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A CLINICAL STUDY ON THE EFFICACY OF CERTAIN HERBAL DRUGS IN THE MANAGEMENT OF MADHUMEHA (NON-INSULIN DEPENDENT DIABETES MELLITUS)

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ABSTRACT

Diabetes is appallingly becoming an epidemic in India, with more than 62 million diabetic individuals currently diagnosed with the disease. India, already the diabetic capital of the world, is heading towards the diabetic explosion. The etiology of diabetes in India is multifactorial which includes genetic factors coupled with environmental influences such as obesity and lifestyle changes. Striking similarities are noted between Diabetes and *Madhumeha* described in Ayurveda. The current study aimed at evaluating the efficacy of *Nishadi Churna* on fifty known cases of *Madhumeha* (Non-insulin depended Diabetes Mellitus) patients selected from the OPD of ACRI, Jaipur. The trial drug was administered in the dose of 5gms twice a day, half an hour before breakfast. The review period was of 15 days. After 60 days therapy, highly significant ($p<0.001$) reduction was observed on Fasting Blood Sugar and Post Prandial Blood Sugar levels. The formulation showed statistically highly significant ($p<0.001$) results in *PrabhutaMutrata (polyuria), Pipasadhikya (polydipsia), Kshudhadhikya (polyphagia), Swedadhikya (excessive sweating) Daurbalya (weakness), Alasya (lassitude), Atinidra(excessive sleep), Vibandha*

(constipation), Karapadadaha (burning sensation in hands and feet), Madhurasyata (sweet taste of mouth), Tandra and *Kricchravyavayata (sexual dysfunction).* No adverse drug reactions or complications were reported during the study.

KEYWORDS: *Madhumeha,* Diabetes Mellitus, *NishadiChurna,* Blood Sugar.

INTRODUCTION

Madhumeha is the disease of metabolic derangement and genetic predisposition related with each constituent of the body with systemic consideration. The word *Madhumeha* consists of two words '*Madhu'* and '*Meha'*. Diabetes mellitus (DM) is described in Ayurveda as *Madhumeha/Kshaudrameha*, which literally means excessive urine with sweet taste like honey. AcharyaMadhava narrates the word *Prameha* as repeated (***Prakarsha***), excessive (***Prabhuta***) and turbid urination which shows increase in terms of frequency and quantity.[1]

Madhumeha is co-related with *Non-Insulin dependent Diabetes Mellitus*. Diabetes mellitus, a metabolic disorder of multiple etiology is characterized by chronic hyperglycemia with derangement of carbohydrate, fat and protein metabolism resulting from defects either in insulin secretion or insulin action or both. The patients of diabetes mellitus present with characteristic symptoms such as thirst, polyuria, blurring of vision and weight loss.

General etiology of *Prameha* coincides with that of *Madhumeha* of Charaka Samhita, with its aetiopathogenesis dealt in Sushruta Samhita and Ashtanga Samgraha, having the common opinion that all *Pramehas* when left untreated or not properly treated lead to *Madhumeha.*[2] Two types of *Prameha* namely *Sahaja* and *Apathyanimittaja*, can be compared to Insulin dependent and Non-insulin dependent diabetes mellitus respectively.[3] As *madhumeha* belongs to *Madhyama Rogamarga (BastiMarma*), therefore it is palliable and needs life long active management strategy.[4]

The number of people suffering from diabetes mellitus all over the world is increasing progressively. According to ***International Diabetes Federation (IDF) Report 2013,*** worldwide ***366 million*** people had *diabetes* in 2011; by 2030 this will rise to ***552 million***. In India, there are nearly ***50 million*** *diabetics*, according to the statistics of the IDF. It is estimated that by 2025, every 5th *diabetic* subject in world will be an Indian. The number of people with *Type 2 diabetes*is increasing in every country. 80% of affected people live in low and middle-income countries. The greatest number of people is between ***40 to 59 years*** of

age. 183 million people (50%) with *diabetes* are undiagnosed. *Diabetes* caused 4.6 million deaths in 2011. *Diabetes* caused at least USD 465 billion dollars in healthcare expenditures in 2011; 11% of total healthcare expenditures in adults (20-79 years). 78,000 children develop *Type 1 diabetes* every year.[5]

