Journal of Ayurveda and Integrative Medicine 15 (2024) 100973

Contents lists available at ScienceDirect

Journal of Ayurveda and Integrative Medicine

journal homepage: elsevier.com/locate/jaim

Efficacy of tryushnadya churna in metabolic syndrome with obesity – A randomized double blind controlled clinical trial

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ARTICLE INFO

Keywords:
Ayurveda
Metabolic syndrome
Obesity
Tryushnadi churna
Ayurveda diet
Yoga

ABSTRACT-

Background: Metabolic syndrome (MetS) with obesity has significant mortality and morbidity. Integrative Ayurveda management is explored for it's possible effect.
Aim: To evaluate the effect of Tryushnadi churna in the management of Metabolic syndrome with obesity.
Methods: Study is a Randomized, Controlled, double blind, parallel group comparative clinical trial. 48 participants meeting the National Cholesterol Education Programme Adult Treatment panel 3 diagnostic criteria were recruited in the study. They were divided in two 2 groups. Placebo group were administered with Placebo 1 gm twice a day, Ayurveda diet and yoga. Tryushnadi Group were intervened with Tryushnadi churna 1 gm twice a day, Ayurveda diet and yoga. Interventions were for 90 days. Assessments criteria included Weight, BMI,Waist circumference (WC), Waist hip ratio, Skin fold thickness (SFT), Body fat, blood pressure, WHO-QOL BREF scale, Clinical Global Impression Scale (CGI)- Severity, Global improvement and Efficacy index, Fasting blood sugar (FBS) were assessed on every 30th day. Other blood parameters like Glycated haemoglobin (HbA1c), Triglycerides, High density lipoproteins (HDL), Low density lipoproteins (LDL), Total cholesterol (TC) were evaluated at pre and post study.
Results: Between groups comparison showed, Tryushnadi group had significant improvements in BMI, Weight, WHOQOL-Bref and had large effect size. Both the groups showed improvement in WC, body fat, SFT, CGI severity, CGI efficacy index and improvement in quality of life in within group assessment.
Conclusion: Study showed that Tryushnadi churna was effective in management of MetS with Obesity. Integrated management of Ayurveda medicine, Ayurveda diet and yoga had beneficial effect.

1. Introduction

Metabolic syndrome (MetS) is a complex multifactorial disease with a cluster of various interrelated cardiometabolic risk factors that promote the development of atherosclerotic cardiovascular disease (CVD) and Type 2 diabetes mellitus (T2DM) [1]. Features of metabolic syndrome include abdominal obesity, elevated blood pressure, insulin resistance, a proinflammatory and prothrombotic state, and atherogenic dyslipidemia (high triglycerides, high apolipoprotein B, high low-density lipoprotein particle (LDL-p) number, and low high-density lipoprotein cholesterol (HDL-C)) [2].

Obesity is the important risk factor for MetS and increases chance for development of MetS and T2 DM. The predisposing factors for MetS are obesity, poor diet with excessive energy, sedentary activity and age. Individuals with obesity and metabolic syndrome (MetS) have an increased risk for Type 2 Diabetes mellitus (T2DM) and cardiovascular disease (CVD) development and premature death [3]. Obese participants have double risk of all-cause of mortality compared to lean counterparts [4]. Obesity is related to an increased prevalence of coronary heart disease, type II diabetes mellitus, asthma and renal disease [5].

Obesity and MetS have become a major public health concerns globally due to their high prevalence. Worldwide estimation showed 25% of adults have MetS [6]. The prevalence of obesity and MetS is rapidly increasing in India and other South Asian countries, leading to increased mortality and morbidity due to CVD and T2DM [7]. The prevalence of MetS has escalated in different parts of India, ranging now from 11% to 41% [8]. Specifically, some segments of the population

Peer review under responsibility of Transdisciplinary University, Bangalore.
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https://doi.org/10.1016/j.jaim.2024.100973
Received 21 January 2022; Received in revised form 3 May 2024; Accepted 14 May 2024

(women and people belonging to middle and low socioeconomic strata) are increasingly becoming vulnerable to obesity and clustering of cardiovascular risk factors (MetS) in India [9]. Approximately about one third of urban south Asians are showing evidences of the MetS [10].

Pathology in MetS is associated with chronic low grade inflammation or meta-inflammation and there is increase in IL-1, IL-6, TNF-α, C reactive protein and decrease in anti inflammatory cytokines like adiponectin [11]. Insulin resistance precedes development of MetS and diabetes [12]. Elevated levels of free fatty acids (FFA) impair insulin signalling and increase the risk of MetS and T2DM.

