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APPLICATION OF THE ISCHEMIA REVERSAL PROGRAM TOWARDS IMPROVING THE TIME TO ONSET OF ISCHEMIA IN PATIENTS WITH CHRONIC ISCHEMIC HEART DISEASE IN URBAN MUMBAI

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ABSTRACT Chronic ischemic heart disease (IHD) is a cardiovascular disease that results in an imbalance between the myocardial oxygen demand and supply. Despite several advances in medical science leading to a better understanding and management of IHD, this disease continues to be one of the worldwide leading causes of mortality. This necessitates the development of supplementary alternatives for the management of chronic IHD. This retrospective study evaluates the effectiveness of an ischemia reversal program developed by clinicians at Madhavbaug cardiac clinic and hospital by exploring its impact on the time to onset of ischemia through an evaluation of primary endpoints (maximum oxygen uptake capacity [VO2max] with the resultant metabolic equivalents of task [METs] and Duke Treadmill score [DTS]) and secondary endpoints [body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and body weight] in patients with chronic IHD within the Mumbai region. Significant improvements in these primary and secondary endpoints indicated that the application of ischemia reversal program can delay the onset of ischemia and result in an improvement in the overall quality of life.

KEYWORDS : Ischemic heart disease; Ischemia reversal program; Metabolic equivalents of task; Duke Treadmill score; maximum oxygen uptake capacity

INTRODUCTION

Chronic ischemic heart disease (IHD) is a cardiovascular condition that results in a transient imbalance between the myocardial oxygen demand and supply.[1] The diagnosis and risk stratification of this condition is undertaken using an ECG exercise stress test.[2] If left untreated, chronic IHD may eventually lead to severe heart damage resulting in life threatening acute symptoms, including heart failure. The management of chronic IHD aims to reduce existing symptoms by prescribing anti-anginal drugs[3] and improve prognosis through a reduction in the burden of coronary risk[4] and administration of antiplatelet agents.[5]

In India, a country of 1·3 billion people with cultural and lifestyle diversities, the burden of IHD is immense. According to the Registrar General of India, within a decade the percentage of total deaths due to IHD increased from 17% (in 2001-2003) to 23% (in 2010-2013).[6] During the same duration, the percentage of adult deaths occurring due to IHD, increased from 26% (in 2001-2003) to 32% (in 2010-2013).

In the city of Mumbai, rapid industrialization and urbanization have increasingly contributed towards an increase in mental stress that when coupled with an inactive lifestyle, poor eating habits, increased use of tobacco and alcohol, and lack of exercise is responsible for the increasing prevalence of chronic ischemic heart disease. It is believed that chronic ischemic heart disease can be effectively managed by controlling risk factors such as tobacco consumption, alcohol abuse and following a healthy diet, and retaining effective control over high blood pressure and cholesterol. The regular use of conventional allopathic medications such as beta blockers, calcium channel blockers, nitrates, acetylsalicylic acid, and statins is a significant factor for controlling chronic IHD. Additionally, supplementary alternatives for management of IHD often include cardiac rehabilitation programs that contribute towards improving physical endurance and the quality of life, and preventing complications. Practicing such supplementary programs does not interfere with the administration of prescribed allopathic medications. However, the rewards of practicing these can lead to an overall dosage reduction of the prescribed allopathic medications that in turn can prevent or prolong the advent of long-term adverse events. Effective application of supplementary approaches such as the ischemia reversal program developed at Madhavbaug cardiac clinic and hospital along with effective counselling and promotion of healthy nutritional and lifestyle choices are considered to effectively control the further aggravation of chronic IHD to life threatening acute symptoms.

Ayurveda Based Ischemia Reversal Program

Clinicians at Madhavbaug cardiac clinic and hospital have developed an ischemia reversal program that is a combination of Panchakarma and allied therapies. Ischemia reversal program is specifically designed to correct the imbalance between demand and supply of myocardial blood flow. This program administered by the clinicians at Madhavbaug, is proposed to be an add on therapeutic regimen that can be easily coupled with any other ongoing treatment regimens.

