Original Article

Clinical study of *Arogyavardhini* compound and lifestyle modification in management of metabolic syndrome: A double-blind placebo controlled randomized clinical trial

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Abstract

Background: Metabolic syndrome (MS) is a cluster of obesity, hypertriglyceridemia, impaired glucose tolerance, and insulin resistance. The sedentary lifestyle settles on the phenotypical expression of a genetically acquired trait in an obese person. Weight control and a healthy lifestyle remain primary and effective strategies for prevention and management of the MS. The lifestyle modifications mentioned for *Santarpanjanya* (disorders due to over nutrition) diseases and *Arogyavardhini* compound that can improve metabolism and reduce weight were selected for a present clinical trial to assess and compare their efficacy in the management of the MS. **Materials and Methods:** Seventy-five patients were registered for the trial and randomly divided into two groups. Patients were treated with lifestyle modification with and without *Arogyavardhini* compound for 8 weeks. **Results:** Thirty-five patients in each group could complete the course of treatment. Lifestyle modification alone and with *Arogyavardhini* compound resulted in 1.32% and 3.06% decrease in waist circumference, 5.81% and 18.03% decrease in serum triglycerides, 4.43% and 6.89% decrease in systolic blood pressure, 3.82% increase and 2.48% decrease in fasting blood sugar, 9.13% and 5.56% increase in high-density lipoprotein, respectively. The decrease in waist circumference, systolic blood pressure was statistically significant in the both groups. **Conclusion:** *Arogyavardhini* compound, along with lifestyle modification was found more effective than lifestyle modification alone in the management of MS.

Keywords: *Apathyanimittaja Prameha*, *Arogyvardhini* compound, Ayurveda, *Medavaha Sroto-Dushti*, metabolic syndrome

Introduction

Metabolic syndrome (MS) is a constellation of three or more metabolic disorders, including obesity, insulin resistance, hypertension and dyslipidemia occurring due to improper diet and lifestyle. It is believed as one of the major public health burdens worldwide, especially in the Indian subcontinent.[1,2] Approximately 25% of the world's population is suffering from MS, and it will increase up to 38% by the year 2023.[3] The prevalence of the MS is higher in adult population throughout the world.[4] People with abdominal obesity are at high risk of having MS, and a sedentary lifestyle settles on the phenotypical expression of a genetically acquired trait. Adoption of a healthy lifestyle and weight control is the effective and primary strategies for the prevention and treatment of the MS.[5] In the etiopathogenesis of MS, reactive oxygen species play an essential role in multiple physiological systems under conditions of oxidative stress and contribute to cellular dysfunction. Oxidative stress also plays a major role in the pathogenesis of a variety of human diseases, including diabetes, hypertension, atherosclerosis, aging, Alzheimer's disease, kidney disease and malignancies. It has been found that in MS, dyslipidemia and elevated extra and intra-cellular glucose concentrations result in oxidative stress, which is defined as an imbalance between oxidants and antioxidants.[6] Lifestyle factors such as a dietary habit, physical activity,

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Access this article online

Quick Response Code:

Website: www.ayujournal.org

DOI: 10.4103/ayu.AYU_79_19

How to cite this article: Padhar BC, Dave AR, Goyal M. Clinical study of *Arogyavardhini* compound and lifestyle modification in management of metabolic syndrome: A double-blind placebo controlled randomized clinical trial. AYU 2019;40:171-8.

Submitted: 05-May-2019 **Revised:** 30-Aug-2019
Accepted: 03-May-2020 **Published:** 08-Aug-2020

smoking habit, and physiological stress are the modifiable determinants of the oxidative stress and the chronic low-grade inflammation is involved in the pathogenesis and progression of many aging-associated diseases, including MS.[7]

Clinical features of MS resemble *Apathya Nimittaja Prameha* or *Avarana Janya Madhumeha* (type 2 diabetes) mentioned in Ayurveda.[8] The initial stage of MS can be compared with *Medavaha Sroto-Dushti* (vitiation of micro-channels of lipid metabolism and transportation), which manifests as a group of symptoms of *Atisthula* (obesity) and premonitory symptoms and signs of *Prameha* (diabetes). *Apathya Nimittaja Prameha* or *Medavaha Sroto-Dushti* which occurs due to *Santarpaka Ahara* and *Vihara* (over nutrition and sedentary lifestyle), can be said *Santarpanjanya* diseases. Disturbed metabolism, fat accumulation, production of *Ama* (reactive oxygen species) and obstructed channels for lipid transportation are the key factors in the pathogenesis of the MS.

