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CLINICAL STUDY TO ASSESS THE SAFETY AND EFFICACY OF *NISHA AMALAKI YOGA* WITH AND WITHOUT HONEY IN PATIENTS OF *PRAMEHA* W.S.R. TO PRE-DIABETES

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ABSTRACT

Introduction: According to Ayurveda classics, *Prameha* is a syndrome and 20 different types of it is explicated with a common characteristic of copious flow of cloudy or turbid urine frequently. The etiological factors, pathogenesis, signs and symptoms of *Prameha* resemble very closely with that of Prediabetes. Prediabetes is the stage before Diabetes in which impaired fasting glucose levels are observed. This stage is the vital period for preventing type II diabetes as it can be reversed and cured completely**.** The aim of this study is to evaluate the safety and efficacy of *Madhu* as *anupana* in the management of *Prameha* (Prediabetes) and to revalidate the efficacy and safety of *Nisha Amalaki yoga* in the management of *Prameha* (Prediabetes). **Material and Methods:** 30 patients were enrolled in this clinical trial and were randomly divided into two groups – Group-A and Group-B with 15 patients in each. The *Nisha Amalaki yoga choorna* was administered in a dose of 8 g daily in 2 divided doses before meals with luke warm water as *anupana* in Group A and 10 gm (7ml) *Madhu* in Group B for 30 days. The patients were followed up every 15 days for one month and the assessments were done. The results of the subjective data were statistically assessed with ' Wilcoxon paired r a n k test' and that of objective data with paired 't' test. **Results:** Significant results were observed in subjective parameters like *prabhutamutrata, avilmutrata*, *trishnadhikya*, *kshudhadhikya, swedadhikya*, *karpadadaha, karapadasuptata,* and *daurbalya* and objective parameters like FBS and lipid profile of both the groups. **Conclusion:** The study confirms that *Nisha Amalaki yoga* with and without honey were equally effective in treatment of *Prameha* by reducing majority of the symptoms.

KEYWORDS: *Prameha,* Prediabetes, Honey, *Nisha, Amalaki, Madhu, Nisha Amalaki yoga.*

INTRODUCTION

Ayurveda is the science of life that confers on health and longevity in the form of both preventive and curative way. *Prameha* is mentioned in ancient *Ayurveda* texts as a syndrome. The *Samanya lakshana* of the disease is described as '*prabhutavila mutrata*[1]*,* which means copious flow of cloudy or turbid urine frequently. On the basis of the colour, smell and feeling of touch of urine, *Prameha* is described to be of 20 types.[2] The aetiological factors, pathogenesis, signs and symptoms, types and principles of management of *Prameha* as described in various Ayurveda classics resemble very closely with that of Prediabetes and similarly, *Madhumeha* with Diabetes Mellitus (DM).

Prediabetes is the stage before DM in which there occur glycemic variability but the sugar level is below the diabetes thresholds. The sole sign observed in Pre-diabetes is rise in fasting glucose level (Impaired Fasting Glucose IFG) and impaired glucose tolerance (IGT). This stage is considered as the most crucial period for preventing type II diabetes because, if identified and treated it can be reversed and cured completely.[3] Among the Prediabetic people, around 5-10% advance to DM and the same proportion revert to normoglycemia per year. According to the experts the prevalence of Prediabetes is increasing worldwide and more than 470 million people will have Prediabetes by 2030.[4]

There are large numbers of drugs in texts advised for *Prameha chikitsa.* In the present study, *Nisha* (*Curcuma longa* Linn.) *Amalaki* (*Emblica officinalis* Gaertn.) and *Madhu* (Honey) have been selected for the management of *Prameha*.[5] *Madhu* is a *dravya* which is mentioned very profoundly in the management of *Prameha* as an *anupana* with other drugs in Ayurveda classical

texts.[6][7][8][9] But due to its sweet nature it is not been used commonly. The effect of *Madhu* in Alloxan induced diabetic rats had shown significant results in providing instant energy without increasing the blood glucose levels.[10]

AIMS AND OBJECTIVES
- To evaluate the safety and efficacy of *Madhu* as *anupana* in the management of *Prameha* (Prediabetes).
- To revalidate the efficacy and safety of *Nisha Amalaki yoga* in the management of *Prameha* (Prediabetes).