Ischemia reversal program involves a 3-step procedure that takes about 65-75 minutes and is performed on patients with IHD after a light breakfast using a variety of decoctions and oils described ahead:

a. Snehana/external oleation or massage: This is a 30-35 minute procedure that involves the administration of an external massage to IHD patients using an oil-based decoction. The massage technique uses centripetal or upward strokes directed towards the heart. This procedure aims at increasing the venous return.

b. Swedana/passive heat therapy: This is a 10-20 minute procedure that is administered to IHD patients while lying inside a sudation box, in a supine position, with their head positioned outside the box. The treatment involves steadily passing steam containing a group of ten herbs (Dashmoola) at a maximum temperature of 40C for 10-15 minutes. After the treatment, patients are suggested to relax for 3-4 minutes. This procedure is aimed at improving the local blood supply through vasodilation.

c. Basti/per rectal drug administration: This is a 15-minute procedure that involves the per rectal administration of a drug to IHD patients. The drug remains inside the body for ≥15 minutes to ensure maximum absorption. This procedure is aimed at increasing the force of contraction of the heart muscles

A combined effect of increased venous return, improved vasodilation, and increased force of heart muscle contraction achieved through the ischemia reversal program and the reduction of body fat by following the recommended nutritional program is expected to provide an improved supply of oxygen to the heart thereby delaying the time to

onset of ischemia. The delay in the time to onset of ischemia can be monitored through an improvement in maximum oxygen uptake capacity (VO_2max)[7] with the resultant metabolic equivalents of task (MET)[8] and the Duke treadmill score (DTS)[9] as the primary endpoints and through a measurement of secondary endpoints such as body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and weight control. The objective of this present observational study was to evaluate the impact of ischemia reversal program on the time to onset of ischemia through an evaluation of these primary and secondary endpoints in ischemia patients.

MATERIALS AND METHODS

This was a retrospective observational study conducted between April 2019 to September 2019. The study used data of patients with IHD who were assessed for the presence of inducible cardiac ischemia using exercise treadmill testing. All patients provided a written informed consent towards publishing the data generated out of this study. 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 Mumbai, 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 137 data files screened for availability of complete data (on Day 1 and Day 90 of the study), 65 patient files were selected and their data were considered for analysis. The present study involved a total of 65 IHD patients with a mean age of 60.27±10.65 years. The age of the patients included in this study ranged from 26 to 77 years of age. Majority of the patients were males (66.15%) as compared to females (33.84%). The baseline demographic characteristics of the patients included in this study is shown in Table 1.

On Day 1 of the ischemia reversal program, all 208 patients underwent VO_2max, Duke treadmill scoring, SBP, DBP, weight, and BMI measurements per the international recommendations. The time for which a patient could exercise during the Duke treadmill test, until the observation of a 1 mm deviation (depression or elevation) of the ST-segment from the isoelectric line, was recorded as the time to onset of ischemia. These readings were considered as baseline readings. Additionally, the metabolic equivalents of task (METs) value was calculated by dividing the oxygen uptake indicated via VO_2max with the oxygen consumption (3.5 ml/kg/min) at rest. These assessments were again repeated on Day 90 of the ischemia reversal program and a percent change from the baseline reading was calculated.

Apart from these evaluations, the dependency of patients on standard allopathic medications on Day 1 and Day 90 of the ischemia reversal program was also assessed by computing and comparing the percentage of the total selected patients, who used a conventional allopathic therapeutic agent before and after the 90-day study period.

VO_2max and Metabolic Equivalents of Task (METs)

The maximum volume of oxygen that an individual can consume during intense, whole-body exercise is called as VO_2max. During exercise, the oxygen consumption in an individual increases as the exercise intensity increases until a point is reached when this consumption plateaus although the exercise intensity can continue to increase. This is defined as the VO_2max or the maximum aerobic capacity of an individual.

In addition to VO_2max, the energy cost of physical activities can also be expressed as METs. A 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/kg/min. Thus, a task at 2 METs would require two times the resting energy expenditure or 7.0 ml/kg/min. The METs are helpful in identifying the intensity of an individual's exercise routine.

For this study, the METs were calculated by dividing the oxygen uptake indicated by VO_2max by the oxygen consumption (3.5 ml/kg/min) at rest. The obtained METs were subsequently used to compute the DTS and were used to classify patients 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.