Due to high prevalence, there is an immediate need to identify a potential treatments for MetS to prevent development of serious comorbid conditions [6]. MetS is a complex disorder and has multi targets for therapy and no single therapy can address all targets. Management strategies in MetS are aimed at reducing low density lipoproteins (LDL), hypertension and impaired glucose tolerance. The first line of therapy for metabolic syndrome is aggressive diet and lifestyle interventions: reducing caloric intake, adopting a healthy diet, and increasing physical activity [13]. High carbohydrate, low fiber, high energy food increase the risk of MetS [14,15]. Saturated fatty acids increase MetS while polyunsaturated fatty acids (PUFA) decrease MetS. PUFA reduces triacylglycerol, hypertension, CRP, IL-6. Monounsaturated fatty acids (MUFA) decrease triacylglycerol, LDL and increase high density lipoproteins (HDL). Whole grain carbohydrates reduce MetS [16]. Dietary fibers also called as non starch polysaccharides available in whole grain cereals, legumes, fruits, vegetables have possible role in prevention of T2DM and MetS [17,18]. Intermittent fasting has shown to reduce weight, decrease insulin resistance, dyslipidemia, reduction in blood pressure, decreased risk of T2DM and cardiovascular diseases [19]. Pharmacological interventions are statins, fibrates, nicotinic acid, ACE inhibitors, metformin, thiazolidinediones or acarbose [20]. Polypharmacotherapy and associated comorbidities compel the participant for lifelong medication which adds burden to the cost of disease and adverse drug effects. Hence study was designed to evaluate the effects of a Polyherbal Ayurveda formulation '*Trayushnadya churna* [21] along with lifestyle modification through diet and yoga in obese participants of MetS. *Ayurveda texts* [21] advocate, *Trayushnadya churna* to have effect on sthoulya (obesity), medoroga (lipid disorders), prameha (Diabetes mellitus), kustha (skin disorders) and other kaphaja diseases.

2. Materials & methods

2.1. Preparation of the drug

The ingredients of Trayushnadya churna were procured from authentic distributors and capsules were prepared in GMP certified KLE Ayurveda Pharmacy as per standard procedures. Qualitative analysis of each raw material and finished product as per API (Ayurvedic Pharmacopeia of India) guidelines were done. Raw drugs (ash, extractive values and loss on drying), finished product assessments were done. For powder of Trayushnadya churna, ash values and loss on drying were assessed and capsule filling was carried out. Wheat powder (Triticum aestivum L.) was used as a placebo.

2.2. Research design

The study was a randomised, double blind, parallel group comparative design clinical study. Investigators were not involved in randomisation, distribution and administration of study articles and were other staff from central research unit. Computer generated random numbers were utilized for the study. Block size was 2, control and trial group allocation was in the ratio of 1:1.

2.3. Sample size

Sample size was calculated from a previous study [22] on the basis of BMI assessment. The sample size was 24 in each group under 5 % alpha error and 80 % power of the test.

2.4. Ethical clearance and CTRI registration

The study was approved by Institutional ethics Committee (Protocol ID BMK/16/PG/KC/01 KLEU BMK Ayurveda Mahavidyalaya Belagavi CTRI Registration Number- CTRI/2018/06/01423). Data collection was from Jan 2018 to May 2019.

2.5. Participants

The participants attending outpatient department of the institute were recruited for the study. The CONSORT statement guidelines [23] have been followed in reporting the outcomes of the study. Total 48 participants diagnosed as Metabolic Syndrome as per National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) [24] were recruited from outpatient department of KLEU Shri BMK Ayurveda Hospital Belagavi, Karnataka, India.

2.5.1. Inclusion criteria

Participants of either sex between age 20–60 years, BMI>25 kg/m2, blood pressure levels equal or above 130/85 mm of Hg in a period of 7 days, FBS >110 mg/dl, were included in the study.

2.5.2. Exclusion criteria

The participants with stage II and stage III hypertension (JNC 8 criteria [25]); participants with K/C/O Type 1 DM, uncontrolled DM, DM complications, on medication for T2 DM; those with comorbid diseases like coronary heart disease (CHD), endocrine diseases, renal diseases; those taking any medications or intervention for dyslipidaemia and obesity within the period of 4 weeks; and pregnant and lactating female participants were excluded from the study.

2.5.3. Screening methods

Study materials and pamplets were displayed in the main visible areas of the hospital and were also distributed in the camps and social media sites. All participants included in the study were examined thoroughly and data were recorded systematically. Various laboratory and Ayurveda variables were assessed. Laboratory investigations were carried out at clinical laboratory, KAHER's Shri BMK Ayurveda Mahavidyalaya, Belagavi in all participants at baseline and 90th day of intervention. Only FBS was assessed on baseline, 30th, 60th and 90th day.

2.5.4. Detailed procedures along with timeline

All the participants were randomly divided into two groups: placebo group and Tryushnadi group. Placebo group (n = 24) received Placebo capsules 1 gm BD while Tryushnadi group (n = 24) received Trayushnadya churna capsules 1 gm BD. Both groups received their respective interventions along with water after food intake. Ayurveda Diet chart and yoga protocol were given to participants of both the groups.

