Published online in http://ijam.co.in ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 15 (1), 2024; 148-153

Randomised Controlled Trial on the efficacy of *Mamajjaka (Enicostemma littorale Linn.*) in the Management of *Madhumeha* (Diabetes Mellitus)

Research Article

Amit R Nampalliwar[1*], Pawankumar Godatwar[2]

1. PhD Scholar, 2. PhD-Guide, PG Department of Roga Nidana and Vikriti Vigyana, National Institute of Ayurveda, Jaipur, Rajasthan, India.

Abstract

Diabetes Mellitus is in top ten list of diseases causing mortality. In the year 2011, estimated 366 million people were found to be suffering from diabetes mellitus. By year 2030 this morbidity data will rise to approximately 552 million people worldwide. India is having the largest number of diabetics in the world and gets the name 'Diabetic capital'. This study was carried out with an aim:-'To Conduct a Randomised Controlled (*Upashayatmaka*) Trial on the role of *Mamajjaka* capsule in the management of *Madhumeha* (DM type-2)'. In this study total 110 patients of Diabetes were selected from NIA hospital and randomly divided into two groups. Group A (Control group) comprise 54 patients were administered with Tab. Metformin and dose was 500mg tablet 1 BD before meals as advised according to allopathic consultant. Group B (Trial group) comprise 56 patients were administered with Cap. *Mamajjaka*, dose: 500 mg Capsule 2 BD, before 30 min. of meal with lukewarm water. Total duration trial was 100 days. Results obtained in subjective and objective parameters were analysed for the statistical significance by adapting paired T test and unpaired T test. The study revealed that Group-B was found to be more effective in bringing symptomatic relief and Group-A was found to be more effective in improving biochemical markers in the patients of *Madhumeha*. Cap. Mamajjaka *(Enicostemma littorale Linn.*) provided better results, suggests that this can be a good complimentary medicine for the patients who are not getting good relief from modern medicine alone.

Keywords: Diabetes Mellitus*, Madhumeha, Mamajjaka. Enicostemma littorale* Linn.

Introduction

Diabetes Mellitus is known to mankind since antiquity is a global health problem which is growing in full pace, and alarming the world as a non infectious pandemic. It is in top ten lists of diseases causing death. With an estimated 366 million people in 2011 and by 2030 this will have risen to 552 million people suffering from Diabetes Mellitus (1). Now India is having the largest number of diabetics in the world and gets the name 'Diabetic capital' (2). Recent epidemiological studies from India point to the great burden due to Diabetes and its micro and macro vascular complication on the society. This is because the status of diabetes control in India is far from the ideal status (3).

Based on available data, the mean GHb (Glycosylated hemoglobin) level is around 9% which is at least 2% higher than the goal currently. It is estimated by International Diabetic Federation (IDF) that by 2025 every fifth diabetic subject in world will be an Indian (4). Genetic predisposition with life-style changes, increased urbanisation and globalisation contributes to this rapid rise of Diabetes Mellitus in India. More over Type-2 Diabetes Mellitus in Indian population appears to occur at least a decade earlier than Europeans (5).

In this scenario we can estimate the economic burden caused because of Diabetes Mellitus. It has strange similarity with *Madhumeha* which is described under subheading of *Prameha* and independently as a result of *Avarana*. Treatment and description of *Madhumeha* is available in almost all of our classics. Gravity of the disease is assessed in the *Brihatrayi* as the eminent Indian surgeon *Acharya Sushṛta* has include it among the eight precarious diseases citing as '*Mahagada'*, *Acharya Charaka* comprised it among eight *'Achikitsya Vyadhi* and *Achrya Vagbhata* counted it in eight '*Maharoga*'(6).

The increased burden of Diabetes Mellitus draws the attention of modern researchers to *Madhumeha*. It is relevant and quite important to analyse *Madhumeha* with the reference of Diabetes Mellitus.