There is no well-established therapeutic intervention for the management of MS in contemporary medical science. Patients of MS are treated with anti-diabetic, antihypertensive, anti-hyperlipidemic, anti-obesity drugs and lifestyle modifications. These drugs have several side effects and patients have to take it for long life.

Arogyavardhini compound is a formulated medicine. The contents of *Arogyavardhini* compound [Table 1] like *Tamra Bhasma* (incinerated copper), *Guggulu, Katuki, Triphala* are having *Lekhana* (weight-reducing), *Dipana* (improving digestion and metabolism) and *Medadoshahara* (correcting lipid metabolism and transportation) properties,[9] *Lasuna* (garlic) is having *Avaranahara* (removal of obstruction in micro channels), *Rasayana* (antioxidant) properties , which may be useful to correct the underline pathology of disease and establish the normal physiology.[10] Recent researches on *Arogyavardhini Rasa* have proved its anti-dyslipidemic and weight lowering effect.[11] Anti-hypertensive, anti-hyperglycemic, anti-hyperlipidemic and antioxidant effects of *Lasuna* (garlic) are also proven by various researches.[12].Furthermore, Acharya Charaka has mentioned that daily exercise, taking food after complete digestion of previously eaten food and eating food articles prepared with wheat and barley flour is beneficial for the prevention and treatment of diseases occurring due to over nutrition, especially obesity.[13] Obesity being the main culprit in the pathogenesis of MS, patients were also advised to avoid diet and lifestyle factors vitiating *Medavaha Srotas* and later helping for manifestation of obesity and type 2 diabetes, such as daytime sleep, sedentary lifestyle, *Kapha* and fat, increasing foods.[14]

The study design is a double-blind randomized clinical trial; placebo (capsules filled with roasted sooji/semolina powder) was given to patients of one of the group where only lifestyle modification was advised, to make the interventions of both the groups appearing identical. The research work was planned to assess the clinical safety and efficacy of *Arogyavardhini* compound and lifestyle modification in the management of the MS. Primary objective of the study was changes in components of MS. While secondary objective was changes in Framingham 10 years' cardiac risk score.

Materials and Methods

Trial design

Patients, who reported to the Outpatient Department of the Kayachikitsa, I. P. G. T and R. A. Hospital, Jamnagar, were investigated for diagnosis of MS. A total of 495 patients having complaint of weight gain and increased waist circumference were screened for the present clinical trial and diagnosed with MS as per National Cholesterol Education Program (NCEP), adult treatment panel III (revised in 2005) guideline.[15] Among them, 75 patients fulfilling the inclusion criteria were included in the study. Selected patients were randomly divided into two groups, irrespective of their age, sex, caste and religion, by computer-generated randomization method. Masking of interventions was done by the neutral third person nominated by the departmental research committee. Patients and researchers were kept blind until the completion of clinical trial and data

Table 1: The ingredients of *Arogyavardhini* compound

Content	Latin/scientific name	Part used	Ratio	Form
Shuddha Parada	Processed mercury	-	1 part	Liquid metal
Shuddha Gandhaka	Processed sulphur	-	1 part	Powder
Loha Bhasma	Processed iron	-	1 part	Incinerated powder
Abharaka Bhasma	Processed mica	-	1 part	Incinerated powder
Tamra Bhasma	Processed copper	-	1part	Incinerated powder
Haritaki	*Terminalia chebula* Linn.	Fruit	2 part	Powder
Amalaki	*Emblica officinalis* Gaertn.	Fruit	2 part	Powder
Bibhitaki	*Terminalia bellirica* Roxb.	Fruit	2 part	Powder
Shuddha Shilajit	Processed asphaltum		3 part	Powder
Suddha Guggulu	*Commiphora mukul* Hook.	Gum resin	4 part	Powder
Eranda Moola	*Ricinus communis* Linn	Root	4 part	Powder
Katuki	*Picrorhiza kurrora* Roxb.	Root/rhizome	22 part	Powder
Nimba	*Azadirachta indica* A.Juss	Leaf juice	As per required for trituration	Liquid
Lasuna (single bulb)	*Allium sativum* Linn.	Bulb	44 part	Powder