2.5.4.1. Diet and yoga. Diet was planned on the basis of *agni* strength and body weight. Diet was planned on the lines of *meda dusti, sthoulya* and *prameha* diseases. Initially all participants' 3 days food record were assessed to know food patterns, quantity, quality of diets. Exercise and daily activity were assessed. Then nutritionist advised them and gave general instructions of diet and estimation of portion sizes. Assessment of *Agni* strength (Increased, decreased, deranged, normal) and weight were carried out. Fruits, vegetables, whole grain cereals, beans, nuts, seeds, millet, *methi, bajra, jowar*, buttermilk, *vrukshamla* (*Garcinia indica*) were used in diet planning. Energy intake was planned to 25 kcal/kg/day ideal body weight to promote weight loss [26]. Proteins intake was up to 15–20 %, carbohydrates 45%, and fats 25–35% of total energy

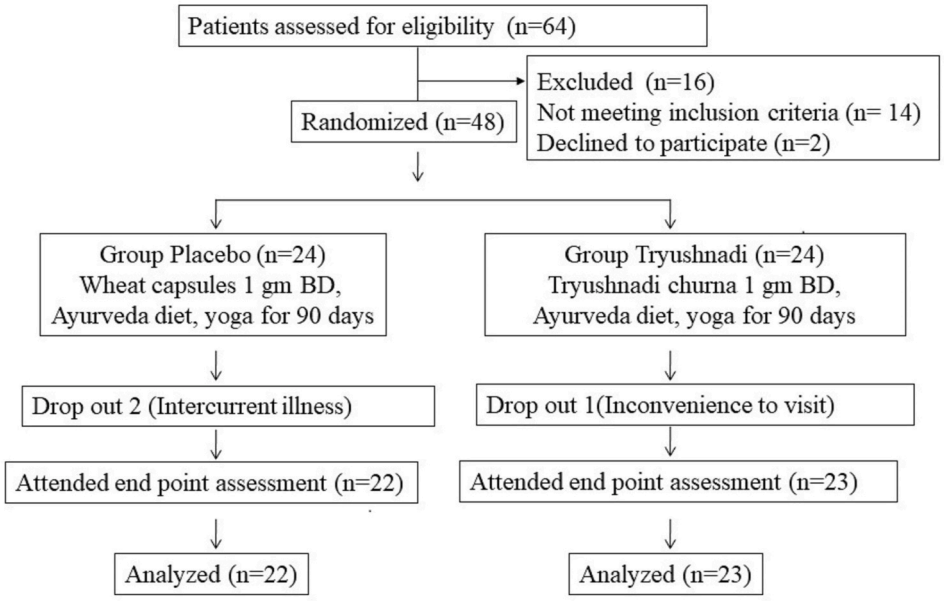

Fig. 1. CONSORT flow chart.

intake. Saturated, cholesterol and trans fat were minimised and Polyunsaturated fatty acids (PUFA) and Monounsaturated fatty acids (MUFA) were recommended. 1200 Kcal diet per day irrespective of weight was planned in decreased Agni. In increased, deranged and normal agni strength the diet chart was planned as per weight. Yoga protocol included in the study consisted of 60 min of different asanas. Beginning with omkara, standing asanas, suryanamaskara, sitting, prone, supine asanasa and ended with pranayama. 3 yoga sessions were carried out and general instructions and advices were provided. Handouts and charts of diet and yoga were provided. Periodic telephonic interactions were conducted to address any difficulties and to motivate, facilitate the adherence of diet and yoga schedules.

Duration of intervention was 90 days with follow-up on every 30th day. The nature and design of the study were explained to the participant and informed consent was obtained. During the study participants were asked to adhere to treatment protocol and report the adverse events, if any, to investigators at the earliest.

2.5.5. *Criteria for assessment*

2.5.5.1. Primary outcomes. Body weight (BW) in kilograms was recorded following standard operating procedures.

2.5.5.2. Secondary outcomes. The secondary outcomes were Body Mass Index (BMI) (kg/m2), Height and weight were measured to nearest 0.1 cm and 0.1 kgs after removing outer clothing and foot wear). Waist circumference (WC) (Smallest girth between costal margin and iliac crest to the nearest 0.1 cms), Waist hip ratio (WHR) (Hip circumference was widest circumference between anterior superior iliac crests and the ischial tuberosities), Skin fold thickness was measured using a skin fold calliper, sum of 4 skinfolds (biceps, triceps, subscapular, suprailac areas) (SFT) and Body fat (BF) was calculated as per Durnin and Womersley [27,28]. BF of 18–24% was considered normal in males, 25–31% in females [29]. All measurements were done with a non stretchable tape, right side of the body as per the recommendations of International Society for the Advancement of Kinanthropometry (ISAK) [30]. Fasting blood sugar (FBS), Glycated haemoglobin (HbA1c), Triglycerides, High density lipoproteins (HDL), Low density lipoproteins (LDL), Total cholesterol (TC) was measured through 8 h fasting venous blood. Consistent values of Supine blood pressure measured in 7 days interval were considered as base line value and subsequent assessments were done. WHO quality of life-BREF (WHOQOL-BREF) scale [31], Clinical Global Impression Scale (CGI)- Severity, Global improvement and Efficacy index [32] were assessed.

