

ROLE OF ISCHEMIA REVERSAL PROGRAM TO REDUCE MYOCARDIAL ISCHEMIA STUDIED WITH CARDIAC STRESS TESTING: AN OBSERVATIONAL STUDYRohit Sane¹, Pramod Manohar², Rahul Mandole^{3*}, Gurudatta Amin⁴ and Pravin Ghadigaokar⁵¹MD Ayurveda, Managing Director, Madhavbaug Cardiac Hospitals and Clinics, India.²BAMS, Head of Madhavbaug Khopoli Cardiac Hospital, Thane, Maharashtra, India.³BAMS, Head of Department of Research & Development, Madhavbaug Cardiac Clinic and Hospital, Thane, Maharashtra, India.⁴BAMS, Chief Medical Officer, Madhavbaug Cardiac Clinic and Hospital, Thane, Maharashtra, India.⁵BAMS, Head Medical Operations, Madhavbaug Cardiac Clinic and Hospital, Thane, Maharashtra, India.**Corresponding Author: Rahul Mandole**

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ABSTRACT

Background: Heart problems are considered a global epidemic, with cardiovascular disease being spread all over the world. Ischemia Reversal Program (IRP) is a form of Ayurvedic therapy which combines use of panchkarma and allied therapy in the management of IHD. **Aim and objectives:** The present study was planned to study the effectiveness of IRP therapy in patients of myocardial ischemia attending Madhavbaug clinics in Vidarbha region, Maharashtra. **Materials and methods:** This was a retrospective study conducted from June 2019 to December 2019, wherein we identified the data of patients suffering from IHD (positive for inducible ischemia from stress test) of either gender or any age, and who had attended the out-patient departments (OPDs) at Vidarbha region, Maharashtra, India. The data of patients who had been administered IRP with minimum 7 sittings over a span of 12 weeks were considered for the study. **Results:** In the present study, medical records of 50 patients of IHD were analyzed. At the end of IRP therapy there was statistically significant reduction in weight, BMI, SBP, and DBP. VO₂ peak was improved at the end of therapy i.e. 26.51±5.93 mL/kg/min as compared to baseline i.e. 15.62±5.36 mL/kg/min and the difference was highly statistically significant (p<0.001). DTS improved from -2.93±5.88 at baseline to 3.21±6.03 at week 12 of IRP therapy and the difference was highly statistically significant (p<0.0001). **Conclusion:** Findings of present study suggest that IRP can serve as effective therapeutic option for the management of myocardial ischemia.

KEYWORDS: Ischemic Heart Disease, Ischemia Reversal Program, Ayurveda, Panchkarma, VO₂ peak, Dukes Treadmill score.

INTRODUCTION

Heart problems are considered a global epidemic, with cardiovascular disease being spread all over the world. Although the general trend has been the decline in its prevalence in developed countries, it has become a problem in developing countries such as India.^[1] It is estimated that about 75 percent of heart deaths occur in developing countries, while the lowest number of deaths are known in developed countries, probably due to better health care services. The main cause of cardiovascular mortality is coronary heart disease (CHD), a common cardiovascular disease (CVD) similar to congenital heart disease (IHD). According to published scientific literature, the prevalence of IHD in India has grown from 2% in 1960 to 14% in 2013.^[2] The increase in the number of IHD is allowed in a number of areas including urban migration and lifestyle changes.^[3] The growing trend in India's cardiovascular disease is evident in the

last few years, with 20.6% of deaths occurring in 1990, rising to 29.0% in 2013.^[4]

These life-threatening illnesses are not curable. Persistently, this leads to an imbalance of demand and the provision of oxygen to the muscles, a specific myocardium. And the progression of these hemodynamic modifications eventually led to damage to the vascular endothelium.^[5]

Due to the multitude of activities, the management of IHD is not always straightforward. Treatment options should be done after looking at age, comorbidities, interaction drugs, etc. Therefore, it is necessary for an hour to explore another new treatment that will not only work to control the disease but also help to reduce the anxiety, fear, and medical costs associated with IHD.^[6] The main purpose of treatment in IHD is to restore the

balance between demand and supply of oxygen to the muscles, improve blood pressure (BP), antiplatelet action, reduce oxidative stress, etc. It has been proven in various studies that most herbal remedies have these effects, so these drugs may serve as a potential treatment option in the management of IHD.^[6] Moreover, patient compliance is one of the major challenge for optimal outcomes in management of IHD.^[7] Thus, it is the need of the hour to explore for a novel therapeutic option which will not only control the disease activity but also help to improve the patient compliance.

