A CONTROLLED CLINICAL STUDY OF KATAMKATAIRYADI KWATHA AND METFORMIN IN PRAMEHA PURVARUPAVASATHA WITH SPECIAL REFERENCE TO PREDIABETES

R. R. Ghungaralekar*

HOD, Dept. of Kayachikitsa, R. A. Podar Medical College.

*Corresponding Author

Dr. R. R. Ghungaralekar

HOD, Dept. of Kayachikitsa,

R. A. Podar Medical College.

ABSTRACT

Prediabetes is the precursor stage before diabetes mellitus in which not all the symptoms required to diagnose diabetes are present, but blood sugar is abnormally high. This stage is often referred to as the "grey area."The term prediabetic is an intermediate stage used to describe a person with impaired blood glucose tolerance levels of fasting between 100 and 126 mg/dl of blood or whose 2-hour postprandial blood glucose was 140-200 mg/dl. In present study, the Prediabetes stage is compared with pramehpurvarupavastha of Ayurveda. And thus, the efficacy of katamkatairyadikwath is compared with established drug metformin on 60 patients divided in two groups for 3 months. The comparison shows that katamkatairyadi Kwath is almost as efficient as metformin and can be use safely in prediabetes.

KEYWORDS: Prediabetes, Pramehpurvarupavastha, Katamkatairyadi Kwath.

INTRODUCTION

In Ayurvedic classics various diseases are described along with their causes signs, symptoms and Samaprapti under the topic Nidan Panchak. Prameha has been described in great detail in all Ayurvedic Samahitas. Prameha is mentioned as Anushangi Vyadhi (Hereditory) and included in Mahagada i.e. difficult to treat and cure. Having cardinal symptoms Prabhut and Avil Mutrata. In brihatrayi Acharya describe Twenty types of prameha on the basis of predominance of Dosha. Over indulgence of Hetus leads to vitiation of all the three Doshas mainly Kaphadosha. and other vital elements Mainly Meda and Mamsa along with Rakta, Shukra, Ambu, Vasa, Lasika, Majja, Rasa and Oja are involved in Samaprapti of Prameha.

Susrutacharya described the shatkriyakal of diseases, In Chaturtha Kala (4th stage) i.e. Sthanshanshrya where the disease shows its picture and we can come across the diagnosis of disease, (purvarupa).

Pramehapurvarupa described in Ayurvedic texts is very much imperative factor because of it has its own pathophysiology. After studying purvarupa of prameha we can imply measures for prevention of its progression to Prameha.

As Prameha is correlate with Diabetes Melitus and diagnosed on the basis of BSL (Fasting and Post Prandial), PramehaPurvarupavastha can be correlate with early stage of Diabetes Melitusi.ePrediabetes.

Diabetes Mellitus is a silent killer. It is spreading epidemic all over the world. India has more diabetics than any other country in the world. The disease affects more than 50 million Indians and kills about 1 million people a year.

Diabetes mellitus is a heterogeneous metabolic disorder of carbohydrate, fat and protein characterized by hyperglycaemia with or without glycosuria. It is associated with long-term potentially catastrophic effects on almost all systems of the body. These can manifest as minor annoyances at first but then insidiously destroy the cellular components of a given body part, organ, or entire system. Diabetes mellitus is expected to continue as a major health problems owing to its serious complications, especially end stage renal disease, Ischemic heart disease, gangrene of lower extremities, blindness in the adults. Diabetes Mellitus is destructively progressive and the prognosis is poor unless definite measures are taken to control the disease.

Prediabetes is a condition in which blood glucose level are higher than normal, but not higher enough to be classified as diabetes. Those with prediabetes are at increased risk of developing type 2 diabetes and also at a risk of developing cardiovascular disease.

As per WHO's global report on diabetes, 422 million adults have diabetes worldwide, India ranks among top 3 countries with diabetic population. Global prevalence of diabetes among adults over 18 years of age has risen from 4.7% to 8.5%. India had 64.5 million people living with diabetes as per 2015 data. Out of these it remained undiagnosed in more than 36 million people and global number of diabetic patient is estimated to be 100 million by 2030. 30% of Indian adults aged 20 years or older have prediabetes which is about 78 million.