Accordingly, most of the *diabetic* patients come from affluent sectors of the society. *Diabetes mellitus* considerably reduces the quality of life and the life expectancy of the patients. The associated complications of Diabetes mellitus worsen the situation and adversely affect almost all the systems of the body e.g. Diabetic Neuropathy, Nephropathy, Angiopathy, Retinopathy etc. The available modern *anti-diabetic* agents have numerous adverse effects. Keeping the gravity of the situation and public health need in view, it is important to find out an alternative non-chemical therapeutic agent to treat this disease. Therefore, a safe combination of certain already experimented *Ayurvedic* drugs was selected for the current study.

AIMS AND OBJECTIVES OF THE STUDY

- To evaluate the clinical efficacy of trial drug in the management of *Madhumeha* (Diabetes mellitus)
- To assess the clinical safety of trial drug in the management of *Madhumeha* (Diabetes mellitus)
- To find out an economical and safe management for *Madhumeha* (Diabetes mellitus)

MATERIAL AND METHODS

1. **Type of study:** **Open Clinical Trial in a single group**
2. **Sample Size:** **50 patients**
3. **Name of the drug:** ***Nishadi churna***
4. **dosage shedule** **5gms twice a day half an hour before meals**
5. **Anupana of the drug:** ***Ushnodaka* (Lukewarm water)**
6. **Study duration of trial drug:** **60 days**
7. **Selection of the patients:** **OPD of the ACRI, Jaipur**

Criteria For Inclusion

a) Age between 35-70 years

b) Sex: Patients of either sex

c) Glycaemic status: Patients having Fasting blood sugar levels>120mg% and Post prandial blood sugar levels>180mg% upto 350%

d) The patients having polyuria, polydipsia, polyphagia, body ache, fatigue and weakness

e) Known *diabetic* patients up to 10 years duration

Criteria For Exclusion

a) Age less than 35years and more than 70years

b) PP blood sugar > 350 mg%

c) *Diabetics* of more than 10 years duration

d) Patients having *diabetic* retinopathy/visual complications

e) Patients with neuropathy/related complications

f) Patients with angiopathy/related complications

g) Patients with nephropathy/related complications

h) Patients complicated with various infections e.g. urinary tract infections, respiratory tract infections and skin infections etc

i) Insulin dependent *diabetics*/patients with ketonuria

Withdrawal Criteria

1. Patient developing any serious adverse effect necessitating his hospitalization
2. Non-compliance of the treatment regimen (minimum 80% compliance is essential to continue in the study)
3. Patient'swill of withdrawal from the study.

LABORATORY INVESTIGATIONS

Following lab investigations were carried out before, during after the trial to observe the effect of formulations under study.

1. Haematological investigations like Hb, TLC, DLC and ESR
2. Routine and microscopic examination of urine, fasting urine sugar (FUS) and post prandial urine sugar (PPUS)
3. Bio-chemical examination – Fasting Blood Sugar, Post Prandial Blood Sugar, Blood Urea, Serum Creatinine and Lipid Profile

ROUTINE EXAMINATION AND ASSESSMENT

A detailed clinical history and physical examination of each trial subject was recorded as per the case record form. The clinical, pathological and bio-chemical investigations were done as recommended in the proforma at 0 day, 30th day and 60th day.

Drug formulation

Drugs were selected on the guidelines given by *Acharyas* and previous research works conducted on these medicines in different Research Institutes.

