Current Research in Pharmaceutical Sciences
Available online at www.crpsonline.com

CRPS 2011; 01: 12-14

Received: 11/11/2011
Revised: 19/11/2011
Accepted: 22/11/2011

Narendra Singh Kushmakar

Department of Pharmacology and ToxicologyBR Nahata college of Pharmacy (A SIRO Recognized by DSIR ministry of Science and technology, GOI) Mhow – Neemuch Road Mandsaur (M.P) 458001

Abhilasha Jumnani
R.N.S. Institute of Pharmacy Sitholi Gwalior (M. P.)

Correspondence:
Narendra Singh Kushmakar

Department of Pharmacology and ToxicologyBR Nahata college of Pharmacy (A SIRO Recognized by DSIR ministry of Science and technology, GOI) Mhow – Neemuch Road Mandsaur (M.P) 458001

E-mail: nsk86pharma@gmail.com

Review on Diabetic Nephropathy

Narendra Singh Kushmakar*, Abhilasha Jumnani

ABSTRACT

Diabetic nephropathy (DN) is one of the most frequent life threatening complications of diabetes mellitus that occurs approximately 30-40%. It is usually attributed to metabolic consequences of abnormal glucose regulations, such as elevated blood and tissue levels of glycosylated proteins and hemodynamic changes within the kidney tissue. Recently there has been a renewed interest in understanding the role of reactive oxygen species (ROS), which play a key intermediate role in the pathophysiology of DN.

Keywords: diabetes mellitus, pathophysiology, Nephropathy, hyperglycaemia, anti oxidative mechanisms.

1. INTRODUCTION

Diabetic nephropathy (DN) is clinically defined as the progressive development of renal insufficiency in the setting of hyperglycaemia. Diabetic nephropathy (DN) is one of the most frequent life threatening complications of diabetes mellitus that occurs approximately 30-40%. Diabetic Nephropathy (DN) is one of the important micro vascular complications of diabetes mellitus. It is usually attributed to metabolic consequences of abnormal glucose regulations, such as elevated blood and tissue levels of glycosylated proteins and hemodynamic changes within the kidney tissue. Recently there has been a renewed interest in understanding the role of reactive oxygen species (ROS), which play a key intermediate role in the pathophysiology of DN. Chronic hyperglycaemia the main determinant of the initiation and progression DN, not only generates more reactive oxygen metabolites but also attenuates anti oxidative mechanisms through non-enzymatic glycation of the scavenging enzymes.[1,2]

Pathophysiology [2]

The pathology of diabetic nephropathy manifests histologically as diabetic glomerulo sclerosis, and is characterized by glomerular basement membrane thickening and mesangial expansion with increased extracellular matrix deposition. Mesangial expansion in diabetic glomerulo sclerosis may be considered the result of an imbalance between mesangial matrix protein production and degradation, favoring matrix protein accumulation. Overproduction of mesangial matrix proteins may be the result of glomerular hypertension and hyperglycemia-driven synthesis of prosclerotic cytokines such as transforming growth factor-B, angiotensin II and other growth factors.

Alternatively, elevated glucose levels may inhibit matrix protein degradation through non-enzymatic glycosylation and through the inhibition of protein degradative pathways. Thus the mediators of mesangial expansion constitute reasonable therapeutic targets when crafting a treatment strategy for diabetic nephropathy.

The diagnosis of diabetic glomerulosclerosis can be made with a renal biopsy. Light microscopic findings include increased mesangial matrix and thickening of the glomerular basement membrane. Immunofluorescence is characterized by increased staining of the glomerular and tubular basement membrane and Bowman's capsule for IgG and albumin in a linear pattern.

The presence of diabetic glomerulosclerosis can also be inferred from the clinical presentation. In the first placebo controlled, double blind study of the effect of ACE inhibitors diabetic nephropathy. A diagnosis of diabetic glomerulosclerosis was inferred if a patient had diabetes at least 7-10 years, exhibited demonstrable diabetic retinopathy, and had macroscopic proteinuria (albuminuria> 300mg/day). Diabetics with heavy proteinuria, but lacking the disease for a sufficient period of time and/or retinopathy, may require renal biopsy. These patients may suffer from primary glomerulopathies such as membranous nephropathy, or other glomerular diseases.

Diabetic glomerulopathy is the most common cause of nephrotic syndrome. Thus, early in the course of the disease, the serum creatinine is normal despite heavy proteinuria (> 3 grams/24 hours). In this regard, a diabetic patient presenting with elevated serum creatinine in the absence of macroscopic proteinuria should suggest additional diagnostic possibilities (such as other glomerulopathies). The diagnostic utility of proteinuria is less useful in patients treated with angiotensin converting enzyme inhibisstors (ACEi) or angiotensin II receptor blockers (ARBs), since both classes of drugs are known to reduce glomerular proteinuria.