Duke Treadmill Score (DTS)

Exercise stress test evaluations, using the exercise treadmill, are helpful in diagnosing the presence of significant coronary disease in patients with IHD symptoms and assessing their future risk towards undesirable cardiac events.[10] Evaluations using exercise stress test offer the advantages of being non-invasive and cost-effective. Computing a prognostic DTS is a well-accepted and routinely used method that provides survival estimates based on the duration of an exercise test using a standard Bruce protocol, maximum deviation of the ST-segment (depression or elevation), and the presence and severity of angina during exercise. For the calculation of the DTS, the exercise time in the Bruce protocol can be replaced with METs.[11] In this study, we have used METs in place of the maximum exercise time in minutes to calculate the DTS using the below formula:

Duke treadmill score = METs – (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. A score of ≥+5 corresponds to a low-risk towards cardiac events and such patients do not appear to demonstrate a need for coronary angiography as a follow-up evaluation and generally exhibit a 4-year survival rate of almost 100%. An intermediate score ranging from -11 to +5 indicates moderate-risk towards cardiac complications and such patients are advised a coronary angiography based on their clinical status. On the other extreme, a score of ≤-11 classifies patients into the high-risk category with such patients requiring a coronary angiography for further evaluation and exhibiting a 4-year survival rate of around 79%.

Additionally, the time for which a patient could exercise during the Duke treadmill test, until the observation of a 1 mm deviation (depression or elevation) of the ST-segment from the isoelectric line, was also recorded as the time to onset of ischemia.

Statistical Analysis

The available data were pooled together and coded in a Microsoft Excel spreadsheet using Excel 2019. Categorical data were presented in the frequency form whereas the continuous data were presented as mean (±SD). The McNemar-Bowker test was used to assess the METs and DTS before and after 90 days of treatment. The paired t-test was used to assess the difference between baseline values and values after 90 days of treatment. Box plot and histogram were used to represent the graphs, as appropriate.

RESULTS

A comparison of the shifts in a patient's potential to perform strenuous activity was assessed using the METs utilization at baseline and after 90 days of therapy and is presented in Table 2. Overall, at baseline, 15 (23.08%), 33 (50.77%), and 17 (26.15%) patients were classified to the vigorous exercise, moderate exercise, and light exercise categories according to the utilization of their METs. Following 90 days of treatment in IRP, 46 (70.76%), 16 (24.61%), and 3 (0.46%) patients got classified to the vigorous exercise, moderate exercise, and light exercise categories according to the utilization of their METs. The average VO_2max improved from 15.41 ml/kg/min to 26.16 ml/kg/min (p-value <0.0001) resulting in a general improvement in patient METs that corresponded to a higher number of patients being able to undertake vigorous exercise. Subsequently, the time to onset of ischemia also exhibited a significant delay from 426.11 seconds observed at baseline to 698.76 seconds (p-value<0.0001) observed 90 days after starting the ischemia reversal program identifying the benefits of this program.

Similarly, a comparison of the shifts in patient risk potential, using the DTS at baseline and after 90 days of therapy, is presented in Table 3. Overall, at baseline, 17 (26.15%), 29 (44.61%), and 19 (29.23%) patients were classified to the high-risk, moderate-risk, and low-risk categories according to their Duke Treadmill Scores. Following 90 days of treatment in IRP, 5 (7.69%), 24 (36.92%), and 36 (56.38%) patients got classified to the high-risk, moderate-risk, and low-risk categories per their DTS. The average DTS improved from -3.51 observed at baseline to +3.82 observed after 90 days of the ischemia reversal program (Figure 1). Thus overall, an improvement in the DTS that resulted in a shift from the higher risk categories to the lower risk categories was observed.

The overall secondary clinical endpoints (body weight, BMI, SBP, and DBP) also showed significant improvement between the baseline values and 90 days after starting the ischemia reversal program (Table 4). The mean systolic blood pressure also attained near normal levels 90 days after starting the IRP (p-value = 0.023). However, the mean diastolic blood pressure that was normal at baseline (77.6 mmHg) showed a significant decline to 74.30 mmHg although it was within the normal range (p-value = 0.018). The average body weight also exhibited a decrease from 66.75 kg to 63.32 kg (p-value<0.0001).

