WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 10, 853-860. Research Article ISSN 2277– 7105

DIABETIC NEPHROPATHY: MEANS OF PHARMACOLOGICAL INTERVENTION

***Dr. Suma Jayaram[1] and Dr. Basavaraj Bhandare[2]**

[1]Post Graduate, [2]Professor and Head, Department of Pharmacology, Rajarajeswari Medical College and Hospital, Bangalore, Karnataka, India.

Article Received on
19 July 2015,

Revised on 11 Aug 2015,
Accepted on 02 Sep 2015

***Correspondence for Author**
Dr. Suma Jayaram
Post Graduate,
Department of Pharmacology,
Rajarajeswari Medical College and Hospital,
Bangalore, Karnataka,
India.

ABSTRACT

Background: Diabetic nephropathy is the leading cause of chronic kidney disease and end-stage renal disease in developing countries. It is characterized by persistent albuminuria and a progressive decline in renal function. **Objective:** The objective of this study was to analyze the prescribing pattern and rationality of drug treatment in diabetic nephropathy patients in accordance to Kidney Disease Outcomes quality Initiative (KDOQI) guidelines. **Material & methods**: After obtaining IEC approval, a prospective, observational non interventional study was conducted in The Department of Nephrology in a tertiary care hospital for six months. A total of 116 consenting diabetic nephropathy patients' demographics and pharmacological interventions were analyzed. Data obtained was evaluated using descriptive statistics. **Results:** The patients were in the age group of 50 - 70 years with a documented diagnosis of diabetes mellitus, hypertension and proteinuria. There was a male preponderance of 77%. Anti hypertensive poly-therapy was observed. As monotherapy, Enalapril (75%) was the most common drug prescribed, followed by Telmisartan (25%). As combination therapy, enalapril with chlorthalidone was the most common. Mixtard 50(50% soluble and 50% isophane) was the most commonly prescribed antidiabetic medication (86%). Statins were administered to all the patients, atorvastatin (78%) being the most common. **Conclusion:** In this study antihypertensive poly-therapy was observed in the majority, with ACE inhibitors being the most frequently prescribed. Insulin mixtard was preferred to hypoglycemic drugs. It was found that the prescription pattern analyzed in this study was adherent to the KDOQI guidelines.

KEYWORDS: Albuminuria, ACE Inhibitors, Diabetic nephropathy, Insulin.

DIABETIC NEPHROPATHY: MEANS OF PHARMACOLOGICAL INTERVENTION

INTRODUCTION

Diabetic Nephropathy (DN) is a microvascular complication of diabetes mellitus ranging from renal hyper filtration to end stage kidney disease and is responsible for significant morbidity and mortality among the diabetic population.[1] It is characterized by persistent albuminuria and a progressive decline in renal function.[2] The overall prevalence of diabetic nephropathy varies from 20 - 40% in diabetic patients.[2]

The pathogenesis of diabetic nephropathy is multifactorial and include genetic predisposition, poor glycaemic control, hypertension, dyslipidemia and smoking.[3]

Microalbuminuria (30-300mg/day) recognized as an early predictor of diabetic nephropathy, reflects a stage of endothelial dysfunction and is a risk factor for cardiovascular disease and mortality.[4]

Prevention, early detection and aggressive intervention are needed to retard the progression of diabetic nephropathy to end stage renal failure. Treatment of DN has focused on the integrated control of hyperglycaemia, hypertension and dyslipidaemia to reduce microalbuminuria.[5]

Reno protective agents like Angiotensin Converting Enzyme inhibitors (ACEI) and Angiotensin receptor blockers (ARBs),[5, 6] have been shown to reduce microalbuminuria as well as overt proteinuria, associated with Diabetes.

Slowing the decline of renal function from Diabetic Nephropathy to End Stage Renal Disease is of paramount importance .The information on drug prescribing patterns can provide a framework for continuous prescription in a hospital setting. This can help the prescribers to improve patient management by rationalizing prescribing practices.

AIMS AND OBJECTIVES

The objective of this study was to analyze the prescribing pattern and to rationality of drug treatment in diabetic nephropathy patients in accordance to Kidney Disease Outcomes quality Initiative (KDOQI) guidelines.

MATERIALS AND METHODS

This study was a prospective observational non interventional study conducted following approval by the Institutional Ethical Committee. 116 inpatients diagnosed with Diabetic Nephropathy in the Department of Nephrology at Rajarajeswari Medical College and Hospital were included in the study. Diagnosis was based on KDOQI guidelines- 2 of 3 urine samples should fall within the microalbuminuric or macroalbuminuric range. Patients fulfilling the inclusion criteria were taken in to the study.

