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Clinical efficacy of *Gokshura-Punarnava Basti* in the management of microalbuminuria in diabetes mellitus

Rajkala S. Ramteke, Anup B. Thakar[1], Amiben H. Trivedi[2], Panchakshari D. Patil[3]

Lecturer, Department of Panchakarma, GJ Patel Institute of Ayurveda and Research, New Vallabh Vidyanagar, Anand, [1]Associate Professor and I/C Head, Department of Panchakarma, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar, [2]Associate Professor, Department of Medicine, MP Shah Medical College and GG Hospital, Jamnagar, [3]Senior Research Fellow, Institute of Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar, Gujarat, India

Abstract

Microalbuminuria is the strong predictor of diabetic nephropathy, which is the main cause of morbidity and mortality in patients with diabetes mellitus (DM). Microalbuminuria is also characterized by increased prevalence of arterial hypertension, proliferative retinopathy, and peripheral neuropathy. The study was planned to evaluate the effect of *Gokshura-Punarnava Basti* in the management of microalbuminuria in DM (*Madhumeha*). Eligible diabetic patients with urine albumin excretion between 30 and 300 mg in 24 h were randomly divided into two groups. *Asthapana Basti* (decoction enema) of *Gokshura* and *Punarnava Kwatha* (decoction), *Kalka* (paste), *Taila* (medicated oil), *Madhu* (honey), and *Saindhava* (rock salt) for 6 consecutive days and *Anuvasana* (unctuous enema) of *Gokshura-Punarnava Taila* on 1st and 8th day by traditional *Basti Putaka* method was given in study group. Tablet Enalapril 5 mg, twice daily for 30 days was given to the patients in control group. The primary outcome measures were percentage change in the presenting complaints of diabetes, urine microalbumin, Blood Sugar Level (BSL), and Blood Pressure (BP). Enalapril showed 33.33% improvement, where as *Gokshura-Punarnava Basti* showed 79.59% improvement in the presenting complaints of diabetes, urine microalbumin, BSL and BP. *Gokshura-Punarnava Basti* has shown superior results in the management of microalbuminuria in DM as compared to control drug.

Key words: *Basti*, diabetes mellitus, *Gokshura*, *Madhumeha*, microalbuminuria, *Punarnava*

Introduction

We are in the midst of an epidemic; the epidemic of diabetes and its micro-vascular complications; without aggressive intervention health-care costs will be devastating to millions of patients predicted to be affected by diabetes over the next decades. One of the early markers of not only diabetic nephropathy, but also vascular disease in patients with diabetes, is the presence of microalbuminuria. It is a leading cause of end stage renal disease and also the leading cause of diabetes mellitus (DM) related morbidity and mortality.[1,2]

Among the diabetic population, 20-40% of patients develop diabetic nephropathy.[3] In type II DM, usually microalbuminuria may be present at the time of diagnosis, which reflects its long asymptomatic period.

Address for correspondence: Dr. Rajkala S. Ramteke, C/7, Ayurveda Staff Quarters, G.J. Patel Institute of Ayurveda and Research, New Vallabh Vidyanagar, Anand - 388 121, Gujarat, India.
E-mail: vaidyarajkala@gmail.com

Madhumeha may be equated with the DM. Charaka explain it as a life-style disorder,[4] due to over indulgence in heavy and richly nutritious food, day-time sleep, lack of exercises, other sedentary habits and not doing seasonal purifications.[5] Even though, there is no direct reference regarding diabetic nephropathy being manifested as a complication of *Madhumeha* in classical texts, but by the help of modern science, it can be concluded that diabetes being a metabolic disorder, manifestation of nephropathy changes in a diabetic patient are a result of metabolic derangements, contributing to hyperglycemia.[6]

As diabetic nephropathy is a complication of *Madhumeha*, so proper treatment of *Madhumeha* will prevent and pacify its complications. Management of diabetes described in classics; can be administered in nephropathy. These include modalities like *Shamana* (palliative), *Shodhana* (purificatory), and *Rasayana* (rejuvenation), etc.