Above data suggest that prediabetes, diabetes is fast gaining the status of potential epidemic in India due to sedentary life style, less physical exercise, eating spicy, junk foods leading to disease like hypertension, coronary artery disease and diabetes.

Treatment to be given to prediabetic are the OHAs namely Biguanides, such as Metformin and alpha glucosidase inhibitor such as Acarbose and Voglibose which control blood sugar level. But OHAs has side effects like Sudden Hypoglycemia, GIT upset etc. These drugs only treat hyperglycemia and not the cause. Thus, modern medicine has its own limitations for the management of metabolic diseases. Today practically we are using modern medicines for primary management or symptomatic relief in these diseases due to which we have to suffer from many side effects. Hence peoples are moving towards Ayurveda. Ayurveda with its holistic approach does the multitargeted actions and hence As Principal of Ayurveda "Treat the Root Cause" We can stop the conversion of Prediabetes into Diabetes and prevent complications also.

In Ayurvedic classics there is an elaborate treatment for Prameha. As modern drugs are unable to give satisfactory cure there is need to find safe and effective Drug which can stop the disease in Prediabetic stage.

Hence, I was decided to work on Ayurvedic combination which is safe, cost effective, multi-targeted with holistic approach and mentioned in Ayurvedic classics. While keeping all the things in mind and going Ayurvedic literature I found, 'Katamkatairyadi Kwatha' mentioned in Bhavprakasha satisfying all the criteria. Katamkatairyadi Kwatha containing Katamkateri (Daruharidra), Yashtimadhu, Triphala, Chitraka. By its LaghuRukshGuna and Tikta Kashaya Rasa it acts on Kapha Dosha and MedaDushya. Due to these properties of Katamkatairyadi Kwatha help to break the Samaprapti of Prameha Purvarupavastha.
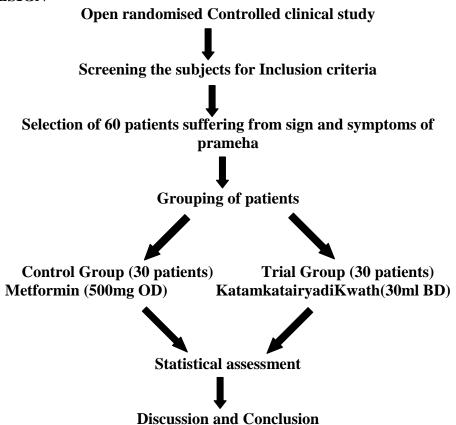
AIM OF STUDY

The present study was conducted to evaluate the Clinical efficacy of Katamkatairyadi Kwatha in Pramehapurvarupavastha with special reference to Prediabetes.

MATERIALS AND METHODS

Type of study: Open Randomized controlled study.

STUDY DESIGN

Open randomised Controlled clinical study

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Screening the subjects for Inclusion criteria

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Selection of 60 patients suffering from sign and symptoms of prameha

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Grouping of patients

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Control Group (30 patients)   **Trial Group (30 patients)**
Metformin (500mg OD)   **KatamkatairyadiKwath(30ml BD)**

↓   ↓

Statistical assessment

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Discussion and Conclusion

METHODOLOGY

60 Patient were enrolled on to study from O.P.D. And I.P.D. of dept of Kayachikitsa of R. A. Podar Medical College, worli Mumbai were selected randomly into two groups.

Group A (Control Group)

The patients were given metformin 500mg OD after dinner.

Group B (Study Group)

Patients were administered 'KatamkatairyadiKwatha' Dose 30ml. twice a day before meals. 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

"KatamkatairyadiKwatha" was prepared under the guidance of "Bhaishajyakalpana Department" of our institute as per classical text reference.

Complete procedure of preparation will be as follows

1) Bharadchoornas of Katamkateri (Daruharidra), Yashtimadhu, Triphala and Chitrak was taken in Samae proportion. that is 3.75 gm each and 16 parts of water (240 ml) was added in it.