The consumption of allopathic medications at baseline on Day 1 and 90 days after starting the ischemia reversal program are presented in Table 5 and Figure 2. Of the total subjects, 57 patients were on prescribed medications. The dependence of patients on most commonly prescribed medications (in ≥25% of the patient population) showed a decrease following 90 days of treatment in the IRP and included statins (from 40.0% to 20.0%), antiplatelets (from 38.46% to 21.53%), biguanides (from 35.38% to 23.07%), beta blockers (from 33.84% to 23.07%), angiotensin II receptor blockers (from 32.30% to 21.53%), nitrates (from 29.23% to 18.46%), calcium channel blockers (from 29.23%to 16.92%), and nonsteroidal anti-inflammatory drugs (from 29.23% to 21.53%). Additionally, the percent of patients on no medications increased from 12.30% at baseline to 20.0% at 90 days after starting the IRP.

DISCUSSION

Mental stress and the changes in lifestyle associated with urbanization are responsible for an increase in the number of chronic ischemic heart disease cases in Mumbai. If left untreated this condition may eventually aggravate and lead to the appearance of life-threatening acute symptoms such as cardiac failure. Along with prescription medications, supplementary alternatives such as an ischemia reversal program, developed by the clinicians, and adoption of healthy nutritional and lifestyle choices can aid in better managing the chronic ischemic heart disease condition and improve the overall quality of life in such patients.

The ischemia reversal program is a combination of Panchakarma and allied therapies. The advantage offered by Panchakarma technique applied in the ischemia reversal program is that it can be administered as an add on procedure and coupled along with any other ongoing treatment regimens. Application of Panchakarma that forms the basis of the ischemia reversal program possibly provides its advantages through Snehana that reduces sympathetic overactivity by exerting anxiolytic effects leading to a reduction in blood pressure, Swedana that reduces myocardial oxygen demand via the reduction of sodium and water load, and Basti that helps in the release of nitric oxide from vascular endothelium using a decoction containing *Tribulus terrestris*, *Curcuma longa*, and *Emblica officnalis*. The nitric oxide released by the 3 herbs used in Basti acts through coronary vasodilation, anti-inflammatory action, and antioxidant action. Additionally, the recommended diet of 1000-1200 kcal per day also assists in body weight reduction and an overall improvement of BMI thereby leading to a reduction in the myocardial oxygen demand.

The analysis of retrospective data obtained following the administration of the ischemia reversal program for 90 days and following the recommended diet exhibited significant improvements in the primary endpoints such as VO_2max that was also used to compute the METs and DTS. A general improvement in the VO_2max with the resultant METs corresponded to a higher number of patients being able to undertake vigorous exercise. The DTS also exhibited a shift from the higher risk categories to the lower risk categories. These improvements seen within the primary parameters led to a significant delay in the time to onset of ischemia. Additionally, significant improvements in the secondary endpoints such as BMI, SBP, and weight were also observed. Systolic blood pressure is one of the prognostic marker in patients with IHD as a reduction in this parameter leads to a reduction in the afterload of the ventricles and improves endothelial health. The study also demonstrated that ischemia reversal program noticeably reduced a patient's dependency on standard allopathic medication at the end of 90 days of therapy.

Thus, the findings of this study identify that the application of an ischemia reversal program along with healthy nutritional and lifestyle choices can lead to an improvement in primary endpoints such as VO_2max, the resultant METs, and DTS that in turn can improve the time to onset of ischemia and result in a reduction in cardiovascular morbidity and mortality. The conduct of other such studies on a national scale, probably with larger sample size, two treatment arms to facilitate direct comparison with the standard therapy, and more follow up period can provide additional support to generalize the findings of this study for a larger population.

CONCLUSION

Application of the ischemia reversal program and following a recommended diet plan results in significant improvements in the primary endpoints (VO_2max with the resultant METs and DTS) and secondary endpoints (BMI, SBP, and body weight) and delays the onset of ischemia. This results in an overall improvement in the quality of life in patients with chronic IHD in urban Mumbai.

Conflicts of interest: Authors have no conflicts of interest.

