Original Research Article

Impact of Ayurveda Based Panchkarma Therapy in change of the VO_{2peak} in Chronic Heart Failure Patients with - An Observational Study

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ABSTRACT

Background and Aim: Reduced peak oxygen uptake (VO2peak) is a primary predictor of mortality in chronic heart failure (CHF) patients which is also an indicator of the exercise capacity of an individual. Traditionally, exercise training during cardiac rehabilitation has been used to improve the patients VO2peak. This however, may not be applicable to patients of all age due to exercise intolerance. Our study therefore, focussed on the use of ayurveda based panchkarma treatment for increasing the maximal oxygen consumption during regular physical activities.

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Methods: An observational study was carried out on 589 CHF patients who had opted for panchkarma treatment at various branches of Madhavbaug clinics. The patients'weight, body mass index (BMI) and blood pressure (BP) were measured before the start of the treatment. A 6 minute walk test (6MWT) and cardiac stress test with modified Bruce protocol was used to measure the initial VO2peakvalue for each patient. Using this value the initial metabolic equivalent was calculated. The study population underwent a minimum of 7 sitting (twice a day) of panchkarma therapy for 7 days. They were asked to follow up after 90 days. During the follow up their weight, BMI, BP, VO2peak and metabolic equivalent (MET) were measured and compared with results of day 1.

Results: The study consisted of 589 CHF patients belonging to the age group of 20 to 90 years, of which 53.24% were males and 46.76% were females. There was a reduction in weight, BMI and blood pressure and an increase in the VO2peakand MET after the treatment.t Age wise comparison showed that the VO2peakdecreases with increasing age and the effect of the treatment also is seen more in younger patients. On the other hand, similar improvement in the oxygen consumption was seen in both genders. The treatment was also able to improve the VO2peakin patients with severe risk i.e. those having initial VO2peakvalue of <12mL/kg/min.

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Conclusion: The ayurveda based panchkarma treatment proved beneficial in improving the exercise capacity measured in VO2peak and MET thus improving the exercise tolerance of the study population and reducing the risk of mortality.

Keywords: Panchkarma, VO2peak, metabolic equivalent, exercise capacity, chronic heart failure, cardiac output.

1. INTRODUCTION

Chronic heart failure (CHF) is considered to be a global pandemic with a prevalence of >37.7 million worldwide. [1]Congestive heart failure develops due to the dysfunctions in either the left ventricular (LV) diastole or systole. This may develop due to various risk factors such as hypertension, or metabolic syndromes including diabetes mellitus, hyperlipidemia and central obesity.[2]

These changes may be related to age. With an increasing age, the changes taking place in the structure and function of the heart may affect the maximal stroke volume thus decreasing the maximum oxygen consumption (VO2peak) of the body. VO2peak is the maximum oxygen uptake during physical activities like running and cycling. The oxygenated blood that is received by the heart needs to be pumped to the body. If the cardiac output is compromised due to dysfunctions of the left ventricle, there will be a load on the heart to compensate for the lower oxygen to the body leading to CHF. [3]Patients with a low VO2peak show symptoms of dyspnea on exertion and it is considered as the primary predictor of mortality in CHF patients. Thus, if we improve the VO2peak using certain interventions, this can reduce the mortality rate in heart patients. [4]

Another method of calculating the exercise intensity is the determination of metabolic equivalent (MET) which represents the baseline metabolic rate. It is the energy needed by an individual at rest. During an activity the MET for an individual can be calculated by dividing the oxygen consumption (VO2) when performing the activity by the VO2 at rest. [5]

Previous studies have shown to increase the VO2peak during the 3 month intervention using cardiac care and exercise training. This increase in peak VO2lead to the decrease in the all-cause mortality of the study population.However, it has been estimated that only 30% of patients reach the target number of training per week post 10-12 months.[6,7]

We have previously carried out studies on CHF patients that underwent panchkarma therapy in order to increase their maximal aerobic capacity (MAC).[8] Also studies were carried out to evaluate the efficacy of the therapy on VO2peak. [9] This study however, is a detailed analysis of the change in the VO2peak with regards to 3 groups based on age, initial value of VO2peak and gender.

2. MATERIAL AND METHODS

2.1 STUDY POPULATION

An observational study was carried out on a group of patients (aged 20-90 years, both genders included) suffering from chronic heart failure (CHF) from 217 centres of Madhavbaug clinic all over India.