Gokshura (*Tribulus terrestris* Linn.) is considered one among the drugs of *Mootra Virechaneeya Gana* (diuretic drugs)[7] by

Charaka. Hence, it acts as *Anulomana* (downward movement) of *Apana Vata*. This corrects the *Gati* (movement) of *Vata* there by influencing it in a positive way. *Gokshura* is also a proven anti-diabetic agent.[8] Its *Bastishodhana*[9] (cleansing) effect reduces *Avarana* of *Kapha* and *Meda* in the microcirculation of kidneys. *Punarnava* (*Boerhaavia diffusa* L. nom. Cons.) has *Ushna Veerya* (hot property), which corrects *Srotosanga* existing in the kidneys. The *Ushna Veerya* assists in the regeneration of renal tissues. It also acts as anti-inflammatory[10] and diuretic.[11]

Basti due to its purification property, eliminates the excess of deranged metabolic waste and in turn clears the *Avarana* of *Vata* and normalizes the functions of *Vyana* and *Apana Vata*. Thus, the normalized *Vata* helps to stop the depletion of vital *Dhatus* (body elements) through urine. Based on these qualities *Gokshura-Punarnava Basti* was selected for the present study. Angiotensin Converting Enzyme (ACE) inhibitor was taken as control drug.[12] The objective of the current work is to study the effect of *Gokshura-Punarnava Basti* in the management of microalbuminuria in DM (*Madhumeha*).

Materials and Methods

Selection of patients

Total 100 patients suffering from DM with microalbuminuria were selected from Out Patient Department (OPD) and Indoor Patient Department (IPD) of Panchakarma Department, IPGT & RA, Jamnagar and Medicine OPD of G.G. Hospital, Jamnagar irrespective of religion, sex, occupation, caste, etc., after screening. The patients were divided into two groups by following the computer generated randomization plan.

Ethical clearance was obtained from the Institutional Ethics Committees vide PGT/7/Ethics/2009-2010/3494/15 dated 08/02/2010 and MCLJ/IEC/113/2010 dated 12/04/2010. This study is registered in Clinical Trial Registry of India with registration No. CTRI/2012/03/002496 dated 15/03/2012.

Inclusion criteria

1. Known type II diabetic patients with urine albumin between 30 and 300 mg in 24 h urine sample.
2. Hypertensive patients with Blood Pressure (BP) <200/120 mm of Hg.
3. Age in between 20 and 70 years irrespective of gender.
4. Patients eligible for *Basti* treatment.

Exclusion criteria

1. Diabetic patients with urine albumin >300 mg in 24 h urine sample.
2. Hypertensive patients with BP >200/120 mm of Hg.
3. Microalbuminuria induced due to other diseases such as pregnancy and chronic renal failure.
4. Patients with other severe complications of DM such as ketoacidosis and paralysis.
5. Plasma creatinine more than 2.5 mg/dl.
6. Any other serious systemic illness.
7. Patient contra-indicated for *Basti*.

Laboratory investigations

Routine hematological, biochemical and urine examination, urine microalbumin in 24 h sample and glomerular filtration rate (GFR) were carried out before and after the treatment.

Methodology

Selected patients were randomly divided into two groups. All of them were advised to continue their anti-diabetic and antihypertensive drugs. Diet control and regular exercise was advised to all patients. Protein restricted diet and proper life-style was advised in both groups. All patients in *Basti* group (BG) were explained the *Pathyapathya* during *Basti*.

Grouping

Study group (BG): Gokshura-Punarnava Basti

i. *Asthapana Basti* (decoction enema) – contents
- *Gokshura-Punarnava* decoction – 350 ml
- *Gokshura-Punarnava* oil[13] – 100 ml
- Honey – 75 ml
- *Gokshura-Punarnava* paste – 15 g
- Rock salt – 5 g.

ii. *Anuvasana Basti* (unctuous enema)
- *Gokshura-Punarnava* oil – 120 ml.

Duration: Total days = 8* (*1st and 8th day *Anuvasana Basti* after food in morning, 2nd to 7th day *Asthapana Basti* before food between 9.00-10.30 am according to *Yoga Basti* pattern).

Basti was prepared by the classical method[14] and administered by traditional *Putaka* method.