Contents of the formulation

Table No. 01: Contents of the formulation

S.No.	Herb	Botanical name	Part used
1.	Haridra	Curcuma longa Linn.	Rhizome
2.	Amalaki	Phyllanthus emblica Linn.	Fruit
3.	Jambu	Syzygium cumini	Seed
4.	Meshashringi	Zymnema sylvestre	Leaves
5.	Karavellaka	Momordia charantia	Fruit
6.	Bimbi	Coccinia indica	Root

Method of preparation

All the raw drugs were taken in equal quantity. The individual drugs were checked for their identity, quality and quantity. All were cleaned thoroughly. Then subjected to size reduction in a pulverizer separately to get crude powder of each drug. Powder of all the drugs was then mixed together in the pulverizer. The prepared powder was then packed in small polybags.

CRITERIA FOR ASSESSMENTOF THE RESULT

The changes in the subjective and objective parameters along with laboratory investigations before and after the treatment were considered for assessment of the efficacy and safety of the drug.

ASSESSMENT CRITERIA

1. **Subjective improvement**

All the patients under trial were specifically asked for any changes of improvement in their general well being either physically or mentally and the clinical manifestations produced by drug under trial.

2. **Clinical improvement**

For the assessment of clinical improvement, the scoring pattern was generated for the severity of the symptoms of the illness and accordingly the improvement was analyzed.

Table No. 02: Clinical parameters for assessment

S.No.	Symptoms	Scoring	BT (0 day)	AT (60 days)
1.	**PrabhutaMutrata(Polyuria)**			
	3-5 times/day, rarely at night	0		
	6-8 times/day, 0-2 times at night	1		
	9-11 times/day, 2-4 times at night	2		
	>12 times/day, > 4 times at night	3		
2.	**Avila Mutrata (Turbidity in urine)**			
	Specific Gravity Urine Sugar Albumin Total			
	1020-1025 (0) Nil (0) Nil (0) 0	0		
	1026-1030 (1) + (1) + (1) 1-3	1		
	1031-1035 (2) ++ (2) ++ (2) 4-6	2		
	1036-1040 (3) +++(3) +++ (3) 7-9	3		
	1041-1045 (4) ++++(4) ++++ (4) 10-12	4		
3.	**Pipasadhikya (Polydipsia)**			
	Feeling of thirst (8-10 times/24 hrs) and relieved by drinking water	0		
	Feeling of moderate thirst (11-13 times/24 hrs) and relieved by drinking water	1		
	Feeling of excessive thirst (14-16 times/24 hrs) and not relieved by drinking water	2		
	Feeling of severe thirst (>16 times/24 hrs) and not relieved by drinking water	3		
	Feeling of thirst not relieved by drinking water	4		
4.	**Kshudhadhikya (Polyphagia)**			
	As usual/in routine	0		
	Slightly increased (one meal extra with routine diet)	1		
	Moderately increased (two meals extra with routine diet)	2		
	Markedly increased (three meals extra with routine diet)	3		
5.	**Swedadhikya (Excessive Sweating)**			
	Sweating after heavy work and fast movements/hot weather	0		
	Profuse sweating after moderate work and movement	1		
	Sweating after light work and movement (stepping ladder)	2		
	Profuse sweating after light work and movement	3		
	Sweating even at rest or in cold weather	4		
6.	**Daurbalya (Weakness)**			

	No weakness	0		
	Mild after doing work	1		
	Moderate after doing work	2		
	Severe after doing work	3		
	Feeling weak without doing work	4		
7.	**Alasya (Lassitude)**			
	Can do routine exercise/work	0		
	Can do moderate exercise with hesitancy	1		
	Can do mild exercise only with difficulty	2		
	Cannot do mild exercise even	3		
8.	**Atinidra (Excessive sleep)**			
	Doing satisfactory work with proper vigour and in time	0		
	Doing satisfactory work/late initiation, likes to stand in comparison to walk	1		
	Doing little work very slow, likes to sit in comparison to stand	2		
	Doing little work very slow, likes to lie down in comparison to sit	3		
	Don't want to do any work/no initiation, likes to sleep in comparison to lie down	4		
9.	**Vibandha (Constipation)**			
	Passes stool as per normal schedule	0		
	Passes stool with strain, sometimes takes purgative	1		
	Passes stool usually after 24hrs, frequently takes purgative	2		
	Passes stool after gap of one day, normal purgative doesn't work	3		
10.	**Hasta, pada&Sandhi-shula (Pain in hands, feet & joints)**			
	Absent	0		
	Mild	1		
	Moderate	2		
	Severe	3		
11.	**Karapadadaha (Burning sensation in hands & feet)**			
	Absent	0		
	Occasional, mild and bearable	1		
	Continuous but bearable and not severe	2		
	Continuous, severe and unbearable	3		
12.	**Madhurasyata (Sweetness in mouth)**			
	Absent	0		
	Mild	1		
	Moderate	2		
	Always	3		
13.	**Karapadasupti (Numbness)**			
	Absent	0		
	Incontinuous	1		
	Continuous but bearable and not severe	2		

