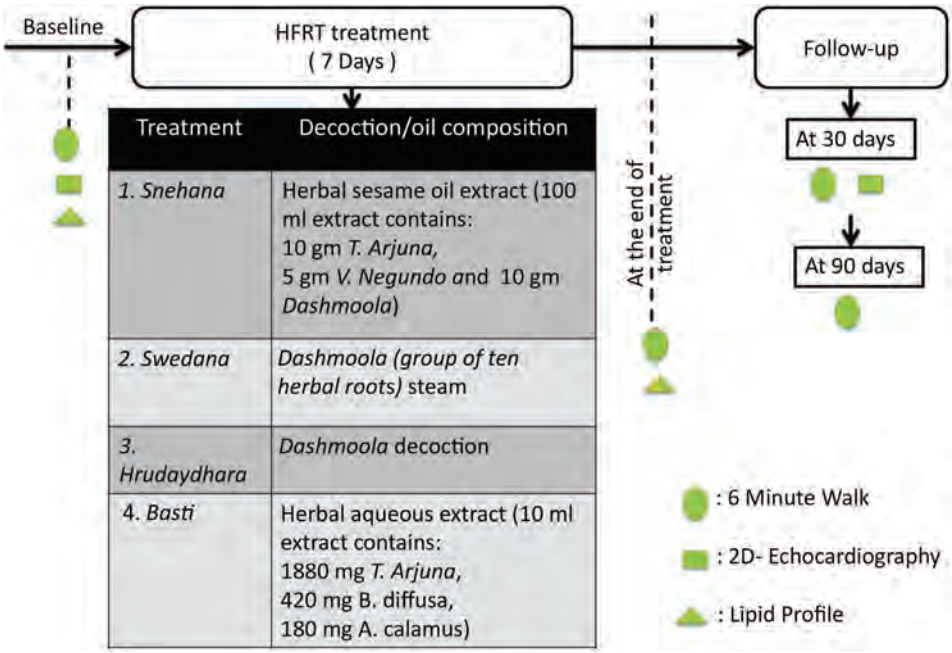

Fig. 1. Study design and therapy.

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Table 1
Study *Dinacharya*.

Activity	Benefit	Inclusion in daily schedule
Wake up early	Improves health, help to excrete, metabolic wastes.	4:30 am
Medicated abhyang	Daily abhyanga rejuvenates body along with it reduces *Shrama* (*breathlessness on exertion*) typical sign of chronic heart failure. It improves quantity of life, quality of sleep, reproducing power of cells.	Twice a day for 7 days then advised for once a day before bath
Exercise	It improves functional capacity, it can improve *Koshthagni* as well as *Dhatwagni* including *rasdhatwagni*	First 7 days walking for 30 min, cycling at speed of 10 km/h and Yoga under supervision of physiotherapist.

References from Ashtanghrudaya Sutrsthan 2nd chapter.

Secondary endpoints included improvement from baseline, in EF (monitored by 2D Echo, after 30 days of follow-up) and lipid profile (at the end of 7 day treatment).

Patient reported outcomes are not considered as efficacy endpoints in this study.

2.5. Statistical methods

2.5.1. Statistical analyses

Statistical analyses were performed using SPSS software version 22 (Chicago, Illinois, USA). The parametric variables are depicted as mean (standard deviation) while non-parametric variables are reported as median (range). The mean change in efficacy endpoints between the time-points was analyzed using non-parametric analysis with baseline values as covariates.

3. Results

3.1. Study population

Out of the 82 screened CHF patients, 52 were enrolled in the present study and received HFRT in addition to their conventional treatment. The study population had mean [SD] age of 53.0 [8.6] years and comprised of 44 (84.6%) men. The baseline demographic and clinical characteristics were comparable among the CHF patients (Table 2). All enrolled patients with CHF completed the 14 sittings of HFRT and the follow-up visits (100% compliance).

3.2. Efficacy measurements

The primary efficacy endpoint was analyzed at baseline, at the end of 7 day treatment, follow-up after 30 days and 90 days.

Table 2
Baseline and clinical characteristics.