Control group / Enalapril group
- Drug: ACE inhibiter – Tablet Enalapril
- Dose: 5 mg twice a day
- Mode of administration: Oral
- Duration: 30 days.

The drugs for *Basti* were procured from Pharmacy, Gujarat Ayurved University and the control drug (tablet enalapril) was provided from the dispensary of Civil Hospital.

Follow-up study

After completion of the therapy, patients were kept under observation to assess the immediate and short-term improvement for 1 month.

Criteria for assessment

i. Improvement observed in patients was assessed mainly on the basis of relief in percentage change in the presenting complaints of *Madhumeha* on the basis of the score decided in a previous study.[15]
ii. Urine microalbumin, GFR, blood sugar level (BSL) and BP.

Statistical analysis

The data obtained in the study was subjected to statistical tests.

Subjective criteria

Percentage of improvement in each parameter of both the treated groups is calculated. Wilcoxon signed-rank test is applied to the statistical data for evaluating the difference in the before and after treatment scores. Chi-square test is applied for comparison between both groups.

Objective criteria

Obtained data of objective parameters between the groups was statistically determined by paired *t*-test, unpaired Student's *t*-test for both the groups with the level of significance set at $P < 0.05$.

Observations

Total 100 patients were registered in the present study with 50 in the study group that is, BG and 50 in the control group, that is, EG. Among them, total 97%, (49 in BG and 48 in EG) completed the treatment.

Maximum registered patients were belonging to 41-55 years age group (48%), average random BSL was more than 281 mg/dl (35%); positive family history of DM (75%) and having the history of diabetes since 5-10 year (54%) and the history of hypertension since 5 years (44%). Maximum patients had *Vishamagni* (48%), *Krura Koshtha* (50%), *Vata Kapha Prakriti* (47%), *Madhyama Atura Bala* (76%), and belonging to overweight criteria (66%). In maximum patients *Kapha Dushti* (50.11%) and *Medovaha Sroto Dushti* (45.03%) *Lakshana* were observed.

The average duration required for *Niruha Basti* administration was 25.75 s and for *Anuvasana Basti* 16.75 s. Average retention time was observed 6.25 min in *Asthapana* and 5.48 h in *Anuvasana*.

Results

Effect of therapies on presenting complaints of diabetes

The effect of BG was significant in almost all complaints of *Madhumeha*. Highly significant ($P < 0.001$) improvement is found in *Prabhuta Mootrata* (frequency of urine), *Avila Mootrata* (turbidity of urine) and *Daurbalya* (weakness). Significant improvement ($P < 0.01$) was found in *Trishnadhikya* (polydypsia), *Karapada Daha* (burning sensation in palms and soles) and *Atisweda* (excessive perspiration) [Table 1].

Table 1: Comparative effect of therapies on presenting complaints of *Madhumeha*

Presenting complaints	BG		EG		χ^2	*P*
	NSI	SI	NSI	SI		
Prabhuta Mootrata (frequency of urine)	18	31	46	02	35.142	<0.001
Avil Mootrata (turbidity of urine)	19	30	39	09	16.472	<0.001
Kshudhadhikya (polyphagia)	33	16	44	04	7.339	<0.01
Trishnadhikya (polydypsia)	36	13	46	02	7.645	<0.01
Karpadadaha (burning sensation)	27	22	39	09	7.624	<0.01
Atisweda (excessive perspiration)	29	20	42	06	9.909	<0.01
Daurbalya (weakness)	02	47	37	11	50.757	<0.001

BG: *Basti* group, EG: Enalpril group, NSI: Non significant increase, SI: Significant increase

Effect of therapies on urine microalbumin

BG provided 61.50% of relief in urine microalbumin, whereas EG provided 26.46% relief. The results in BG were statistically highly significant ($P < 0.001$) whereas in EG, the result was statistically significant ($P < 0.01$) in reduction of urine microalbumin. In BG statistically insignificant decrease in urine creatinine was observed although in EG insignificant increase in urine creatinine was seen [Table 2].

Effect of therapies on GFR

BG and EG both were shown statistically insignificant ($P > 0.05$) results on GFR.

