Research Article

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CLINICAL EFFICACY OF TRIPHALADI GRANULES IN MANAGEMENT OF APATHYANIMITTAJA PRAMEHA (TYPE 2 DIABETES MELLITUS)

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ABSTRACT

Aim of the study was conducted with an objective of evaluating the role of Triphaladi granules in clinically diagnosed cases of Apathyanimittaja Prameha which was confirmed by laboratory investigations. The 51 registered patients were administered with Triphaladi granules in a dose of 5 gm twice a day with lukewarm water before meals for duration of two months in 2 Groups; Group A (Triphaladi granules) and Group B (ongoing oral hypoglycemic agent with Triphaladi granules). Statistically highly significant improvement was observed in subjective criteria like Prabhutmutrata, Kshudhadhikya, Trishnadhikya, Daurbalya and Pindikodweshtana; where as in objective criteria significant results were obtained in FBS in both the Groups, Group A showed significant results in PPBS and Serum Triglyceride and Group B showed significant result in Serum HbA1c after completion of treatment. In Group-A moderate improvement was observed in 37.5% of cases, 50% cases showed mild improvement in diseased condition and 12.5% cases obtained grade-unchanged. In Group-B, 16% of cases showed moderate improvement and 56% were categorized as mildly improved after the treatment. The 28% patients were under grade unchanged. Based on results, it has been concluded that Triphaladi granules is effective in management of uncomplicated cases of Apathyanimittaja Prameha.

Key words: Apathyanimittaja Prameha, Diabetes mellitus type 2, Oral hypoglycemic agents, Triphaladi granules.

INTRODUCTION

The 21st century is the age of science, technology, computer and atomic energy. The advancement of science and technology is been observed in every field including modern medical science. Besides the miraculous achievement of modern medical science humanity is passing through a horror of disease and drug phobia particularly in developing countries like India. Improper unbalanced diet and sedentary lifestyle are showing upward trend in India. This has lead to emergence of several health problems, among those diabetes mellitus is a giant disease considered as one of the arch enemy of mankind. Diabetes and its complications pose a major threat to future public health resources throughout the world. The manifestation of disease is described as "Prabhutavilamutrata" which means frequent and copious urine with turbidity. [1,2] It is also believed that, if not treated properly in due course of time, Prameha changes in Madhumeha, which is very similar to a debilitating disease Type 2 diabetes mellitus. [3,4] Although conventional modern medicine has number of drug of choice for controlling the blood sugar level in patients of type-2 Diabetes mellitus. However, with prolonged treatment doses of the drugs often needs to be increased to control blood sugar level and a time comes when patient has to be switched over to Insulin. With a view to help the suffering community there is a need to find a safer drug, which can be used to control blood sugar level for longer periods. Ayurvedic classics provide references on herbal and herbomineral drugs which can be safely used in controlling the blood sugar in patients of Diabetes mellitus. And hence, Ideal therapy is still obscure. In present study a protocol is made to manage Apathyanimittaja Prameha by herbal compound mentioned in Yogratnakara in Prameha Chikitsa.[5] Patients were also advised for brisk walking for 30 minutes morning and evening. Healthy lifestyle was also suggested to these patients as per their constitution (Prakriti).

DRUG REVIEW

The drug Triphaladi Kwatha is mentioned in Yogaratnakar Prameha Chikitsaadhyaya shloka 73 for management of Prameha.

Preparation of drug and dosage

All the authenticated drugs (Table 1) taken in equal proportions were crushed to a coarse powder [6]separately and mixed thoroughly with 8 parts of water in a stainless steel container and then continuous mild heat was applied until it was reduced to one-fourth of its initial quantity. During the heating process, continuous stirring was done to facilitate the evaporation and avoid any deterioration due to burning of materials. After a desirable reduction in volume was achieved, the Kwatha was filtered through single folded cotton cloth and collected in a separate vessel. Subsequently, the Kwatha was boiled again over slow fire on a gas stove, maintaining the temperature between 90 °C and 95 °C till a semisolid consistency was

obtained. As water evaporates, viscosity of extract increases, resulting in Ghana[7] form. Ghana was mixed with the powder of Triphaladi Kwatha (up to 10% of extract) further forming a solid mass. The solid mass (Ghana) was passed through a no. 8 sieve and granules were prepared and then dried at 50 °C in a hot air oven for 5 hours. [8,9] Both the groups were administered with Triphaladi granules in a dose of 5 gm twice a day with lukewarm water before meals for duration of two months.

