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"Clinical Evaluation Of Rasanjan In The Management Of Obesity"

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Abstract:

Background – WHO's latest projection indicates that globally obesity has nearly tripled since 1975. Obesity (Sthaulya) is defined as abnormal or excessive fat accumulation that may impair health. Ashtang Hridaya has mentioned Rasanjan as best treatment of Sthaulya in Agrya Dravya. Rasanjan is a herbal and animal origin (Jangama) product, which is prepared mainly by Daruharidra Kvath (Extracts of Berberis aristata) and Ajakshir (Goat's milk) or Gokshir (Cow's milk) Rasanjan is known to have Katu and Tikta Ras, Ushna Veerya, Kaphanashak and Chedana Karma. Aim - To evaluate the efficacy of Rasanjan in the management of obesity (Sthaulya). Material and Methods - A randomized control clinical trial was conducted for 60 days with Sample size of 48 divided in two groups. Rasanjan along with diet and exercise was given in study group whereas only diet and lifestyle advice was given in control group. Results- Study group showed statistically significant (P<0.05) results in reduction of weight, BMI, Circumference - Abdomen, Arm, Neck, Thigh, Waist, Hip, Waist-Hip ratio, Total body fat %, Biceps fat, Triceps fat, Subscapular and Abdominal fat percentage when analysed by 2 way ANNOVA test. Conclusion - Rasanjan's properties are opposite to that of Kapha and Meda, therefore with Samanya-Vishesh siddhant it helps in reducing Meda in body and thus helps in obesity. Obesity is a lifestyle related disorder and it cannot be managed without making lifestyle changes. Rasanjan along with diet and exercise works well in management in Sthaulya as compared to only diet and exercise.

Keywords: BMI, Fat percentage, Obesity, Rasanjan, Sthaulya

Introduction

World Health Organization's latest projection indicates that globally obesity has nearly tripled since 1975. In 2016, more than 1.9 billion adults (age 18+) were overweight, out of these over 650 million were obese. About 39% of adults aged 18 years+ were overweight in 2016, and 13% were obese. 41 million children under the age of 5 were overweight or obese in 2016. Overweight and obesity are linked to more death worldwide than underweight.^[1] WHO states two main causes of obesity which are consumption of energy dense food that are high in fats and decrease in physical activity due to urbanization, transportation and sedentary lifestyle at work.

According to Ayurveda, Acharya Sushrut mentions that Sthaulya and karshya are due to rasa dhatu^[2] and also states that madhyam sharir is best^[3] as both sthula and karshya are always affected by some diseased condition. Ayurveda includes Atisthula (Obese) and Atikrisha(emaciated) persons in Astha Ninditiya purushas^[4] (eight despised or undesirable physiques). Sthaulya has been categorized as disease cause due to santarpan. Atisthula purusha is said to suffer from the following defects- Javaparodha (Decreased Activities), Alpa-vyavayita (Reduced Vyavya), Daurbalya (Weakness), Daurgandhya (Excessive smell), Swedabadha (Excessive sweating), Ati-trisha (Excessive thirst), Ati-kshudha (Excessive Hunger). One reference from Sushrut Samhita for treatment of obesity stated that if the condition develops person should use Shilajatu, Guggulu, Gomutra, Triphala, Loharaja, Rasanjan, Madhu, Yava, Mudga, Koradusaka, Syamaka, Uddalaka etc which create dryness and clear the obstructed channels and also physical exercise, scarificant enemas etc can be done.^[5]

Similarly Acharya *Vagbhat* has also mentioned *Rasanjan* in treatment of *Sthaulya* in Chapter 14 – "*Dvividhupakramaniya Adhyay*" in *Sutra Sthana*. (A.H. Su. 14/23)^[6] *Ashtang Hridaya* has mentioned *Rasanjan* as best treatment of *Sthaulya* in *Agrya Dravya* explained in 40th Chapter of *Uttartantra* – "*Vajikarana Vidhi Adhyay*" (A.H. Ut. 40/49)^[7] *Rasanjan* is a herbal and animal origin (*Jangama*) *Dravya* which is prepared in laboratory mainly by *Daruharidra kvath* (Extracts of Berberis aristata) and *Ajakshir* (Goat's milk) or *Gokshir* (Cow's milk).^[8] *Rasanjan* is known to have *Katu* And *Tikta Ras, Ushna Veerya, Kaphanashak And Chedana Karma*.^[9]

Aim

To evaluate the efficacy of Rasanjan in the management of obesity (Sthaulya).