	Continuous, severe and unbearable	3		
14.	**Tandra (Drowsiness)**			
	No drowsiness	0		
	Mild drowsiness but able to do usual work	1		
	Moderate drowsiness but able to do usual work with errors	2		
	Severe drowsiness which hampers usual work	3		
	Patient unable to do any work because of drowsiness	4		
15.	**Kricchravyavayata (Erectile Dysfunction)**			
	Absent	0		
	Mild loss of libido	1		
	Moderate loss of libido	2		
	Severe loss of libido	3		
	Complete loss of libido	4		

OBSERVATIONS AND RESULTS

Wilcoxon Signed Rank Test was used to statistically analyze the data:

Table No. 03: Symptomatic improvement after therapy in 50 patients:

Symptom	Mean B.T.	Mean A.T.	Mean Diff.	Mean %	Number	S.D.	S.E.	p value	Result
PrabhutaMutrata (Polyuria)	2.07	1.52	0.55	26.37%	27	0.63	0.09	< 0.001	H.S.
Avila Mutrata (Turbid Urine)	1.29	1.00	0.29	22.22%	10	0.53	0.10	< 0.050	S.
Pipasadhikya (Polydipsia)	1.86	1.35	0.51	27.47%	27	0.54	0.08	< 0.001	H.S.
Kshudhadhikya (Polyphagia)	2.40	1.69	0.71	29.63%	31	0.51	0.08	< 0.001	H.S.
Swedadhikya (Excessive Sweating)	1.74	1.32	0.42	24.24%	18	0.55	0.09	< 0.001	H.S.
Daurbalya (Weakness)	1.82	1.38	0.44	23.94%	19	0.55	0.09	< 0.001	H.S.
Alasya (Lassitude)	1.53	1.16	0.37	24.14%	16	0.54	0.09	< 0.005	H.S.
Atinidra (Excessive sleep)	1.39	0.79	0.61	43.59%	19	0.57	0.11	< 0.001	H.S.
Vibandha (Constipation)	1.93	1.18	0.75	38.89%	21	0.44	0.08	< 0.001	H.S.
Hasta, pada & Sandhi-shula (Pain in hands, feet & joints)	1.31	1.06	0.25	19.15%	9	0.44	0.07	< 0.001	H.S.
Karapadadaha (Burning sensation in hands & feet)	1.68	1.28	0.40	23.88%	18	0.55	0.09	< 0.001	H.S.
Madhurasyata (Sweetness in mouth)	1.07	0.43	0.64	60.00%	9	0.50	0.13	< 0.001	H.S.
Karapadasupti (Numbness)	1.24	1.06	0.18	14.29%	3	0.39	0.10	> 0.2	I.S.
Tandra (Drowsiness)	1.28	0.93	0.35	27.12%	16	0.48	0.07	< 0.001	H.S.
Kricchravyavayata (Erectile dysfunction)	1.53	1.26	0.26	17.24%	10	0.45	0.07	< 0.001	H.S.

