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CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF VIDANGADI YOGA (AYURVEDIC POLYHERBAL MEDICINE) IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background and objectives: Prevalence of diabetes mellitus (DM) is rapidly rising throughout the globe at an alarming rate, where India leads with largest number of diabetics and became "diabetes capital of the world." Incidence of diabetes mellitus is increasing due to genetic predisposition, high body fat, and insulin resistance. Though multiple oral hypoglycaemic agents and insulin are available, these are associated with side effects, primary and secondary failure. Hence, evaluation of antidiabetic potential of medicines described in traditional health sciences such as Ayurveda (Indian system of medicine) is also important. This study aimed to assess the efficacy and safety of Vidangadi Yoga (ayurvedic polyherbal medicine) in the management of type 2 diabetes mellitus (T2DM). Methods: Total 31 patients were taken for this clinical research. They are divided into two groups, group A and B, given Vidangadi Yoga 4 g & 2 g TDS respectively for three-month follow up. They are investigated against their blood glucose, HbA1C and liver profile tests. Patients were also investigated for subjective parameters viz polyurea, polyphagia, exhaustion and constipation and their response has also been noted regarding palatability acceptance and ease of administration. Results: Patients has responded positively for formulation. Decrease in FBS and PPBS were found highly significant ($P < 0.001$) in both groups but more in higher dose (group A). Decrease in HbA1C is also found highly significant in both groups. In LFT, SGOT level were also decreased more in group B in comparison to group A, and it is significant ($P = 0.017$ and 0.002). SGPT level were also decreased more in group B in comparison to group A, and it is significant in group B ($P= 0.085$ and 0.002). Conclusions: Vidangadi Yoga was found significant not only in controlling blood sugar but also in management of other factors related to diabetes mellitus.

KEYWORDS: Ayurveda, type 2 diabetes mellitus; ayurvedic polyherbal medicine; Vidangadi Yoga; herbal treatment; n; blood glucose; Diabetes mellitus, Clinical study trial.

INTRODUCTION

Background

Diabetes is not the disease of 19-21st century, but it was known since ancient times in the name of Prameha with synonyms of madudhatu, madhuprameha, ojomeha, kshoudrameha. Types and symptom along with management approach was discussed and dictated in ancient texts elaboratly. Madhumeha can be considered as diabetes mellitus (DM) by different perspectives based on clinical symptoms and attempts have been made by ayurvedic physicians and researchers to treat these two entities by using classical formulations mentioned in Prameha Chikitsa.[1] DM is not a single disease but it is a group of metabolic disorders that are characterized by hyperglycemia caused by reduced insulin secretion, decreased glucose utilization and increased production of glucose. Metabolic derangement taking place in the body as an outcome of the pathology of DM causes secondary pathological changes in multiple organs and systems. It imposes unbeatable load on systems, leading to increased incidences of end stage renal disease, nontraumatic amputations, adult blindness, and cardiovascular diseases, and finally resulting in death. Prevalence of DM is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. With more than 62 million diabetics currently present in India, it is fast gaining the status of a potential epidemic. It is predicted that by 2030 DM may afflict up to 79.4 million individuals.[3] This rising prevalence undoubtedly is going to pose a potential burden on the healthcare system. Over the past 30 years, the status of DM has changed as a mild disorder of the elderly to one of the major causes of mortality and morbidity affecting the youth and middle-aged people. Though advances in modern medicine have helped scholars to develop multiple oral hypoglycemic agents (OHA) and insulin therapy, achieving glycemic control becomes the sole purpose in clinical practice, let alone think of reversing

the pathology. Control of hyperglycemia also becomes tricky in some individuals due to primary and secondary failures. Along with it, limited role of good glycemic control in preventing long term complications has always kept the window open for better remedy for overall control of the disease.

Researchers have correlated DM with Prameha mentioned in Ayurveda. The disease has been explained in great details in all ancient ayurvedic treatises. In Ayurveda, treatments of DM have been described in details, including multiple mono-herbal, multi-herbal, herbo-mineral combinations and Panchakarma (~bio-purification treatments) treatments. Such mono or multi-herbal medicines have been widely studied, but many potential combinations remain unexplored. Vidangadi decoction (kwatha) is one of such classical Ayurvedic formula- tions. It is widely used in DM treatment. All the ingredients of the combinations are herbal in origin and are known to have antidiabetic/hypoglycemic effects.

METHODS

Study design Total 36 patients were registered for clinical trial at OPD of department of kayachitiksa, jammu institute of Ayurveda and research Hospital in which 5 patients were dropped out.