MATERIALS AND METHODS
Drug review: Many pharmacological and clinical researches of *Nisha Amalaki* on Glucose metabolism and Glycemic control are already done and proven efficacious. *Nisha Amalaki* administered with honey in diabetic rats had shown significant (p<0.01) lowering of blood glucose level comparable to that of the Pioglitazone treated group.[11] Since no clinical study was conducted to assess the combined effect of *Nisha Amalaki* with honey, the present work was planned to assess the combined efficacy of *Nisha Amalaki* and *Madhu*.

Preparation of drug and dosage: Fine *Nisha choorna* (powder) was triturated repeatedly five times with 2.5 part of *Amalaki swarasa* (juice) in an end runner machine until it became dry. The trial drugs were taken in ratio 1:12.5. This was calculated according to the dose of these drugs advised for *Prameha chikitsa* in the Hindi commentary of *Bhaishajyaratnavali* by *Sidhinandan Mishra.*[12]

The *choorna* was administered in a dose of 8 g daily in 2 divided doses before meals with luke warm water as *anupana* in group A and 10 gm (7ml) *Madhu* in group B. As *nava madhu* (new honey) is *brimhana* and not good enough to reduce *kapha,*[13] *madhu* needed for the trial was collected and stored in clean dry glass bottles 1 year before use.

Study design: Simple randomized open label clinical trial.

Selection of Cases: 30 diagnosed patients of *Prameha* (Prediabetes) fulfilling the inclusion criteria were chosen from xxxxxxxxxxxx. These patients were randomly divided into two groups – group-A and group-B with 15 patients in each group. Patients were selected irrespective of caste, religion, nationality, gender, socio-economic status etc.

Ethical Clearance: Ethical clearance was obtained from Institutional Ethics Committee, xxxxxxxxxxxxx, with Ref No. IEC/ACA/2019/1-10, dated 28/05/2019 for clinical study at xxxxxxxxxxxxx.

CTRI registration: The trial was registered in CTRI with registration number CTRI/2020/03/023724.

Inclusion Criteria: Patients in the age group 20-70 years with Fasting Blood Sugar (FBS) in the range of 100-125 mg/dl, Post Prandial Blood Sugar (PPBS) in the range of 140mg/dl – 199 mg/dl were included.

Exclusion Criteria: Patients those who were suffering from Type 1 DM, Type 2 DM, Pregnant women and lactating mother or with any serious illness like coronary artery disease, malignancy, kidney failure etc. were excluded.

Criteria for assessment: The duration of treatment was 30 days and all the enrolled patients were advised to come for the follow up on every 15 days. The effect of trial drug was assessed on the basis of the following parameters.

Prabhutamutrata (**Polyuria-** Frequency of Urine) Score
- 3-6 times/day, 1 time at night   0
- 6-9 time/day, 1-2 times/night   1
- 9-12 time/day, 3-4 times/night   2
- >12 times/day, >4 times/night   3

Avilamutrata (**Turbidity**)
- Crystal clear Urine   0
- Faint but news print easily read through test tube   1
- News Print not easily read through test tube   2
- News Print cannot be seen through test tube   3

Trishnadhikya (**Polydipsia**)
- 6-8 times /day   0
- 9-11 times / day   1
- 12-14 times/day   2
- > 14 times/day   3

Kshudhadhikya (**Polyphagia**)
- Normal / As Usual   0
- Slightly increased (1-2 meals)   1
- Moderately increased (3-4 meals)   2
- Markedly increased (5-6 meals)   3

Swedadhikya (**Perspiration**)
- Sweating after heavy work   0
- Profuse sweating after moderate work   1
- Sweating after very mild work   2
- Profuse sweating after mild work   3

Karapadadaha (**Burning sensation of both palms and feet**)
- No *daha*   0
- Mild *Daha* but not continuous   1
- Moderate *daha* but continuous   2
- Severe continuous *daha*   3

Karapadasuptata (Numbness of both palms and feet)

- No *Suptata*   0
- Mild *Suptata*, not continuous   1
- Moderate continuous *suptata*   2
- Severe and continuous *suptata*   3

Daurbalya (Weakness)

- Can do routine work   0
- Can do moderate work   1
- Can do mild work only with difficulty   2
- Cannot do even mild work   3

Objective parameters assessed: Fasting and Post Prandial blood sugar have been assessed on 0th day, 15th day and 30th day. Lipid profile and Urine – Routine and Microscopic Examination have been assessed before and after completion of the treatment.