Comment [OL5]: How many participants?

Inclusion criteria: Known CHF patients that complied with the New York Heart Association (NYHA) class I to III were included in the study.

Exclusion criteria: CHF patients that belonged to NYHA class IV and those who were contraindicated for cardiac stress testing were excluded.

2.2 STUDY EVALUATION

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At the start of the study the know CHF patients were screened according to the New York Heart Association (NYHA) classification. Patients were included as per the study criteria mentioned above. Their weight, BMI, blood pressure (BP) was noted. Using the 6 minute walk test (6MWT) method the VO2peak and metabolic equivalents (MET) was calculated based on Cardiac Stress Testing with Modified Bruce Protocol and then average for the study population was calculated. After a period of 90 days, the weight, BMI, BP, VO2peak and MET were measured and the average was compared to the average of day 1.

2.3 STUDY THERAPY

The study population was given a minimum of 7 sittings twice a day of ayurvedic based herbal detoxification for a period of 7 days to a maximum of 21 sittings for 90 days. Thetherapy consists of 4 steps- centripetal oleation, thermal vasodialtion, thoracic drip and per rectal herb decoction administration [10].

- Centripetal oleation (Snehana): This step includes massaging the patient using sesame oil containing essence of lavender oil. The patient is made to lie on his back and the massage is carried in a circular manner from the wrist towards the heart, upto the abdomen in clockwise and anticlockwise direction. Same procedure is followed for the back. Also the vertebral column is massaged from the lumbar region towards the cervical region in a zigzag manner. The duration of this step is 20 minutes

- Thermal vasodialtion: During this procedure, the patient is made to lie in supine position in a sudation box. Steam (temperature maintained at 40°C) generated by the boiling of Dashmula (ten root) decoctions is allowed to flow uniformly in the closed box for 10-15 minutes. The patient is then made to relax in the box for 3-4 minutes. The entire procedure takes 20 minutes.

- Thoracic drip: A warm dashmoola decoction is allowed to drip over the thoracic cavity (7-8 com height) of the patient with constant speed. This procedure is a variation of shirodhara technique and it takes 15 minutes to complete.

- Per rectal herb decoction administration: A decoction (10 ml aqueous extract) is prepared with a mixture of T. arjuna (1880 mg), B. diffusa (420 mg) and A. calamus (180 mg). This decoction is filled in an enema can and the decoction is administered into the rectum of the patient. The total duration of the basti is 10 minutes and the solution must be retained in the body for at least 15 minutes for maximum absorption.

The study was approved by institutional review board and conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

2.4 STATISTICAL ANALYSIS

The data collected were analysed using in Microsoft Excel using the one-way Analysis of variance (ANOVA) test. The mean ± standard deviation (SD) data of the study population recorded for the various parameters on day 1 and day 90 were compared. Comparison of the change in the VO2peak before and after the treatment were divided into three categories- Age group wise VO2peak distribution, value of initial VO2peak and gender group wise VO2peak. The mean ± SD values were plotted on graphs in order to compare the effect of the treatment on the VO2peak.

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3. RESULTS

3.1 STUDY POPULATION

A total of 647 CHF patients were screened of which 589 patients from 217 centres all over India were selected based on the inclusion criteria. The population consisted of 269 (46.76%) females and 320 (53.24%) males belonging to the age group of 20 to 90 years. Along with CHF, some patients were suffering from diabetes mellitus (DM) (18%), Hypertension (HTN) (14.43%) and obesity (8.49%).

3.2 STUDY EVALUATION

All investigations carried out before and after the treatment

The mean results of day 1 and day 90 were tabulated and compared. There was a decrease observed in the average weight, BMI and BP of the study population. The oxygen consumption measured in VO2peakand MET increased post treatment. (Table 1)

Table 1: Change in the investigations carried out before and after the treatment.

Test Performed	**Day 1 (mean ± SD)**	**Day 90 (mean ± SD)**	***P*-value**
Weight (kg)	69.47 ± 13.80	66.19 ± 12.56	0.0001
BMI (kg/cm^2)	27.50 ± 4.92	26.07 ± 4.42	0.0001
SBP(mm Hg)	128.68 ± 13.37	121.46 ± 14.60	0.0001
DBP (mm Hg)	79.75 ± 11.	76.07 ± 8.58	0.0001
VO_{2peak} (mL/kg/min)	16.74 ± 7.47	24.65 ± 8.67	0.0001
MET	4.78 ± 2.13	7.07 ± 2.47	0.0001
Index: BMI- Body mass index, SBP- systolic blood pressure, DBP- diastolic blood pressure, MET- metabolic equivalent, SD- standard deviation			

The treatment lead to a reduction in medication for the study population with the only exception being the antiplatelet medicine. Highest reduction is seen in proton pump inhibitor (PPI) and calcium channel blockers (CCB) allopathic medications.