Material and Methods

- 1. Rasanjan was prepared after authentication and standardization of the raw materials i.e *Daruharidra* and Goat Milk.

 *Daruharidra Kwath + Goat's Milk (1:1/4) was followed in preparation of *Rasanjan*. [10] The powdered final product was filled in Capsules of 500 mg each. Packet of 60 capsules for 15 days was prepared with silica gel packs in it for moisture absorption.
- 2. Diet chart was prepared and was verified by experts in the field and dietician. Do's and Don't's in the diet and lifestyle according to Ayurveda were explained in the form of attractive poster.
- 3. Digital weighing Scale- The smart weighing scale of company RENPHO was used.. It also shows 11 Essential Measurements Scale shows body weight, data including Weight, BMI, Body Fat Percentage when connected to app. It has maximum capacity of 180 kg and is FDA/CE/FCC/ROHS Certified.
- 4. Measuring Tape- Measuring tape with locking tip and push button of company caretouch were used for measuring circumference of body parts for assessment of obesity. The sturdy vinyl tape measured 60 inches (150 cm) in length
- 5. Skin Fold callipers- These were used of company caretouch for assessment of body fat percentage for assessment of obesity. Measurement of fat with skin fold callipers can be done in three easy steps: Pinch, Click and Read.
- 6. Complete Body Fat Percentage Monitor- The Omron Body Fat Analyzer is a small handheld body fat analyser device that uses a method called Bioelectrical Impedance Analysis to calculate body fat percentage and body mass index. The fat loss monitor sends an extremely low level electric current of 50kHz and 500 μA through body to determine the amount of fat tissue. This weak current is safe and is not felt while operating the machine. Muscles, blood vessels and bones have high water content that conduct electricity easily. Body fat does not hold water and therefore has low electrical conductivity. It also helps in analysing whether reduction of weight is due to fat loss or muscle loss.

The study got approved by Institutional Ethics Committee (dated: 4 March 2017) and trial was registered in Clinical Trial Registry of India dated: May 29, 2018) Trial registered Prospectively. Randomized control clinical trial was conducted in which 48 patients were registered from outpatient department of Hospital. They were randomly allocated into two groups following computerized randomization after getting informed consent.

Study group - Rasanjan in the form of capsules (2 gms per day - 500 mg capsules twice a day empty stomach with warm water) along with Diet and lifestyle advice.

Control Group – Diet and lifestyle advice.

Patients were enrolled after baseline assessment and assessment of inclusion and exclusion criteria. Complete history was taken including demographic details, present and past history of illness, addictions, dietary history, family history etc. Continuous reminders for intake of medicines, diet and exercise motivation and follow up reminders were given through SMS and phone calls. Drug dispensed was always given for 15 days and patient was called for follow up after 15 days. Data was collected after every 15 day follow up. Study was conducted for 60 days which consisted of total five visits i.e on Day 0, Day 15th, Day 30th, Day 45th and Day 60th

Inclusion criteria: Patients of either gender aged between 18 and 65 years with BMI > 30kg/m2 and < 40kg/m2 were included in this study.

Exclusion criteria: Patients with known history Pathophysiologic /genetic syndromes, evidence of malignancy, prolonged medication with corticosteroids, major systemic illness, atrial fibrillation, Acute coronary syndrome, Myocardial infarction, stroke, serious hepatic and pulmonary disorders, Alcoholics and drug abusers, Prior surgical therapy for obesity, Pregnant or lactating women were excluded from the study.

Criteria for Assessment:

Assessment was done by considering changes in the subjective as well as objective parameters before the treatment, during the treatment and after the treatment. Anthropometric parameters included Weight, Height, BMI, Inches Calculation – Abdomen circumference, Arm C, Thigh C, Neck C, Waist C, Hip C, Waist-Hip Ratio, Fat percentage – Abdomen, Triceps, Biceps, Subscapular and Total Body Fat percentage. Subjective parameters included signs and symptoms of Sthaulya such as Level of enthusiasm, Excess sweating, Dyspnea on exertion, excessive sleep, excessive hunger, excessive thirst, decreased physical exercise, feeling of heaviness, Flabbiness of body, Fatigue and Unpleasant Odor.

Statistical analysis:

The data obtained in clinical study were subjected to statistical tests.