Diagnostic parameters are:

- Renal biopsy
- Microalbuminurea
- Proteinurea
- Hypertension
- Glomerular filtration rate (GFR)
- Creatinine level
- Blood urea nitrogen (BUN)
- BGL
- Urine volume
- Body weight

TREATMENT AND MANAGEMENT [5,6,7]

Blood glucose control

Strict blood glucose control has been shown to delay the progression of diabetic related complications. The diabetic control and complication trail research (DCCT) reported that blood glucose control can delayed the progression of micro vascular complication. In this regard, every attempt should be made to obtained a glycosylated haemoglobin level>7% in patient with diabetes mellitus.

Blood pressure control

Both systolic and diastolic hypertension increases the progression of nephropathy. Aggressive treatment of hypertension may slow progression of nephropathy. At the time of diagnosis 30 present of non insulin dependent diabetes mellitus (NIDDM) patient have hypertension. Once nephropathy develops, close to 70 percent will be found to have high blood pressure. Therefore, blood pressure should be carefully monitored. In person with existing diabetic nephropathy or with evidence of either micro or macrovascular complication of diabetes, blood pressure should not be higher than 130/80.

Angiotensin II inhibition

Randomized, placebo controlled trial that showed the beneficial effect of ACE inhibitors in the treatment of diabetic glomerulosclerosis. Subsequent studies have confirmed this observation for both ACE inhibitors and ARBs. ACEi are first line therapy for diabetic glomerulosclerosis, but ARBs are regarded by some as equivalent. The beneficial effect of angiotensin II inhibition may result from:

a) A decline in glomerular hypertension (with slowing of mesangial expansion),

b) A reduction in proteinuria (with an expected decrease in proteinuria-associated prosclerotic events), and/or

c) A decrease in angiotensin II stimulated TGF-ß synthesis.

Dietary protein restriction

In some reports, dietary protein restriction has been shown to slow the loss of GFR in proteinuric diabetics, although the data are not conclusive. Protein restricted diets decrease glomerular hypertension, the production of prosclerotic cytokines, proteinuria, glomerulosclerosis and remain a viable therapeutic option for compliant patients.

Microalbuminuria

Microalbuminuria predates the development of macroscopic proteinuria. Macroscopic proteinuria is a major risk factor for progression to ESRD, thus measures to reverse Microalbuminuria may retard development of clinical nephropathy. Patients with microalbuminuria treated with ACEi demonstrate slower progression to macroproteinuria and renal failure. ADA guidelines suggest assessing for microalbuminuria (normal < 30 mg/24 hours or less 30 mcg/mg creatinine for a spot urine collection) at the time of diagnosis in all type 2 diabetics, in all type I diabetics with disease duration > 5 yrs and annually thereafter in both groups. Early and aggressive therapy of microalbuminuria, taken along with angiotensin II inhibition, is expected to slow disease progression.

Macroproteinuria

Heavy proteinuria is a risk factor for progressive renal failure, including diabetic nephropathy. There is abundant evidence that abrogating proteinuria with dietary and antihypertensive interventions, and/or ACE inhibitors, and/or ARBs, results in a slower loss of GFR in proteinuric states. In this regard, combination therapy with both ACE inhibitors and ARBs may provide benefit over ACE inhibitors alone. Finally, nephrotic diabetics treated with ACE inhibition, and exhibiting a reduction in proteinuria to < 1 gm / day, demonstrated stable renal function for up to 8 to 15 years. Taken together, therapeutic measures directed at reducing macroscopic proteinuria would be expected to slow the progression of diabetic nephropathy, and angiotensin II inhibition is the mainstay of therapy for attaining that goal.

Diabetic Nephropathy complications include

- Hypoglycemia
- Rapidly Progressing Chronic Kidney failure
- End-Stage Kidney Disease
- Hyperkalemia
- Severe Hypertension
- Complications of Hemodialysis
- Complications of Kidney Transplant
- Increased Infections

REFERENCES

1. Sharma S, Kulkarni SK, Chopra K. Curcumin, The active principal of turmeric, ameliorates diabetic nephropathy in rates. Clin exp pharmacol 2006; 33: 940-945.

2. Mclaughlin NG, Bhatt UY. Udayan. A review of the diagnosis and therapy of diabetic nephropathy.Northeast Florida Medicine Spring 2005; 27-32.

3. Vivian EM, Rubinstein GB. Pharmacologic management if Diabetic Nephropathy. Clinical Therapeutics. 2002; 24: 41-55.

4. Shumway TJ, Gambert RS. Diabetic nephropathy-pathophysiology and management. International Urology and Nephrology. 2002; 34:257-264.

5. Mclaughlin GN, Bhatt UY, Mars LR. A review of the diagnosis and therapy of Diabetic Nephropathy. Northeast Floroda Medicine 2005:27-31.

6. Fraser DJ, Phillips AO. Diabetic nephropathy. Medicine 2007; 35:503-506.

7. Watkins JP. ABC of Diabetes. 5th ed. BMJ Publishing Group Ltd, London 2003.