In this study we tried to decide prevalence of type of *Madhumeha* which could be of help in deciding effective treatment. In present study *Mamajjaka churna* was prepared by giving three *bhavana* by its own *svarasa*, so it became concentrate. Then it was filled in the capsule and used for administration in the patients of *Madhumeha* (Diabetes Mellitus).

*** Corresponding Author:**
Amit R Nampalliwar
Reader & HOD,
Department of Roga Nidan Evam Vikriti Vigyana,
Government Ayurveda College & Hospital,
Bilaspur-495001, Chhattisgarh, India.
Email Id: dr.n.amitkumar@gmail.com

Aims and objectives:

1. To Conduct a Randomised Controlled (*Upashayatmaka*) Trial on the hypoglycemic activity of *Mamajjaka* capsule.
2. To assess the efficacy of *Mamajjaka* on other aspect of *Madhumeha* (Diabetes Mellitus)

Materials and Methods

IEC approval: Before trial this clinical study was placed in IEC(Institutional Ethics Committee) for approval. The trial was started after IEC approval.

This study is conducted under a strict protocol to prevent bias and to reduce the sources of error in the study. This Controlled clinical trial was conducted under the following steps:-

1. Selection of patients
2. General observation
3. Administration of Drug
4. Follow up study
5. Assessment of progress

Selection of patients

The patients for *Upashayatmaka Adhyayana* (clinical trial) were selected from OPD and IPD of NIA Hospital (*Arogyashala*) Jaipur, after screening them as per *Ayurvedic* and Modern criteria for *Madhumeha* (Diabetes Mellitus). Selection was carried out according to relevant history, sign, and symptoms including laboratory investigations

A written information and consent letter had been given to patients. The patients were explained about the purpose, procedures and possible dangers of the trial.

Total 110 patients were registered for the study, but only 92 patients completed the course.

Criteria for the selection of the patient:

Inclusion criteria

1) Patients were selected randomly irrespective of sex
2) Patient of age group between 16-75 years.
3) Diagnosed case of *Madhumeha* (D.M. type-2)
4) Patient giving clinical history of Diabetes.
5) Hyperglycaemia confirmed by lab. in new cases. (Reference range: F. >120mg/dl, P.P. >200mg/dl.)

Exclusion criteria

1) Patient of IDDM (D.M.type-1)
2) Complicated cases of Diabetes Mellitus
3) Type-2 Diabetes patient on insulin therapy.
4) Unconscious and uncooperative patients.
5) *Garbhini* and *Sutika*

Diagnostic Criteria

The following criteria were developed to select the cases on clinical ground, which is based on the signs and symptoms, described in *Ayurvedic* and modern texts and lab. investigations.

All the patients were assessed on the basis of assessment criteria as follows

Subjective parameters

- *Prabhuta mutrata* (Frequency of urine)
- *Avila Mutrata* (Turbidity of urine)

Objective parameters

The following laboratory criteria were used on investigation ground:

- Biochemistry – FBS, PPBS, GHb (HbA1C)
- Urine examination – FUS (Fasting Urine Sugar)

All of these laboratory investigations were conducted in the central laboratory of NIA.

General observations

Demographic Profile:

The patients registered under the present trial were closely interviewed according to the proforma of study. In incidence of their age, sex, socio-economic status, marital status, religion, habitat, dietary habits, nature of Job and other relevant information's were worked out.

Physical Measurement:

All the measurement was made with the patients in empty stomach before, during follow-up and after the treatment.

- **Height –** Standing height was measured with the subject in bare feet, back against a wall and the eyes looking straight ahead. A set square resting on the scalp and the tape measurement from the wall was used to measure the height to the nearest centimetres.
- **Weight** – Weight was measured with minimum clothing using a platform scale to the nearest kilograms. The scale was standardised to 'Zero' before each use.
- **Body Mass Index –** The body mass Index (BMI) was calculated by dividing weight in kilograms by height in meters squared.
- **General physical examination –** like Pulse rate (PR), Respiration rate (RR), Body temperature, Blood pressure etc. were also assessed.