analysis. The study was approved by the Institutional Ethics Committee of I. P. G. T and R. A., Gujarat Ayurved University, Jamnagar (No. PGT/7-A/2014-15/2652, Dt. 19/12/2014) and the trial was also registered in the clinical trial registry of India (CTRI No: CTRI/2015/06/005833, Date: 01/06/2015.) Prior informed written consent was taken from each patient before including in the study. A detailed clinical research pro forma, incorporating all the points of history taking, physical examination, and assessment of the treatment, was maintained for record and analysis purpose.

Inclusion criteria

1. Patients having age between 20 and 60 years of either sex
2. Abdominal obesity (waist circumference >90 cm in men and >80 cm in women)
3. Hyper-triglyceridaemia (s. triglycerides level 150–600 mg/dl)
4. Low high density lipoprotein (HDL) cholesterol (S. HDL cholesterol <40 mg/dl for men and <50 mg/dl for women)
5. Elevated blood pressure (systolic blood pressure 130–139 mmHg and/or diastolic blood pressure 85–90 mmHg)
6. Impaired fasting glucose (fasting plasma glucose 100–125 mg/dl).

Exclusion criteria

1. Age below 20 and above 60 years
2. Patients suffering from diabetes mellitus, hypertension, and taking anti-diabetic and antihypertensive or anti-hyperlipidemic drugs
3. Systemic illness such as tuberculosis, carcinoma and endocrine disorders like Cushing's syndrome, hypothyroidism
4. Patient having the history of myocardial infarction or unstable angina
5. The patients suffering from congestive cardiac failure
6. Patients having major renal or liver disorders.

Medication and treatment plan

Details about trial drugs

Arogyavardhini compound

Arogyavardhini compound is a formulated medicine, which contains *Arogyavardhini Rasa* and single bulb *Lasuna* powder in equal (1:1) proportion. The ingredients of *Arogyavardhini* compound are depicted in Table 1. Most of the raw materials of *Arogyavardhini* compound were procured from Pharmacy, Gujarat Ayurved University, Jamnagar. *Lasuna* was purchased from Ahmedabad, Gujarat. All herbal raw drugs were authenticated by Pharmacognosy laboratory, I. P. G. T, and R. A, Gujarat Ayurved University, Jamnagar.

For the preparation of *Arogyavardhini Rasa*, *Shodhana* (purification) of *Guggulu* was carried out by the *Swedana* (steaming) method using *Triphala* decoction.[16] Herbal ingredients were powdered by grinding and sieving and passed through sieve no # 80. Fresh juice of *Nimba* leaves (*Azadirachta indica* A.Juss.) was prepared by grinding and squeezing.[17] *Dhatukajjali,* which is the mixture of *Kajjali* (black sulfide of mercury), *Lauha Bhasma* (incinerated ash of purified iron), *Abhraka Bhasma* (incinerated ash of purified mica) and *Tamra Bhasma* (incinerated ash of purified copper) was made by sequential *Mardana* (trituration).[18] *Dhatu-Kajjali* was taken in a polythene bag with the addition of powdered drugs and mixed thoroughly by shaking. Then, the mixture was added little by little in a butterfly wet– grinder, initially containing a mixture of *Guggulu*, (*Commiphora mukul (Stocks) Hook.*) *Shilajatu* (purified asphaltum) and *Nimba* leaves juice. The required quantity of *Nimba* leaves juice for optimum levigation was added until the mixture was immersed completely. Approximately 300–310 ml leaves juice was added three hourly. Grinding and soaking was carried out for 12 h/day for 2 days. The final material of *Arogyavardhini* was subjected to complete drying and was powdered, weighed, packaged, labeled, and stored in a glass container.

Good quality of *Lasuna* (garlic) bulbs, were selected to prepare powder. *Lasuna* was added little by little in a butterfly wet-grinder to make its paste. The paste was dried for 5 days. When paste became slightly reddish yellow and brittle enough to be powdered, it was added into the grinder to make powder. The fine powder of *Lasuna* was sieved in mesh no. 80.