Effect of therapies on BP

BG shows 15.04% and EG shows 3.45% relief on systolic BP. On diastolic BP, BG shows 15.49% and EG shows 03.03% relief. On comparison of results within the groups there was a highly significant difference ($P < 0.001$) in systolic and diastolic BP [Table 3].

Effect of therapies on BSL

BG treated group shows highly significant ($P < 0.01$) decrease in fasting blood sugar by 13.50% and EG also shows a significant decrease ($P < 0.05$) in fasting blood sugar by 16.06%. In post-prandial blood sugar also BG showed statistically highly significant ($P < 0.001$) relief by 15.21% and EG showed statistically insignificant decrease ($P > 0.05$) by 9.92%. In comparison, no significant differences were observed in both fasting and post-prandial BSL when the values from BG were compared with EG [Table 4].

Effect of therapies on hematological and biochemical parameters

There was statistically insignificant change ($P > 0.05$) in all hematological and biochemical parameters in both the groups. However, there is a change from pre-test to post-test mean value of above parameters, which is within the physiological limit.

Overall effect of therapies

In BG, 40.81% showed moderate improvement, 38.78% showed mild improvement, whereas 20.41% patients were unchanged. In EG, 31.25% showed mild improvement, none of them got complete remission and marked improvement, 2.08% got moderate improvement, whereas 66.67% remained unchanged.

Discussion

Microalbuminuria comes under the heading of incipient nephropathy and it is not associated with significant clinical signs or any changes other than a very small increase in BP. However, symptoms like frothy urine can be seen in some patients with incipient nephropathy in OPD.

The study drug was adopted based on the expert practitioners' views. Registered patients were administered trial therapy for 8 days and control drug for 1 month. *Basti* schedule was consisted of *Anuvasana Basti* on 1st and last day and consecutive *Asthapana Basti* for 6 days. The *Yoga Basti* schedule was not followed *per se* because; *Anuvasana* is not indicated in *Bahudoshavastha* like *Prameha*, where it may produce deleterious effects due to its *Utkleshana* (dislodgement of *Dosha*) property.[16] To attain unctuousness to the gastrointestinal tract and avoid vitiation of *Vata* due to

Table 2: Effect of therapies on urine microalbumin and creatinine level

Group	*N*	Mean score		Mean difference	% Relief	SD	SEM	*t*	*P*
		BT	AT						
Microalbuminuria (mg/24 h)									
BG	49	149.676	57.624	92.051	61.500↓	116.844	16.692	5.515	<0.001
EG	48	116.525	85.694	30.831	26.459↓	76.335	11.018	2.798	<0.01
Creatinine level (µmol/L)									
BG	49	37.299	29.099	8.200	21.985↓	33.987	4.855	1.689	>0.05
EG	48	32.140	41.098	–8.958	27.872↑	31.258	4.512	1.985	>0.05

BG: *Basti* group, EG: Enalapril group, SD: Standard deviation, SEM: Standard error of mean, BT: Before treatment, AT: After treatment, ↓: Decrease, ↑: Increase

Table 3: Effect of therapies on blood pressure

Blood pressure (mmHg)	Mean difference		SD	SEM	*t*	*P*
	BG	EG				
Systolic	22.000	5.042	11.205	2.276	7.452	<0.001
Diastolic	14.735	2.833	7.559	1.535	7.753	<0.001

BG: *Basti* group, EG: Enalapril group, SD: Standard deviation, SEM: Standard error of mean

Table 4: Effect of therapies on blood sugar level (paired '*t*' test)

Group	*N*	Mean score		Mean Diff	% of Relief	SD	SEM	*t*	*P*
		BT	AT						
Fasting blood sugar (mg/dl)									
BG	49	180.082	155.776	24.306	13.497↓	55.114	7.873	3.087	<0.01
EG	48	185.063	155.333	29.729	16.064↓	87.197	12.586	2.362	<0.05
Post prandial blood sugar (mg/dl)									
BG	49	236.592	200.612	35.980	15.208↓	69.816	9.974	3.607	<0.001
EG	48	230.708	207.833	22.875	9.915↓	96.872	13.982	1.636	>0.05