Administration of Drug

110 clinically diagnosed *Madhumeha* patients were divided randomly into two groups:-

- **Group A: -** Control group – 54 patients were administered with Tab. Metformin (Allopathic treatment)
- **Dosage:** 500 mg Tablet 1 BD, before 30 min. of meal as advised according to allopathic consultant.
- **Group B: -** Trial group – 56 patients were administered with Cap. *Mamajjaka*
- **Dosage:** 500 mg Capsule 2 BD, before 30 min. of meal.
- ***Anupana*** : with luke-warm water
- **Duration of Trial:** 100 days for both groups.

Follow up study

- Patients were followed every 15 days.
- Laboratory investigation was repeated after complete treatment.
- Improvement and other side effects were noted.

Assessment of progress

After the completion of the treatment, the results are assessed by adopting the following criteria.

Improvement in signs and symptoms of disease on the basis of symptoms score. In this particular research work, subjective criteria were taken from the reference book-'Developing Guidelines for Clinical Research Methodology in Ayurveda'(7), under the chapter of Gradation of Symptoms: *Medovaha Srotas* are as follows

Sl.No	Parameters	Grading
***Prabhuta- mutrata* (Frequency of urine)**		
1	3 – 6 times per day, rarely at night	**0**
2	6 – 9 times per day, 0 – 2 times per night	**1**
3	9 – 12 times per day, 2 – 4 times per night	**2**
4	More than 12 times per day, more than 4 times per night	**3**
A*vila* -m*utrata* (Turbidity of urine): News Paper Test:		
1	Crystal clear fluid	**0**
2	Faintly cloudy, smoky or hazy with slight turbidity.	**1**
3	Turbidity clearly visible but newsprint easily read through test tube-	**2**
4	Newsprint not easily read through test tube	**3**
5	Newsprint can not be seen through test tube	**4**
Assessment of Body Mass Index (B.M.I.)		
1	18.5-24.9	**0**
2	25-29.9	**1**
3	30-34.9	**2**
4	35-39.9	**3**
5	>40	**4**

Improvement in laboratory Investigation (i.e. reduce levels) on the basis of lab reports also Reduction in objective assessment parameters.

Assessment of overall effect of the therapy

1) Control of the disease: improved FBS and PPBS > 50 mg/dl or under normal range and sign- symptoms approach to normal.
2) Markedly improved: Relived sign symptoms and improved FBS and PPBS 30-50 mg/dl.
3) Improved: Nominal improved in sign/symptom and improved FBS and PPBS 10-29 mg/dl.
4) Unchanged: No reduction in sign/symptom and improvement <10 mg/dl.
5) Deteriorate: Increased blood sugar and deterioration of other sign or symptoms.

Observations & results

Table 1: Group wise status of 110 patients registered for this study

Type	Number of patients		Total
	Group A	Group B	
Registered	54	56	110
Completed	43	49	92
Drop Out	11	7	18

In the present study, total 110 patients were registered out of which 92 patients completed the study and 18 patients Dropout.

Table 2: Showing pattern of Clinical improvement in *Prabhuta-mutrata* (Frequency of urine)

Group	N	Mean		Diff.	% of Change	SD	SE	W	P
		BT	AT						
A	43	2.21	0.91	1.30	58.95	0.67	0.10	820	<0.0001 (ES)
B	49	2.18	0.41	1.78	81.31	0.85	0.12	1081	< 0.0001 (ES)

Group	Mean diff.		% of Change		SD	SE	U	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	1.30	1.78	58.95	81.31	0.97	0.15	707.5	0.0036 (VS)

Group A showed 58.95% relief in *Prabhuta-mutrata* which was extremely significant result, Group B showed 81.31% relief in *Prabhuta-mutrata.* A & B were compared with each other. It is seen that there was very significant difference (p=0.0036) between the two groups. This implies that clinically Group B is better than Group A

Table 3: Showing pattern of Clinical improvement in *Avila-mutrata* (Turbidity of urine)