OBSERVATIONS AND RESULTS
A Pre-Test and Post–Test design was adopted in this clinical trial. The observations and results were drawn on the basis of the effect on each sign and symptoms before and after treatment. Subjective data was assessed with 'Wilcoxon paired rank test' and objective data with paired 't' test. During the course of clinical trial 1 patients from group-A and 1 patient from Group-B were dropped out due to poor follow-up. [Table 1]

Table 1: Status of Patients in the Clinical Trial.

S. No.	Status in the Clinical Trial	Group-A	Group-B
1.	Registered	15	15
2.	Completed	14	14
3.	Dropped out	1	1

The current study data on the basis of age group had shown peak incidence of Prediabetes in younger adults[14] and sex wise distribution shown more incidences in males than females justifying the previous study findings.[15] The data on the basis of occupation showed more incidences in patients having sedentary works and this is justifying the *Prameha nidana 'asyasukham, avyayam, alasya'*.[16] The data of socioeconomic status shows high incidence in upper middle class, and this can be due to the changes in the life style.[17] Majority of the individuals had shown incidence of family history.[18] As per the data on *agni*, most of the patients were of *mandagni* and *vishmagni* which results in production of *ama* which is one of the important steps in *samprapti* of *Prameha*. *Teekshnagni* found in some patients may be the *Prameha lakshana "kshudhadhikya."* Most of the patients had *krura koshta* which may be due to excessive fluid loss in *Prameha*. Most of the patients were belonging to *pitta kapha prakruti*. *Abhyavaharana shakti* and *jarana shakti* was *madhyama* in majority of individuals. Dominant *rasa* and *guna* in the diet showed high dominance of *madhura, amla, lavana rasa* and *guru, snigdha, sheeta guna* which are *kapha vardhak*. The nature of diet shown dominance in carbohydrate diet which might have led to the present disease condition.[19] Most of the patients

were consuming quantitatively *madhyama* diet but had habitual supplementary foods like tea, cool drinks etc. and addiction of alcohol and tobacco, which are *prameha nidana*. The incidence of *purvaroopa* had shown dominance of *alasya, mukha kantha talu shosha, nakhativruddhi*. Most of the patients had *prabhutamutrata, trishnadhikya* and *daurbalya* which is 93.33% followed by *kshudhadhikya* in 86.66% of patients and *swedadhikya* and *avilmutrata* in 73.33% of patients. *Karapadadaha* and *karapadasuptata* was noticed in 40% of patients.

DISCUSSION
As per Wilcoxon paired r a n k test, both groups showed statistically significant result in all the subjective parameters. The average percentage of relief of *Prameha lakshana* - *prabhutamutrata, avilmutrata, trishnadhikya, kshudhadhikya, swedadhikya, karapadadaha, karapadasuptata,* and *daurbalya* were 83.33%, 88.89%, 92.86%, 92.86%, 86.67%, 95.24%, 95.24%, 83.33% in group A and 71.43%, 77.78%, 92.57%, 95.23%, 85%, 92.86%, 100% and 79.76% in group B respectively. Here *Nisha Amalaki choorna* with honey provided more benefit in *Karapadadaha* and *karapadasuptata lakshana,* which can be due to its overall antioxidant property[20] [Table 2-9].