BG: *Basti* group, EG: Enalapril group, BT: Before treatment, AT: After treatment, ↓: Decrease

Asthapana; *Anuvasana Basti* was scheduled for the 1st and last day of trial therapy. Continuous six *Asthapana* were given looking into the pathogenesis of the research question; that is, *Kapha* and *Meda* in excess causing *Avarana* to movement of *Vata*, *Bahudoshatva* and to attain cleansing effect. Though in classics, continuous *Asthapana* is contraindicated; however, still according to conditions (*Avastha*) it can be done.[17] As nephropathy patients are in a state of *Bahudoshavastha*, in such condition purification through *Basti* will be the best treatment. Therefore, the experiential (*Anubhuta*) combination of *Basti* was followed.

Mode of action of *Gokshura-Punarnava Basti* in microalbuminuria

In *Avaranajanya Madhumeha*, etiological factors mainly vitiates the *Kapha* and *Pitta* in turn affect the *Jatharagni* and *Dhatwagni* and disrupts metabolism and produces an excess of deranged quality *Rasa*, *Meda*, *Kleda*, *Rakta*, etc.[18] All these vitiated *Dushyas* obstructs the path of *Vata* (*Avarana*), which gets aggravated and changes its path and carries vital *Dhatus* toward *Basti* and excretes them out causing depletion.[19]

It could increase the digestive power (*Agni*); purifies each and every channel of the body and also helps to normalize the function of *Rasavaha*, *Medovaha*, *Mootravaha Srotasa*. *Basti* drugs after absorption conceivably helps in disintegration of pathogenesis as it possess anti-diabetic activity. It may alter the absorption of carbohydrate and fat from the intestine.

The *Gokshura-Punarnava Basti* was found effective in decreasing *Prameha* symptoms by virtue of *Kledaharana*, *Kapha-Pitta Nirharana*[20] and *Basti Nanakarmakartwat*.[21] *Basti* itself is a procedure having rejuvenation effect. Furthermore, due to correction of digestive fire and *Sroto Shodhana* adds to the effect of drug properties. That in turn may help to form the *Dhatus* in proper proportion with appropriate qualities. *Ruksha* quality of *Punarnava* and honey may help to reduce the *Kleda*. Drugs such as *Punarnava* and sesame oil with their *Ushna Veerya* may act over *Vata* and vitiated *Kapha* by combating their *Sheeta Guna*. Maximum drugs are having *Katu Vipaka* that reduces vitiated *Kapha* and may cause *Sroto Shodhana*. All these factors probably help in reduction of *Bahudrava Shlesma* and in turn reduction of vitiated *Meda* and *Kleda*. Thus, once these factors get normalized in the body they in turn make clear the path of *Vata*, which stops the depletion of vital *Dhatus* and restore normal physiology. Thus, pathology gets alleviated. Drug used in *Basti* on virtue of its properties are proven as an anti-diabetic and *Tridoshashamaka* effect. Researches proved chloroform extract of *B. diffusa* has significant anti-diabetic activity[22,23] and hypoglycemic function of *T. terrestris* is primarily concentrated in the phytochemicals known as sapopin.[24]

T. terrestris and *B. diffusa* acts as ACE inhibitors[25] and anti-oxidant.[26] *B. diffusa* is clinically proved as a useful and safe drug in patients of nephrotic syndrome[27] and its action as kidney regeneration.[28] Antioxidant action of study drug and procedure may prevent further formation of reactive oxygen species, exerting antioxidant properties.

No adverse effects (*Vyapada*) were observed during and after the study. Insignificant variations (increase or decrease) were observed in hematological and bio-chemical parameters (excluding BSL). This proves that this treatment is safe.

Conclusion

Microalbuminuria in DM can be considered as a complication of *Madhumeha*. There is no direct correlation of diabetic microalbuminuria as such in Ayurveda. *Gokshura-Punarnava Basti* was found to be more effective in reducing microalbuminuria in DM as compared to enalapril. A significant decrease was seen in BP and BSL in BG. The variations in biochemical and hematological parameters were within the physiological limits, hence *Gokshura-Punarnava Basti* can be safely practiced in cases of microalbuminuria.

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