A CONTROLLED CLINICAL STUDY OF ELADI VATI AND METFORMIN IN PRAMEHA PURVARUPAVASTHA WITH SPECIAL REFERENCE TO PREDIABETES

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ABSTRACT

Diabetes mellitus is a metabolic disorder of multiple aetiologies characterized by insulin resistance, relative insulin deficiency and hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism. But diabetes can be identified at its pre stage called prediabetes. At this stage by providing proper treatment one can prevent this pre stage from converting into post stage of diabetes and then its complication. In this present study, the prediabetes stage is compared with the Prameha purvarupavastha of Ayurveda. And thus, the efficacy of a drug mentioned in Ayurveda for diabetes 'Eladi vati' is compared with the already established drug Metformin. Total 60 patients have completed the study in which 2 groups of trial and control was made. Trial group received Eladi vati and controlled group received metformin in a fixed dose for a period of 2 months. At the end of the study, the results were compared. The comparison shows that Eladi vati is almost as efficient as metformin and can be used safely in prediabetes.

KEYWORDS: Prediabetes, prameha, purvarupa, metformin, eladi vati.

INTRODUCTION

In today's busy lifestyle, health has become most compromised factor. Peoples don't have time for their own health. Today we can see population is mostly affected by lifestyle disorders rather than any infectious disease. Diabetes is one of those lifestyle disorders that are caused by our faulty lifestyles. Luckily, diabetes does not develop at once, rather it progresses gradually. So by identifying diabetes at its earlier stage its progression can be checked. Earlier stage of diabetes is known as the pre-diabetic condition. Our ancestors were well known about both the pre-diabetic and diabetic conditions.

Ayurved has paid due attention to the preventive as well as curative aspect of various diseases.

Diabetes is also described very elaborately under the name of prameha. According to Ayurved, Prameha is considered as a Mahagad i.e Very difficult to cure. Negligence in management and care of Prameha may result into Madhumeha i.e. diabetes mellitus. Charak has described Madhumeha as the subtype of Vataj Prameha whereas Sushruta said that all types of Prameha if not treated in time ultimately leads to madhumeha.

The sign and Symptoms, etiopathogenesis and line of treatment mentioned for Prameha in Ayurvedic texts coincide with the present disease diabetes mellitus.

The recently concluded National Urban Diabetes study (NUDS) carried out by the Diabetes Epidemiology Study in India (DESI) estimated that the prevalence rate of Diabetes in the adult population is 12.10%, while the prevalence rate of Impaired Glucose Tolerance (IGT), a pre-diabetic condition is 14%.

Presently over 387 milliion people have diabetes worldwide, with type 2 DM making up about 90% of the cases. The number of people with diabetes is expected to rise to 592 million by 2035. There are estimated 77.2 million people in India who are suffering from Prediabetes. ICMR estimated that the country already had around 65.1 million diabetes patients.

The rapid increase in prevalence of diabetes is due to rapid lifestyle and socioeconomic changes, reduction in physical activity and eating spicy junk foods etc. leading to diseases like coronary artery disease, hypertension and Diabetes.

Complication of diabetes begin early in the progression from normal glucose tolerance to prediabetes to diabetes, which indicate that till the time of diagnosis type 2 DM other complications have already travelled half of their way. Hence, prevention of Type 2 DM at the prediabetes level is better than cure after its occurrence.

As our Acharyas have described the shatkriyakal of diseases, purvarupavastha is 4th stage i.e.

Sthanshanshryaa where the disease shows its picture and we can come across the diagnosis of disease, same is with Type 2 DM where at purvarupavastha ie prediabetes stage we can imply measures for prevention of its progression to Diabetes.

