Diabetic Nephropathy and Chronic Renal Failure

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Diabetes in our time is an expression of success of prevention and treatment of past infective diseases. In the beginning of 20 century the life expectancy was 50 years, whereas today it is 75 years. This prolongation of life have resulted in a more frequent occuring of Ischemic Cardiomyopathy, Cancer and Diabetes. Diabetic Nephropathy is considered nowadays as a medical catastrophe of world wide dimensions.(1) This is a consequence of the vast widespread of Diabetes Mellitus in the world. While in 1994 there were 120 million people with Diabetes Mellitus, in 2010 this number will be 240 million and in 2025 there will be 300 million diabetics all over the world. Diabetes Mellitus present now an important social and medical problem. In U.S.A. type 2 diabetes is present in 12 % of people above 40 years of age. Type 2 diabetes affects now 135 million people worldwide. There is a great difference in the prevalence of type1 and type 2 diabetes. So the frequency of type 1 diabetes is ten times lower than type 2 diabetes. Type 2 diabetes is caracterised by insulin resistance i.e. the failure to respond to normal concetration of insulin and this is accompanied by compensatory hyperinsulinemia. The cinetics of insulin secretion are abnormal very early but in the later stages β cell secretion fails to overcome insulin resistance (2).

How one can diagnose Diabetes Mellitus? Today the diagnosis is performed no longer on the basis of oral glucose test but on the consistent increase of fasting glucose concetration.(> 7 mmol/l)(3).

Diabetic Nephropathy is in many countries the most frequent cause of ESRD. From 1982-1992 in US the prevalence of Diabetes as cause of ESRD increased from 27 % to 36 %. The annual incidence of ESRD from Diabetes Mellitus is 70 pts /million/year. The treament of Diabetic Nephropathy is rather expensive. In US the cost of Diabetic Nephropathy is 10 billion USD/year. Per patient the cost is 50.000 USD/year. The mortality rate of diabetics in Hemodialysis is 1.5-2.5 time higher than in non diabetics.Only 20 % of diabetics survive for 5 years in Hemodialysis.

Diabetic Nephropathy begins with Microalbuminuria which is considered as Incipient Nephropathy. Microalbuminuria is considered when its level is on the range: 30-300 mg/24hours. Measurement of microalbuminuria must be done in two separate ocasions 3-6 months apart. Nearly 20 % of type 2 diabetics have Microalbuminuria.(4) Overt Nephropathy is caracterised by persistent albuminuria > 300 mg/24 h. associated with high blood pressure, relentless decline of GFR and high risk of cardiovascular morbidity and mortality.measurement of albuminuria is based on 24 hours urine collections or Alb/creatinine ratio in spot morning urine sample. The presence of Albuminuria in a diabetic patient with retinopathy is virtually diagnostic of Diabetic Nephropathy. If Retinopathy is absent then a renal biopsy is indicated for a precise diagnosis.

Risk factor of Diabetic Nephropathy are: male sex, older age, Albuminuria, increased HbA1C, retinopathy, colesterol and increased GFR. Microalbuminuria strongly predicts cardovascular mortality.Hyperglicemia is the primary inciating factor in the pathogenesis of diabetic complications. High level of glucose induce the production of reactive oxygen species which are involved in the development of diabetic complications.Proteins modified by glucose such as Amadory products and Advance Glycation End Products play an important role in the renal diabetic complications.Also Protein Kinase C pathway is a significant pathogenic mechanism in the genesis of these complications(5). TGF-β has a central role in renal hypertrophy and accumulation of extracelular matrix.(6) In fact both hemodynamic and structural changes are important.(7). Is it useful to control hyperglicemia in Diabetic Nephropathy? In the past, it was thought that beyond a certain point tight glicemic control fail to prevent the further decline of renal function(2) but later studies confirmed that glycemic control (although less than lowering the high blood pressure) influence the rate of progression of renal damage. Hypertension has a great role on the onset and progression of DN. In type 2 diabetic pts, hypertension is a powerful predictor of cardiovascular death increasing the risk by a factor of 20. (8).Genetic factors also also play an important role in the progressive renal injury. Among them the I/D polymorphism of ACE gene is decisive in the occuring of of a progressive disease.

Among 493 pts with diabetes we found the presence of diabetic Nephropathy in 30 % of them. In pts with diabetic nephropathy we found incresed levels of uremia (54 % of type 1 diabetes vs 43 % of type 2 diabetes.),. hypercolesterolemia (34 % vs 58 %), tryglicerides (33 % vs 44 %) , retinopathy (95 % vs 55 %)and high blood pressure (31% vs 41 %).Our results and recent studies on this field suggest that baseline urine Albumine/Creatinine ratio is apowerful indipendent predictor of progression of diabetic nephropathy.This is very important because proteinuria is easily quantifiable and also a modifiable risk factor. Other indipendent risk factors explaining renal outcomes are: 1) the level of renal dysfunction 2) anemia 3) hypoalbuminemia. Although the lower serum albumin level can be explained in part by the magnitude of proteinuria it is clear that other factors such as nutrition and inflammation can also may contribute to a reduction in serum albumin level.(9)(10)

Briefly concluding: All diabetic patients with nephropathy can benefit from good metabolic control (mostly in the incipient phase), raised blood pressure correction and renin angiotensin system inhibition.

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