Ayurveda is a pillar of traditional Indian medicine, used by many different doctors in the treatment of various ailments. Panchakarma and combined therapies are administered by Ayurvedic physicians to bring relief to patients suffering from various ailments. One of the integrated approaches to the management of IHD patients is the management of the Ischemia Reversal Program (IRP) Kit. This IRP treatment method involves the incorporation of Snehana (Centripetal oleation), Swedana (Thermal vasodilation), and Basti (through the control of certain drugs), which are known to bring recovery to IHD patients.^[6]

Although there is scientific evidence available on the improvement of exercise capacity in IRP patients treated with IRP,^[6] still the data is scarce in Vidarbha region of India. Hence the present study was planned to assess the

effectiveness of IRP in patients of known IHD from Vidarbha region of India.

Subjects and Methods

This was a retrospective observational study conducted between June 2019 to December 2019. The study used data of patients with IHD who were assessed for the presence of inducible cardiac ischemia using exercise treadmill testing. Male or female patients of any age were included in this study. These patients had attended the out-patient departments (OPDs) of various Madhavbaug clinics located in Vidarbha, India. Only the data of patients who had been administered an IRP package with a minimum of 7 sittings over a period of 90 days (± 15 days) were considered for this study. The inclusion of patient data files for this retrospective analysis, was based on the availability of complete relevant baseline data (on Day 1 of the IRP) and final day data (on Day 90 of the IRP).

Of a total of 54 data files screened for availability of complete data (on Day 1 and Day 90 of the study), 50 patient files were selected and their data were considered for analysis.

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.^[6]

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	<i>Dashmoola</i> (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 <i>GHA</i> decoction 100 ml	15 minutes

Where: GHA stands for Gokshura/Tribulus terrestris (antihypertensive action, antispasmodic, hypolipidemic, cardioprotective actions); Haridra/Curcuma longa (hypotensive, anticoagulant, antioxidant); Amalaki/Embllica officinalis (cardioprotective, hypolipidemic, antioxidant).^[8-12]

Baseline recordings of Duke's treadmill score (DTS), VO₂ peak, DBP, SBP, MET and other secondary parameters like body mass index (BMI) as per standard recommendations.^[6] These parameters were again recorded at week 12 of IRP therapy. The dependency on standard medication was calculated both at baseline and week 12 of IRP as the percentage of patients out of the total enrolled ones who required a conventional allopathic therapeutic agent during the study period.

Duke's treadmill Score (DTS) is calculated by the formula^[12]

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.

The DTS is typically used for stratifying patients based on their risks and typically ranges from -25 to +15. Depending on the score, the patients were categorized into risk groups as shown in table 2.

Table 2: Risk groups of patients of IHD according to Duke's treadmill score (DTS).^[12]

Risk Category	DTS criteria	Need for coronary angiography	4- year survival
Mild	≥ 5	No	99%
Moderate	+4 to -10	May require	-
Severe	≤ 10	Requires	79%

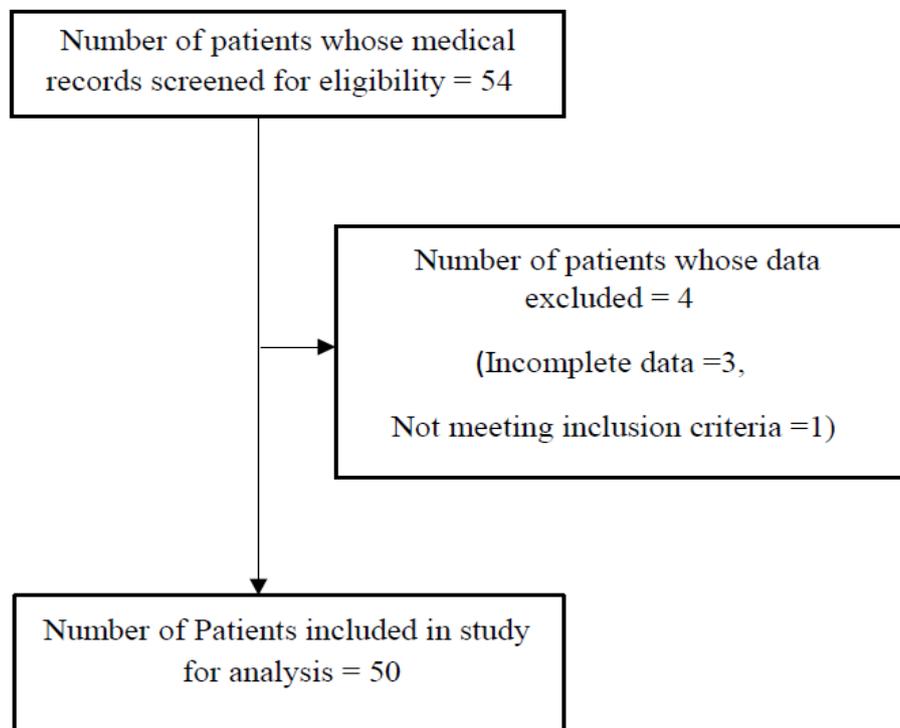
The maximum volume of oxygen that an individual can consume during intense, whole-body exercise is called as VO₂max/ maximal aerobic capacity (ml/kg/min). A metabolic equivalent (MET) is defined as the amount of oxygen consumed by an individual at rest (also known as resting energy expenditure) ie, approximately 3.5 ml O₂/kg/min.^[13]