Inclusion criteria for selection of patients was either sex, age group of 30 – 70 years, 8 hour fasting blood sugar (FBS) >126 and < 250 mg/dl and 2 hour postprandial blood sugar (PPBS) >200 to <= 350 mg/dl. We exclude the patients not lying in parameter of inclusion criteria and patients suffering from retinopathy, nephropathy, cardiovascular problems, hormonal imbalance, regnant and lactating mother. Their blood sugar (FBS and PPBS) has been investigated at starting, after one month, two months and after 3 months while HbA1C, SGOT, SGPT, and creatinine has been investigated at starting and end of the study (3 month).. Patients were also questioned for astringency of taste, acceptability, other related problems like constipation, exhaustion, polydipsia.

Trial drugs

For this study, vidangadi Kashaya spray dried powder has been made available to patients by modifying the kashaya (decoction) form into powder dosage form, using spray drier. In order to maintain its principle administrable form as kashaya, it was recommended to dissolve unit dose into luke warm water to make in to kashaya form etc.

Table 1: Ingredients of Vidangadi Kashaya.

Sanskrit Name	Latin name		
Vidanga	*Embelia ribes* Burm.f.	Fruit	1 part
Shala	*Shorea robusta* Gaertn.	Bark	1 part
Arjun	*Terminalia arjuna* (Roxb) W. & A.	Bark	1 part
Kataphal	*Myriae sculeuta* Buch-Ham	Bark	1 part
Kadamba	*Anthocephalus indicus* Miq.	Bark	1 part
Lodhra	*Symplocos racemosa* Roxb.	Bark	1 part
Asana	*Pterocarpus marsupium* Roxb.	Bark	1 part
Kutaj	*Holarrhena antidysenterica* (Linn.) Wall.	Bark	1 part

Patients grouping

Total 31 patients were divided into two groups, group A and group B having 14 patients and 17 patients respectively. Group A (patients having fasting blood sugar more than 160) was given a dose of 4 g TDS while group B (patients having fasting blood sugar less than 160) was given 2 g TDS of vidangadi yoga. The patients were strictly advised to dissolve suitable quantity of powder into 100 ml luke warm water just before administration and drink it. Patients are advised to do regular exercise and diet control as prescribed to avoid high sugar content diet. Patients are also advised to examine blood sugar on regular interval and council to take vidangadi Kashaya in proper manner

Statistical analysis

Findings were analysed statistically by SPSS 16.00 version applying the paired t-test, one-way ANOVA, Friedman test and Chi square test. The results are interpreted with possible co relation of ayurvedic and contemporary point of view. $P < 0.05$ was considered statistically significant and $p < 0.001$ were considered highly significant in the results of this study.

RESULT

All the patients were selected independently of their sex, age, caste, economy and religions. Total 36 patients were registered while 5 have left the study due to their own consent. Patient's variable and their profile were given in Table 2. Patients were also investigated against their subjective parameters like polyurea, polyphagia, exhaustion feeling of patients and constipation as shown in Table 3-6. All the parameters were accessed by oral assessment of patients by questioner. Very less patients have complaint about polyurea and polyphagia while reported patients claiming for improved status. There is significant improvement in case of exhaustion of patients. In case of constipation, this formulation shows highly significant effect and makes patients feel good.

Table 2: Effect of Vidangadi yoga.

Patients variables	Division of variables	Group A (% of patients)	Group B (% of patients)
No. of patients	Total	14	17
Age Group	30-40 years	7.10	17.64
	41-50 years	28.57	29.41
	51-60 years	35.71	29.41
	61-70 years	28.57	23.52
Sex	Male	100	82.2
	Female	0	11.8
Diabetic family history	Yes	28.10	17.6
	No	71.6	82.4
Diet	Vegetarian	57.1	29.4
	Mixed	42.9	70.6
Addiction	Tobacco	35.7	11.8
	Smoking	14.3	0
	Alcohol	7.1	0
BMI	(≤ 18)	0	0
	(≥18 to ≤24.9)	21.42	41.17
	≥ 25	78.57	58.82
Review on astringency of Vidangadi Yoga	0	0	0
	1	7.1	0
	2	42.9	47.1
	3	50	51.6

Table 3: Effect of Vidangadi Kashaya in polyuria.

	Polyurea (Number of cases)				Within the group comparison Friedman test
Groups Grade	0 Days	30 Days	60 Days	90 Days	
0 1 A 2 3	1 1 2 1 0	1 1 3 0 0	1 2 2 0 0	1 2 2 0 0	X^2 =4.71 P=0.194
0 1 B 2 3	1 4 1 1 1	1 5 2 0 0	1 5 2 0 0	1 5 2 0 0	X^2 =3.000 P=0.392
Within the group comparison Chi square test	X^2 =0.562 P=0.755	X^2 =0.530 P=0.403	X^2 =0.043 P=0.835	X^2 =0.043 P=0.835	

Table 4: Effect of vidangadi Kashaya on polyphagia.

