Clinical Research

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

Rajkala S. Ramteke, Anup B. Thakar¹, Amiben H. Trivedi², Panchakshari D. Patil³

Lecturer, Department of Panchakarma, GJ Patel Institute of Ayurveda and Research, New Vallabh Vidyanagar, Anand, ¹Associate Professor and I/C Head, Department of Panchakarma, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar, ²Associate Professor, Department of Medicine, MP Shah Medical College and GG Hospital, Jamnagar, ³Senior 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 (decocion enema) of Gokshura and Punarnava Kwatha (decocion), 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.

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 Moothra Virechaneeya Gana (diuretic drugs)[⁷] by
Charaka. Hence, it acts as Anulomana (downward movement) of Apana Vata. This corrects the Gati (movement) of Vata thereby influencing it in a positive way. Gokshura is also a proven anti-diabetic agent.[9] Its Bastishodhana[10] (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[9] 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 MCI/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.

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 lifestyle was advised in both groups. All patients in Basti group (BG) were explained the Pathyaapathy 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 inhibitor – 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 Dushhti (50.11%) and Medovaha Sroto Dushti (45.05%) Lakshana were observed.

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

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), Karpadadaha (burning sensation) in BG and Prabhuta Mootrata (frequency of urine), Daurbalya (weakness) in EG [Table 1].

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 Anuvasa Basti on 1st and last day and consecutive Asthapaana Basti for 6 days. The Yoga Basti schedule was not followed per se because; Anuvasa is not indicated in Bahudoshavastha like Prameha, where it may produce deleterious effects due to its Utkleshana (dislodgement of Dosha) property.[6] 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

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean score</th>
<th>Mean difference</th>
<th>% Relief</th>
<th>SD</th>
<th>SEM</th>
<th>t</th>
<th>P</th>
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<tbody>
<tr>
<td></td>
<td>BT</td>
<td>AT</td>
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<tr>
<td>Microalbuminuria (mg/24 h)</td>
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<tr>
<td>BG</td>
<td>49</td>
<td>149.676</td>
<td>57.624</td>
<td>92.051</td>
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<td></td>
<td></td>
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<tr>
<td>EG</td>
<td>48</td>
<td>116.525</td>
<td>85.694</td>
<td>30.831</td>
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<td>Creatinine level (μmol/L)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>BG</td>
<td>49</td>
<td>37.299</td>
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<td>EG</td>
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<td>32.140</td>
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<td>−8.958</td>
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Table 3: Effect of therapies on blood pressure

<table>
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<tr>
<th>Blood pressure (mmHg)</th>
<th>Mean difference</th>
<th>SD</th>
<th>SEM</th>
<th>t</th>
<th>P</th>
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<tr>
<td></td>
<td>BG</td>
<td>EG</td>
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<tr>
<td>Systolic</td>
<td>22.00</td>
<td>5.042</td>
<td>11.205</td>
<td>2.276</td>
<td>7.452</td>
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<tr>
<td>Diastolic</td>
<td>14.735</td>
<td>2.833</td>
<td>7.559</td>
<td>1.535</td>
<td>7.753</td>
</tr>
</tbody>
</table>

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)

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean score</th>
<th>Mean Diff</th>
<th>% of Relief</th>
<th>SD</th>
<th>SEM</th>
<th>t</th>
<th>P</th>
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<tbody>
<tr>
<td></td>
<td>BT</td>
<td>AT</td>
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<td>Fasting blood sugar (mg/dl)</td>
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<td></td>
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<tr>
<td>BG</td>
<td>49</td>
<td>180.082</td>
<td>155.776</td>
<td>24.306</td>
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<td>EG</td>
<td>48</td>
<td>185.063</td>
<td>155.333</td>
<td>29.729</td>
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<tr>
<td>Post prandial blood sugar (mg/dl)</td>
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<tr>
<td>BG</td>
<td>49</td>
<td>236.592</td>
<td>200.612</td>
<td>35.980</td>
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<td></td>
<td></td>
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<tr>
<td>EG</td>
<td>48</td>
<td>230.708</td>
<td>207.833</td>
<td>22.875</td>
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</table>

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

Asthapana; Anuvasaana 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 Asthapaana is contraindicated; however, still according to conditions (Avastha) it can be done. As nephropathy patients are in a state of Bahudoshavastha, in such condition purification through Basti will be the best treatment. Therefore, the experiencial (Anubhuta) combination of Basti was followed.

Mode of action of Gokshara-Punarnava Basti in microalbuminuria

In Avaranajanyaya Madhumeha, etiological factors mainly vitiates the Kapha and Pitta in turn affect the Jatharagni and Dhatvagni and disrupts metabolism and produces an excess of deranged quality Rasa, Meda, Kleda, Rakta, etc. 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.

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, Moortavaha 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 Gokshara-Punarnava Basti was found effective in decreasing Prameha symptoms by virtue of Kledaharana, Kapha-Pitta Nirharana and Basti Nanakarmakartwat. 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 Bahudhra 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 and hypoglycemic function of T. terrestris is primarily concentrated in the phytochemicals known as sapopin.
T. terrestris and B. diffusa acts as ACE inhibitors and anti-oxidant. B. diffusa is clinically proved as a useful and safe drug in patients of nephrotic syndrome and its action as kidney regeneration. 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.

References