Group	N	Mean		Diff.	% of Change	SD	SE	W	P
		BT	AT						
A	43	1.53	1.19	0.35	22.73	0.92	0.14	285	0.0196 (S)
B	49	2.12	0.78	1.35	63.46	0.69	0.10	1035	< 0.0001(ES)

Group	Mean diff.		% of Change		SD	SE	U	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	0.35	1.35	22.73	63.46	1.12	0.17	473.5	< 0.0001(ES)

Group A showed 22.73% relief in *Avila-mutrata* which was extremely significant result, Group B showed 63.46% relief in *Prabhuta-mutrata.* A & B were compared with each other. It is seen that there was significant difference (p=0.0196) between the two groups. This implies that clinically Group B is better than Group A.

Effect of therapy on Laboratory Parameters

In randomised selection of sample with different sample size, Paired 't' test for paired(Group A & B) and Unpaired 't' test for unpaired parametric variables(Group A vs B) were used to Analyse the following data:

Table 4: Showing pattern of improvement in FBS

Group	N	Mean		Diff.	% of Change	SD	SE	T	P
		BT	AT						
A	43	195.37	130.79	64.58	33.05	31.30	4.77	13.53	< 0.0001 (ES)
B	49	191.43	131.27	60.16	31.43	36.52	5.22	11.53	< 0.0001 (ES)

Group	Mean diff.		% of Change		SD	SE	T	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	64.58	60.16	33.05	31.43	59.01	9.00	0.49	0.5380 (NS)

The effect of therapy on fasting blood sugar is statistically extremely significant (p<0.0001) in both Group A& B. Though maximum difference in percentage of change is observed in Group A, the difference is not statistically significant (p=0.5380) when compared with group B. Clinically Group A(33.05%) was more effective in reducing Fasting Blood sugar than Group B(13.43%).

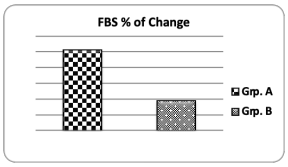


Table 5: Showing pattern of improvement in PPBS

Group	N	Mean		Diff.	% of Change	SD	SE	T	P
		BT	AT						
A	43	269.53	193	76.53	28.39	41.53	6.33	12.08	< 0.0001 (ES)
B	49	265.69	189.71	75.98	28.60	45.65	6.52	11.65	< 0.0001 (ES)

Group	Mean diff.		% of Change		SD	SE	T	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	76.53	75.98	28.39	28.60	70.52	10.75	0.05	0.9525 (NS)

The effect of therapy on post prandial blood sugar is statistically extremely significant (p<0.0001) in both Group A& B. the difference is not statistically significant (p=0.9525). When compared Group A with Group B. Clinically both group A(28.39%) & group B (28.60%) was more effective in reducing post prandial blood sugar.

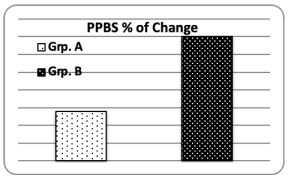


Table 6: Showing pattern of improvement in GHb (HbA_1C):

Group	N	Mean		Diff.	% of Change	SD	SE	T	P
		BT	AT						
A	43	7.75	6.62	1.13	14.55	0.68	0.10	10.82	< 0.0001 (ES)
B	49	7.42	6.27	1.14	15.43	0.89	0.13	9.05	< 0.0001 (ES)

Group	Mean diff.		% of Change		SD	SE	T	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	1.13	1.14	14.55	15.43	1.26	0.19	0.09	0.9191 (NS)

The effect of therapy on Glycosylated haemoglobin (GHb/HbA_1C) is statistically extremely significant (p<0.0001) in both Group A & B. Clinically both group A(14.55%) & group B(15.43%) was more effective on Glycosylated haemoglobin(GHb). The difference is not statistically significant (p=0.9191). When compared Group A Vs Group B.