The medicines given in modern science only treat hyperglycemia and not the cause and hence to stop the progression of disease global concern is increasing towards Ayurveda.
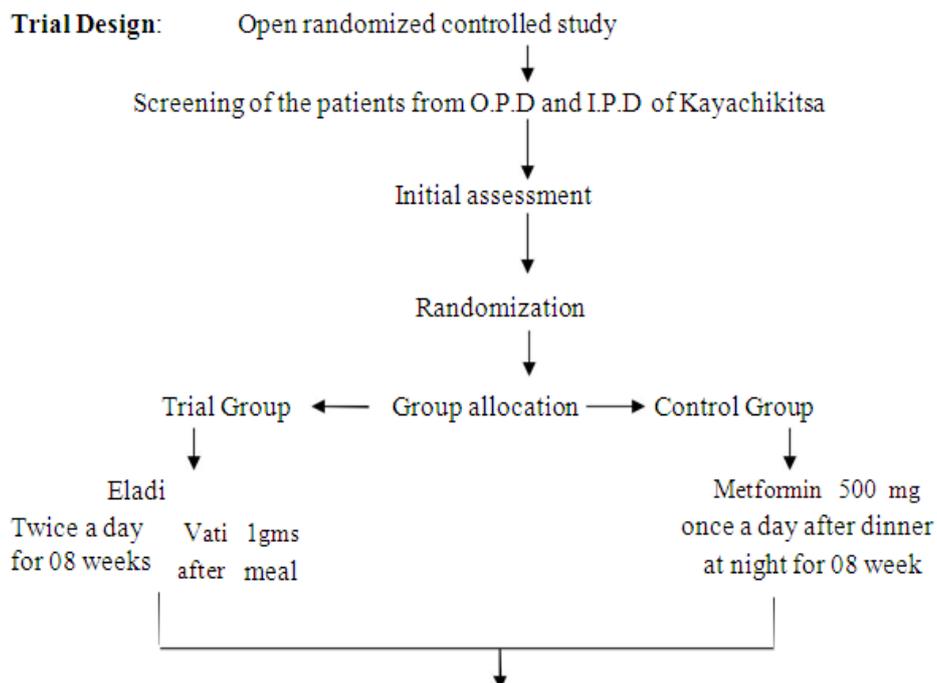
Ayurveda classics have mentioned various measures like Pathya, Aahar, Vihar and Aaushad. Aaushad (Ayurvedic herbs) mentioned in the classics are useful in reduction of blood sugar, decrease in insulin resistance and improvement in beta cell activity.

As earlier mentioned treatment in Prediabetic stage can avoid diabetes and its complications, similarly if Prameha is treated in Prameha Purvarupavastha i.e. Sthanasanshraya avastha or Chaturtha kriyakala of Shatkriyakaal. It is easy to cure and reduce its prevalence and complications.

Therefore I have chosen a kalpa known as 'Eladi Vati' described in Harit Samhita. It is described in the form of churna, mentioned in the contest of prameha. It has 4 contents- ela, shilajita, pippali and pashanbhed. These drug poses gunas or properties which helps to break the chain of samprapti of prameha.

Overall this Eladi Vati acts as an Apatarpan Chikitsa in Prameha vyadhi. Dravyas in Eladi Vati are Katu-Tikta rasatmaka, Madhur-Vipaki, Laghu, Ruksha, Kapha-Medohara, Kledashoshak dravyas which are exactly opposite to the properties of Dosha-Dushyas Involved in samprapti.

Diagnosis of Prameha is confirmed with the help of criteria for diagnosis of DM. Therefore criteria for diagnosis of Pre-diabetes can be beneficial to diagnosis of Prameha Purvarupavastha and help to specify the diagnostic criteria of Prameha Purvarupavastha.
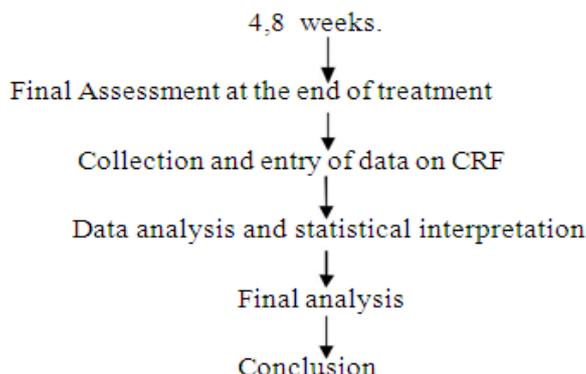
Prediabetes being in co-relation with Prameha-purvarupavastha this kalpa can be successfully used in treating this condition of prediabetes.

So considering these points, the study was undertaken to evaluate the role of Eladi Vati in the management of patients of prameha purvarupavasatha. The efficacy of eladi vati is examined by comparing it with the effect of metformin. Hence, a controlled clinical study was undertaken.

AIM OF STUDY
The present study was conducted to evaluate the clinical efficacy of Eladi-vati in Prameha purvarupavastha with special reference to Prediabetes.

MATERIALS AND METHODS
Type of Study: Open Randomized Controlled Study.

Subjective Assessment at intervals of 2,4,6,8 weeks

Objective assessment before and after treatment and at intervals of

4,8 weeks.

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Final Assessment at the end of treatment

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Collection and entry of data on CRF

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Data analysis and statistical interpretation

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Final analysis

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Conclusion

METHODOLOGY
Sixty outpatients attending R.A. Podar medical (Ayurvedic) college, Worli, Mumbai, Maharashtra, were selected randomly and divided into two groups-Group A and Group B.