Quantitative data was compiled, segregated and analysed through statistical tests such as Paired T-Test and 2 Way ANOVA. Wilcoxin test and Fisher's exact test was applied on subjective criteria of assessment. Statistical analysis was done with the help of Medcalc- "medcalc@version 9.2" and GraphPad – "GraphPad Prism 8 version". After obtaining P value, it was observed as insignificant if P > 0.0001 and significant if P < 0.0001.

Observation and Results

Sthaulya has been mentioned in detail in Samhitas along with aetiology, etiopathogenesis, symptoms, complications, treatment, diet and lifestyle advice. Charak Samhita has mentioned Sthaulya in Ch. Su. 21 – Asthau-Nindita-Purush, [11] Sushrut Samhita has mentioned Sthaulya in Su. Su. 15 Dosha-Dhatu-Mala-kshya-Vriddhi Vigyaniya, [12] Ashtang Hriday has mentioned AH.Su. 14 - Dwividha-upakramaniya, [13] Ashtang Sangrah has mentioned in AS.Su. 24 - Dwividha-Upakramaniya, [14] Madhav Nidaan has mentioned in Chapter 34- Medoroga Nidanam, [15] Sharangdhar has mentioned in Chapter 7 - Rogaganana, [16] Bhav Prakash has mentioned in Chapter 39 – Sthaulya Adhikar, [17] Bhel has mentioned Sthaulya in Chapter 11-Samshanparighniya, [18] Chakradatt has mentioned in Chapter 36- Treatment of Sthaulya, [19] Vangasen has mentioned in Chapter 42 – Sthaulya, [20] Bhaishajya Ratnavali has mentioned in Chapter 39 – Medorog Chikitsa Prakaran [21]

Out of 48 patients in clinical trial in study and control group, 79% were female and 21% male. Maximum patients were in age group 18-30 yrs (23) followed by 31-45 yrs (14) and lowest in 46-65 yrs (11). 28 patients were married, 19 unmarried and 1 widow. 43 patients were hindu, 2 were muslim and 1 each of sikh, Christian, buddhist. Diet preference of maximum patients (31) was non vegetarian and 17 were vegetarian. 45 patients had none addiction.

Various parameters of quantitative data were recorded in study and control group and this data was compiled, segregated and analyzed through statistical tests such as Paired T-Test and 2 Way ANOVA.

2 way - ANOVA test for study and control group data analysis shows P < 0.0001 which means significant improvement in all the parameters such as weight, BMI, Abdominal Circumference, Arm Circumference, Neck circumference, Thigh circumference, Waist Circumference, Hip Circumference, Waist-Hip Ratio, Total Body Fat percentage, Biceps Fat percentage, Triceps Fat Percentage, Abdominal Fat Percentage and Sub Scapular Fat Percentage.

Same quantitative data analysed using Paired T Test shows P < 0.0001 which means significant improvement in various parameters in Study Group such as weight, BMI, Abdominal Circumference, Neck circumference, Thigh circumference, Waist Circumference, Hip Circumference, Total Body Fat percentage, Biceps Fat percentage, Triceps Fat Percentage, Abdominal Fat Percentage and Sub Scapular Fat Percentage. However Arm Circumference and Waist hip Ratio in study group shows Insignificant improvement with P = 0.0014 and P = 0.6399 respectively. Paired T test when applied on control group data shows insignificant improvement in all parameters i.e. weight (P=0.5385), BMI (P=0.4259), Abdominal Circumference (P=0.4878) , Arm Circumference (P = 0.4912), Neck circumference (P = 0.7466), Thigh circumference (P = 0.2325), Waist Circumference (P = 0.1670), Hip Circumference (P = 0.0036), Waist-Hip Ratio (P = 0.4647), Total Body Fat percentage (P = 0.9622), Biceps Fat percentage (P = 0.8024), Triceps Fat Percentage (P = 0.2567), Abdominal Fat Percentage (P = 0.7466) and Sub Scapular Fat Percentage (P = 0.5748).

When all the Qualitative parameters of all the patients of study and control group were combined, it was observed that there were 341 parameters of control group of Day 0 which reduced to 336 on Day 30 and 334 on last follow up i.e Day 60. Whereas in study group sum of parameters was 365 on Day 0 which reduced to 305 on Day 30 and 275 on Day 60 showing significant decline in overall gradings.