For the present study MET values were classified into three levels of exercise intensity: light exercise (<3.0 METS) an activity that results in only minimal perspiration and a very slight increase in breathing above normal; moderate exercise (3.0 to 6.0 METS) an activity that results in definite perspiration and above normal breathing; and heavy exercise (>6.0 METS) an activity that results in heavy perspiration and heavy breathing.^[14]

Patient compliance was noted by evaluating the number of patients who successfully completed the IRP therapy for 12 weeks.

Statistical analysis: Data were pooled and coded in Microsoft Excel spreadsheet. R Version 3.4.1 software was used to analyse the data. Categorical data were represented in the frequency form and continuous data were presented as the Mean \pm SD. McNemar-Bowker test was used to assess Duke treadmill score before and after week 12 of treatment. Paired t-test was used to assess the difference between baseline values and 12 weeks after treatment. Box plot and histogram were used to represent the graphs.

Patient record data selection for the present study is depicted in figure 1.

**Figure 1: Patient record selection for the present study.**

RESULTS

In the present study, medical records of 50 patients of IHD were analyzed. Mean age in the present study was 59.42 ± 10.36 years. Out of these, 26 were male (52%) and 24 were females (48%). Thus, male: female ratio was 1.08 (table 3).

Table 3: Baseline characteristics of the study subjects (n= 50)

Variable	N = 50
Age (years)	59.42 ± 10.36
Gender	
Male	26 (52%)
Female	24 (48%)

Data was expressed in % and mean \pm SD

At the end of IRP therapy there was statistically significant reduction in weight as compared (63.24±10.16 kg) to baseline (67.62±9.85 kg) with a p-value of 0.01. Similar trend was observed in BMI, SBP, and DBP. VO₂ peak was improved at the end of therapy i.e. 26.51±5.93 mL/kg/min as compared to baseline i.e.

15.62±5.36 mL/kg/min and the difference was highly statistically significant (p<0.001). DTS improved from -2.93±5.88 at baseline to 3.21±6.03 at week 12 of IRP therapy and the difference was highly statistically significant (p<0.0001) [table 4].

Table 4: Summary of mean change observed from baseline after 12 weeks for different parameters.

Parameter	Baseline	After 12 weeks	p-value
Weight	67.62±9.85 kg	63.24±10.16 kg	0.01
Body Mass Index	26.14±5.22 kg/m ²	23.72±5.78 kg/m ²	0.04
Systolic Blood Pressure	132.82±20.25 mmHg	123.92±18.36 mmHg	0.01
Diastolic Blood Pressure	80.21±11.36 mmHg	72.37±9.74 mmHg	0.01
VO ₂ Max	15.62±5.36 mL/kg/min	26.51±5.93 mL/kg/min	<0.001
Duke Treadmill Score (DTS)	-2.93±5.88	3.21±6.03	<0.0001

On analyzing the angina index, it was found that mean angina index was 1.44 at baseline and it reduced to 0.41 at week 12 of IRP (p<0.001) [figure 2].