Group A (Control group): The patients were given Metformin each day.
Dose: Metformin 500mg after dinner.

Group B (Study group): In study group patients were administered Eladi Vati.
Dose: 2 BD after food. i.e. 1gm (each tab is of 500mg).

The study protocol was approved by the hospital's and institute's Ethics Committee. Informed written consent was obtained from all study participants.

Method of preparation of drug
"Eladi Vati" will be prepared under the guidance of "Bhaishajyakalpana Department" of our institute as per classical text reference. Standardization and authentification of the drugs was carried out in a standard pharmacy.

Composition of drug:
1) Ela
2) Pippali
3) Pashanbhed
4) Shilajit

All four contents are in equal quantity and a tablet of 500mg each was made.

Inclusion Criteria
✓ Both sexes of age between 18 – 65 years.
✓ Signs and symptoms of Prediabetes and that of Prameha Purvarupavastha.
✓ Newly diagnosed with Prediabetes (IFG between 100-125 and PPBS 140- 199)
✓ Not suffering from any other chronic infections including HIV.
✓ Having HbA1c between 5.7 to 6.4%.

Exclusion Criteria
✓ Pregnant & lactating mothers.
✓ Prior use of medication to treat diabetes except gestational diabetes.
✓ Have been diagnosed with diabetes by result of IFG more than or equal to 126mg/dl.
✓ Abnormal liver function study.
✓ Patients having Acute Complications like Coronary Heart Disease, Acute Infective Hepatitis or Alcoholic Hepatitis.
✓ Those who are not ready to complete the trial protocol were excluded.

Criteria of Assessment
Both the subjective and objective parameters are taken into consideration to assess the severity of the disease. Different symptoms graded into four grad scales (0-3) on the basis of severity to assess the change in Clinical symptoms of Prediabetes.

Table No. 1: Subjective parameters.

	Subjective parameters	Gradations
1.	Dantadina maladhyatvam	Grade 0 –No Symptoms
2.	Fatigue	Grade 1 – Mild Symptoms
3.	Shayyasana, swapna, sukhe-Rati	Grade 2–Moderate Symptoms
4.	Skin &urogenital infections	Grade 3 – Severe calculus Symptoms
5.	Kara-pada daha	
6.	Pipasaativriddhi (excluding environmental variation)	
7.	Swedatipravritti (excluding environmental variation)	

Table No. 2: Objective parameters.

Objective parameters	Range
1. FBS	100 - 125
2. PPBS	140 – 199
3. HbA1c	5.7 -6.4 %

Assessment of Total Effects of Therapy
Percentage of relief in symptoms and signs with respect to each patient is as follows and is classified as-

Table No.-3.

Cured	Complete relief in signs and symptoms
Markedly improved	>50% relief in signs and symptoms
Improved	25% to 50% relief in signs and symptoms
Unchanged	No relief or <25% relief

Duration of study: 2 months.

Follow-up – Clinically patients will be screened after every 15 days for 2 month.

End Point of the study: The Drug Metformin will be given for 2 month to Group A patient; after 1 month and 2 month required study investigations will be repeated and before and after comparison will be done. For Group B patient will be given Eladi Vati for 2 month; after 1 month and 2 month before and after assessment of required study investigations will be done and the comparison between group A & group B will be done.

Clinical Examination - Complete Clinical examination will be done to diagnose & assess the condition of patient.

Statistical Evaluation
Clinical data obtained from patients was analyzed statistically in terms of Mean score, Percentage of relief, Standard Deviation (S.D.), Standard Error (S.E.) by following tests.

Wilcoxon matched –pairs signed –ranks test:
Wilcoxon matched–pairs signed–ranks test was applied for assessment of effect of treatment on symptom grade within Trial group and within Control group.

Mann-Whitney Test
Comparison between two groups before and after treatment with respect to symptoms grade score by Mann-Whitney Test.

Paired 't' test
For assessment of effect of treatment on haematological parameters (BSL F PP, HbA1C) before and after treatment within Trial Group and within Control Group.

Unpaired 't' test
Comparison between two groups before and after treatment.
The minimum level of significance was fixed at $P < 0.05$.

RESULT
Effects of Treatment on Symptoms
It was observed that the percentage relief in symptoms of skin and urogenital infection and Kara-pada daha are more in trial group than control group. But the overall percentage of relief was less in Trial group (68.90%) than in Control group (76.26%).