		MEAN	SD	SEM	ANNOVA	SIGNIFICA NCE	
	WT_C_D0	77.29	7.35	1.50			
	WT_C_D60	77.25	7.36	1.50	B 0 0001	G:	
	WT_S_D0	88.58	10.32	2.10	P <0.0001	Significant	
	WT S D60	84.95	10.02	2.04			
	BMI C D0	31.84	1.99	0.40			
	BMI C D60	31.82	1.96	0.40	D <0.0001	S::6:t	
	BMI S D0	33.79	3.86	0.78	P <0.0001	Significant	
	BMI S D60	32.51	4.20	0.85			
	Abd CF C D0	99.54	7.43	1.51			
	Abd CF C D60	98.91	6.99	1.42	P <0.0001	g: :c	
	Abd CF S D0	108.08	8.61	1.75	P <0.0001	Significant	
	Abd CF S D60	102.79	7.34	1.49			
	Arm CF C D0	31.25	2.64	0.53			
	Arm CF C D60	31.33	2.56	0.52	P <0.0001	Significant	
	Arm CF S D0	32.20	3.09	0.63			
	Arm CF S D60	30.70	3.20	0.65	7	7	
	Neck CF C D0	32.87	1.70	0.34			
	Neck CF C D60	32.83	1.68	0.34	P <0.0001	Cignificant	
	Neck CF S D0	36.04	4.23	0.86		Significant	
	Neck CF S D60	34.16	3.30	0.67			
	Thigh CF C D0	59.54	5.79	1.18			
	Thigh CF C D60	59.16	5.58	1.14		Significant	
	Thigh CF S D0	61.29	6.11	1.24	P <0.0001		
	Thigh CF S D60	57.29	5.74	1.17			
	Waist CF C D0	108.25	7.60	1.55			
	Waist CF C D60	107.50	7.45	1.52			
Tab	Table 1 – Effect on various quantitative parameters by ANNOVA						
	Waist CF S D60	108.20	10.73	2.19			

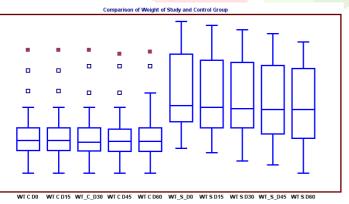
	MEAN	SD	SEM	ANNOVA	SIGNIFICA NCE
Hip CF C D0	112.62	7.15	1.46		0
Hip CF C D60	111.58	7.05	1.44	D 0.0455	
Hip CF S D0	119.20	9.24	1.88	P= 0.0465	Significant
Hip CF S D60	113.54	9.45	1.93		
W/H C D0	0.95	0.03	0.0070		Significant
W/H C D60	0.95	0.03	0.0061		
W/H S D0	0.95	0.02	0.0059	P <0.0001	
W/H S D60	0.94	0.03	0.0080		
TBF% C D0	39.79	4.07	0.83		Significant
TBF% C D60	39.80	3.92	0.80		
TBF% S D0	37.94	5.94	1.21	P <0.0001	
TBF% S D60	35.95	6.29	1.28		
BI F% C D0	26.33	5.64	1.15	P <0.0001	Significant
BI F% C D60	26.25	5.90	1.20		
BI F% S D0	26.75	5.77	1.17	P <0.0001	
BI F% S D60	23.75	5.93	1.21		
TRI F% C D0	33.41	4.47	0.91		
TRI F% C D60	33.08	4.82	0.98	D 0 0001	g: :c: ,
TRI F% S D0	31.41	7.16	1.46	P <0.0001	Significant
TRI F% S D60	28.16	6.21	1.26		
ABD F% C D0	42.08	6.68	1.36		Significant
ABD F% C D60	42.16	6.82	1.39		
ABD F% S D0	42.83	6.56	1.34	P <0.0001	
ABD F% S D60	37.91	6.83	1.39		
SSF% C D0	30.83	5.33	1.08		
SSF% C D60	31.00	4.71	0.96	D 0000	
SSF% S D0	34.33	5.73	1.17	P <0.0001	Significant
SSF% S D60	31.25	6.09	1.24		