2) The whole mixture was boiled until $1/8^{th}$ of it remains (30 ml)

3) Then it was filtered and ready for administration.

Inclusion Criteria

- Both sexes

- Age between 18 to 65 yrs

- Signs and symptoms of Prediabetes and that of PramehaPurvarupavastha.

- Newly diagnosed with Prediabetes (IFG between 100-125 and PPBS 140- 199)

- suffering from any other chronic infections including HIV.

Exclusion Criteria

- Age below 18 years & above 65 years

- 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.

- Patients having Acute Complications like Coronary Heart Disease, Acute Infective Hepatitis or Alcoholic Hepatitis.

- Patients having disorders like Carcinoma anywhere in the body or any other major life threatening disease

- Those who are not ready to comply 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.

Subjective Criteria

1. Unexplained weight gain

2. Fatigue

3. Shayyasanaswapnasukhe-rati

4. skin &urogenital infections
5. Kara-padadaha
6. Pipasaativriddhi (excluding environmental variation)
7. Swedatipravritti (excluding environmental variation)

Objective Criteria

(1) BSL fasting blood glucose and postprandial blood glucose.

(2) HbA1c before and after treatment.

(3) Clinical assessments are made before, during and at the end of the treatment After 3 month.

Assessment of Total Effect of Therapy

Percentage relief in symptoms and signs with respect to each patient is as follows and classified as per definition described of cured, markedly improved, Improved and Unchanged.

1) Cured: Complete relief in sign and symptoms along with certain lab parameters was considered as cured.

2) Markedly Improved: More than 50% relief in sign and symptoms of the patients along with certain definite changes in physical and lab parameters was considered as markedly improved.

3) Improved: 25 to 50% relief in sign and symptoms as mentioned in criteria of assessment was considered as to be improved.

4) Unchanged: Patients who don't have any relief in sign and symptoms or no change in biochemical parameters was considered as Unchanged. Along with this, the patient exhibiting improvement <25% also kept under this group.

Duration–3 month.

Follow-up: Clinically patients was screened after every 15 days for 3 month.

End point of the study: The drug metformin was given for 3 months to group A patients, After every 4 weeks required study investigations was repeated, and before and after comparison were done. For group B Katamkatairyadikwath was given for 3 monthsAfter

every 4 weeks required study investigations was repeated and before and after comparison weredone. and the comparison between Group A and group B was done.

Clinical Examination

Complete Clinical examination was done to diagnose & assess the condition of patient.

Statistical Evaluation of Treatment

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.

1. Wilcoxon matched –pairs signed –ranks test

Comparison of symptoms grade score before and after treatment within Trial Group and within Control Group is a qualitative data, so Wilcoxon matched–pairs signed–ranks test was applied for assessment of effect of treatment on symptom grade within Trial group and within Control group.

2. Mann-Whitney Test

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

3. 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 is a quantitative data, Paired 't' test was applied.

4. Unpaired 't' test

Comparison between two groups before and after treatment with respect to quantitative data, Unpaired 't' test was applied.

Results were interpreted as

P<0.05 Improvement

P<0.01 Significant improvement

P<0.001 Very significant improvement

RESULTS

Table No. 31 Showing Effect on Symptoms Score of 60 Patients of Prediabetes.

Sr. No.	Symptoms	Trial Group				Control Group			
		BT	AT	Diff	%of relief	BT	AT	Diff	%of Relief
1.	Unexplained weight gain	31	04	27	87.00	33	15	18	54.54
2.	Fatigue	35	08	27	77.14	44	11	33	75.00
3.	Shayyasana Swapn sukhe-rati	40	11	29	72.50	46	10	36	78.26
4.	Skin And Urogenital Infection	10	2	8	80.00	21	4	17	80.95
5.	Kara-Pada Daha	30	9	21	70.00	25	3	22	88.00
6	Pipasaativrid Dhi	43	8	35	81.48	43	6	37	86.04
7	Swedatiprav Ritti	44	13	31	70.45	48	11	37	77.08
	Average Score	33.28	7.85	25.43	76.41	37.14	8.57	28.57	76.92

Average Effect of Objective Parameters

Parameters	Trial Group Averege % Relief	Control Group Averege % Relief
Bsl Fasting	24.89	25.09
Bsl Post Prandial	30.56	31.56
HbA1c	9.53	10.07

Effect of therapy on symptom score: Total effect of therapy: In case of Trial group 16 patients (53.33%) were markedly improved and 14 patients (46.66%) were improved. In case of Control group, 18 patients (60.00%) were markedly improved and 12 patients (40.00%) were improved.