Parameters	Total ($N = 52$)
Age, years, mean (SD)	58.8 (10.9)
Men, *n* (%)	44.0 (84.6)
Weight, kg, mean (SD)	62.6 (11.2)
Body mass index, kg/m^2, mean (SD)	23.7 (3.7)
Medical history	
Diabetes, *n* (%), yes	25 (48.1)
Hypertension, *n* (%), yes	19 (36.5)
Intervention	
PTCA	1 (1.9)
CABG	8 (15.4)
Concomitant medicines	
Non-steroidal anti-inflammatory drugs	17 (32.7)
Angiotensin receptor antagonists	12 (23.1)
Vasodilators	10 (19.2)
β-blockers	8 (15.4)
Calcium channel blockers	7 (13.5)
Diuretics	6 (11.5)
ACE inhibitors	4 (7.7)
No record available	16 (30.8)

Patients with CHF showed significant improvement in MAC_{levels} (7.11%, $p = 0.029$), at the end of 7 day treatment as compared to baseline. This improvement was maintained at two follow-up visit (Fig. 2).

Secondary efficacy endpoints namely EF showed significant improvement (6.38%, $p = 0.012$) at 30 day follow-up visit (Median (range): 25.0 (22.0/29.75)) as compared with baseline (23.5 (20.0/26.0)).

The serum lipid levels i.e. HDL-cholesterol and LDL-cholesterol were increased leading to an increase in total cholesterol levels, at the end of treatment as compared with baseline whereas VLDL-cholesterol levels and triglyceride levels were decreased (Table 3).

3.3. Safety and tolerability

Overall, no TEAEs, abnormal laboratory results or ECG values were reported from baseline to follow-up.

4. Discussion

Chronic Heart Failure is inability of heart to pump sufficient amount of oxygenated blood, which is required for normal metabolic activity of body. Factors like high blood pressure, uncontrolled diabetes, valvular heart diseases and ischemic heart disease can lead to dysfunction of myocardium which in turn may cause CHF [9]. The CHF is also referred as a disabling disease mainly because patients suffer from fatigue and delayed recovery after exertion due to reduced MAC. Therefore, MAC is considered as a strong predictor of mortality [10].

According to Acharya Charak if agni of an individual is vitiated, the entire metabolic activity in the body is disturbed and the person suffers from disease. Ayurveda uses an umbrella term 'Hrudrog' for cardiac problems.

In Ayurveda all causes of heart disease are dysfunctional *rasa dhatvagni* which causes production of poor quality of *rasa dhaatu* which when goes in heart cause various cardiac diseases. This *dhatvagni* or bioenergy can be denoted by metabolic rate. Ratio of metabolic rate at rest and during exercise is denoted as metabolic equivalent (Met) value and Met × 3.5 = MAC. Hence MAC can be correlated with *rasa dhatvagni*, suggesting that reduced MAC may cause *rasa dhatvagni maandya* (reduction in function of *rasa dhatvagni*) which may lead to *Hrudrog*. [11].

This is a first follow-up study to report that 7 day HFRT improves MAC of CHF patients with low ejection fraction (<30) and is maintained for 90 days after the therapy.

There is a plethora of literature related to different methods of MAC estimations. However 6MWT is known to be most convenient and affordable test for MAC estimations [12].

Over the years, several equations for MAC estimation based on 6MWT were developed depending upon the population. For heart failure, various MAC equations are proposed namely Lipkin 1986, Cahalin 1996, Faggiano 1997, Roul 1998, Lucas 1999, Opasich 2001 etc. Several studies have highlighted that a good correlation

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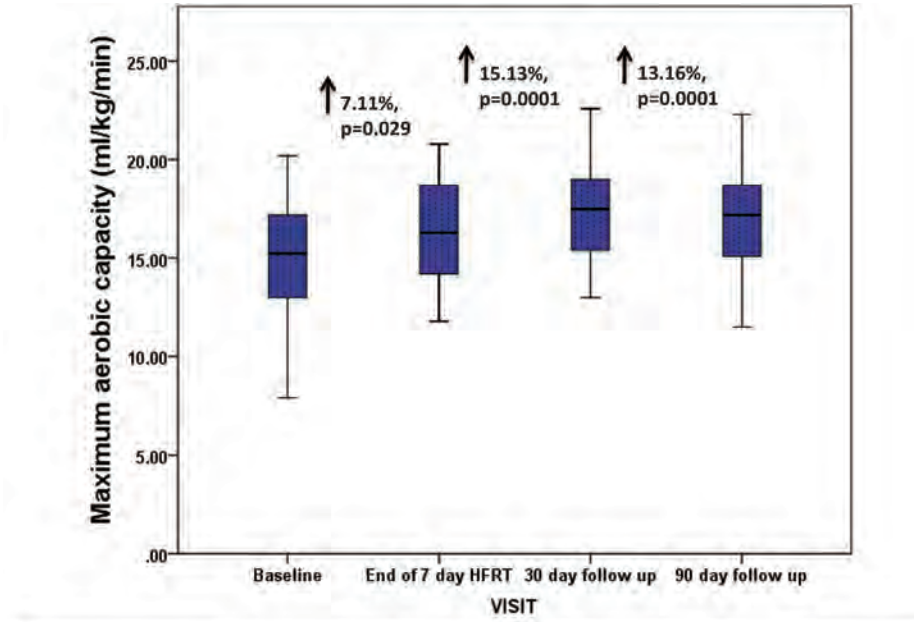