Inclusion Criteria

1. Patients above 50 years of age.
2. Patients of both sexes.
3. Patients diagnosed with diabetic nephropathy.

Exclusion Criteria

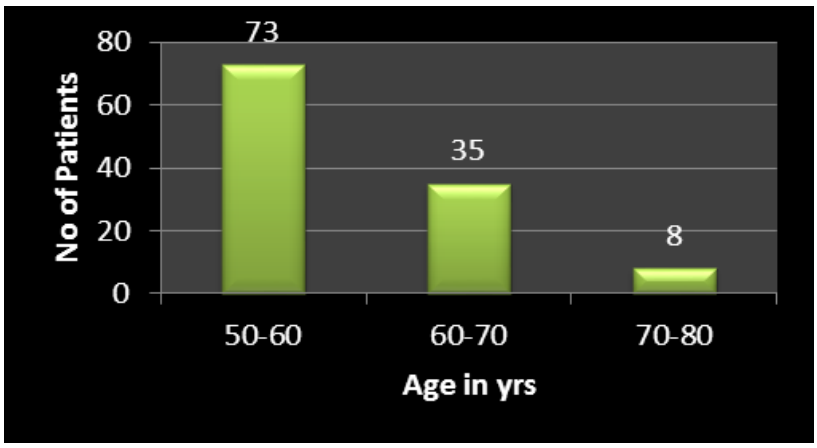
1. Pregnant & lactating women.
2. Patients with Type 1 diabetes mellitus.
3. Patients with non diabetic kidney disease.
4. Patients who are on dialysis support.

Statistical analysis

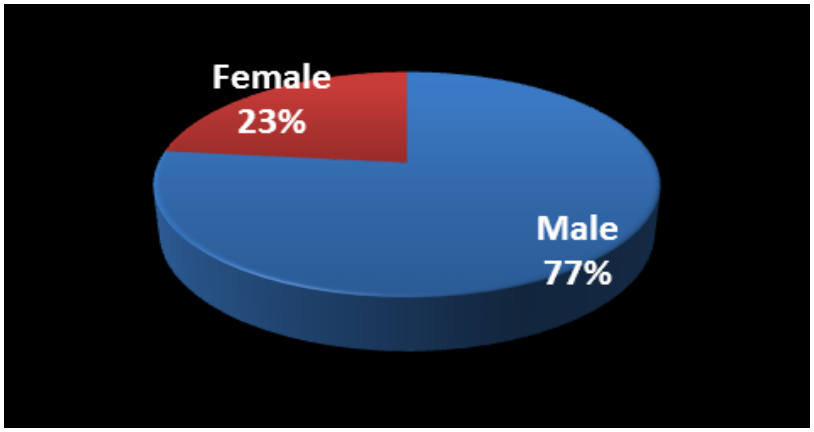
Results were analyzed using descriptive statistics and expressed as percentages and mean.

RESULTS

Majority of the patients were in the age group of 50-60 years. Out of the 116 patients 77% were male and 23% female.