Then, equal quantity of garlic powder and *Arogyavardhini Rasa* was mixed well with each other in the mass mixing machine until the homogeneous mixture was obtained. The final product, namely *Arogyavardhini* compound, was packaged, labeled, and stored in a glass container.

Lifestyle modification

The lifestyle modification was advised to patients in both the groups like to perform;

- Exercise like -brisk walking for 30 min daily in the morning .[13] To take food only when previously taken food is properly digested, *Jirna Ahara* (complete digestion of food) with symptoms like as good appetite, lightness of body, clear belching, proper evacuation of stool and urine and cheerfulness of mind[19]
- They were advised to eat food prepared with wheat and barley.[19] Patients were asked to avoid day sleep, milk and dairy products, sweets and sedentary lifestyles.[14]

Grouping and posology

Patients in one group were treated with lifestyle modifications and *Arogyavardhini* compound capsule, while in another group lifestyle modification and placebo capsule (filled with roasted Sooji powder), each capsule of 500 mg, two capsules twice a day before lunch and dinner with *Anupana* of water for 8 weeks. De-masking the interventions after completion of the clinical trial, it was found that patients in Group A had received the placebo capsules, while patients in Group B had received *Arogyavardhini* compound capsules.

Investigations

Following investigations were carried out at baseline and after completion of 8 weeks' course of treatment;

- Routine hematological investigations such as hemoglobin, total white blood cell (WBC) count, differential WBC count, red blood cell count, platelet count and erythrocytes sedimentation rate
- Complete lipid profile and fasting blood sugar, renal function test (serum creatinine, serum proteins, serum albumin, serum Globulin, and blood urea.), liver function test (serum glutamic pyruvic transaminase [SGPT], serum glutamic oxaloacetic transaminase [SGOT], serum alkaline phosphates, total bilirubin, direct bilirubin and indirect bilirubin)
- Physical, chemical and microscopic urine investigations.

Sample size

It was estimated that a total of 70 patients, 35 patients in each group would be needed to detect a difference between groups, with a two-tailed α of 0.05 and a (1-β) of 0.80, for a comparison of two independent proportions, if there was an absolute decrease of 12% in the composite outcome measure. As 5%–10% drop out was expected, so sample size of total of 75 patients for this trial was kept.

Assessment criteria

Differences of initial and after 8 weeks' observations on waist circumference, s. triglycerides, s. HDL, fasting blood sugar, systolic blood pressure, and Framingham's 10 years cardiac risk score were used to assess the effect of therapy. The information gathered based on observations was subjected to statistical analysis. Sigma state software (3.5 Version) was used to find the SD, SE, "*t*," and "*P*" values.

To check the significance of changes due to intervention in a single group, student paired "*t*"-test was applied and $P < 0.05$ was considered as statistically significant changes. The effect of both the drugs on various objective parameters was compared and unpaired "*t*"-test was used to check the statistical significance of changes in outcomes.

Results

Patients for the present clinical trial were registered between June 2015 and July 2016. A total of 75 patients were registered for the present study, among them 70 patients, 35 patients in each group completed the course of treatment. One patient in group A drop out due to shifting of his job to another city and 2 patients in group A were dropped out due to irregular follow-up of the treatment. One patient in group B drop out due to unknown reasons while another patient in group B dropped out due to personal reasons [Figure 1].

Group A and group B provided 1.32% and 3.06% decrease in waist circumference, 5.81% and 18.03% decrease in serum triglycerides, 3.82% increase and 2.48% decrease in fasting blood sugar, 9.13% and 5.56% increase in serum HDL, 4.43% and 6.89% decrease in systolic blood pressure, respectively. The reduction in waist circumference in both the groups was statistically highly significant. Reduction in serum triglycerides in group B was statistically significant. An increase in fasting blood sugar in the placebo controlled group (group A) and a reduction in fasting blood sugar in group B were statistically insignificant. An increase in serum HDL in placebo controlled group was statistically significant while the increase in serum HDL in group B was statistically insignificant. The decrease in systolic blood pressure in both the groups was statistically highly significant [Table 2].