Analysis of change in VO2peak within different study groups.

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The study population was divided into 3 study groups based on age, initial VO2peak value and gender.

- Age group wise VO2peak distribution:

The study population was divided into 3 groups based on age- 20-40 years, 41-60 years and 61-90 years. It was observed that the initial value of the average VO2peak decreased with increasing age group. Also the increase in VO2peak post treatment varied among the 3 groups, with 20-40 years showing highest change (9.36 mL/kg/min) followed by 41-60 years (8.62 mL/kg/min) and lowest change in 61-90 years (6.69 mL/kg/min). (Figure 1)

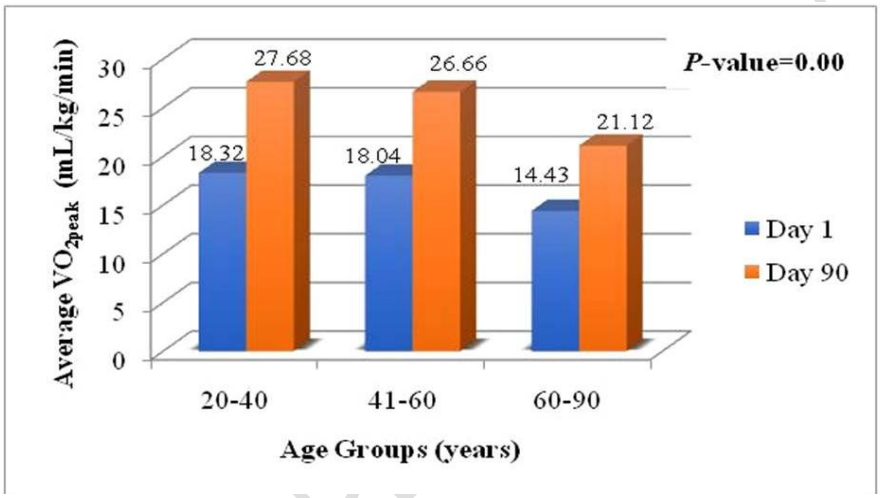

Figure 1: Change in the average VO2peak in the study population between different age groups post treatment.

- Initial VO2peakGroup distribution:

Additionally, similar to the study conducted by Keteyian SJ et.al. 2008 [10] we divided the study population according to the initial values of VO2peakof each patient into 3 groups- Severe (1-12 mL/kg/min), Intermediate (13-18 mL/kg/min) and low risk (>18 mL/kg/min). The change in the oxygen consumption post treatment within each group was studied. The increase in VO2peak value of patients under the severe group (9.38 mL/kg/min) was higher compared to intermediate (8.07 mL/kg/min) and low risk (6.95 mL/kg/min) patients. (Figure 2) This helped us to understand the efficacy of the study therapy in patients with different severity.

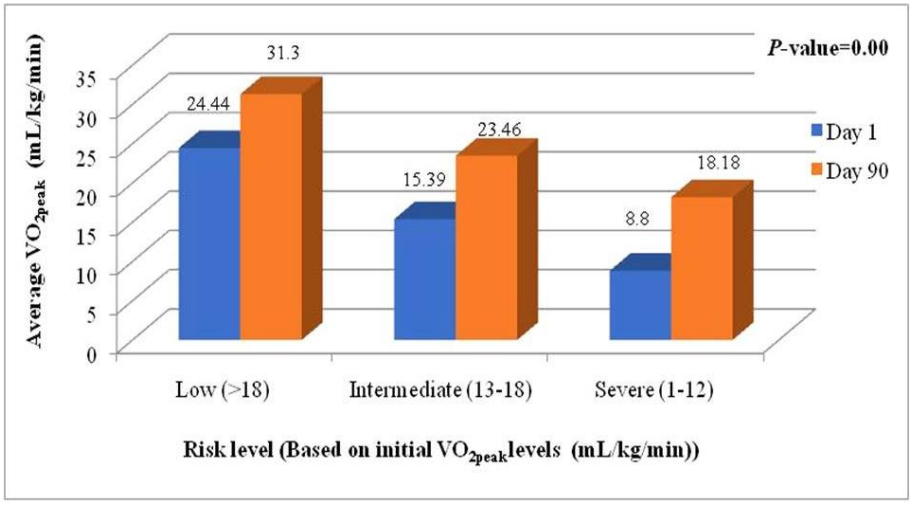

Figure 2: Risk profile of study population based on initial VO2peak value at baseline (day 1) and Day 90.