Table 2 – Effect on various quantitative parameters by ANNOVA

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	MEAN	SD	SEM	Paired T test	SIGNIFICANCE	
WT_C_D0	77.29	7.35	1.50	D 0.5205	N. G. G.	
WT_C_D60	77.25	7.36	1.50	P= 0.5385	Not Significant	
WT_S_D0	88.58	10.32	2.10			
WT S D60	84.95	10.02	2.04	P < 0.0001	Significant	
BMI C D0	31.84	1.99	0.40	P = 0.4259	N-+ C:-nificent	
BMI C D60	31.82	1.96	0.40	P = 0.4239	Not Significant	
BMI S D0	33.79	3.86	0.78	D < 0.0001	Cignificant	
BMI S D60	32.51	4.20	0.85	P < 0.0001	Significant	
Abd CF C D0	99.54	7.43	1.51	D = 0.4979	Not Cignificant	
Abd CF C D60	98.91	6.99	1.42	P = 0.4878	Not Significant	
Abd CF S D0	108.08	8.61	1.75	D < 0.0001	Significant	
Abd CF S D60	102.79	7.34	1.49	P < 0.0001		
Arm CF C D0	31.25	2.64	0.53	P = 0.4912	N-4 C:: E:4	
Arm CF C D60	31.33	2.56	0.52	P = 0.4912	Not Significant	
Arm CF S D0	32.20	3.09	0.63	P = 0.0014	Not Cignificant	
Arm CF S D60	30.70	3.20	0.65	P = 0.0014	Not Significant	
Neck CF C D0	32.87	1.70	0.34	P = 0.7466	Not Cignificant	
Neck CF C D60	32.83	1.68	0.34	F = 0.7400	Not Significant	
Neck CF S D0	36.04	4.23	0.86	P < 0.0001	Significant	
Neck CF S D60	34.16	3.30	0.67	F < 0.0001	Significant	
Thigh CF C D0	59.54	5.79	1.18	D = 0.2225	N-4 C:: C:+	
Thigh CF C D60	59.16	5.58	1.14	P = 0.2325	Not Significant	
Thigh CF S D0	61.29	6.11	1.24	P < 0.0001	Significant	
Thigh CF S D60	57.29	5.74	1.17	P < 0.0001	Significant	
Waist CF C D0	108.25	7.60	1.55	P = 0.1670	Not Cignificant	
Waist CF C D60	107.50	7.45	1.52	P = 0.10/0	Not Significant	
Waist CF S D0	113.45	10.31	2.10	P < 0.0001 Significa	Cignificant	
Waist CF S D60	108.20	10.73	2.19	P < 0.0001	Significant	