Table No. 4: Showing Effects of treatment on subjective symptoms of 60 Patients of Prediabetes.

Sr. No.	Symptoms	Trial Group				Control Group			
		BT	AT	Diff	% of relief	BT	AT	Diff	% of relief
1.	Dantadina maladhyatvam	32	9	23	71.87	32	5	27	84.37
2.	Fatigue	45	16	29	64.44	40	10	30	75.00
3.	Shayyasana swapn sukhe-rati	40	11	29	72.50	38	10	28	73.68
4.	Skin and Urogenital Infection	20	7	13	65.00	11	4	7	63.63
5.	Kara-Pada Daha	29	8	21	72.41	27	8	19	70.37
6	Pipasaativriddhi	42	12	30	71.42	43	7	36	83.72
7	Swedatipravritti	46	16	29	65.21	45	12	33	73.33
	Average Score	36.28	11.28	25	68.9%	33.71	8	25.71	76.2%

Table No. 5: Showing Effects of treatment on objective symptoms of 60 Patients of Prediabetes.

S.No.	Haematological Parameters	Mean±SD		Mean ofDiff.± SD
		BT	AT	
1.	BSL (Fasting) Trial	115.73±6.153	94.90±6.402	20.83 ± 6.948
	Control	114.03±5.898	89.83±6.879	24.200 ± 8.454
2.	BSL (PP) Trial	170.10±15.52	127.23±12.36	42.86± 15.26
	Control	163.23±17.26	123.07±12.87	40.16± 15.15
3.	HbA1C Trial	5.907±0.2982	5.455±0.2263	0.4500±0.2162
	Control	6.067±0.2881	5.650±0.1925	0.4167±0.2102

There was no significant difference found between Trial and Control group in all symptoms. The P value is >0.05, which means the drug in Trial group was equally effective as in control group with respect to above symptoms.

Effect of therapy on symptoms score
Total effect of therapy: In case of Trial group 13 patients (43.33%) were markedly improved and 17 patients (56.66%) were improved. In case of Control group, 09 patients (30%) were markedly improved and 21 patients (70%) were improved.

Table No. 6: Showing Total effect of therapy in 60 patients of Prediabetes.

S. N.	Total effects of therapy	Trial Group		Control Group		Total	
		No. of Patients	%	No. of Patients	%	No. of Patients	%
1	Cured	00	00	00	00	00	00
2	Markedly Improved	07	23.33	13	43.33	20	33.33
3	Improved	23	76.66	17	56.66	40	66.66
4	Unchanged	00	00	00	00	00	00

There was no significant difference found between Trial and Control group in all symptoms. The P value is >0.05, which means the drug in Trial group was equally effective as in control group with respect to above symptoms.

DISCUSSION
In contemporary literature, Prediabetes is the pre-stage of diabetes and it results due to metabolic disorder later on developing into Diabetes with its hazardous complications like Ischemic Heart disease, Hypertension, Coronary Heart disease etc. It is mostly based on unbalanced diet, Endocrine Factors, Sedentary life style, Stressful mental conditions and Heredity etc. Still appropriate remedy is awaited, which will conquer Diabetes without any adverse effects on body. Only few studies have been conducted to evaluate the effect of 'Ayurvedic Herbal Medicine' formulae to treat prediabetes for prevention of diabetes among alternative therapies, but still there is a scope to work in the area of its etio-pathology and Management.

The disease 'Prameha' and its stage Prameha purvarupavastha is well-recognized from Samhita period. Prameha purvarupavastha is similar to prediabetes. Prameha can be caused by Sahaj and apathyanimitaj nidanas. Sahaja is due to beeja dushti showing genetic predisposition in the pathophysiology. Chakrapani opines that it can be caused by father, mother or grandparents which means the disease is beeja (ovum and sperm), beejabhaga (chromosomes), or beejbhagavyava (genetic coding). Chakrapani commented to this as it is caused due to the faulty indulgence of food during pregnancy. But apathy nimithaja may be due to intake of madhura, curd, paneer, sweets, sheeta, guru, snigdha, picchila aharas, ksheera vargas, guda vargas, pishtannas and performing diwaswapna, avvyayama, aalasya etc. All these are being practiced today because of industrialization and urbanization, sedentary occupations leads to obesity which leads to glucose intolerance. Depression, anxiety, frustration and loneliness may also increase excess food intake. All this vitiates kapha dosha in quantity and volume leading to manifestation of Prameha Purvarupavastha ultimately leading to Prameha. Similar are the cause which accelerates Prediabetes.