	Polyphagia (Number of cases)				Within the group comparison Friedman test
Groups Grade	0 Days	30 Days	60 Days	90 Days	
0 1 A 2 3	12 1 1 0	13 1 0 0	13 1 0 0	13 1 0 0	X^2 =1.00 P= 0.801
0 1 B 2 3	17 0 0 0	17 0 0 0	17 0 0 0	17 0 0 0	X^2 =000 NA
Within the group comparison Chi square test	X^2 =2.596 P=0.273	X^2 =1.255 P=0.283	X^2 =1.255 P=0.283	X^2 =1.255 P=0.283	

Table 5: Effect of vidangadi Kashaya on exhaustion feelings of patient.

Groups Grade	Exhaustion (Number of cases) 0 Days	30 Days	60 Days	90 Days	Within the group comparison Friedman test
0 A 2 3	6 2 4 2	7 4 3 0	7 6 1 0	7 6 1 0	X^2 =13.68 P= 0.003
0 1 B 2 3	1 0 3 3 1	1 1 5 1 0	1 4 2 1 0	1 4 3 0 0	X^2 =13.036 P= 0.005
Within the group comparison Chi square test	X^2 =1.399 P=0.706	X^2 =1.726 P=0.422	X^2 =4.081 P=0.130	X^2 =4.081 P=0.130	

Table 6: Effect of vidangadi Kashaya on constipation.

Groups Grade	Constipation (Number of cases) 0 Days	30 Days	60 Days	90 Days	Within the group comparison Friedman test
0 1A 2 3	4 4 3 3	9 4 1 0	9 4 1 0	10 4 0 0	X^2 =23.174 P< 0.001
0 B 1 2 3	8 2 4 3	11 2 3 1	12 2 2 1	12 3 1 1	X^2 =18.559 P< 0.001
Within the group comparison Chi square test	X^2 =1.870 P=0.600	X^2 = 2.601 P=0.457	X^2 =2.158 P=0.540	X^2 =2.054 P=0.561	

Table 7: Effect of vidangadi Kashaya on blood sugar (fasting and postprandial).

Groups	Fasting Blood Sugar (Mean ± SD) 0 day	30 days	60 days	90 days	Postprandial Blood Sugar (Mean ± SD) 0 days	30 days	60 days	90 days
A	175.93 ± 12.12 135.59 ± 4.66	162.21 ±	142.07 ± 14.38	134.50 ± 12.30	291.50 ± 51.12	216.50 ± 49.16	192.07 ± 34.12	177.50 ± 21.84
B	120.70 ± 8.76	8.06	115.41 ± 8.32	115.41 ± 8.86	230.82 ± 26.09	170.82 ±26.99	157.76 ± 24.11	144.53 ± 18.31
Within the group comparison Paired t test BT-AT	For Group A 41.42 ± 18.44 t= 8.403 P < 0.001		For Group B 20.17 ± 7.22 t= 11.51 P < 0.001		For Group A 114.00 ± 34.90 t= 12.22 P < 0.001		For Group B 86.29 ± 17.20 t= 20.68 P < 0.001	

Table 7: Effect of vidangadi Kashaya on blood sugar (fasting and postprandial).

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B	120.70 ± 8.76	8.06	115.41 ± 8.32	115.41 ± 8.86	230.82 ± 26.09	170.82 ±26.99	157.76 ± 24.11	144.53 ± 18.31
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Table 8: Effect of vidangadi Kashaya on HbA1C, SGOT, SGPT and creatinine.

Group	Mean ± SD						
	bA1C		SGOT		SGPT		Serum Creatinine
	0 Day	90 Days	0 Day	90 Days	0 Day	90 Days	0 Day 90 Days
A	8.52 ± 1.46	7.07 ± 0.60	28.42 ± 10.56	24.12 ± 8.11	33.63 ± 9.79	29.35 ± 8.16	0.89 ± 0.11	0.72 ± 0.10
B	7.67 ± 0.89	6.77 ± 0.48	28.62 ± 7.99	25.55 ± 6.43	38.73 ± 12.82	32.68 ± 9.62	0.93 ± 0.15	0.85 ± 0.12

Patients were investigated for objective parameters, blood sugar level (fasting and postprandial), HbA1C and LFT (SGOT, SGPT) and creatinine as given in Table 8. Effect of Vidangadi Kashaya was found highly significant in case of fasting blood sugar as well as postprandial blood sugar in group A and group B as given in Table 7. Among them group A shows more significant in comparison to group B in both the cases.