Table 2: Mean change in *Prabhutamutrata*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	2.43	0.5	1.93	83.33	105	0.0001
Group B	2.64	0.86	1.78	71.43	105	0.0001

*BT -Before treatment, AT- After treatment

Table 3: Mean change in *Avilamutrata*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	2.14	0.29	1.85	88.89	78	0.0005
Group B	2.75	0.67	1.79	77.78	78	0.0005

Table 4: Mean change in *Trishnadhikya*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	2.43	0.21	2.22	92.86	105	0.0001
Group B	2.29	0.21	2.07	92.571	105	0.0001

Table 5: Mean change in *Kshudhaadhikya*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	2.79	0.21	2.57	92.86	105	0.0001
Group B	2.57	0.14	2.42	95.23	105	0.0001

Table 6: Mean change in *Swedadhikya*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	3	0.4	1.86	86.67	55	0.0020
Group B	2.8	0.4	2.4	85	55	0.0020

Table 7: Mean change in *Karapadadaaha*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	3	0.14	2.86	95.24	28	0.0156
Group B	1.57	0.14	1.42	92.86	28	0.0156

Table 8: Mean change in *Karapadasuptata*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	3	0.14	2.86	95.24	28	0.0156
Group B	2.71	0	2.71	100	28	0.0156

Table 9: Mean change in *Daurbalya*.

Group	Mean BT	Mean AT	Mean Difference	Mean %	W	P
Group A	2.42	0.29	2.14	83.33	91	0.0002
Group B	2.07	0.28	1.78	79.76	78	0.0005

As per paired *t* test, the change in FBS level was significant in both group A and group B [Table 10].

Table 10: Mean change in FBS.

Group	Mean BT	Mean AT	Mean Difference	Mean %	T	P
Group A	118.0	99.8	18.2	13.18167	6	<0.0001
Group B	118.00	99.80	18.2	13.181	3.285	0.0059

Nisha Amalaki choorna along with luke warm water was slightly more beneficial in reducing blood sugar. Statistically non-significant improvement was seen in PPBS [Table 11].

Table 11: Mean change in PPBS.

Group	Mean BT	Mean AT	Mean Difference	Mean %	T	P
Group A	159.2	133.068	26.132	13.7889	1.214	0.2462
Group B	157	142.6	14.40	5.33	1.720	0.1091

This may be because the cases were of Prediabetes and there was not much variation from the normal PPBS level at the time of enrolment. On comparing the % of relief of lipid profile, group B was found to be more effective in lowering the cholesterol and LDL [Table 12].

Table 12: Percentage of Relief in Lipid Profile in Group A and Group B.

S. No.	Lipid profile	Group A				Group B			
		Mean B.T.	Mean A.T.	Mean Dif.	% Of Relief	Mean B.T.	Mean A.T.	Mean Dif.	% Of Relief
1	Cholesterol	209.54	209.9	0.357	2.756	196.95	185.14	11.81	78.73
2	Triglycerides	166.65	171.85	5.203	6.584	151.48	146.29	5.19	34.6
3	HDL	44.94	48.66	3.72	9.83	43.33	48.36	5.03	33.53
4	LDL	133	130.12	2.87	0.58	118.74	101.49	17.25	115

This may be due to the *lekhana* property of honey and hypolipidemic action of *Nisha*[21] and *Amalaki*.[22] The drugs having antioxidant property and *rasayana* property prevents the *oja kshaya* occurring in *Prameha*.

According to Vasavda Krup et al. Curcumin, present in *Nisha* has anti-inflammatory, antioxidant, antimutagenic, antidiabetic, antibacterial, hepatoprotective, expectorant and anticancerous pharmacological activities.[23] According to Yokozawa et al. *Amalaki* is helpful in reducing the oxidative stress and potent in preventing hyperlipidemia associated with ageing.[24] Study by Emordi et al. showed that honey had both good hypoglycemic activity and good effects on cardiovascular risk factors.[25] This way total effect of *Nisha Amalaki choorna* corroborate with the results of previous studies.

CONCLUSION
The present study confirms that, *Nisha Amalaki yoga* with and without honey is effective in treatment of *Prameha* and undeniably reduces majority of the symptoms. *Nisha Amalaki yoga* with both the *anupana* gave good result in subjective and objective parameters. The present study confirms that honey even being sweet in taste it does not increased the sugar level and thus it is safe and effective in *Prameha.* The condition of the patients were stable even after discontinuing the drugs. Since the quality of honey available at markets in India remains doubtful, it is advisable to use *Nisha Amalaki choorna* with luke warm water as *anupana* in clinical setup.

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