MATERIALS AND METHOD

A series of 51 patients with signs and symptoms of Apathyanimittaja Prameha were selected from OPD or IPD. Irrespective of sex, caste, occupation and religion. The study was approved by Institutional Ethics committee and was registered under CTRI (CTRI/2011/12/002195T)

Inclusion criteria

- Age between 30 years to 70 years.
- Known patient of Type 2 Diabetes mellitus, and also the patients preliminarily diagnosed Type 2 Diabetes mellitus on the basis of signs and symptoms of the disease was confirmed by FBS and PPBS and then were included in study.
- Patients presenting with Type2 DM having, Random serum glucose level more than 200 mg/dl, Fasting Blood Sugar greater than 126 mg/dl,[10] patients of Type 2 Diabetes mellitus under modern medication and still having uncontrolled blood sugar level.

Exclusion Criteria

- Age below 30 years and above 70 years.
- Patients of Sahaja Prameha and having Bala and Dhatukshaya, gestational diabetes mellitus and Type I Diabetes mellitus.
- Patient having any one or more of condition, malignant and accelerated hypertensive, CVS disorder (CAD), Pregnant woman or planning to be gravida within six months, Lactating mother, Secondary Diabetes mellitus, CNS disorder e.g. encephalopathy, Patient under going regular treatment for any other severe illness and also patients suffering from Tuberculosis, Carcinoma, HIV positive patients and endocrinal disorders like, Thyrotoxicosis, Cushing Syndrome etc. was excluded from the present study.

Treatment Protocol

Group A: Recently diagnosed patients, mild to moderate cases of type 2 Diabetes - Apathyanimittaja Prameha was administered 'Triphaladi granules' along with Pathyapalana i.e. Controlled diet and exercise.

Group B: known patients of Type 2 Diabetes mellitus with ongoing modern antidiabetic drugs, whose blood glucose level is not well under control was administered with Triphaladi granules additionally along with Pathyapalana i.e. Controlled diet and exercise.

Criteria to assess the effect of trial drug
Gradation of the symptoms: (Table 2)
Objective assessment:
Results of the treatment has been assessed on the basis of

- FBS and PPBS levels
- Urine sugar estimation
- Effect in S. cholesterol, S. Triglyceride and HDL levels
- S. Insulin, S. Apolipoprotein B and Glycated haemoglobin levels (in selected cases).
- Hamiltons Anxiety and Depression rating scale.

OBSERVATIONS

The 51 patients of Apathyanimittaja Prameha were registered for study. Out of those 49 patients completed the course of treatment and 2 patients discontinued. 24 patients completed the treatment and 1 patient discontinued in Group A, while 25 patients completed the treatment and 1 patient discontinued in Group B.

The observations are based on demographic, constitutional and clinical profile of 51 patients reported that maximum cases in study were female (58.82%), age Group of 51-60 yrs. most cases (50.89%) were from middle socio-economic Group and maximum cases (49.01%) were housewives. Incidence in dietary habits was found more in persons with vegetarian diet (68.82%). BMI wise maximum cases found in study were overweight (53.06%) and 31.37% of patients belonged to Pitta-Vataj Prakriti. Cases were reported with a positive family history (33.32%) and duration of illness was more than 5 yrs in maximum cases (54.90%). About 90.19% cases were presented with Daurbalya followed by about 86.27% with Trishnadhikya and 80.39% with Prabhutmutrata. About 74.50% cases registered with complaint of kshudhadhikya and 13.72% with Swedadhikya. Pindikodweshtana was complaint in 50.98% cases and Karapadatala Daha in 13.72% cases, least number of cases 7.84% were registered with the complaints of Karapadatala Suptata.