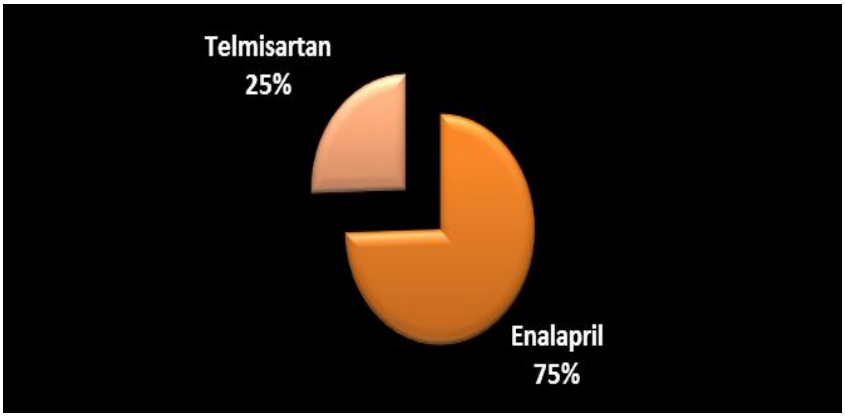
Graph 1: Age Distribution



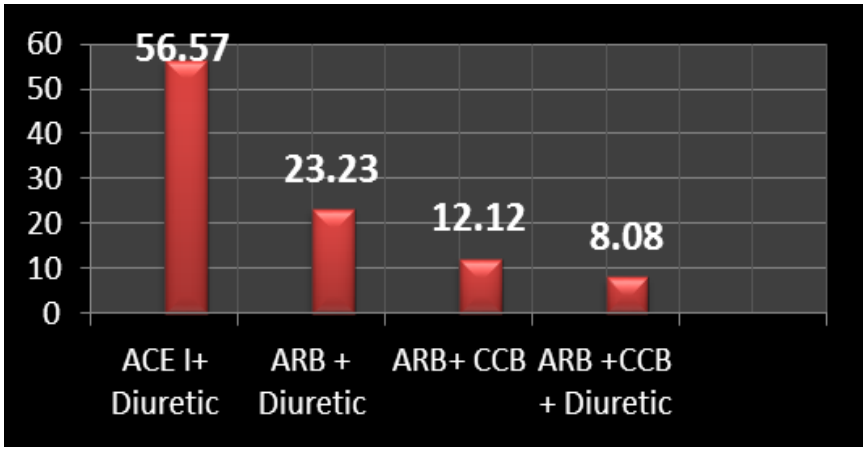
Graph 2: Gender Distribution

Table 1: Associated Risk factors

Smokers	67.2%
Dyslipidemia	59.4%
obesity	36.2%



Graph 3: Drugs used as monotherapy



Graph 4: Combination therapy

Table 2: Classes of drugs utilized

Classes of Drugs	No of patients received the drug
ACE inhibitor	68
ARB	48
CCB	20
Diuretics	85
Statins	116
Insulin and/or OHAs	116
Phosphate binders	12

Table 3: Percentage distribution of various drugs

Drug class	Percentage of usage
ACE inhibitors	Enalapril (75%), Ramipril (25%)
ARBs	Telmisartan(76%), Losartan (24%),
CCBs	Amlodipine (84%), Cilnidipine (16%)
Statins	Atorvastatin(78%), Rosuvastatin (22%)
Insulin	Mixtard (93%)
Sulfonylurea	Glimepiride (89%), Glipizide (11%)
Phosphate binders	Calcium carbonate (10.34%)

DISCUSSION

In our study there was a male preponderance with the mean age above 50 years as similar to a previous study.[7] Hypertension and diabetic retinopathy were the two associated major co-morbid factors of DN.

According to the KDOQI guidelines, hypertensive patients with diabetes and kidney disease stages 1-4 should be treated with an ACE inhibitor or an ARB, usually in combination with a diuretic. Target blood pressure being < 130/80 mm Hg and patients with LDL-C > 100 mg/dL should be treated with a statin.[4]

Anti-hypertensives were prescribed to all study patients which is an indication of the high prevalence of cardiovascular morbidity in DN.[8] 85.4% patients were prescribed multidrug combinations as per, The seventh report of the Joint National Committee (JNC VII) to achieve the target blood pressure of 130/80 mm of Hg in diabetic hypertensive patients.[9] Antihypertensives prescribed were ACEI/ARB (68.5%) followed by diuretics (64.6%) and was similar to previous study done by Mogensen et al.[10]

As monotherapy, Enalapril(70.68%) was the most common drug prescribed, followed by Telmisartan (29.32%). As combination therapy, enalapril with hydrochlorothiazide was the most common, which is similar to a study conducted by Patel et al.[11]

In addition to antihypertensive effect of ACEIs and ARBs in Diabetic nephropathy, there is reduction in the risk of doubling of plasma creatinine and developing renal failure.[12,13] Diuretics potentiate the antihypertensive and anti-proteinuric effect of ACEIs and ARBs which is observed in 64.6% of patients who were on hydrochlorothiazide.[14]

A study by Robert D et al, suggests that administration of Fixed drug combinations of an ACEI with a calcium channel blocker can effectively reduce albuminuria in type 2 diabetics with hypertension and nephropathy.[15]

Intensive glycaemic control reduces the rate and progression of microalbuminuria in diabetics. 93% patients received insulin as hypoglycemic agent, while Glimepiride was the most commonly used Oral hypoglycemic agent. This transfer to insulin treatment is due to avoidance of oral hypoglycaemic drugs, which can accumulate in uraemia and lead to hypoglycaemia.[16]

The usage of calcium carbonate is explained by the need for phosphate binders in late stage of DN.