If factors analogues to the peculiar Dhatu are carried consecutively the Ahar rasa continuously arrives through the Srotas of Dhatu give rise to exaggeration of that dhatu. Thus in this manner Bahu & Abaddha Meda vriddhi occurs in Prameha Purvarupavastha.

Similarly if we consider Pre-diabetes, high risk factors especially excessive intake of carbohydrates with lack of exercise reduce metabolic activities in the body & accelerate fat deposition as there is no oxidation of the excessive glucose in the body. This deposition mainly occurs over abdomen, hip region, cheeks & rest is all over body. Thus produce laxness in the body. Here we can correlate Kapha & Meda dushti in Prameha Purvarupavastha.

The aim of treatment is to achieve normal metabolism. The ideal management would allow the patient to lead a completely normal life, to remain not only symptom free but in good health to achieve a normal metabolic state and to escape the long term complication of diabetes. Screening for prediabetes should be done particularly in high risk groups such as first degree relatives of known cases and appropriate vigorous management measures like lifestyle intervention and use of medicines should be done.

Discussion on mode of Action of Eladi Vati
All the ingredients are having 'Katu-Tikta Rasa', which is famous for its 'Kleda Shoshana, Medoghana and Lekhana karyas'. Also it will do 'Absorption i.e. Shoshana of Kleda, Medo, Vasa, Majja, Pitta and Kapha as it's having 'Tikta Rasa'.

Pashanbhed has kashaya and Tikta rasa with katu vipaka, this increases the activity of kledasoshana and lekhana especially. Pashanbhed has kaphanihsarak karma.

This vati has overall laghu, ruksha and tikshana guna which reduces guruta and pichhilata of kapha and meda dhatu. This action helps in kaphashamana and sampraptibhanga of prameha.

Additionally, 'Predominant Madhura Vipaka' will play a role in rejuvenation by rasayana karma, nourishes dhatus and increases deha bala.

Shilajatu has chhedana karma because of its prabhav, this expel the kaphadi dosha from srotas. Thus removes the obstructive vitiated dosha from each and every srotas of the body. It is described in Ayurvedic texts that there is no kaphaj vyadhi which cannot be treated with shilajatu. This explains its prabhavjanya karma.

Pipaali also has chedan karma which causes the vilayan of the doshas from the srotas thus removing the obstracted doshas. Apart from this Ela has dipan and pachana karma which helps in the proper digestion of the food and helps in relieving agnimandya. As Ayurved has described agnimandya as the root cause of all the vyadhis in the body, this action of ela is very helpful.

The most important feather of this vati is 'Rasayana Quality of Pipaali and shilajit', so as to gain up resistance power against the said disease by maintaining equilibrium of Tridoshas in the body as per 'Rasayana' Principle.

Overall properties of Eladi-Vati have a very important role in sampraptibhanga of prameha. Here all the dravyas possess qualities opposite to Medo Dhatu and Teekshna (most potent) in nature, (predominant for increasing the ability of Jatharagni). This will increase the strength of Pachakagni leading to metabolism of Meda, by Lekhana (scraping) and Chedana (clearing) actions because of which prasarana of Meda will be restricted. With this classical background this study was planned to find the role of Eladi - Vati' in comparison with 'Metformin' in the management of Prameha purvarupavastha with special reference to Prediabetes.

Discussion on Total Effect of Therapy
In case of Trial group 7 patients (23.33%) are Markedly improved and 23 patients (76.66%) are improved whereas in control group 13 patients (43.33%) are markedly improved and 17 patients (56.66%) are improved, none of them remain unchanged and none of them are cured completely.

Comparison between two groups was statistically evaluated by Chi-Square Test. The value is 1.875, P > 0.05 which was statistically insignificant which suggested that there is no significant difference between two groups with respect to total effect of therapy.

CONCLUSION
In this study patients had shown better results in both the groups i.e. Trial group (Eladi vati) and Control group (Metformin). The trial group has shown better reduction in BSL PP values (24.86%) than BSL FASTING (18.08%). It was observed that overall percentage of relief was less in Trial group (43.45%) than in Control group (46.77%). In case of Trial group 07 patients

(23.33%) are markedly improved and 23 (76.66) patients are improved whereas in control group 13 patients (43.33%) are markedly improved and 17 patients (56.66%) are improved, none of them remain unchanged and none of them are cured completely. Comparison between two groups statistically showed that the changes were insignificant suggested that there is no significant difference between two groups with respect to total effect of therapy. Thus eladi vati can be safely used in the prameha poorvaroop i.e. prediabetes.

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