Gender group wise VO2peak distribution: A similar improvement in the VO2peak was observed in the female group (7.82 mL/kg/min) and male group (7.98 mL/kg/min). (Figure 3)

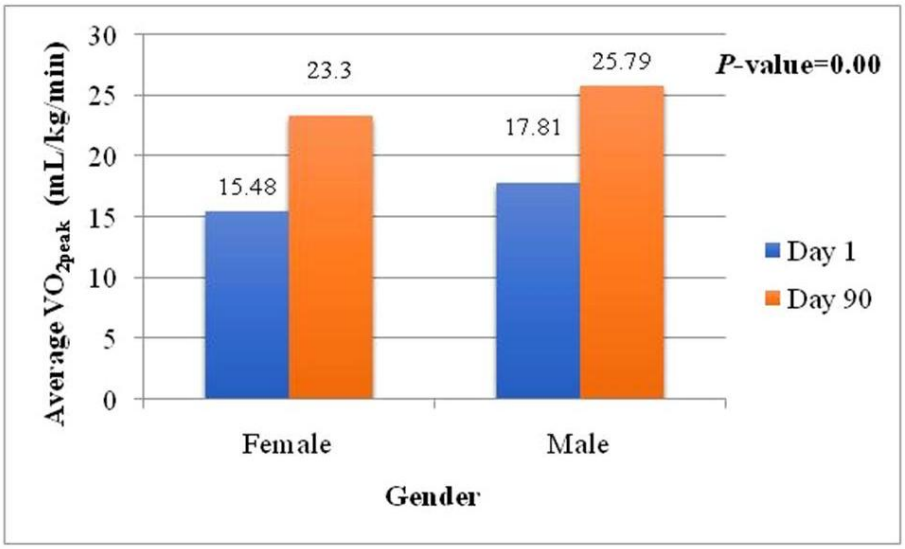

Figure 3: Change in the average VO2peak in the female and male study population post treatment

Medicine reduction: Dependency of the study population on allopathic medicines for blood pressure, heart failure and diabetes reduced considerably (Table 2).

Table 2: Change in the medication of the study population after the treatment.

Allopathic medicine	Day 1*	Day 90*	Medicine Reduction (%)
Beta Blocker	139	93	33.09
ARNI	16	8	50.00
ACE inhibitor	31	19	38.71
Sulfonylurea	81	51	37.04
Bigunide	118	78	33.90
Dpp 4 Inhibitor	21	13	38.10
CCB	56	25	55.36
PPI	42	15	64.29
Nitrate	62	30	51.61
Antiplatelet	224	147	77.00
Vasodilator	22	15	31.82

*Values indicate the number of patients that were prescribed the medication.

ARNI-Angiotensin receptor-neprilysin inhibitor, ACE- Angiotensin-converting enzyme, DPP-dipeptidyl peptidase, CCB- calcium channel blockers, PPI- proton pump inhibitors, NSAID-nonsteroidal anti-inflammatory drugs

4. DISCUSSION

We conducted an observational study on 589 CHF patients that had approached the different branches of Madhavbaug clinics all over India. The patients were considered for the study based on their NYHA classification.

On admission, the weight, BMI and BP was measured. 14.43% patients were hypertensive and it was needed to treat the high BP as well. On day 1, the patients underwent a 6 MWT during which the VO2peak was measured. Using the maximum oxygen consumption, the MET values for each patient was calculated. The value of VO2peak was divided with 3.5 (resting VO2) to obtain the value of MET. [12] The therapy helped to reduce the weight and BMI. The centripetal massage improves the circulation of the blood and helps to remove the toxins from the cells via the lymphatic system. The rise in body temperature caused by the steam leads to increase in the rate of metabolism thus leading to an increase in the

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generation of waste products. The steam also causes the body vessels to expand enabling improved circulation and transfer of the toxins to the gastrointestinal (GI) tract. [13]