Table 3 – Effect on various quantitative parameters by Paired 't' test



Graph 1 - Comparison of weight of study and control group

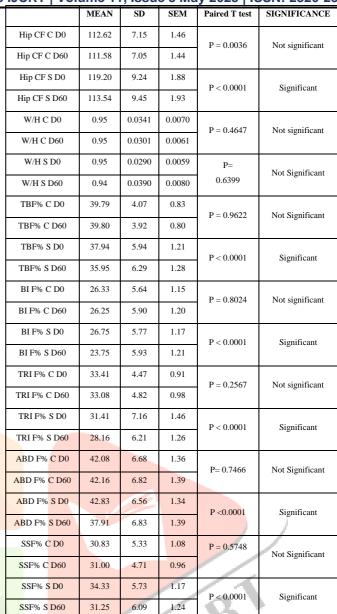
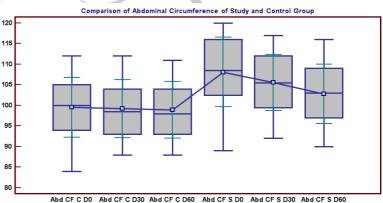
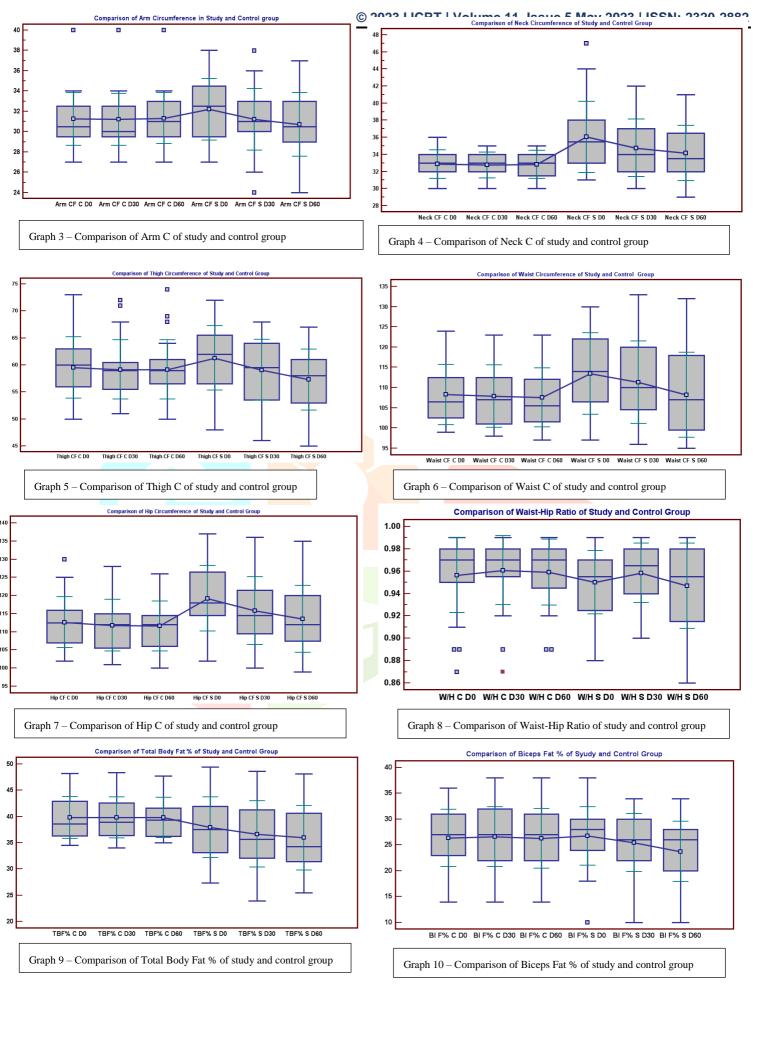
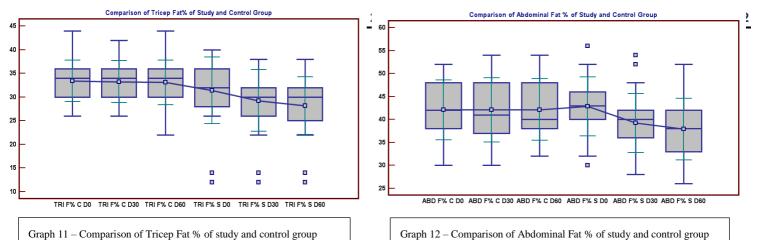


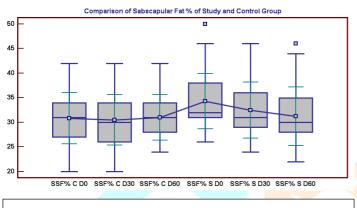
Table 4- Effect on various quantitative parameters by Paired 't' test

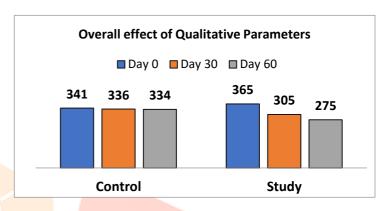


Graph 2 – Comparison of Abdominal Circumference of study and control group.









Graph 13 - Comparison of Subscapular Fat % of study and control group

Graph 14 - Overall effect of Qualitative Parameters.