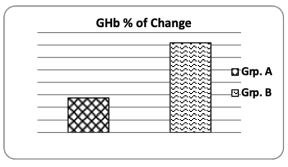


Table 7: Showing pattern of improvement in FUS (*Fasting Urine Sugar*)

Group	N	Mean		Diff.	% of Change	SD	SE	T	P
		BT	AT						
A	43	2.12	0.67	1.45	68.13	0.59	0.09	16.03	<0.0001 (ES)
B	49	2.55	0.94	1.61	63.20	0.79	0.11	14.36	<0.0001 (ES)

Group	Mean diff.		% of Change		SD	SE	T	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	1.45	1.61	68.13	63.20	1.11	0.17	2.05	0.2479 (NS)

Statistically extremely significant(<0.0001) improvement in FUS (*Fasting Urine Sugar*) was observed in both Group A & B. Inter group comparison showed no significant difference (p=0.2479) between two groups, Clinically Group A showed better effect with 68.13% of change than Group B 63.20% of change.

Table 8: Showing pattern of improvement in BMI (Body mass Index)

Group	N	Mean		Diff.	% of Change	SD	SE	T	P
		BT	AT						
A	43	26.41	25.34	1.07	4.06	0.26	0.04	26.80	<0.0001 (ES)
B	49	25.59	25.19	0.40	1.57	0.98	0.14	2.86	0.0062 (VS)

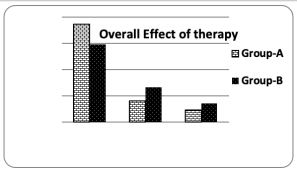
Group	Mean diff.		% of Change		SD	SE	T	P
	Grp. A	Grp. B	Grp. A	Grp. B				
A vs B	1.07	0.40	0.67	62.58	1.04	0.16	4.21	<0.0001 (ES)

Statistical evaluation of studied groups showed extremely significant (P<0.0001) result in Group A and very significant (p=0.0062) result in Group B. The inter-group comparison showed extremely significant difference (p<0.0001) in between group A & B. Clinically Group A with 4.06% of change was more effective than Group B with 1.57% of change.

Table 9: Overall comparison of effect of the therapy in 92 patients of *Madhumeha*

Sr. No.	Total effect of therapy	Group-A (N= 43)		Group-B (N= 49)		Total (N= 92)	
		No. of Pts.	%	No. of Pts.	%	No. of Pts.	%
1	Controlled	32	74.42%	29	59.18%	61	66.30%
2	Markedly improved	7	16.28%	13	26.53%	20	21.74%
3	Improved	4	9.30%	7	14.29%	11	11.96%
4	Unchanged	0	0.00%	0	0.00%	0	0.00%

In case of control Group-A 32 patients (74.42%) were controlled, 7(16.28%) patients were markedly improved and 4(9.30%) patients were improved. In case of trial Group-B 29(59.81%) patients were controlled, 13(26.53%) patients were markedly improved and 7(14.29%) patients were improved.



Discussion

Effect of trial drug Cap. *Mamajjaka(Enicostemma littorale Linn.*):

Previous studies had confirmed the blood glucose lowering effect of *E. Littorale Linn.* in alloxan induced diabetic rats with no change in normoglycemic control rats. The effective dose was found to be 1.5 g dry plant equivalent extract /100 g body wt. The above dose caused significant decrease in glycosylated haemoglobin, liver glucose-6-phosphatase activity and significant increase in serum insulin levels of the diabetic rats. No significant changes were observed in the toxicity parameters of extract treated diabetic rats as compared to diabetic control rats. The above results suggest that *E. littorale* a potent antidiabetic agent without any toxic effect at this particular dose. The chemical composition of *Mamajjaka* shows presence of bitter principle - *swertiamarine* along with alkaloids like gentianine, this acting principle may be potentiating the glucose dependent insulin release from pancreases β-cell, this possibly reflects one of the factor responsible for the decrease blood sugar level (8).