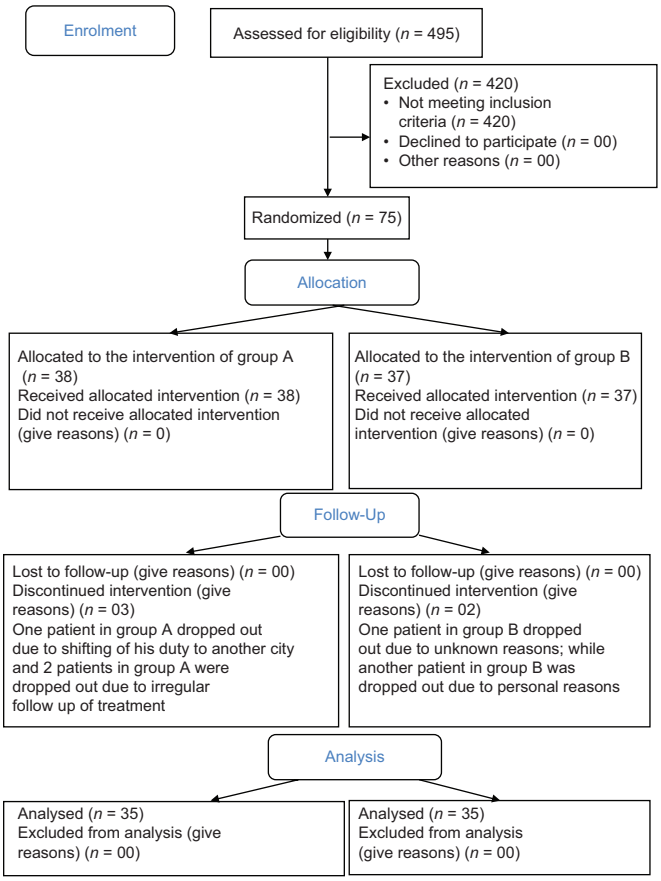

Figure 1: CONSORT flow chart

Group A and group B provided 40.87% and 51.66% decrease in Framingham coronary heart disease risk score, respectively. The decrease in Framingham coronary heart disease risk score in both the groups was statistically highly significant [Table 3].

On applying the Un-paired "*t*"-test, the difference of decrease in waist circumference in group A and group B was statistically highly significant while the difference of decrease in systolic blood pressure was statistically significant [Table 4].

On applying the Un-paired "*t*"-test, the difference of decrease in Framingham coronary heart disease risk score in group A and group B was statistically insignificant. This indicates that the difference of decrease in Framingham coronary heart disease risk score in group A and group B was due to chance [Table 5].

Group A and group B provided 5.85% increase and 4.62% decrease in SGOT, 7.70% increase and 1.24% decrease in SGPT, 13.07% and 0.37% decrease in alkaline phosphatase, 6.90% increase and 3.45% decrease in the direct bilirubin,

Table 2: Results of interventions on primary outcomes

Variable	Group	Mean values			Percentage	Paired *t*-test			Remarks
		BT	AT	Difference		SDM (±)	*t*	*P*	
Waist circumference (cm)	A	106.94	105.51	1.43	1.32↓	1.420	5.951	<0.001	HS
	B	107.29	104.23	3.06	2.84↓	1.514	11.950	<0.001	HS
Serum triglycerides (mg/dL)	A	187.43	177.14	10.29	5.81↓	72.63	0.838	0.4080	IS
	B	198.29	162.54	35.74	18.03↓	80.21	2.636	0.0125	S
FBS (mg/dL)	A	104.50	106.91	−2.40	3.82↑	22.56	0.629	0.5300	IS
	B	104.83	102.03	2.80	2.48↓	17.44	0.949	0.3490	IS
Serum HDL (mg/dL)	A	38.09	41.91	3.83	9.13↑	6.55	3.458	0.0015	S
	B	42.20	44.69	2.49	5.56↑	7.86	1.870	0.0710	IS
Systolic blood pressure (mmHg)	A	133.14	127.20	5.94	4.43↓	5.77	6.094	<0.001	HS
	B	133.60	124.40	9.26	6.89↓	5.07	10.810	<0.001	HS

n=35 in group A (placebo controlled group), *n*=35 in group B (*Arogyavardhini* compound treated group). ↓: G decrease, ↑: Gn increase. BT: Gefore treatment, AT: After treatment, FBS: Fasting blood sugar, HDL: High density lipoprotein, SDM: Standard deviation of mean, S: Significant, HS: Highly significant, IS: Insignificant, *t*: Students paired *t*-test calculated value, *n*: Number of patients