Effect of vidangadi Kashaya were also investigated for Glycated haemoglobin (haemoglobin A1c), and showed significant decrease in both group, A & B as given in Table 8. In LFT profile, SGOT was analysed for both groups, it was reduced significantly as shown in Table 8. SGPT was also screened at starting and end of the study and it was reduced significantly in group B while no significant decreased in group A as in Table 8

DISCUSSION

Herbal medicines have great demand in the developed and developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins, consumer own interest and reasonable cost. Here a formulation which was shown in Table1 having natural ingredients was selected. This formulation was indicated to take as kashaya form so here we made an attempt to dissolve the kashaya powder into luke warm water just before administration so that we can stick to fundamental prescribed dosage form while validating the ancient wisdom. Kashaya was indicated to take in 2 pala (Sharangdhar Samhita) or 1 pala (Yadav ji Tikkam Ji) in divided dose while in API (The Ayurvedic Pharmacopoeia of India) suggest to take kashaya from 48 g of kwath churna. If we make kwath and dry it, then we gat yield of about 12 g/6 g in a day. So on this basis two dose i.e. 4 g TDS and 2 g TDS dose has been decided for human being. Patients were grouped into A (FBS $\geq$ 160) and B (FBS < 160) were given treatment with 4 g TDS and 2 g TDS respectively. Ayurveda also have upper hand in recognition of prediabetic stage described in ayurvedic science like knotted hair, burning sensation, numbness, sweetness in mouth, laziness, body odour like fish whereas modern science has no such criteria. DM is due to increase in vata caused by either blockage of strota (body channel) by aggravated kapha and medo dhatu or due to mental stress food habit, life style etc. So ancient wisdom always talks about management of disease not only targeting the hypoglycaemic action but also use the additive drugs in formulation to manage other possible complication or problems in future.

In clinical study, the patients were showed improvement of the subjective clinical symptoms i.e. polyurea, polyphagia, exhaustion/tiredness and constipation. The comparison done with respect to the all clinical symptoms, patients showed that both groups having significant improved in case of exhaustion feeling of patients and constipation after intervention has given as shown in Table 5 and 6. Patients were also investigated against their subjective parameters like polyurea polyphagia as in Table 3 and 4. All the parameters were accessed by oral assessment of patients by questioner. Very less patients have complaint about polyurea and polyphagia, and the reported patients showed improved status. There is significant improvement in case of exhaustion of patients but group A is more significant to group B (P= 0.003 and P= 0.005). Plants are having many of phytoconstituents like glycosides, tannins and polyphenols that are hypolipidemic in their action. They are also reported for their antioxidant activity thus they play major role in reducing exhaustion. In case of constipation, this formulation shows highly significant effect (P < 0.001) for both the groups among them group A patients showed better response.

In clinical assessment FBS and PPBS both were decreased due to the effect of vidangadi Kashaya. It was found highly significant in case of fasting blood sugar (P < 0.001) as well as PPBS (P < 0.001) as given in Table 7, 8 in group A and group B. Among them group A shows more significant (t= 8.403, P < 0.001) in comparison to group B (t= 11.51, P < 0.001) for FBS. Currently, HbA1c test has been recommended for screening and diagnosis of diabetes. The use of A1c may offer some advantages such as sampling at convenient time, no need for overnight fasting or availability of 75 g glucose and providing a measure of hyperglycaemia over a prolonged duration, which are the major limitations of FPG or the OGTT. In addition, the result is unaffected and has a low biological variability and better pre-analytic stability.[13] Effect of Vidangadi Kashaya on glycated haemoglobin (haemoglobin A1c) was found significant in both group, A & B as given in Table 8. The hypoglycaemic activity is mainly due to the phytoconstituents presents in the ingredients of vidangadi Kashaya. All the ingredients are separately reported for their hypoglycemic action. Lodhra is reported for hypoglycemic and suggested that

Symplocos racemosa Roxb might exert insulin-like effect on peripheral tissues by either promoting glucose uptake metabolism by inhibiting hepatic gluconeogenesis or by absorption of glucose into the muscle and adipose tissues. It also acts through the stimulation of a regeneration process and revitalization of the remaining beta cells.

In LFT profile, SGOT was analyzed for both groups, it showed significant decrease as given in Table 8, which indicate that vidangadi kashaya act as hepatoprotective as well as revitalizer for liver cell and its metabolic reactions. SGPT was also reduced significantly in group B while no significant decreased found in group A as given in Table 8. Hepatoprotective action has also been reported for its ingredients through their several mechanism of action. So it can be concluded that vidangadi Kashaya is not only beneficial in managing blood sugar level but also it is helpful in managing LFT and symptomatic problems like tiredness and constipation.

To conclude, Vidangadi Yoga exhibited more significant effects on lowering blood glucose level and alleviating other symptomatic parameters studied in this study than metformin. Vidangadi Yoga has better tolerability and is considered safe. However, findings from this study need to be further validated.

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