The insulinotropic action of aqueous extract of *E. littorale* was further investigated using rat pancreatic islets. Extract has the potential to enhance glucose-induced insulin release from isolated rat pancreatic islets (9).

In Present research work, we have studied the effect of Cap. *Mamajjaka* (*Enicostemma littorale Linn.*) (2 gm/day) daily for 100 days in Diabetes type-2 (NIDDM) patients. After 100 days of treatment with regular follow-up, it observed that symptomatic parameters of *Madhumeha* like *Prabhuta-mutrata*(Frequency of urine) and *Avil-mutrata*(Turbidity of urine) were significantly(p<0.0001) decreased in the treatment with Cap. *Mamajjaka,* also decreased the Fasting blood sugar (FBS), Postprandial blood sugar (PPBS) levels, Glycosylated haemoglobin (GHb/ HbA_1C), and Fasting urine sugar (FUS) in Diabetes type-2 patients. It also reduced maximum symptoms associated with *Madhumeha* (Diabetes mellitus)

This data suggest that *Cap. Mamajjaka* is a potent herbal antidiabetic. It control blood sugar levels, normalises metabolism and provides good felling of health. *Cap. Mamajjaka* thus can be considered as supplementary therapy for effective treatment of various complications of Type- 2 diabetic patients.

Conclusions

Cap. *Mamajjaka* is effective in the management of all symptomatic parameters of *Madhumeha.* Cap. *Mamajjaka* effectively reduces FBS, PPBS, GHb (HbA_1C) and FUS, when used for long duration i.e. 100 days of trial. Comparison between result of Group A and B was insignificant in FBS, PPBS, GHb (HbA_1C) which suggest equal improvement in both groups. In minimising body weight and BMI, clinically it was seen that Group A (Tab. Metformin) was very effective as compared to in Group B. No side effect was noted in any of the groups during the trial. Cap. *Mamajjaka* provided better results, suggests that this can be a good

complimentary medicine for the patients who are not getting good relief from modern medicine alone.

Acknowledgement

We would like to thank the Staff of Pathology laboratory under the department of Roga Nidana and Vikriti Vigyana for their constant support during this research study. We would like to thank the participants for their active participation in this clinical trial.

References

1. Whiting D.R., Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011 Dec;94(3):311-21.
2. Pandey SK, Sharma V. World diabetes day 2018: Battling the Emerging Epidemic of Diabetic Retinopathy. Indian J Ophthalmol. 2018 Nov;66(11):1652-1653.
3. Ramachandran A, Snehalatha C. Current scenario of diabetes in India. J Diabetes. Epub 2009 Mar;1(1):18-28.
4. Verma R, Khanna P, Mehta B. National programme on prevention and control of diabetes in India: Need to focus. Australas Med J. Epub 2012 June 30;5(6):310-5.
5. Shashank R. Joshi, Diabetes Care in India, Annals of Global Health,Volume 81, Issue 6, 2015, Pages 830-838.
6. Vrddha Vagbhatta. Ashtang Hridaya. with Shashilekha Sanskrit Commentary by Indu. Edited by Kaviraj Atridev Gupta. Varanasi: Chaukambha Publication, Vol.-1 Reprint 2012, Nidansthana, Chapter 8 verse 30, p.p.- 235.
7. Baghel M.S. et.al., 'Developing Guidelines for Clinical Research Methodology in Ayurveda, Edition: 2011; WHO-DFC Sponsored Project; IPGTR&A, Jamnagar, Gujrat; 2011; pp-64-66.
8. Maroo J, Vasu VT, Gupta S.Dose dependent hypoglycemic effect of aqueous extract of Enicostemma littorale Blume in alloxan induced diabetic rats. Phytomedicine: International Journal of Phytotherapy & Phytopharmacology. 2003;10(1):196-199.
9. Maroo J, Vasu VT, Aalinkeel R, Gupta S.Glucose lowering effect of aqueous extract of Enicostemma littorale Blume in diabetes: a possible mechanism of action.J Ethnopharmacol. 2002; 81(3): 317-20.

*****