Table No. 36 Showing Total effect of therapy in 60 patients of Prediabetes.

S. No.	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	16	53.33	18	60.00	34	56.66
3	Improved	14	46.66	12	40	26	43.33
4	Unchanged	00	00	00	00	00	00

Comparison between two groups was statistically evaluated by Chi-Square Test. The value is 0.06787, $P > 0.05$ which was statistically insignificant which suggested that there is no significant difference between two groups with respect to total effect of therapy.

DISCUSSION

In contemporary literature, prediabetes is pre stage of diabetes and it result deu to metabolic disorder later on developing into diabetes with its hazardous complications only few studys have been conducted to evaluate the effect of ayurvedic herbal medicine formulae to treat prediabetes for prevention.

The disease prameha and its stage pramehapurvarupavastha is well recognised from samhita period. pramehapurvarupavastha is similer to prediabetes.

Discussion on probable mode of action of drug

Action on Dosha

Amalaki, Haritaki acts as Tridoshahara and Daruharidra, Bibhitaka acts as Kapha-pittaghna and chitraka acts as a vatkaphaghnaSo, it works on all types of prameha. Maximum of the drugs have Tiktakashaya rasa, and Madhura Katuvipaka similarly. As per guna most of drugs are of laghu Rukshaguna also as per Virya they have Ushna & Shita properties. So, it's very effective in Prameha.

Action on Dushyas

Katamkatairyadi Kwatha formulation has tridoshaharaproperty but specifically Kaphaharaproperty. Its acts on vitiated Kafa, Medaand Kleda. It has capacity to improve tone of sapta-dhatus. With the help of madhuravipaka, Shit veerya, Rasayana and Vrushya properties it causes nourishment of all dhatus. As it is Medohara it reduces Abaddha Meda and others dushyas easily.

Action on Agni & Aam

Due to its Deepan and Pachanproperties, Katamkatairyadi Kwatha works on Jatharagni and Dhatwagni, which reduces the Amapresent in the body. Deepandravyas help to improve Agni and disturbed metabolism.

Action on Srotodushti

In Katamkatairyadi Kwatha Deepan, Pachan and Anuloman properties. By Deepan, Pachan, Anuloman properties it works on srotodushti. With the help of Rasayanaproperties, it causes nourishment of Dhatus. Daruaridra works on mutravahsrotas & reduce the vimargagaman & Atipravruti type srotodushti.

Discussion on Total Effect of Therapy

In case of Trial group 16 patients (53.33%) are Markedly improved and 14 (46.66%)patients are improved whereas in control group 18 patients (60.00%) are markedly improved and 12 patients (40.00%) 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 0.06787, $P > 0.05$ 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 trial patients, had shown better results in both the groups i.e. Trial group (KatamkatairyadiKwatha) and Control group (Metformin).

✓ There is significant reduction in BSL FASTING values in both the groups, but trial group has shown better reduction in BSL PP values.

✓ Among all, maximum percentage of relief found in Kara-padadaha, pipasaativruddhi, Uro-genital infection and Swedatipravritti than other lakshanas.

✓ It was observed that overall percentage of relief was almost same in Control group (76.92%) and in Trial group (76.91%).

✓ No side effects were observed during treatment.

✓ In case of Trial group 16 patients (53.34%) are Markedly improved and 14 patients (46.66%) are improved whereas in control group 18 patients (60%) are markedly improved and 12 patients (40%) 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 0.6787, $P > 0.05$ which was statistically insignificant.

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