Table 1: Ingredients of Triphaladi Granules

Drug	Latin Name	Part Used	Proportion
Haritaki	*Terminalia chebula* Retz.	Pericarp	1 Part
Bibhitaki	*Terminalia bellerica* Roxb.	Pericarp	1 Part
Amalaki	*Embelica officinalis* Gaertn.	Pericarp	1 Part
Asana	*Pterocarpus marsupium* Roxb.	Heart wood	1 Part
Kalinga	*Hollarrhena antidysenterica* Wall.	Bark	1 Part
Musta	*Cyperus rotundus* Linn.	Rhizome	1 Part
Daruharidra	*Berberis aristata* D.C.	Stem	1 Part

Table 2: Gradation of Symptoms

Gradation of the symptoms:	
Prabhuta mutrata	
▪ 3 – 6 times per day, rarely at night	0
▪ 6 – 9 times per day, 0 – 2 times per night	1
▪ 9 – 12 times per day, 2 – 4 times per night	2
▪ More than 12 times per day, more than 4 times per night	3
Avila Mutrata	
▪ Crystal clear fluid	0
▪ Faintly cloudy or smoky (turbidity barely visible)	1
▪ Turbidity clearly present but newsprint easily read through test tube	2
▪ Newsprint not easily read through test tube	3
▪ Newsprint cannot be seen through test tube	4
Kshudhadikya	
▪ As usual	0
▪ Slightly increased (1 – 2 meals)	1
▪ Moderately increased (3 – 4 meals)	2
▪ Markedly increased (5 – 6 meals)	3
Trishnadhikya	
▪ Feeling of thirst 7 – 9 times/24 hours, either/or Intake of water 5 – 7 times/24 hours with quantity 1.5 – 2.0 liter/24 hours	0
▪ Feeling of thirst 9 - 11 times/24 hours, either/or Intake of water 7 - 9 times/24 hours with quantity 2.0 - 2.50 liter/24 hours	1
▪ Feeling of thirst 11 – 13 times/24 hours, either/or Intake of water 9 – 11 times/24 hours with quantity 2.50 -3.00 liter/24 hours	2
▪ Feeling of thirst >13 times/24 hours, either/or Intake of water >11 times/24 hours with quantity >3.00 liter/24 hours	3
Pindiko-udveshatan (Cramps)	
▪ No cramps	0
▪ Cramps after walking more than 1 km.	1
▪ Cramps after walking	2
▪ Cramps after walking ½ km	3
▪ Inability in walking even ½ km	4
Kara-Pada-Tala-Daha/Supti	
▪ No Daha	0
▪ Kara-pada-tala-daha/Supti discontinous	1
▪ Kara-pada-tala-daha/Supti continous but not severe	2
▪ Kara-pada-tala-daha/Supti continous and severe	3
Daurbalya (Weakness)	
▪ Can do routine exercise/work	0
▪ Can do moderate exercise with hesistancy	1
▪ Can do mild exercise only, with difficulty	2
▪ Cannot do mild exercise too	3

Table 3: Effect of therapy on objective criteria Group-A

Objective criteria	n	Mean		% relief	d	SD	SE	t	p
		BT	AT						
FBS (mg/dl)	24	199.21	173.17	13.07↓	26.04	52.83	10.78	2.41	<0.05[**]
FBS (chronicity 1-5 yrs)	18	207.66	169.22	18.51↓	38.44	54.88	12.93	2.97	<0.05[**]
PPBS (mg/dl)	24	286.58	244.37	14.72↓	42.21	82.64	16.87	2.50	<0.05[**]
PPBS (chronicity 1-5 yrs)	18	310.66	255.11	17.88↓	55.55	87.30	20.57	2.70	<0.05[**]
S.Cholesterol (mg/dl)	24	204.25	196.75	3.67↓	7.50	30.69	6.26	1.19	>0.05[*]
S.Triglyceride (mg/dl)	24	303.12	287.29	5.22↓	15.83	161.91	33.05	0.48	<0.05[**]
HbA1c	6	7.217	6.87	4.84↓	0.35	0.38	0.15	2.27	>0.05[*]
S.Insulin (mg/dl)	6	8.65	8.18	5.41↓	0.47	4.28	1.75	0.27	>0.05[*]
S.Apolipoprotein B (mg/dl)	6	149.0	105.66	29.08↓	43.33	117.42	47.93	0.90	>0.05[*]
BMI	24	25.09	24.90	0.76↓	0.19	0.27	0.06	3.39	<0.05[**]
Urine sugar fasting	15	2.27	1.60	29.42↓	0.66	1.92	0.49	1.35	<0.05[**]

[**]= significant, [*]= insignificant, ↓ = Decrease.