Tables Used in the Manuscript

Table 1: Demographics

Total Subjects	65
Females	22 (33.84%)
Males	43 (66.15%)
Mean Age	60.27±10.65 years
Median Age	62 (range 26-77) years

Table 2: Shifts in the Metabolic Equivalents over time

	Metabolic equivalent of task (MET)	After 90 days				p -value
		Light Exercise (3.0 METs)	Moderate Exercise (3.0 to 6.0 METs)	Vigorous Exercise (6.0 METs)	Total	
At Baseline	**Light Exercise (3.0 METs)**	3	10	4	17 (26.15%)	<0.0001
	Moderate Exercise (3.0 to 6.0 METs)	0	6	27	33 (50.77%)	
	Vigorous Exercise (6.0 METs)	0	0	15	15 (23.08%)	
	Total	3 (0.46%)	16 (24.61%)	46 (70.76%)	**N=65**	

Table 3: Shifts in the Duke Treadmill Score over time

	Duke Treadmill Score	After 90 days				p-value
		Low risk (≥+5)	Moderate risk (-11 to +5)	High risk (≤-11)	Total	
At Baseline	**Low risk (≥+5)**	19	0	0	19 (29.23%)	< 0.0001
	Moderate risk (-11 to +5)	13	16	0	29 (44.61%)	
	High risk (≤-11)	4	8	5	17 (26.15%)	
	Total	36 (56.38%)	24 (36.92%)	5 (7.69%)	**N=65**	

Table 4: Summary of mean change observed from baseline after 90 days for different parameters

Parameter	Baseline	After 90 days	p-value
Weight	66.75±12.27 kg	63.32±11.70 kg	<0.0001
Body Mass Index	26.06±4.56 kg/m^2	24.81±4.37 kg/m^2	<0.0001
Systolic Blood Pressure	127.07±19.49 mmHg	121.63±15.68 mmHg	0.023
Diastolic Blood Pressure	77.6±9.93 mmHg	74.30±9.99 mmHg	0.018
VO_2max	15.41±7.02 mL/kg/min	26.16±8.71 mL/kg/min	<0.0001
Time to onset of ischemia	426.11±225.8 seconds	698.76±204.185 seconds	<0.0001

Table 5: Consumption of Allopathic medication at baseline and post 90 days

Medication	Baseline	After 90 days
Angiotensin II receptor blockers	21 (32.30%)	14 (21.53%)
B-blocker	22 (33.84%)	15 (23.07%)
Diuretics	6 (9.23%)	5 (7.69%)
Ca^{2+} channel blockers	19 (29.23%)	11 (16.92%)
NSAIDs	19 (29.23%)	14 (21.53%)
Biguanides	23 (35.38%)	15 (23.07%)
DPP4	5 (7.69%)	2 (3.07%)
Sulfonylureas	16 (24.61%)	13 (20.00%)
Antiplatelets	25 (38.46%)	14 (21.53%)
Statins	26 (40.00%)	13 (20.00%)
Nitrates	19 (29.23%)	12 (18.46%)
No medication	8 (12.30%)	13 (20.00%)

Figures Used in the Manuscript

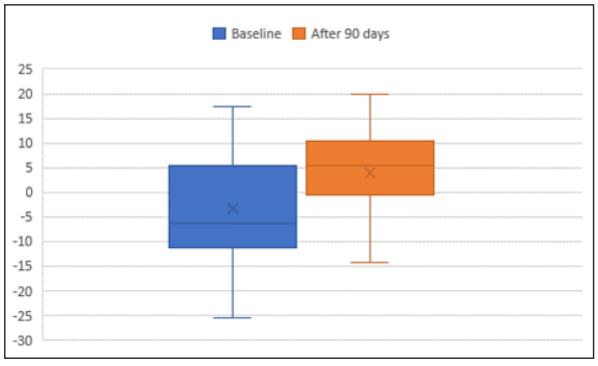

Figure 1: Comparison of Duke Treadmill Score

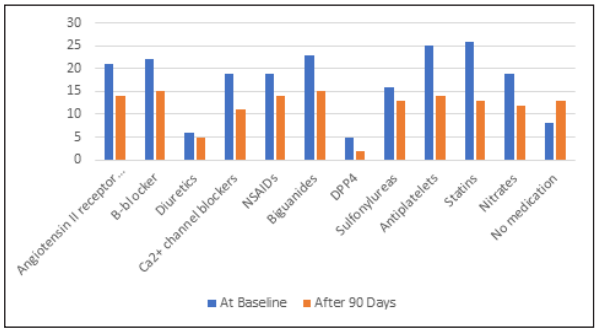

Figure 2: Reduction in Consumption of Allopathic Medication

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