Statins were prescribed to all patients along with advice for smoking cessation, dietary protein restriction and salt restriction.[17] as they play a major role in retarding the progression of diabetic nephropathy.[18]

In this study, about 53 % of 116 patients received anti-microbial agents which indicated the high prevalence of infections in patients hospitalized with DN.

Co prescribed medications were Proton pump inhibitors and multi vitamins. This multi-interventional approach is mandatory to slow the progression of the condition and for the reversal of renal micro vascular complications.

Early detection of DN, the multifactorial approach targeting the main risk factors (hyperglycemia, hypertension, dyslipidemia and smoking), and the use of renoprotective

agents such as the drugs that act on the renin-angiotensin-aldosterone system, may delay progression of kidney disease in DM, besides reducing cardiovascular mortality.

CONCLUSION

ACE inhibitors/ARBs + Diuretics are the preferred anti hypertensives with insulin as antidiabetic agent which was consistent with KDOQI Guidelines.

The principal limitation of the study was that it was collected from the outpatient and thus not be representative of prescription patterns across the state.

REFERENCES

1. Ranjith unnikrishnan, Mohan rema, Rajendra pradeepa M, Mohan deepa M. Prevalence and Risk Factors of Diabetic Nephropathy in an Urban South Indian. The Chennai Urban Rural Epidemiology Study (CURES 45) Blood Pressure., 2007; 30(8): 2019-24.
2. Clinical Practice Guidelines: Diabetic Nephropathy. July 2004 (Ministry of health, Malaysia) p.1-38.
3. Kanasaki K, Taduri G, Koya D. Diabetic nephropathy: The role of inflammation in fibroblast activation and kidney fibrosis. Front Endocrinol (Lausanne)., 2013; 4: 7.
4. Perkovic V, Verdon C, Ninomiya T, Barzi F, Cass A, Patel A, et al. The Relationship between Proteinuria and Coronary Risk: A Systematic Review and meta-analysis. PLoS Medicine., 2008; 5(10): 1486-95.
5. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. Am J Kidney Dis., 2007; 49: S12-154.
6. Freedman BI, Tuttle AB, Spray BJ. Familial predisposition to nephropathy in Africans and Americans with non-insulin dependent diabetes mellitus. Am J Kidney Dis., 1995; 25: 710-3.
7. John L, Rao PS, Kangasabapathy AS. Prevalence of diabetic nephropathy in non-insulin dependent diabetes. Indian J Med Res., 1991; 94: 24-9.
8. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICROHOPE substudy. Lancet., 2000; 355(9200): 253-9.
9. Weir MR, Hanes DS, Klassen DK. Antihypertensive drugs. In: Brenner, Rector, editors. The Kidney. Vol 2. 7th ed. Philadelphia: Saunders Publishers., 2004; 2387-94.
10. Mogensen CE, Neldam S, Tikkanen I, Oren S, Viskoper R, Watts RW. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with

hypertension, microalbuminuria, and non-insulin dependent diabetes: The candesartan and lisinopril microalbuminuria(CALM) study. BMJ., 2000; 321: 440-44.

11. Patel A, MacMahon S, Chalmers J, Neal B, Woodward M, Billot L, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. Lancet., 2007; 370: 829-40.
12. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD for The Collaborative Study Group. The effect of angiotensin converting enzyme inhibition on diabetic nephropathy. N Engl J Med., 1993; 329(20): 1456-62.
13. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S for the RENAAL Study Investigators. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med., 2001; 345(12): 861-9.
14. Flack JM. Maximising antihypertensive effects of angiotensin II receptor blockers with thiazide diuretic combination therapy: focus on irbesartan / hydrochlorothiazide. Int J Clin Pract., 2007; 61(12): 2093-102.
15. Robert D. Toto, Min Tian, Kaffa Fakouhi, Annette Champion, Peter Bacher. Effects of Calcium Channel Blockers on Proteinuria in Patients With Diabetic Nephropathy. The Journal of Clinical Hypertension., 2008; 10(10): 761-9.
16. Marshall SM. Clinical features and management of diabetic nephropathy. In: Pickup, Willams G, editors. Text book of diabetes. Vol 2. Oxford: Blackwell; 2003; 76.6.
17. Hong Sung, Yang Yuan and Zi-Lin Sun. Cholesterol contributes to Diabetic nephropathy through SCAP-SREBP2 pathway, Int J of Endocr., 2013; 1: 1-9.
18. Koya D, Haneda M, Inomata S, Suzuki Y. Long-term effect of modification of dietary protein intake on the progression of diabetic nephropath : A randomised controlled trial. Diabetologia., 2009; 53: 2037-45.