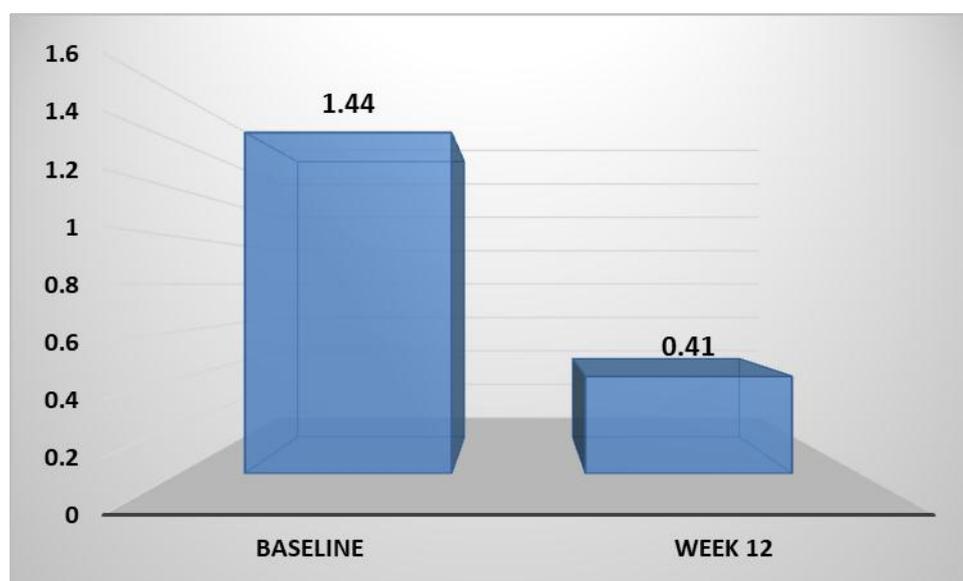


Figure 2: Mean Angina index in patients of the IHD in the present study.

On analyzing the DTS, number of patients in low risk category increased from 11 (30%) at baseline to 23 patients (62%) at 12 weeks of IRP therapy. Similarly, there was reduction in number of patients in moderate to

severe risk categories after 12 weeks of IRP therapy. Overall there was shift of patients from severe risk to low risk group. The difference was highly statistically significant (p<0.001) [table 5].

Table 5: Duke's trade mill score in patients of IHD in the present study.

Timeline	Duke's treadmill score (DTS) [n=37]			p-value
	Low risk (≥5)	Moderate risk (-10 to 4)	Severe risk (≤ -11)	
Baseline	11 (30%)	22 (59%)	4 (11%)	<0.001
Week 12	23 (62%)	12 (32%)	2 (5%)	

Ability to perform strenuous activity was evaluated on the basis of MET usage. At baseline 13 (29%), 25 (58%), and 6 patients (12%) were able to perform light, moderate and vigorous exercise, respectively. After 12 weeks of IRP therapy 2 (2%), 13 (29%), and 29 patients (69%) were able to perform vigorous exercise,

respectively. Thus, there was increase in number of patients who were able to perform rigorous activities after IRP therapy as compared to baseline and the difference was highly statistically significant (p<0.001) [table 6].

Table 6: Table indicating shift in the Metabolic Equivalent of Task over time

Timeline	Metabolic equivalent of task (MET) [n=37]			p-value
	Light exercise (< 3.0 METS)	Moderate exercise (3 to 6 METS)	Vigorous exercise (> 6 METS)	
Baseline	11 (30%)	21 (57%)	5 (13%)	<0.001
Week 12	3 (8%)	10 (27%)	24 (65%)	

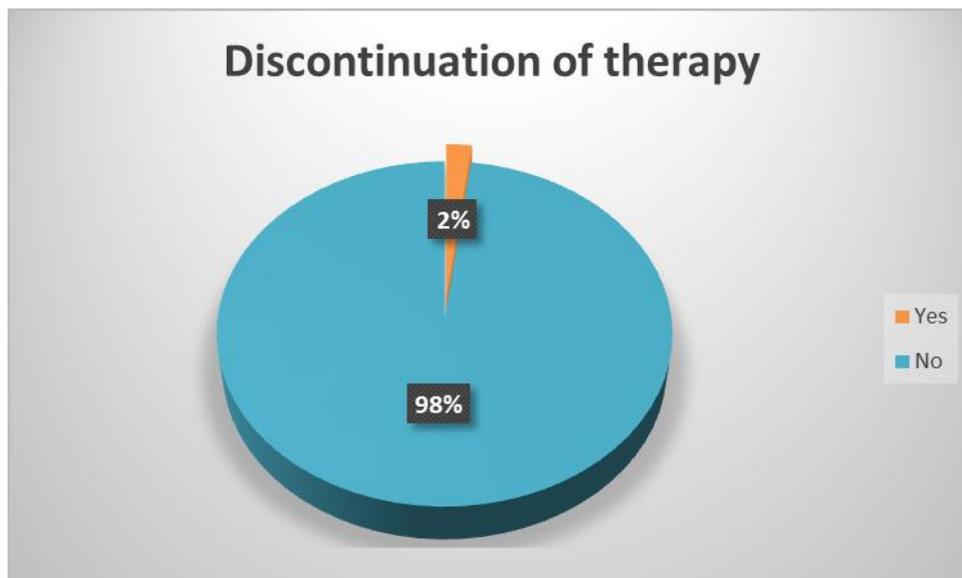
On analyzing the dependency on conventional drugs, it was found that overall the consumption of all drug categories was reduced after IRTP therapy. 2 (4%)

patients were not taking medications at baseline which increased to 15 patients (30%) after 12 weeks of IRP therapy (table 7).