Table 3: Results of interventions on secondary outcomes

Variable	Group	Mean values			Percentage	Paired *t*-test			Remarks
		BT	AT	Difference		SDM (±)	*t*	*P*	
Framingham coronary heart disease risk score	A	5.26	3.11	2.15	40.87↓	3.080	4.126	<0.001	HS
	B	3.31	1.60	1.71	51.66↓	2.545	3.978	<0.001	HS

n=35 in group A (placebo controlled group), *n*=35 in group B (*Arogyavardhini* compound treated group). ↓: A decrease, ↑: An increase. BT: Before treatment, AT: After treatment, SDM: Standard deviation of mean, HS: Highly significant, *t*: Students paired *t*-test calculated value, *n*: Number of patients

Table 4: Comparison of results on primary outcomes

Variable	Group	*n*	Difference in means	Unpaired *t*-test			Remarks
				SDM (±)	*t*	*P*	
Waist circumference (centimetres)	A	35	1.43	1.420	−4.642	<0.001	HS
	B	35	3.06	1.514			
Systolic blood pressure (mmHg)	A	35	5.94	5.770	−3.314	0.013	S
	B	35	9.26	5.066			

n=35 in group A (placebo controlled group), *n*=35 in group B (*Arogyavardhini* compound treated group). SDM: Standard deviation of mean, S: Significant, HS: Highly significant, *t*: Students *t*-test calculated value, *n*: Number of patients

Table 5: Comparison of results on secondary outcomes

Variable	Group	*n*	Difference in means	Unpaired *t*-test			Remarks
				SDM (±)	*t*	*P*	
Framingham coronary heart disease risk score	A	35	2.15	3.080	0.437	0.520	IS
	B	35	1.71	2.545			

SDM: Standard deviation of mean, IS: Insignificant, *t*: Students *t*-test calculated value, *n*: Number of patients

2.22% and 10.87% decrease in indirect bilirubin, respectively. No change was observed in total bilirubin in group A, while an 8% decrease was observed in total bilirubin in group B, which were statistically insignificant. The decrease in serum alkaline phosphates in group A was statistically significant, while it was statistically insignificant in group B [Table 6].

Group A and group B provided 0.58% decrease and 3.57% increase in blood urea, 1% decrease, and 1.12% increase in serum creatinine, 4.45%, and 7.85% decrease in total serum proteins, respectively. The decrease in total serum proteins in group A was statistically significant while decrease in total serum proteins in group B was statistically highly significant. Changes in other renal function parameters were statistically insignificant [Table 7].

Liver function parameters (SGOT, SGPT, s. alkaline phosphatase, total serum bilirubin) and renal function parameters (blood urea, serum creatinine and total serum proteins) were within normal limit before and after treatment. No adverse drug reaction was observed in any of the groups throughout the study.

Table 6: Effect of interventions on liver function tests

Variable	Group	Mean values			Percentage	Paired *t*-test			Remarks
		BT	AT	Difference		SDM (±)	*t*	*P*	
SGOT (units/L)	A	25.83	27.34	−1.51	5.85↑	7.26	−1.23	0.23	IS
	B	26	24.80	1.2	4.62↓	6.75	1.05	0.30	IS
SGPT (units/L)	A	20	21.54	−1.54	7.70↑	6.39	−1.43	0.16	IS
	B	21.03	20.77	0.26	1.24↓	7.45	0.20	0.84	IS
Serum alkaline phosphatase (IU/L)	A	63.20	54.94	8.26	13.07↓	19.41	2.52	0.017	S
	B	61.43	61.20	0.23	0.37↓	15.66	0.09	0.93	IS
Total serum bilirubin (mg/dL)	A	0.75	0.75	0	0.00	0.26	−0.20	0.84	IS
	B	0.75	0.69	0.06	8.00↓	0.49	0.72	0.48	IS
Direct bilirubin (mg/dL)	A	0.29	0.31	−0.02	6.90↑	0.11	−1.24	0.22	IS
	B	0.29	0.28	0.01	3.45↓	0.17	0.49	0.63	IS
Indirect bilirubin (mg/dL)	A	0.45	0.44	0.01	2.22↓	0.20	0.42	0.68	IS
	B	0.46	0.41	0.05	10.87↓	0.36	0.70	0.49	IS

n=35 in group A (placebo controlled group), *n*=35 in group B (*Arogyavardhini* compound treated group). ↓: Decrease, ↑: An increase. BT: Before treatment, AT: After treatment, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, SDM: Standard deviation of mean, S: Significant, IS: Insignificant, *t*: Students paired *t*-test calculated value, *n*: Number of patients