	Baseline	7 day	30 day	90 day
Maximum Aerobic Capacity (Median (Range))	15.2 (12.9 / 17.2)	16.28 (14.03 / 18.68)	17.5 (15.3 /19.1)	17.2 (15.1 / 18.8)

Fig. 2. Maximum aerobic capacity estimations.

Table 3
Lipid profile.

$N = 52$	Baseline	At the end of 7-day HFRT treatment
Total cholesterol	132.9 114.15/161.075	153.2 138.5/180.8 $p =$ **0.011**
HDL cholesterol	39.6 33.15/48.8	40.8 34.8/50.8 $p = 0.231$
LDL cholesterol	73.4 58.1/96.2	92.5 75.0/115.7 $p =$ **0.010**
VLDL cholesterol	20.8 15.8/25.5	19.8 16.7/26.0 $p = 1.00$
Triglycerides	103.8 78.8/127.5	99.0 83.4/130.1 $p = 0.997$

HDL: high density lipoprotein, HFRT: heart failure reversal therapy, LDL: low density lipoprotein, LV: left ventricular, 6-MWD: 6-minute walk distance, VLDL: very low density lipoprotein.
Results are reported as median (range). The difference between the parameters at each visit is evaluated using Mann–Whitney *U* test. *p* value < 0.05 is considered significant.

equation between 6 minute walk distance and MAC has low standard error of estimate (SEE) [12–18]. Therefore present study uses improved Cahalin et al., 1996 correlation equation that has lower SEE as compared to other equations.

Our results corroborate with several other studies that highlight, the improved MAC level is prognostic marker for CHF. However, these studies had different interventions such as exercise, etc. A retrospective study, even associated 1 unit (mL/kg/min) increase in MAC with ~15% decrease in risk of mortality [19]. Additionally, the result of current study underlines the improvement in MAC reported by earlier studies with HFRT as an intervention [7,8].

HFRT, as described earlier uses several herbs such as *T. Arjuna*, *Vitex negundo* and/or *B. diffusa* that are reported to increase antioxidant reserves. *A. calamus* possesses hypolipidemic activity. Also, the Dashmoola formulation has anti-inflammatory, analgesic and anti-platelet effect [20–26]. These herbs used in HFRT, provide an additional cardiac conditioning to CHF patients.

In the present study, there is a statistically significant increase in LDL-cholesterol and total cholesterol levels. But this change did not have viable clinical significance as the increased levels of LDL-cholesterol and total cholesterol were within the diagnostic normal range. Moreover, it should be noted that LDL-cholesterol is not harmful unless there is inflammation and a simultaneous increase in HDL-cholesterol levels may indicate less chance of progressive inflammation [27].

Additionally, HFRT is a combination of panchakarma and allied therapies which is known to have a nourishing effect on the body. Therefore, this treatment may have added to nutritive value of rasa dhatu as shown by changed serum lipid levels.

However, the present study had a small sample size and was restricted to CHF patients with reduced ejection fraction. Future studies in a larger sample-size and different levels of CHF severity are warranted to establish HFRT as a part of maintenance treatment for patients with CHF.

5. Conclusion

HFRT promises significant therapeutic effects with improvement in MAC and no safety concerns. This non-invasive ayurvedic regime can be considered as a good candidate to be included in maintenance treatment of patients with CHF.

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Conflict of interest

Dr. RM is an employee of Vaidya Sane Ayurvedic Education and Agricultural Trust. Dr. RS received honoraria from Vaidya Sane Ayurvedic Education and Agricultural Trust.

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