2.5.6. *Statistical methods*

Statistical analysis were carried out in using SPSS Version 25.0. Homogeneity of the data between the groups was accessed by the $\chi 2$ test. Comparison of between groups across different time points was evaluated through repeated measure ANOVA test and within group comparison was carried out by Bonferroni post-hoc test. Dependent and independent paired T test were applied to the objective parameters. Clinical outcomes considering the differences in pre and post values were subjected to assessments. Values are reported as mean ± standard deviation. Effect size was calculated by Partial Eta Square method. Effect of treatment was evaluated through outcome from base line to 30th day. Effect size interpretation was 0–0.2 minimal, 0.2–0.5 was small, 0.5 to 0.8 was medium and above 0.8 was large effect [33] size. All tests were considered statistically significant at $p < 0.05$.

3. Results

Forty eight participants were recruited in the study. Twenty four participants were enrolled in each groups. Two participants from placebo group and 1 participant from Tryushnadi group dropped out of the study. Reason for the drop out was intercurrent illness in 2 participants, inconvenience in travelling to the centre in other participant. (Fig No 1). No adverse events were noted in both the groups.

3.1. *Demographic profile*

Mean age of the participants was 43.5 years. Majority of participants were females (70.8%), with middle socioeconomic status (75%), graduate level educated (56%), married (98%), showing mean duration of illness as 6.28 years, Vata kapha and Pitta Kapha prakurti (33% each). Clinical profile of the participants at base line were, mean BMI was 30.96, mean weight was 99.36 kgs, mean waist circumference (Female −98.85, male −100.60), mean BMI (30.96), mean weight (76.93 kg), mean FBS (106.75 mg/dl), mean HbA1C (5.93), mean Systolic blood pressure (SBP) was 135.62 mm of Hg, mean Diastolic blood pressure (DBP) was 90.25 mm of Hg, mean Triglycerides (132.06), mean LDL (112.25), mean Total Cholesterol (180.5) and mean HDL (Female-

Table 1
Patients profile.

Clinical profiles	Group Placebo (n = 24)	Group Tryushnadi (n = 24)	p-Value
Age (yrs)	43.75 ± 7.89	43.25 ± 9.52	0.84
Gender- Male	7	7	1
Female	17	17	
Education- Primary	4	5	0.41
Secondary	8	4	
Graduate	12	15	
SE Status -Lower middle class	0	3	0.16
middle class	20	16	
Upper middle class	4	5	
Marital status- Unmarried	0	1	0.31
Married	24	23	
Duration of illness (Years)	5.04 ± 4.08	7.52 ± 5.37	0.07
Prakurti - Vata Pitta	7	5	0.38
Vata kapha	5	11	
Pitta Kapha	9	7	
Kapha Vata	2	1	
Kapha Pitta	1	0	
Agni - Sama agni	12	10	0.63
Manda agni	2	1	
Teekshna agni	10	13	
Sleep- Normal	19	20	0.71
Disturbed	5	4	
Kostha - Madhyama	17	16	0.66
Mridu	2	4	
Krura	5	4	
Obesity-Severity (BMI)			
Grade I(25–30)	13	11	0.56
Grade II(>30)	11	13	
Hypertension (SBP>130 Hg)	20	22	0.386
Hypertension (DBP>85 Hg)	18	22	0.813
Hypertension (SBP>130,DBP>85 Hg)	21	22	
HDL (M < 40, F < 50)	18	23	0.191
Abdominal obesity (Male>102, Female>88) (waist circumference in cms)	16	20	
Abdominal obesity (Male>90, Female>80. In cms)	24	24	0.028
Waist hip ratio (M > 0.9,F > 0.8)	22	23	–
Fasting blood glucose (>100 mg/dl)	8	18	–
Fasting blood glucose (>126 mg/dl)	4	2	–
Diabetes Mellitus(HbA1C>6.5%)	4	3	–
Hypertriglyceridemia(>150 mg/dl)	10	6	–
Drop outs	2	1	–
Study completed	22	23	–
Total	24	24	–

41.14, Male-43.42). Seven participants met T2DM criteria of HbA1C greater than 6.5 % [34] and 6 participants of FBS greater than 126 mg/dl [35]. The mean age, gender, socio economic status, marital status, education, prakurti, duration of illness, *agni*, sleep, *kostha* were comparable between groups (Table 1). Clinical assessments like BMI, body weight, waist hip ratio, body fat index (BFI), SFT, SBP, DBP, FBS, WHOQOL-Bref, CGI-Severity, HBA1C, Triglycerides, Total cholesterol, HDL, LDL were comparable between both the groups at base line. Only waist circumference was not comparable between groups (p = 0.02) (Table 2). Diet chart adherence was 75% and Life style and yoga adherence was 82%.

3.2. Primary outcome

Assessment on body weight showed that the clinical outcomes between the groups were significant (p < 0.001). Decrease in BW was higher in Tryushnadi group (Table 3). Assessment at different time points showed that significant decrease was noted in only Tryushnadi group. Effect size was large (1.89) favouring improvements in Tryushnadi group (Table 3).