Table 7: Effect of interventions on renal function test

Variable	Group	Mean values			Percentage	Paired *t*-test			Remarks
		BT	AT	Difference		SDM (±)	*t*	*P*	
Blood urea (mg/dL)	A	26.06	25.91	0.15	0.58↓	6.06	0.14	0.89	IS
	B	24.66	25.54	−0.88	3.57↑	6.83	−0.77	0.44	IS
Serum creatinine (mg/dL)	A	1.00	0.99	0.01	1.00↓	0.26	0.13	0.90	IS
	B	0.89	0.90	−0.01	1.12↑	0.15	−0.35	0.73	IS
Serum proteins (g/dL)	A	6.96	6.65	0.31	4.45↓	0.69	2.74	0.01	S
	B	7.01	6.46	0.55	7.85↓	0.71	4.52	<0.001	HS

n=35 in group A (placebo controlled group), *n*=35 in group B (*Arogyavardhini* compound treated group). ↓: A decrease, ↑: An increase. BT: Before treatment, AT: After treatment, SDM: Standard deviation of mean, S: Significant, IS: Insignificant, HS: Highly significant, *t*: Students paired *t*-test calculated value, *n*: Number of patients

Discussion on the Result on Primary Outcomes

Waist circumference

Lifestyle modifications such as regular exercise, avoidance of *Adhyashana* (eating food before complete digestion of previously taken food) and daytime sleep can improve the condition of MS in several ways. Intensive and regular practice of exercise stimulates adipose tissue to utilize fatty acid for energy production instead of glucose, which results in the decrement of triglycerides and increment of serum HDL. Owing to regular exercise, increased usage of fatty acids by adipose tissues decreases fat accumulation and obesity, resulting in diminished insulin resistance and prevents the occurrence of type 2 diabetes and co-morbidities related to obesity.

The habit of eating before complete digestion of previous food is defined as *Adhyashana*, which stimulates and accelerates the secretion of insulin. Adipose tissues use glucose for energy production instead of fatty acid in the presence of insulin, leading to less expenditure and thus, storage of fatty acids in adipose tissue, result in obesity and insulin resistance. Avoidance of *Adhyashana* increases the post-absorptive period and decreases insulin levels in the blood. Adipose tissues utilize fatty acids for energy production at a lower level of insulin in the blood, which results in depletion of fatty acids, decreased fat mass and triglycerides, the increment of HDL, and improvement in insulin sensitivity resulting in fall of fasting blood sugar.

Contents of *Arogyavardhini* compound like, *Tamra Bhasma* (incinerated copper),[20] *Guggulu*[21] and garlic[22] are having *Lekhana*, *Pachana*, *Medodoshahara* properties and hence due to their effect, on fat metabolism and lipolysis, becomes accelerated which results in burning of fat from the abdomen and waist region, resulting in the reduction of waist circumference.

Fasting blood sugar

Contents of *Arogyavardhini* compound like; *Tamra Bhasma* plays an important role in carbohydrate metabolism by stimulating insulin binding, hexose transport and lipogenesis.[20] *Katuki* (*Picrorhiza kurroa* Royle ex Benth.) increases the insulin-mediated translocation of glucose transporter type 4from the cytosol to the plasma membrane which results in better glucose uptake by skeletal muscles

and improves glycemic control.[23] *Triphala* lowers fasting blood sugar and inhibit lipid peroxide formation and scavenge hydroxyl and superoxide radicals.[24] *Shilajatu* (Asphaltum Punja-Bianum) reduces uptake of sugar and lipid from the gut.[25]

