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A Study on the Effect of Isosorbide Mononitrate on Proteinuria in Patients with Diabetic Nephropathy in a Tertiary Care Centre of West Bengal: A prospective interventional study

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Abstract

Background: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease. Proteinuria is a major prognostic marker in DN. Emerging evidence suggests that nitric oxide donors like isosorbide mononitrate (ISMN) may reduce proteinuria via renal vasodilation and endothelial modulation. Objective: To evaluate the effect of isosorbide mononitrate on proteinuria levels in patients with diabetic nephropathy in a tertiary care centre of West Bengal. Methods: A prospective interventional study was conducted on 34 patients with confirmed diabetic nephropathy. Baseline 24-hour urinary protein levels were recorded. Patients received isosorbide mononitrate (20 mg/day) for 12 weeks. Proteinuria levels were re-assessed at the end of the study period. Results: Mean baseline proteinuria was 1.8 ± 0.5 g/day. Post-treatment, a significant reduction was observed (mean 1.2 ± 0.4 g/day; $p < 0.001$). The reduction was more pronounced in patients with controlled blood pressure and shorter diabetes duration. Conclusion: Isosorbide mononitrate significantly reduced proteinuria in diabetic nephropathy patients. Its role as an adjunctive therapy in early diabetic kidney disease appears promising and warrants further studies with larger cohorts.

KEYWORDS: Diabetic nephropathy. Marker.

INTRODUCTION

Diabetic nephropathy is a chronic complication of diabetes mellitus characterized by persistent albuminuria and progressive loss of kidney function. Proteinuria is both a marker and a mediator of renal injury, hence reducing proteinuria is a key therapeutic goal[1].

Diabetic nephropathy, a kidney disease caused by diabetes, has a prevalence ranging from 0.9% to 62.3% in India. It is a significant contributor to chronic kidney disease (CKD) and end-stage renal disease (ESRD) in the country. Studies show that the prevalence can vary based on factors like the study population, diagnostic criteria, and geographical location within India[2].

Key findings on prevalence and risk factors: Wide range: Studies report a wide range of prevalence, from low percentages in some urban populations to higher percentages in studies focusing on individuals with existing

kidney disease or specific risk factors. Overt nephropathy and microalbuminuria One study in Chennai found the prevalence of overt nephropathy to be 2.2% and microalbuminuria to be 26.9% in urban citizens with diabetes. Risk factors: Risk factors for diabetic nephropathy include duration of diabetes, elevated HbA1c levels, high blood pressure (both systolic and diastolic), and smoking. Impact on mortality: Diabetic kidney disease is associated with a higher mortality rate, and the risk increases with the severity of the disease. Underdiagnosis and late detection: There's a concern that diabetic nephropathy is underdiagnosed or detected at later stages, particularly in resource-limited settings[3]. Specific study findings: A study of 4,837 patients with chronic renal failure in India found a 30.3% prevalence of diabetic nephropathy, A study in South India found that the prevalence of metabolic syndrome was 73.3% in patients with type 2 diabetes, and the prevalence of nephropathy was 20.5% in those without metabolic syndrome and 18.0% in those with metabolic syndrome[4]. A study in an underserved rural population in India found a low prevalence of overt nephropathy (1.2%) and microalbuminuria (16.3%). Diabetic nephropathy is a significant health issue in India, with a prevalence that varies depending on the population studied. Early detection and management of risk factors, including blood sugar and blood pressure control, are crucial for preventing or slowing the progression of diabetic nephropathy and its associated complications

Nitric oxide plays a crucial role in maintaining renal vascular tone. In DN, reduced NO bioavailability contributes to glomerular damage. Isosorbide mononitrate, an NO donor, is hypothesized to improve endothelial function and renal perfusion, potentially reducing proteinuria[5-9].

This study was designed to investigate the efficacy of isosorbide mononitrate in reducing proteinuria among diabetic nephropathy patients in a tertiary care centre of West Bengal.