Table 2
Base line characteristics of the Clinical assessments in two groups.

S. no	Parameters	Group Placebo	Group Tryushnadi	P (Independent *t*-test)
1.	BMI	30.59 ± 3.58	31.33 ± 3.30	0.467
2.	BW(Kgs)	75.28 ± 7.73	78.18 ± 7.06	0.182
3.	WC (cms)	97.19 ± 7.69	101.54 ± 5.40	0.028
4.	WHR	0.90 ± 0.04	0.9200 ± 0.42	0.175
5.	BFI (%)	35.55 ± 4.94	35.53 ± 4.59	0.98
6.	SFT (mms)	85 ± 16.52	86.83 ± 11.76	0.66
7.	FBS (mg/dl)	107.67 ± 22.39	105.83 ± 21.39	0.773
8.	BP-S (mm of Hg)	134.58 ± 8.83	136.67 ± 7.61	0.386
9.	BP-D (mm of Hg)	90.00 ± 7.22	90.50 ± 7.30	0.813
10.	WHOQOL-BREF	74.96 ± 8.49	74.21 ± 10.54	0.787
11.	CGI-S	3.46 ± 1.021	3.54 ± 1.06	0.783
12.	HbA1c (%)	6.00 ± 0.59	5.87 ± 0.69	0.502
13.	TG (mg/dl)	136.42 ± 28.68	127.71 ± 23.16	0.253
14.	TC (mg/dl)	180.71 ± 49.86	180.29 ± 16.77	0.969
15.	HDL (mg/dl)	43.58 ± 11.26	40.04 ± 6.64	0.191
16.	LDL (mg/dl)	110.29 ± 44.10	114.21 ± 13.45	0.679

Expressed in Mean and standard deviations (S.D.).

3.3. Secondary outcome

Effect of interventions on clinical outcomes showed that secondary parameters like BMI, Waist circumference, Waist hip ratio, Body fat index, Skin fold thickness, FBS, HbA1c, systolic blood pressure (SBP), diastolic blood pressure (DBP), Triglycerides, HDL, LDL, Total cholesterol, Clinical Global Impression Scale (Severity, global improvement and efficacy index) were comparable between groups. However clinical outcomes of WHOQOL- BREF scale showed significant difference (p = 0.002) favouring Tryushnadi group (Table 3).

Within group assessment showed that Waist circumference, BFI, SFT, HbA1C, WHOQOL- BREF, Clinical Global Impression Scale-Severity and CGI-Efficacy index improved in both the groups. Triglycerides showed decrease (p = 0.003) in placebo group. LDL (p = 0.03) and total cholesterol (p = 0.02) showed decrease in Tryushnadi group only. However triglycerides, LDL and total cholesterol were in normative ranges at pre and post assessments. Within group assessment at base line to 60th day showed significant improvement of BFI (p = 0.028), waist circumference (p = 0.006) in Tryushnadi group.

Effect size was large in BMI (1.98), WHOQOL-Bref (1) and was medium in SFT, HbA1C, Triglycerides favouring improvements in Tryushnadi group. It was small in Waist circumference, BFI, FBS, HDL, BP systolic, CGI-Severity, CGI-Global Improvement. Effect size was minimal in WHR, LDL, Total Cholesterol, BP-Diastolic and CGI-Efficacy index (Tables 3 and 4).

4. Discussion

Study showed that Trayushnadya churna intervention in participants of Metabolic syndrome with obesity produced significant reduction in primary outcome i.e. body weight and few of the other secondary outcome like BMI and WHOQOL Bref. Both the groups were comparable in other secondary outcome criteria like waist circumference, waist hip ratio, body fat index, skin fold thickness (mean of biceps, triceps, subscapular, suprailac areas), FBS, HbA1c, blood pressure, triglycerides, HDL, LDL, total cholesterol, clinical global impression scale (Severity, global improvement and efficacy index). Both the groups vis a vis Ayurveda diet and yoga showed improvement in waist circumference, BFI, SFT, HbA1C, WHOQOL-BREF, Clinical Global Impression Scale-Severity

Table 3
Effect of Interventions on various clinical assessments. Expressed in Mean and standard deviations (S.D.).