During basti the herbal decoction may get absorb per rectally and enters into systemic circulation that might have cardiac specific activity thereby imparting cardiotonic action on myocardium. A double blind crossover study reported potential cardiotonic properties of one or more constituents of the herb T. Arjuna (glycosides) that is alsoused in Basti procedure included in the current study protocol [14,15].Additional two herbs used in Basti are B. Diffusa and A. calamus.B. Diffusa is reported to have cardioprotective effect owing to its protective effect against mitochondrial dysfunction that plays a critical role in cardiac hypertrophy or heart failure. An animal study reported cardioprotective effect of A. Calamus by increasing the antioxidant enzyme levels glutathione, catalase, and superoxide dismutase and decreasing the levels of malondialdehyde. Additionally the herb, A. calamus is also reported to have hypolipidemic activity.

CHF leads to patients having a limited exercise capacity and this exercise intolerance is associated with a higher risk of mortality. [18] It is therefore important to increase the exercise capacity using different interventions. Traditionally, exercise training is used to help CHF patients increase their exercise tolerance.

Panchkarma therapy is known to improve the left ventricular systolic and diastolic dysfunction which increases the cardiac output thus improving the VO2peak.[10] In this study, we compared the increase in the VO2peak after treatment between 3 groups based on age, initial value of VO2peak and gender.

It was observed that with increasing age, the initial VO2peak values decreases. This corresponds to previous findings wherein a 10% per decade decrease was seen after the age of 25 years and a 15% reduction between the ages of 50 and 75 years.[19] Additionally, our therapy is also designed to activate the attenuated muscle tissues in young population. However the same in elderly patient is not possible due to quantitative muscle loss related to aging. Therefore, the results of current study might seem more promising for young CHF patients as compared with the older one.

Next the study population were divided based on the initial value of VO2peak- Severe (1-12 ml/kg/min), Intermediate (13-18 ml/kg/min) and low risk (>18 ml/kg/min). The therapy helped to increase the VO2peakvalue of the severe and intermediate risk groups to more than 18 ml/kg/min thus lowering the risk of mortality.

The initial oxygen consumption in females were less than that of males. Women have more fat than muscle as compared to men so this results in a lower VO2peak in females. Also haemoglobin content in men is higher than that in women leading to a higher oxygen carrying capacity and hence higher oxygen consumption. [20] It was observed that the increase in oxygen consumption post therapy was almost the same between men and women. Thus, the therapy showed similar effects in both men and women.

The study population who were prescribed different allopathic medicines at the beginning of the study reported to have reduced dependency on these medications post-therapy. The prescriptions of antihyperglycemic agents were found to have tapered based on the continuous blood sugar level measurements and blood pressure. Post therapy, the prescribed dosage/strength of vasodilators was reduced as compared to before treatment based on the reduction in angina pectoris. Additionally the Angiotensin Receptor-Neprilysin

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Inhibitor (ARNI) were tapered to almost 50% based on the symptoms and follow up NT-proBNP levels.

Limitations: Although the study sample size was appropriate to arrive at plausible conclusion, the age and gender matched control arm was not present to make a head-to head comparison. Further, being an observational single arm study this study design had in built limitation of not being randomised and controlled study.

5. CONCLUSION

The observational study was carried out on 589 CHF patients inorder to assess the effect of the ayurveda based panchkarma treatment on the increase in oxygen consumption. The treatment led to a reduction in BMI thus, reducing the burden on the heart to supply adequate oxygen during regular activities. Patients with CHF have reduced exercise tolerance and our study also focused on using panchakarma to increase their exercise intensity measured in MET. We concluded that increase in VO2peak is dependent on age but independent of gender. Also all the patients reached the low risk category of more than 18 ml/kg/min of VO2peakirrespective of their initial maximum VO2. Also the therapy reduced the dependency on allopathic medication. The patients were therefore less dependent on medicines for maintaining their health and had could carry out regular physical activities due to increased exercise capacity.

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9. CONSENT (WHERE EVER APPLICABLE)

Consent to participate: Informed consent from each participant was registered

Consent for publication Non-disclosure of personal information was agreed and consent for research publication was obtained.

10. ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Institutional review board approval and in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration

11. REFERENCES

1. Boback Ziaeian GCF. Epidemiology and aetiology of heart failure. Nat Rev Cardiol. 2016;13(6):368–378.

2. Sarah A. Dick SE. Chronic Heart Failure and Inflammation What Do We Really Know? Circ Res. 2016;119(1):159–76.

3. Strasser, B., & Burtscher M. Survival of the fittest: VO2max, a key predictor of longevity. Front Biosci (Landmark Ed). 2018;23(23):1505–16.