Serum triglycerides

Contents of *Arogyavardhini* compound like *Tamra Bhasma* decrease serum triglycerides by activating lysyl oxidase enzyme and improving fat metabolism.[26] The other contents of *Arogyavardhini* compound such as *Guggulu*,[27] *Lasuna*,[28] *Triphala*[29] having anti-hyperlipidemic activity has caused decrease in serum cholesterol and triglycerides. Guggulsterone present in *Guggulu* having hypolipidemic, antioxidant, and anti-inflammatory activities had provided cardiovascular benefits through various mechanisms. Farnesoid x receptor, the key transcriptional regulator for the maintenance of cholesterol and bile acid homeostasis gets blocked by guggulsterone, results in the hypolipidemic effect of *Guggulu*. Guggulsterone also up-regulates bile salt export pump, an efflux transporter responsible for the removal of cholesterol metabolites and bile acids from the liver, which results in cholesterol metabolism into bile acids, and thus reduces lipid levels.[30] Garlic reduces lipid levels through inhibition of HMG-CoA reductase and 14-alpha-demethylase.[31]

S. high density lipoprotein

Obesity is one of the causes of the decrease in serum HDL. Lifestyle modification, as well as *Arogyavardhini* compound, has reduced weight and body mass index. Hence, the improvement in obesity increased serum HDL.[32]

Systolic blood pressure

Sulfides present in garlic decrease metabolism of bradykinin, inhibit prostaglandin synthesis; produce H_2S and nitrous oxide which results in vasodilation. It also inhibits the renin-angiotensin-aldosterone system. The combined effect of these sulfides results in low blood volume and cardiac output which decreases systolic blood pressure.[33]

Effect of trial drug on secondary outcomes-Framingham coronary heart disease risk score

Framingham coronary heart disease risk score estimates the chance of heart attack or death in 10 years. It was calculated by the use of software MD + CALC. Age of patients, sex (gender), smoking history, total cholesterol, HDL cholesterol, systolic blood pressure, and history of use of antihypertensive drugs were taken into consideration to calculate the coronary heart disease risk score.[34]

In both groups, patients were advised to quit smoking. Furthermore, lifestyle modification and *Arogyavardhini* compound resulted in a reduction of total cholesterol, systolic blood pressure, and an increase of HDL-cholesterol, which resulted in the lowering of coronary heart disease risk score.

Vitiation of *Jatharagni* (factor responsible for digestion), *Rasa* and *Meda Dhatvagni* (factor responsible for the formation of *Rasa* and *Meda Dhatu*), *Rasa, Mamsa, Meda Dhatu, Kapha* and *Vata Dosha*, *Rasavaha* and *Medavaha Srotasa* are the key components in the pathogenesis of the MS. The contents of *Arogyavardhini* compound like *Tamra Bhasma*, *Triphala*, *Lasuna*, *Guggulu* having *Dipana*, *Pachana* properties correct the functions of *Agni* and removes *Ama* (intermediate product of digestion and metabolism), *Triphala*, *Shilajita*, *Kutaki* reduces *Kleda* (fluidity) and *Meda, Lasuna* and *Guggulu* remove *Avarana* of *Vata* and clear the channels of lipid transportation. Lifestyle modifications like; daily exercise improve the function of *Agni* and reduce *Kapha, Meda,* and *Mamsa,* avoidance of *Adhyashana* helps to maintain the normal function of *Agni* and prevent *Ama* formation; avoidance of day time sleep and *Kapha, Meda* increasing foods improve functions of *Meda Dhatvagni* and *Medavaha Srotasa.* Hence, the lifestyle modification and *Arogyavardhini* compound having their multivariate effect on normalizing the various components of the pathogenesis of metabolic syndrome (MS) resulted in the overall improvement in metabolic syndrome.

Conclusion

Arogyavardhini compound combined with lifestyle modification had provided statistically highly significant improvement in reduction in waist circumference, systolic blood pressure and a statistically significant decrease in serum triglycerides. Hence, it can be stated that *Arogyavardhini* compound along with lifestyle modification is more effective than lifestyle modification alone in the management of metabolic syndrome.

Data access and responsibility

The corresponding author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Acknowledgment

Authors are very thankful to authority of Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar for their financial support for drugs, investigations and equipments required for present clinical trial.

Financial support and sponsorship

Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar, supported for drugs, investigations and equipment required for present clinical trial.

Conflicts of interest

There are no conflicts of interest.

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