S. No	Clinical Variables	Groups P=Placebo T-Tryushnadi	Baseline	30th day	60th day	90th day	Difference of 0^{th} -90^{th}day	P value	Effect Size (0–90days)
1.	BW (kgs)	P	74.94 ± 7.55	74.88 ± 7.62	74.31 ± 7.47	74.00 ± 7.92	1.05 ± 1.70	<0.001	1.89
		T	77.99 ± 7.42	76.83 ± 7.71	76.55 ± 7.41	74.10 ± 7.23	3.85 ± 1.23		
2.	BMI	P	30.04 ± 3.21	30.0 ± 3.39	29.82 ± 3.24	29.66 ± 3.38	0.42 ± 0.64	<0.001	1.98
		T	31.41 ± 3.42	30.94 ± 3.60	30.32 ± 3.88	29.85 ± 3.35	1.54 ± 0.48		
3.	WC (cms)	P	97.11 ± 7.68	96.15 ± 7.92	96.08 ± 8.08	95.01 ± 8.06	2.14 ± 2.98	0.21	0.38
		T	101.00 ± 5.26	99.92 ± 5.97	99.38 ± 5.48	98.19 ± 5.24	3.26 ± 2.93		
4.	WHR	P	0.90 ± 0.04	0.89 ± 0.06	0.91 ± 0.05	0.91 ± 0.05	−0.01 ± 0.04	0.29	0.14
		T	0.91 ± 0.03	0.91 ± 0.03	0.91 ± 0.03	0.91 ± 0.04	−0.005 ± 0.03		
5.	BFI (%)	P	34.62 ± 4.20	33.88 ± 4.42	33.84 ± 4.18	33.4 ± 4.17	2.35 ± 2.64	0.49	0.32
		T	35.17 ± 4.76	34.31 ± 4.78	33.94 ± 5.05	33.46 ± 4.91	2.9 ± 2.60		
6.	SFT (mms)	P	82.10 ± 13.24	77.33 ± 14.16	76.76 ± 12.87	75.62 ± 13.14	6.72 ± 4.84	0.17	0.43
		T	84.95 ± 9.28	80 ± 9.79	79.24 ± 10.08	76.19 ± 8.62	8.52 ± 3.87		
7.	FBS (mg/dl)	P	105.57 ± 21.44	102.38 ± 16.50	96.48 ± 6.53	99.67 ± 11.42	7.77 ± 19.75	0.13	0.46
		T	106.33 ± 22.87	104.24 ± 21.88	101.95 ± 14.97	99.71 ± 27.88	−3.6 ± 29.15		
8.	BP-S (mm of Hg)	P	134.29 ± 9.25	134.76 ± 9.28	131.43 ± 7.27	131.90 ± 9.80	1.25 ± 7.18	0.47	0.25
		T	136.19 ± 8.04	134.29 ± 5.97	137.14 ± 8.45	134.2 ± 7.46	3.15 ± 8.20		
9.	BP-D (mm of Hg)	P	89.52 ± 7.40	89.52 ± 8.04	87.14 ± 5.60	88.86 ± 6.27	0.25 ± 6.4	0.78	0.13
		T	90.10 ± 7.52	87.24 ± 5.34	87.62 ± 4.36	89.81 ± 4.55	0.84 ± 0.63		
10.	WHOQOL-BREF	P	74.57 ± 9.00	77.67 ± 8.33	83.67 ± 6.88	87.81 ± 6.90	13.40 ± 4.88	0.002	1
		T	74.14 ± 10.84	77.14 ± 11.08	84.33 ± 11.87	93.43 ± 8.62	19.04 ± 6.31		
11.	CGI-S	P	3.33 ± 1.01	3.14 ± 0.85	2.86 ± 0.79	2.57 ± 0.74	−0.87 ± 0.95	0.558	0.2
		T	3.48 ± 1.07	3.29 ± 0.84	3.05 ± 0.80	2.90 ± 0.76	−0.68 ± 0.94		
12.	CGI-GI	P	–	3.24 ± 0.43	3.29 ± 0.46	3.10 ± 0.62	0.06 ± 0.68	0.22	0.42
		T	–	3.24 ± 0.53	2.95 ± 0.66	2.86 ± 0.65	0.36 ± 0.76		
14.	CGI-EI	P	–	10.33 ± 1.93	10.14 ± 2.57	8.43 ± 2.61	2 ± 2.06	0.90	0.04
		T	–	9.95 ± 2.15	8.62 ± 2.50	7.67 ± 2.92	2.1 ± 2.7		

Table 4
Effect of Interventions on HbA1c and lipid parameters. Expressed in Mean and standard deviations (S.D.).

S.No	Parameters	Groups P=Placebo T-Tryushnadi	Baseline	90th day	Paired *t*-test BL-90th day	P value-Independent *t*-test	Effect size
1	HbA1c (g/dl)	P	6.04 ± 0.57	5.34 ± 0.48	<0.001	0.10	0.51
		T	5.88 ± 0.71	5.42 ± 0.61	<0.001		
2	Triglycerides (mg/dl)	P	133.09 ± 26.97	108.82 ± 21.44	0.003	0.06	0.64
		T	126.05 ± 22.60	120.86 ± 22.68	0.24		
3	HDL (mg/dl)	P	44.05 ± 11.66	38.59 ± 2.75	0.055	0.361	0.31
		T	39.95 ± 6.93	38.32 ± 3.92	0.385		
4	LDL (mg/dl)	P	110.68 ± 46.13	106.50 ± 28.73	0.704	0.621	0.16
		T	115.95 ± 9.76	105.68 ± 20.60	0.035		
5	Total Cholesterol (mg/dl)	P	183.55 ± 50.21	166.55 ± 18.79	0.119	0.673	0.14
		T	181.82 ± 15.19	172.41 ± 16.74	0.025		

and CGI-Efficacy index.