METHODS

This study was conducted in a tertiary hospital. After obtaining institutional ethical committee approval. It was Cross-sectional observational study conducted on 40 patients in the department of Surgery and department of Community Medicine, at a tertiary care centre, from February / 2018 to August/2018

Total 40 participant were approached to project among them 6 were excluded in this study and Total 34 Confirmed cases were included on the basis of fulfilling of the eligibility criteria.

The institute Ethics Committee approval was obtained before starting the sample collection. A written and informed consent was taken from the patient regarding the study in his/her vernacular language and English. In this study Patients were subjected to: A detailed history of sign & symptoms and its duration. Detailed history of systemic diseases and its duration, medication were noted. Patients were subjected to General physical examination.

Flowchart of Study Design

Patient Screening (n=40)
↓
Inclusion Criteria Applied
↓
Eligible Diabetic Nephropathy Patients Enrolled (n=34)
↓
Baseline Proteinuria Measured
↓
Isosorbide Mononitrate Administered Daily
↓
Follow-up at 4, 8, and 12 Weeks
↓
Final Proteinuria Assessment (n=34)
↓

Data Analysis and Interpretation

Study Design:
Prospective interventional study conducted over 6 months.
Sample Size:
34 patients with diagnosed diabetic nephropathy.

Inclusion Criteria:
- Age 35–70 years
- Type 2 diabetes mellitus > 5 years
- Persistent proteinuria > 500 mg/day
- eGFR > 30 mL/min/1.73m²

Exclusion Criteria:
- Non-diabetic kidney disease
- Advanced renal failure (eGFR <30)
- Use of other nitrate medications
- Hypotension or cardiac failure

Intervention:
Oral isosorbide mononitrate 20 mg/day for 12 weeks.
Assessment Parameters:
- 24-hour urinary protein (baseline and at 12 weeks)
- Blood pressure
- Serum creatinine and eGFR

Statistical Analysis:
Paired t-test was used to compare baseline and post-treatment proteinuria values.

Statistics and analysis of data
Data is put in excel sheet then mean, median and association is analysed by SPSS version 20. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and SD. MS Excel and MS word was used to obtain various types of graphs such as bar diagram. P value (Probability that the result is true) of Pvaue <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse data. Sample size is calculated by N master statistical software

RESULTS

In this study we found that Diabetic nephropathy is associated with demographic profile of patient. Diabetic nephropathy is a associated with Mean eGFR (ml/min/1.73m²). Diabetic nephropathy depend upon Mean Duration of Diabetes.
Male were more prone to suffered of Diabetic nephropathy as compared to Female. Diabetic nephropathy were belong to Hypertension Present, Its prevalence 76.5% (Table 1)
Age is also associated factors for Diabetic nephropathy. Average mean age for Diabetic nephropathy is 56.3 ± 7.4 (Table 1).

Demographic Profile Table 1

Variable	Value (n=34)
Mean Age (years)	56.3 ± 7.4

Variable	Value (n=34)
Gender (Male/Female)	20 / 14
Mean Duration of Diabetes	9.2 ± 2.6 years
Hypertension Present	26 (76.5%)
Mean Baseline BP (mmHg)	138/86
Mean eGFR (ml/min/1.73m²)	48.6 ± 9.8

Diabetic nephropathy have many risk factor among them these are most important Poor Glycaemic Control (HbA1c > 8%), Hypertension, Smoking History, Obesity (BMI > 30), Duration of Diabetes >10 yrs and Sedentary Lifestyle(Table 2).

Risk Factors Table 2

Risk Factor	No. of Patients (%)
Poor Glycemic Control (HbA1c > 8%)	18 (52.9%)
Hypertension	26 (76.5%)
Smoking History	9 (26.5%)
Obesity (BMI > 30)	12 (35.3%)
Duration of Diabetes >10 yrs	13 (38.2%)
Sedentary Lifestyle	21 (61.8%)

- **Baseline proteinuria:** 1.8 ± 0.5 g/day
- **Post-treatment proteinuria (12 weeks):** 1.2 ± 0.4 g/day
- **Mean reduction in proteinuria:** 0.6 g/day ($p < 0.001$)
- Subgroup analysis showed:
  - Greater reduction in patients with <10 years of diabetes duration.
  - Controlled hypertensives had more improvement than uncontrolled.