Discussion

Any food which is sweet, heavy, cold, oily with sheeta virya; madhura vipaka; santarpana, brihana, rasayana and abhishyandi karma; Parthiv and jala mahabhoot will increase kapha and meda and will lead to Sthaulya. Kapha and meda have similar properties and from samanya Vishesh siddhant, it will lead to vriddhi of them. Acharya Charak has mentioned eight main symptoms of Sthaulya which are Ayushorhasa (Decrease in life span), Javoparodha (Early signs of senility), kricchravyavayata (Difficulty in Intercourse), Daurbalya (Fatigue), Daurgandhya (Foul body odor), Vyayama Asahatva (Inability to do physical exercise), swedabadha (Excessive perspiration), Kshudhatimatram (Increase in appetite) and pippasatiyoga (Increase in thirst). Consumption of etiological factors leads to formation of medo dhatu in excess leading to strotoavrodh (Obstruction of passages) and thus hampering formation of further dhatus. As a result, meda keeps increasing in body. Kothagata vayu leads to increase in digestive fire due to which person feels excess hunger, which inturn leads to excessive eating and Sthaulya. Treatment principle mentioned by Acharya Charak for Sthaulya is "Guru Apatarpana" which means food which are Heavy but does apatarpana should be used. Food which is heavy in nature will help managing excessive digestive fire. If laghu food is given, it will lead to further increase in vata in koshta and thereby elevating digestive fire. Sthaulya is santarpana janya vyadhi and therefore it's important to give apatarpana. This explains that guru apatarpana is most appropriate treatment for Sthaulya. Nidaan parivarjana is essence of any treatment. While mentioning agrya dravya, vagbhat has stated Rasanjan as best for Sthaulya. Acharya Sushrut has also mentioned Rasanjan in treatment of Sthaulya. Rasanjan is a formulation made from Daruharidra kwath and Goat's milk. Properties of Rasanjan are Katu, Tikta rasa, Ushna Virya, Katu Vipaka, Tikshna, snigdha, Sandra and laghu guna and Chedana, kaphashamak karma. Due to these properties it acts well on Sthaulya. Rasanjan along with modified diet and exercise when compared to only diet and exercise shows statistically significant (P<0.05) results in reduction of weight, BMI, Circumference - Abdomen, Arm, Neck, Thigh, Waist, Hip, Waist-Hip ratio, Total body fat %, Biceps fat, Triceps fat, Subscapular and Abdominal fat percentage when analysed by 2 way ANNOVA test (Table -1,2). Significant results were seen in all the parameters on applying paired 't' test except on Arm Circumference and Waist-Hip Ratio. BMI calculation is highly dependent on weight and therefore as weight reduced in study group, there is significant reduction in BMI too. (Table -3,4). As meda is

significantly more on udara and Rasanjan acts on medo dhatu and therefore was helpful in reducing abdominal circumference along with diet and exercise (Graph -2). Study²² shows neck circumference as potentially useful screening tool for obesity and a neck circumference > or = 35.5 cm in men and > or = 32 cm in women should be considered the cut-off point for overweight/obesity (Graph- 4). Values of waist-hip ratio vary from 0.50 -1.0. WHO states that waist -hip ratio above 0.90 for males and above 0.85 for females is a criterion for abdominal obesity. Minute change in waist-hip ratio will not be statistically significant (Graph-8). Subjects taking Rasanjan commonly showed symptom of decreased appetite which can be action of Rasanjan on agni due to which false hunger got diminished. Action of Rasanjan can also be on Krimi which can be the reason of false hunger previously. Stamina build up and improvement in ability of physical exercise takes time and is not evident in such short period. Subjects were given physical exercise of 30 minute walk morning - evening which will improve stamina but gradually over a long period of time. Lightness in body can be indicator of improved metabolism, increase in stamina and dissolving meda dhatu. Reduced levels of flabbiness are evident through decrease in localized fat percentage calculated through skin fold callipers also. Decrease in level of fatigue can also be correlated with lightness in body and improved metabolism. It was noted that subjective parameters such as level of enthusiasm, sweating, dyspnea, sleep, hunger, thirst, physical exercise, heaviness, flabbiness, fatigue and body odor are difficult to access accurately in such short study period (Graph -14). Some incidental findings apart from obesity were also observed during the trial. Patients taking Rasanjan gave essential information during follow ups - Lightness in body, Decrease in appetite, Increase in bowel movements 3-4/day, Improvement in skin texture, Relief from fungal skin infections (In 2 patients), Relief from generalized body itching, Decrease in knee joint pains (1 patient), Decrease in swelling in joints (1 patient). Daruharidra has also been used in treatment of variety of ailments like jaundice, enlargement of spleen, leprosy, rheumatism, fever etc. There were no serious adverse effects seen in patients due to Rasanjan. Although two patients had mild headache, four had nausea and loss of appetite. These effects were self-limiting and did not require any kind of medicine or withdrawal from the trial.

Conclusion

Obesity cannot be managed without making lifestyle changes. The main cause of obesity is poor diet preferences and sedentary lifestyle. Sthaulya depends on ahara, nidra and rasa dhatu and therefore Nidaan parivarjana remains essential factor in treatment. Rasanjan as per ayurvedic principles, its Katu, tikta rasa, ushna veerya, katu vipaka, Tikshna laghu guna, chedana and lekhana karma is helpful in management of Sthaulya. Rasanjan when combined with diet and exercise provides better results in Sthaulya rather than diet and exercise only.

Conflict Of Interest

The authors have no conflicts of interest regarding this investigation.

Acknowledgment

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