Participant profile showed that majority of participants were middle aged, female, middle socioeconomic status, graduate level educated, married, mean duration of illness was 6.28 years, obesity was grade II as per the BMI, FBS and HbA1C were in prediabetic range, hypertension was in grade I category and HDL was in border line low category. Triglycerides, LDL and Total Cholesterol were in normative ranges. SBP was within normative ranges but DBP was in grade I category of Hypertension (JNC 8). 14% participants met the Diabetes mellitus criteria (HbA1c>6.5%). Waist circumference in female were elevated as per as per NCEP ATP III criteria and as per India specific criteria of [36] waist circumference (Male >90 cms, Female >80 cms) was elevated in all participants. Prakurti was Vata kapha and pitta kapha predominant.

Trayushnadya churna, Ayurveda diet and yoga produced significant decrease in weight, the only primary outcome criteria of the study. Obesity reduced from grade II to grade I. Other group with placebo, ayurveda diet and yoga did not produce significant changes in weight, however trends of weight reduction were observed.

Trayushnadya churna, Ayurveda diet and yoga produced significant reduction in many of the secondary outcome criteria like BMI and WHOQOL-Bref. BMI improvement is directly related to reduction in weight. WHOQOL-Bref reduction could be due to a comprehensive effect of Trayushnadya churna on multiple components of the disease apart from weight and BMI. Within group assessment showed significant reduction in Waist circumference, BFI, SFT, HbA1C, Clinical Global Impression Scale-Severity and CGI-Efficacy index. These cumulative effects could have caused improvements in WHOQOL-Bref.

Improvements in FBS and SBP were significant and were below the diagnostic criteria of Metabolic syndrome (NCEP ATP III criteria). FBS reduced below 100 mg/dl. SBP reduced below 135 mm of Hg. HbA1C levels reduced to prediabetic criteria of 5.7 %. Skin fold thickness suggest subcutaneous fat depots and has a major role in obesity-related insulin resistance and glucose insulin homeostasis [37]. Skin fold thickness and body fat were high in both male and female participants. SBP values were within the normative limits but DBP was raised in both groups as per JNU 8 criteria. A per NCEP ATP III, both SBP and DBP were

Table 5
Tryushnadi churna- Ingredients, Latin name, part used and proportion.

Sl. no	Name	Latin name	Part used	Proportion
1.	Pippali	*Piper longum* L.	Fruit	1
2.	Maricha	*Piper nigrum* L.	Fruit	1
3.	Shunti	*Zingiber officinale* Roscoe	Root	1
4.	Amalaki	*Emblica officinalis* Gaertn	Fruit	1
5.	Haritaki	*Terminalia chebula* (Gaertn.) Retz.	Fruit	1
6.	Vibhitaki	*Terminalia belerica* (Gaertn.) Roxb.	Fruit	1
7.	Chavya	*Piper chaba* Trel. & Yunck.	Root	1
8.	Chitraka	*Plumbago zylanica* L.	Root	1
9.	Bakuchi	*Psoralia corylifolia* Linn.	Seed	1
10.	Vida lavana	Sodium chloride, sodium sulphate		1
11.	Oudbida lavana	Sodium chloride, sodium bicarbonate		1
12.	Saindhava lavana	Sodium chloride		1
13.	Souvarchala lavana	Black salt (Sodium chloride)		1

raised in Tryushnadi group and in placebo group only DBP was raised. Non significant changes were observed in both groups. In Tryushnadi group, improvement lead to normative values in diastolic BP (JNU 8 criteria) and systolic BP (NCEP ATP III).

Trayushnadya churna has ingredients like *pippali, maricha, shunti, haritaki, vibhitaki, amalaki, chavya, chitraka, bakuchi, vida lavana, saindhava lavana, souvarchala lavana, audbidha lavana* (Table 5). Piperine, active ingredient of pippali showed to decrease body weight, improves insulin resistance and leptin sensitivity in High Fat Diet-induced rat [38]. Itrifal saghir [39], a triphala formulation, 5 gms twice a day for 12 weeks in obese participants showed decrease in weight, waist circumference. Other ingredients of Trayushnadya churna have properties like *laghu, teekshna, sukshma, ushna guna, kapha nissararana*, might have done *lekhana* and *meda hara karma*. Ayurveda diet and yoga was administered in both the groups. Studies have shown beneficial effects of Ayurveda medicines in MetS related manifestations. OBERAY [40], a proprietary Ayurveda medicine in obese and over weight participants showed increase in mean HDL and decrease in LDL, very low density lipoprotein, triglycerides. Decrease was also in plasma adiponectin, BMI, Waist Circumference, total body fat, skin fold parameters, subcutaneous and skeletal muscle fat levels. Water-soluble cinnamon extract (Cinnulin PF®) supplementation in diet for 12 weeks in participants of MetS showed decrease in fasting blood sugar, SBP and increase in lean body mass [41].