Table 4 : Effect of therapy on objective criteria Group-B

Objective criteria	n	Mean		% relief	d	SD	SE	t	p
		BT	AT						
FBS (mg/dl)	25	172.08	158.92	7.65↓	13.16	37.79	7.56	1.74	>0.05[*]
FBS (chronicity 1-5 yrs)	09	310.66	255.11	17.88↓	55.55	87.30	20.57	2.70	<0.01[**]
PPBS (mg/dl)	25	234.24	240.72	2.77↑	6.48	76.22	15.24	-0.42	>0.05[*]
PPBS (chronicity 1-5 yrs)	09	208.77	254.66	21.97↑	45.88	63.51	21.17	2.17	>0.05[*]
S.Cholesterol (mg/dl)	25	196.28	199.92	1.85↑	3.64	22.26	4.45	-0.82	>0.05[*]
S.Triglyceride (mg/dl)	25	205.20	204.56	0.31↓	0.64	53.16	10.63	0.06	>0.05[*]
HbA1c	06	7.23	6.75	6.67↓	0.48	0.37	0.15	3.24	<0.05[**]
S.Insulin (mg/dl)	05	9.14	8.06	11.81↓	1.08	4.22	1.89	0.57	>0.05[*]
S.Apolipoprotein B (mg/dl)	05	125.40	101.20	19.29↓	24.20	40.62	18.16	1.33	>0.05[*]
BMI		26.68	26.55	0.50↓	0.13	0.27	0.05	2.42	<0.05[**]
Urine sugar fasting	14	1.86	1.86	0	0.00	1.47	0.39	0.00	>0.05[*]

[**]= significant, [*]= insignificant, ↓ = Decrease, ↑ = Increase.

Table 5: Effect of Therapy on Hamiltons Anxiety and Depression Rating Scale Group-A

n=24	Mean Score		% Relief	diff	SD(±)	SE(±)	't'	p
	B.T.	A.T.						
Anxiety	16.125	11	31.78↓	5.125	1.650	0.337	15.216	<0.001[***]
Depression	7.750	2.792	63.97↓	4.958	1.781	0.364	13.639	<0.001[***]

[***]= highly significant, ↓ = Decrease

Table 6: Effect of Therapy on Hamiltons Anxiety and Depression Rating Scale Group-B

n=25	Mean Score		% Relief	diff	SD(±)	SE(±)	't'	p
	B.T.	A.T.						
Anxiety	15.320	10	34.72↓	5.320	1.574	0.315	16.902	<0.001[***]
Depression	6.960	3.280	52.87↓	3.680	2.512	0.502	7.325	<0.001[***]

[***]= highly significant, ↓ = Decrease

Table 7: Overall effect of therapy of both the Groups

Group	Group – A (n=24)	%	Group – B (n=25)	%
Marked	0	0	0	0
Moderate	9	37.5	4	16
Mild	12	50	14	56
Unchanged	3	12.5	7	28

Table 8: Comparison between overall effects of therapy of both the Groups

Overall effect of therapy				t	p
Group	No of patients			2.945	>0.05[*]
	<50%	>50%	Total		
A	15	9	24		
B	21	4	25		
Total	36	13	49		