The effect of *Nishadi Churna*on chief complaints indicated that it provided statistically highly significant ($p<0.001$) in *Prabhuta Mutrata (*26.37%), *Pipasadhikya*(27.47%), *Kshudhadhikya* (29.63%), *Swedadhikya*(24.24%), *Daurbalya*(23.94%), *Alasya*(24.14%), *Atinidra*(43.59%),

Vibandha(38.89%), *Hasta, pada & Sandhi-shula*(19.15%), *Karapadadaha*(23.88%), *Madhurasyata*(60.00%), *Tandra (27.12%) and Kricchravyavayata*(17.24%).

Statistically, the formulation showed significant (p<0.050) results in *Avila mutrata*(22.22%) while it was insignificant (p>0.02) in *Karapadasupti*(14.29%).

Table No.04: Changes in the clinical parameters after therapy in 50 patients:

Clinical parameter	Mean B.T.	Mean A.T.	Mean Diff.	Mean %	Number	S.D.	S.E.	t value	p value	Result
Blood pressure (Systolic)	136.72	133.64	3.08	2.25%	50	4.37	0.62	4.98	< 0.001	H.S.
Blood pressure (Diastolic)	88.40	88.16	0.24	0.27%	50	2.64	0.37	0.64	> 0.1	I.S.
BMI	24.93	24.57	0.36	1.43%	50	0.32	0.05	7.87	< 0.001	H.S.

Effect of therapy on laboratory profile

The formulationshowed highly significant (p< 0.001) results on *Fasting Blood Sugar* (15.18%), *Post Prandial Blood Sugar* (14.50%), *Fasting Urine Sugar* (13.33%) and *Post Prandial Urine Sugar* (33.33%).

DISCUSSION

Madhumeha is a grave and refractory illness hence is considered as one among the *Astamaharoga.*[6] It seems that disease is as old as the humanity is. In present scenario, modern medicine has its own limitations to manage the disease and its complications efficiently. The ancient Ayurvedic principles of prevention *(Nidanaparivarjana)*, purificative measures *(Shodhana Chikitsa)* and rejuvenative measures (rasayana therapy) with due consideration of appropriate single / polyherbal formulations *(Aushadhi)* and strict diet and exercise regimen*(Pathya-apathya)*, have proved to be profitable in managing the illness.

The present study drug, ***Nishadi Churna***, was selected on the guidelines given by *Acharyas* and previous research works conducted on these medicines at different Research Institutes. Drugs chosen in the formulation are such that they act in synergistic way *(prakritisamasamvetasiddhanta)*[7] and break the pathogenesis of the illness (*sampraptivighatana*) by acting against the *kaphavargeeyadushya* involved in *Madhumeha* viz. as *meda, mamsa, kleda, shukra, shonita, vasa and majja* etc. The *anupana* was *Ushnodaka*(warm water) which is *kapha-medas-vata* and *amanashaka, agnideepana* and also has role in purification of *Basti.*[8] The present study has provided significant results in the

managing the disease which can hence be used as a good complimentary medicine for the patients who are not getting good results from modern medicine alone.

CONCLUSION

At the end of the present study, the following conclusion can be drawn on the basis of the observations made, results achieved and thorough discussion in the present context:

1. The humankind is facing the *madhumeha* disease since long time. It has been well documented in all perennial sources of Ayurvedic wisdom.
2. The gravity of the disease *Diabetes Mellitus* can be made by the fact that WHO has declared it as an epidemic.
3. Faulty diet and sedentary lifestyle including stress and obesity play an important role in the etiopathogenesis of *Madhumeha.*
4. The incidence can be prevented by increasing awareness about the disease, early detection, disciplined lifestyle, proper food habits and routine exercise.
5. The clinical manifestation, etiology, pathogenesis and treatment of the two entities *Madhumeha* and *Diabetes Mellitus* show striking similarity which proves that there is a correlation between both of them.
6. The chosen drug formulation was found effective in reducing both Fasting and Postprandial Blood Sugar; and also Urine sugar (both fasting and postprandial).
7. All the patients tolerated medicines very well and no side effects were reported by any of the patients thereby suggesting that the drug formulation selected in current clinical trial is completely safe for internal use.

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