Ayurveda diet chart had a good acceptance. Dietary changes and increased exercise were more effective than metformin in reducing risk of T2DM [42]. Diets like Mediterranean diet rich in olive oil rich in MUFA, fruits, vegetables, cereals, beans, nuts, seeds causes decrease in LDL, increase in HDL and increased insulin sensitivity in healthy individuals [43]. Low Glycaemic index food like whole grains are digested slowly, gradual increase in glucose and controlled insulin response [44]. Dietary approaches to stop Hypertension (DASH) diet has more of low-fat dairy, vegetables, fruit, dietary fibre, whole grains and less of refined grains, saturated fat and total fat [45]. DASH diet decreases hypertension, total cholesterol and LDL [46]. DASH decreases weight, hypertension, FBS and increases HDL in MetS [47]. Diet (Ingestion of whole-grain products, vegetables, fruits, low-fat milk and meat products, soft margarines, and vegetable oils rich in monounsaturated fatty acids) along with physical activity (moderate exercise for at least 30 min per day) interventions for 3.9 yrs showed decrease in incidence and risk factors associated with MetS like abdominal obesity, blood pressure, low HDL, increase Triacylglycerol. At first year, decrease in prevalence of metabolic syndrome, abdominal obesity and elevated blood glucose were noted [48,49]. Butter milk intake leads to decrease in total cholesterol and triacylglycerol [50]. *Vrukshamla (Garcinia indica*) has hydroxycitric acid that has shown anti obesity, antidiabetes, antioxidant effect [51]. Bioactive peptides of Milk and plant (cinnamon, green tea, berberine and ginseng) have shown to decrease the risk factors associated with MetS [52].

Yoga protocol was well accepted and adhered by the participants. Studies [53] recommend 150 min or more of moderate-to-vigorous intensity activity weekly, spread over at least 3 days/week, with no more than 2 consecutive days without activity in diabetes. Study on Intensive yoga for 12 weeks reduced abdominal obesity with reduction in waist circumference, waist-hip ratio, BMI, body weight, and body fat percentage [54]. Study on yoga (asana, pranayama, relaxation and meditation) for 14 weeks, showed improvement in anthropometric parameters, body weight, BMI, waist circumference and skinfold thickness [55]. A case report [56] with Integrated yoga and naturopathy module for 6 weeks considerably decreased various manifestations of MetS.

Strengths of the study is double blind, randomized controlled trial. Control group with placebo, Ayurveda diet and life style practise like yoga is the strength of the study. As diet and life style modification is one of the main interventions in MetS. Comparator as placebo adds strength to the study. Comprehensive assessment of various manifestations of MetS like BMI, weight, anthropometric measures, blood pressure, lipid profiles, glycemic indices like fasting blood sugar and HbA1C, quality of life and gross clinical assessments for 90 days are the noticeable components of the study. Study evaluated the effect of integration of ayurveda drug, diet and lifestyle modifications. This is the strength and novelty of the study.

Ayurveda protocol with Tryushnadi churna decreased obesity, anthropometric measures, glycemic levels, lipids, blood pressure and improved quality of life. This suggests of it's role in metabolic syndrome and is the notable component of the study. It validates the experiential ayurveda documentation of Tryushnadi churna as lekhana, kapha medohara effect and is the valuable outcome of the study. Tryushnadi churna produced no adverse effects. Diet and yoga adherence have a considerable role and participants needs periodic communication and motivation for their active participation. This factor could be an issue in effectiveness of this protocol. Ayurveda protocol did not contain panchakarma procedures and forms the limitation. However study needs to be conducted in large diverse, multi cultural population and multi centric study is essential. This will show the acceptability and feasibility in global scenarios. Current study can contribute to the ayurveda evidences in MetS as there is scarcity of publications in the same. Study conducted with a long term follow ups will be helpful. Measurements with blood insulin levels, C peptide, body fat assessment with Dual energy X-ray absorptiometry will be helpful in better assessments of the interventions.

5. Conclusion

Study showed that Tryushnadi churna is effective in decreasing weight, BMI and improving quality of life in obese participants with MetS. Effect size was large in these parameters favouring Tryushnadi churna. Ayurveda diet and yoga with and without Tryushnadi churna produced decrease in waist circumference, body fat, skin fold thickness, CGI severity and CGI efficacy index in within group assessment. Integrative management with Ayurveda medication, Ayurveda diet and yoga is beneficial approach in MetS with obesity.

Source of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

NIL.

Author contribution

SC- Conceptualization,Visualization, Data collection, Writing - Reviewing and Editing.

BRT- Conceptualization, Methodology, Writing - Original draft preparation, Writing -Reviewing and Editing, Statistical analysis.

VBG- Methodology, Writing - Original draft preparation, Writing -Reviewing and Editing.

OS- Visualization, Data collection, Writing - Reviewing and Editing.

Decleration on use of generative AI in scientific writing

Nothing to disclose.

Acknowledgements

We would like to thank Dr Krsihnapriya and Dr Rajat Sharma for their contribution in the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2024.100973.

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