4. Inamdar, A. A., & Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. J Clin Med. 2016;5(7):62.

5. Coelho-Ravagnani C de F, Melo FCL, Ravagnani FCP, Burini FHP, Burini RC. Estimation of the metabolic equivalent (met) of an exercise protocol based on indirect calorimetry. Rev Bras Med do Esporte. 2013;134–8.

6. Ann M. Swank, John Horton, Jerome L. Fleg, Gregg C. Fonarow, Steven Keteyian, Lee Goldberg, Gene Wolfel, et.al. Modest Increase in Peak VO2 Is Related to Better Clinical Outcomes in Chronic Heart Failure Patients. Circ Hear Fail. 2012;5:579–85.

7. De Maeyer, C., Beckers, P., Vrints, C. J., & Conraads VM. Exercise training in chronic heart failure. Ther Adv chronic Dis. 2013;4(3):105–17.

8. Sane Rohit MR. Efficacy of heart failure reversal treatment in patients with low ejection fraction. J Ayurveda Integr Med. 2018;9(4):285–9.

9. Sane R, Sugwekar V, Nadapude A, Hande A, Depe G, Mandole R. Study of efficacy of ischemia reversal program (IRP) in ischemic heart disease (IHD) patients with VO2max and Duke's treadmill score. Int J Basic Clin Pharmacol. 2018;

10. Sane, Rohit & Aklujkar, Abhijeet & Patil, Atul & Mandole R. Effect of heart failure reversal treatment as add-on therapy in patientswith chronic heart failure: A randomized, open-label study. Indian Hear Journal. 2017;69(3):299–304.

11. Keteyian SJ, Brawner CA, Savage PD et al. Peak aerobic capacity predicts prognosis in patients with coronary heart disease. Am Hear Journal. 2008;156(2):292-300.

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12. M. Jette. K. Sidney. G. Blumchen. Metabolic Equivalents (METS) in Exercise Testing, Exercise Prescription, and Evaluation of Functional Capacity. Clin Cardiol. 1990;13:555–65.

13. Soni G. Physio-Anatomical relation of Snehana & Swedana with Lymphatic System Physio-Anatomical relation of Snehana & Swedana with Lymphatic System. AYUHOM. 2017;4(1):64–6.

14. Bharani A, Ganguly A, Bhargava KD. Salutary effect of Terminalia arjuna in patients with severe refractory heart failure. International Journal of Cardiology. 1995 May 1;49(3):191-9.

15. Maulik SK, Wilson V, Seth S, Bhargava B, Dua P, Ramakrishnan S, Katiyar CK. Clinical efficacy of water extract of stem bark of Terminaliaarjuna (Roxb. ex DC.) Wight & Arn.in patients of chronic heart failure: a double-blind, randomized controlled trial. Phytomedicine. 2016 Feb 23.

16. Prathapan A, Vineetha VP, Raghu KG. Protective effect of Boerhaavia diffusa L. against mitochondrial dysfunction in angiotensin II induced hypertrophy in H9c2 cardiomyoblast cells. PLoS One. 2014 Apr 30;9(4):e96220.

17. Kumar MS, Hiremath VS. Cardioprotective effect of Acorus calamus against doxorubicin-induced myocardial toxicity in albino Wistar rats. Indian Journal of Health Sciences and Biomedical Research (KLEU). 2016 May 1;9(2):225.

18. Gademan, M. G., van der Laarse, A., Swenne, C. A., & van der Wall EE. Oxygen uptake in heart failure: how much, how fast? Neth Heart J. 2009;17(6):224–5.

19. Kim, C. H., Wheatley, C. M., Behnia, M., & Johnson BD. The Effect of Aging on Relationships between Lean Body Mass and VO2max in Rowers. PLoS One. 2016;11(8):e0160275.

20. Huldani, Achmad H, Arsyad A, Putra AP, Sukmana BI, Adiputro DL, et al. Differences in VO2 Max Based on Age, Gender, Hemoglobin Levels, and Leukocyte Counts in Hajj Prospective Pilgrims in Hulu Sungai Tengah Regency, South Kalimantan. Syst Rev Pharm. 2020;11(4):9–14.

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