[*]= insignificant
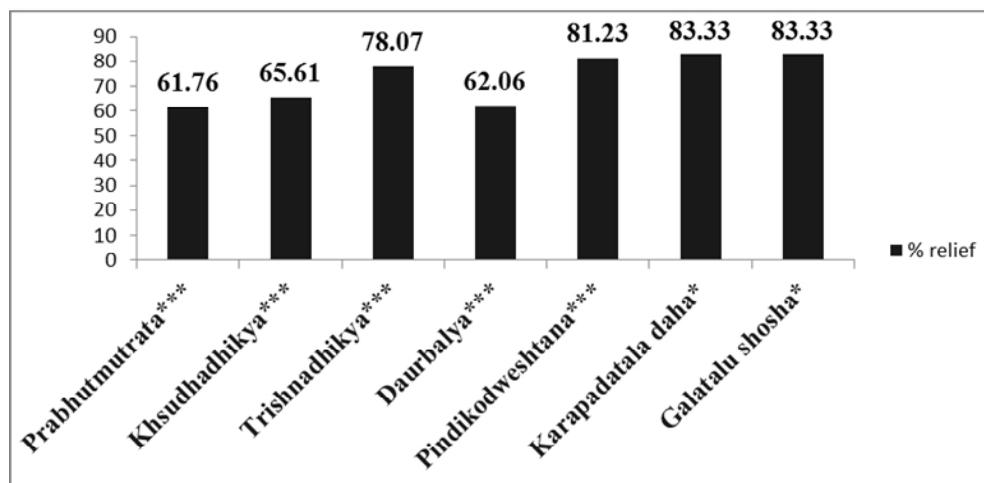
[***]= highly significant, [*]= insignificant, Wilcoxon's signed rank test.

Graph 1: Effect of therapy on symptoms Group-A

***= highly significant, **= Significant, wilcoxon's signed rank test.
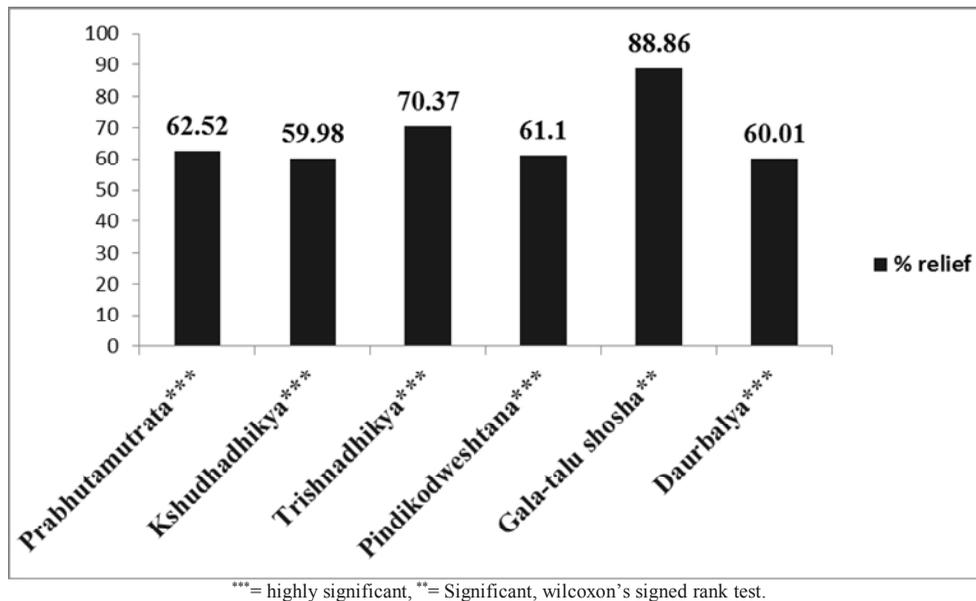
Graph 2: Effect of therapy on symptoms Group-B

RESULTS

In both the Groups statistically highly significant improvement was observed in symptoms - Prabhutmutrata, Kshudhadhikya, Trishnadhikya, Daurbalya and Pindikodweshtana (Graph 1 and 2). In biochemical parameters significant results were obtained in FBS in both the Groups, Group A showed significant results in PPBS and Serum Triglyceride, whereas in Group B significant result in Serum HbA1c were reported after completion of treatment. Both the Groups showed significant decrease in BMI levels by 0.76% and 0.50% in Group-A and Group-B respectively. Group A showed insignificant decrease and Group B showed insignificant increase in Serum Cholesterol. Statistically insignificant decrease was noted in Serum Insulin and Serum Apolipoprotein B in both Groups (Table 3 and 4). Group A showed significant decrease in fasting urine sugar level (Table 4). Stress is leading factor in etiology of type 2 diabetes mellitus Triphaladi granules showed statistically highly significant decrease in Hamiltons anxiety and depression rating scale (Table 5 and 6). In Group-A Moderate Improvement was observed in 37.5% of cases, 50% cases showed Mild Improvement in diseased condition and 12.5% cases obtained grade-Unchanged In Group-B, 16% of cases presented Moderate Improvement and 56% were categorized as Mildly Improved after the treatment. The 28% patients were under grade Unchanged. Analyzing above results, Group-A showed better results than Group-B (Table 7). On statistical analysis, both the Groups showed statistically similar results, as there is statistically insignificant difference between the trial Groups (Table 8).