Table 7: Consumption of Allopathic medication at baseline and post 12 weeks.

Medication	Baseline	After 12 weeks
Angiotensin II receptor blockers	11	7
β-blocker	7	4
Diuretics	4	2
Ca ²⁺ channel blockers	6	2
NSAIDs	7	4
Biguanides	25	15
DPP4	17	10
Sulfonylureas	20	9
Insulin	15	9
Antiplatelets	11	6
Statins	12	7
Nitrates	8	3
No medication	2	15

On analyzing the patient compliance, it was found that only 1 patient (2%) discontinued the therap. Patient compliance was good in 98% of the patients (figure 3).

**Figure 3: Patient compliance in the patients of present study.****Figure: Patient compliance.****DISCUSSION**

Despite advances in medical science leading to a better understanding of IHD, the availability of more diagnostic techniques, and the development of more drugs to control it, IHD continues to be one of the leading causes of death worldwide. One of the ways to reduce sudden

death and improve the quality of life for patients with IHD involves providing alternative therapies that can be easily but effectively managed and ultimately lead to tangible benefits for the patient. Regular administration of anti-ischemic drugs has provided therapeutic benefits in this chronic condition by taking measures such as

correcting the imbalance between oxygen demand and cardiovascular delivery, lowering blood pressure, lowering platelet aggregation, hypolipidemic action, and using antioxidant effects to name a few. Several natural remedies commonly used in Ayurveda remedies and techniques such as Panchakarma also offer alternative therapies.^[6]

Doctors at Madhavbaug's clinics and hospitals have developed an ischemia reversal program (IRP) which is a combination of Panchakarma and combination therapy. The main benefit of the Panchakarma procedure used in the IRP is that it can be added as a supplement and combined with any other ongoing treatment regimens. The use of Panchakarma which forms the basis of the IRP may provide its benefits through the use of Snehana which reduces excessive use of anxiolytic effects leading to lower blood pressure, Swedana which reduces the need for myocardial oxygen by reducing sodium and water load, and Basti that aids in the release of nitric oxide endothelium uses a decoction containing Gokshura (*Tribulus terrestris*), Haridra (*Curcuma longa*), and Amalaki (*Emblca officinalis*). Nitric oxide released from 3 herbs used in Basti acts with coronary vasodilation, anti-inflammatory action, and antioxidant action.^[6]

After an analysis of the retrospective data obtained following the 90-day IRP administration, significant improvements in endpoints such as the Duke treadmill score (DTS) and metabolic equivalent (MET) were observed. Duke Treadmill scores have led to a shift from high risk categories to low risk categories. The general development of patients' METs has resulted in a higher number of patients being able to perform strenuous physical activity. In addition, significant improvements in the second extremities such as high oxygen intake (VO₂ max), body mass index (BMI), systolic blood pressure (SBP), and weight were also observed. SBP is one of the predictors of patients with IHD as lowering SBP reduces loading behind the ventricles and improves endothelial health. Studies have also shown that IRP significantly reduces a patient's dependence on common allopathic drugs at the end of 90 days of treatment.

Patient compliance is one of the significant determinant of outcome in a chronic disease like IHD. It was found in a clinical study that patient compliance with conventional allopathic medicines is very less in chronic diseases like IHD, hypertension, DM. This leads to sub optimal outcomes, increased incidence of complications and ultimately the morbidity and mortality rates are also increased.^[7] Thus, excellent patient compliance in the present study seen with IRP is a welcome sign as this increases the likelihood of positive outcomes in IHD.

Therefore, the findings of the present study suggest that the reduction of these structures should be associated with a reduction in heart disease and death. However, some such studies should be performed on a national scale, perhaps with a larger sample size, 2 treatment arms

to make direct comparisons with standard treatment, follow-up time, so that the findings of our study are not made for more people.

As this is a retrospective study, the findings of the current study can only be generalized after appropriate studies are carried out with a prospective design, large sample size, extra arm making direct comparisons with standard treatment, and more follow-up time.

CONCLUSION

From the findings of the present study, IRP was found to be effective in improvement of all important parameters like Duke treadmill score (DTS), metabolic equivalent (MET), maximal oxygen uptake capacity (VO₂ max), body mass index (BMI), systolic blood pressure (SBP). Thus, it can be inferred that IRP can serve as effective therapeutic option for the management of myocardial ischemia.

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