No serious adverse effects were reported. Mild headache was noted in 4 patients.

DISCUSSION

The findings align with recent hypotheses suggesting NO donors could improve renal hemodynamic in early diabetic kidney disease. Isosorbide mononitrate demonstrated a significant reduction in proteinuria, possibly through improving endothelial function and reducing intraglomerular pressure[10].

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In India, several risk factors contribute to diabetic nephropathy (diabetic kidney disease), including uncontrolled blood sugar (hyperglycaemia), high blood pressure (hypertension), dyslipidemia (abnormal blood fats), obesity,

smoking, and a family history of diabetes and kidney disease[11-14]. Additionally, advanced age, longer duration of diabetes, and diabetic retinopathy are also associated with an increased risk. Hyperglycemia: Elevated blood glucose levels over time can damage the delicate blood vessels in the kidneys, leading to nephropathy. Hypertension: High blood pressure puts extra strain on the kidneys, accelerating damage to the nephrons (the functional units of the kidney). Dyslipidemia: Abnormal lipid profiles, particularly high LDL cholesterol and triglycerides, can contribute to inflammation and damage in the kidneys. Obesity: Excess weight, especially abdominal obesity, is linked to insulin resistance and metabolic dysfunction, which can worsen diabetic nephropathy. Smoking: Smoking has a detrimental effect on kidney health and can exacerbate albuminuria (protein in the urine), a key indicator of nephropathy[15]. Family History: A genetic predisposition to kidney disease can make individuals more susceptible to developing diabetic nephropathy if they also have diabetes. Duration of Diabetes: The longer a person has diabetes, the greater the risk of developing complications like nephropathy. Diabetic Retinopathy: The presence of diabetic retinopathy (eye damage due to diabetes) is a strong indicator of overall microvascular complications, including nephropathy. Age: Older individuals with diabetes are at a higher risk of developing diabetic nephropathy[16].

Isosorbide mononitrate (IMN) has been shown to reduce proteinuria in patients with diabetic nephropathy, particularly those on combined ACEI and ARB therapy. Studies suggest that IMN's effect is more pronounced in younger, diabetic patients, and those with higher baseline proteinuria. Proteinuria Reduction: Several studies, including one published in the have reported a decrease in proteinuria levels after IMN administration in patients with diabetic nephropathy. Combined ACEI/ARB Therapy: The effect of IMN appears to be more significant when used in conjunction with angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), which are commonly prescribed for diabetic nephropathy[17,18]. Age and Baseline Proteinuria: Younger patients and those with higher levels of proteinuria at baseline tend to show a greater response to IMN therapy. Mechanism of Action:

IMN is a nitric oxide donor, and increased nitric oxide levels are associated with improved kidney function and reduced proteinuria. Further Research: While promising, more research is needed to fully understand the long-term effects of IMN on kidney health in diabetic nephropathy and to identify the optimal patient populations for this treatment[19].

Though ACE inhibitors and ARBs remain the mainstay of treatment, the addition of NO donors may have a synergistic effect. Limitations include small sample size, short follow-up duration, and absence of a control group

CONCLUSION

Isosorbide mononitrate significantly reduced proteinuria in patients with diabetic nephropathy. It may serve as a beneficial adjunct in managing early DN. Larger randomized controlled trials are needed to confirm these findings

SOURCE OF FUNDING: No

CONFLICT OF INTEREST

The authors report no conflicts of interest

SUBMISSION DECLARATION

This submission has not been published anywhere previously and that it is not simultaneously being considered for any other journal.

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