DISCUSSION

In clinical trial Group-A showed significant reduction in FBS, PPBS parameters along with insignificant decrease in Serum HbA1c level (Table 2). It shows the potential of Ayurvedic formulation to be used in freshly detected cases of type 2 diabetes mellitus. Also it can be supportive therapy to conventional medicine as it shows a significant decrease in Serum HbA1c level in Group-B (Table 3). The results of test drug in Group-A and Group-B are almost same. Of course, Group-B shows the synergistic action when Triphaladi granules are combined with modern anti-diabetic drugs. Fasting Urine Sugar in Group-A was reduced significantly. Sugar in blood as well as in urine is the result of either deranged metabolism, lowered urinary threshold point, production of Ama Dosha, or due to their cumulative effect. Results indicate that reduction in urine sugar was well managed by Triphaladi granules. In both the Groups statistically highly significant improvement was observed in symptoms - Prabhutmutrata, Kshudhadhikya, Trishnadhikya, Daurbalya and Pindikodweshtana (Graph 1 and 2). Ingredients of Triphaladi granules i.e. Haritaki,[11] Amalaki,[12] Asana,[13] Kutaja,[14] Musta[15] and Daruharidra[16] are quoted as Pramehara in Ayurveda classics. Most of ingredients are Tridoshashamaka property. Apathanimittaja Prameha shows dominancy of Kapha among the Doshas, Meda among the Dooshyas. Most of ingredients of Triphaladi granules are having Tikta, Katu, Kashaya Rasa, Laghu, Ruksha Guna, Ushna Virya and Katu Vipaka which might have corrected Kapha Dushti and Medo Dhatu Dushti thus acts on pathogenesis of Apathyanimittaja Prameha. Most of the ingredients of Triphaladi granules have known hypoglycemic, antihyperglycemic, hypolipidaemic, hypocholesterolemic, insulin releasing, antistress, and antioxidant and immunomodulatory activities. So, it can be a good solution to the complex metabolic derangement of type 2 diabetes mellitus. According to modern pharmacology active principle of Haritaki and Bibhitaki i.e. chebulinic acid which has reported alpha glucosidase inhibitory action,[17] Bibhitaki also contains gallic acid which helps in

regeneration of β cells of pancreas,[18] similar action is observed by flavonoid, epicatechin in Vijaysara.[19] Berberine in Daruharidra promotes regeneration and functional recovery of β cells.[20] Mixture of turpenoids in Musta stimulates glucose uptake,[21] whereas Kutaja retards the carbohydrate absorption from intestine,[22] thus helping in relieving the signs and symptoms of diabetes mellitus type 2.

CONCLUSION

Pathogenesis of Apathanimittaja Prameha shows dominancy of Kapha-Pitta Dosha and Meda Dhatu. Triphaladi granules acts on pathogenesis of Apathyanimittaja Prameha and showed highly significant decrease in symptoms like Prabhutmutrata, Kshudhadhikya, Trishnadhikya, Daurbalya and Pindikodweshtana. Triphaladi granules showed significant reduction in parameters like FBS, PPBS, Serum Triglyceride, fasting urine sugar in Group-A and Serum HbA1c in Group-B. It has also relieved anxiety and depression significantly in diabetic patients along with BMI levels. Healthy dietetics and healthy life-style with the use of Ayurvedic formulation Triphaladi granules singularly or in combination with modern drugs, depending upon the need, will contribute significantly to achieve the goal of improvement in the quality of life in patients of type 2 diabetes mellitus.

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