MONITORING THE PROGRESSION OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH DIABETIC NEPHROPATHY- A PERMANENT CHALLENGE

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Abstract

Aim of study *– The monitoring of renal function in 2 statistically comparative groups of patients, first group with diabetic kidney disease (DKD) and the second with non-diabetics patients with the same degree of chronic kidney disease (CKD).* ***Materials and methods*** *– The prospective study was based on data collected from 785 patients hospitalized in the interval January 2006 - December 2010, 316 of them diagnosed with moderate CKD (creatinine clearance = 30-60 ml/min/1.73 sqm). Two statistically comparative groups of 70 patients were each chosen to continue our study, first group with DKD and the second, non-diabetics with the same degree of CKD.* ***Results.*** *CKD particularly affected the males, especially between 50-70 years old for the first group and 40-60 years old for the second group. The decline of GFR was about 7.8±3.8 ml/min/year for the diabetic patients and about 5.9±2.9 ml/min/year for the non-diabetics. The quarterly referral to nephrologists was better for diabetics (56% vs 24%). The most frequent co-morbidities were detected in diabetics: ischemic heart disease (57% vs 33%), arterial hypertension (90% vs 76%), congestive heart failure (28% vs 12%, $p<0.03$). The use of renoprotective therapy was more frequent in diabetics: ACEI (54% vs 35%), angiotensin II blockers (24% vs 13%) and statines (77% vs 60%). Almost 10% of our patients died during the study, 60% from the diabetic group.* ***Conclusions*** *– The decline of renal function was more rapid in diabetics with moderate CKD, than in non-diabetics, with almost 3 ml/min/year. Renoprotective therapy is still insufficiently used in diabetic patients and metabolic control is hard to achieve, but the increased referral to nephrologists of this special group of patients makes their monitoring a permanent challenge.*

keywords*: diabetic kidney disease, chronic kidney disease, progression, renoprotection*

Introduction

Diabetic kidney disease is one of the leading causes of primary kidney disease in patients starting renal replacement therapy (RRT) and affects almost 40% of type 1 and type 2 diabetic patients. The risk of death increases mainly for cardiovascular causes and is defined by increased urinary albumin excretion (UAE), in the absence of other renal diseases [1,2]. In the United States, diabetes mellitus accounts for more than 44% of patients with end stage renal failure [3]. In Romania, the Dialysis and Transplant Registry 2006 reported that diabetic nephropathy was the predominant cause of ESRD, accounting for 47% of new cases. This places an enormous burden on clinical, public health and economic resources, as such patients have frequently multiple comorbid conditions [2].

Despite multiple therapies that demonstrated their efficiency in slowing the disease progression, approximately 40% of the estimated 21 million patients with diabetes in the United States develop overt nephropathy [3,4]. Hyperglycemia, uncontrolled hypertension (HT), dyslipidemia, smoking habits, as well as genetic predisposition, are the main risk factors for the development and progression of diabetic nephropathy [5,6]. Effective strategies for preventing the development of microalbuminuria, delaying the progression to more advanced stages of nephropathy and reducing cardiovascular mortality in patients with type 1 and type 2 diabetes [11,12] are the best metabolic control (HbA1c <7%), proper control of hypertension (<130/80 mmHg or <125/75 mmHg if proteinuria >1.0g/24 h and increased serum creatinine), using drugs with blockade effect on the renin-angiotensin-aldosterone system [7,8,9,10], and treating dyslipidemia (LDL cholesterol <100 mg/dl).

Aim of study

The aim of our study was to monitor the decline of renal function in 2 statistically comparative groups of patients, first group with DKD and the second with patients with the same degree of moderate CKD, but non-diabetics.

Material and methods

The prospective study was based on data collected from 785 patients examined between january 2006 – december 2010, 316 of them with moderate CKD (creatinine clearance MDRD = 30-59 ml/min/1,73 sqm). Two statistically comparative groups of 70 patients were each chosen to continue our study, first group with DKD (group A) and the second, non-diabetics (group B) with the same degree of CKD. The well-known risk factors usually blamed for the decline of renal function, were followed, as well as the influence of the therapeutic strategies in CKD progression.

Participants were recruited from Nephrology and Diabetes clinics of the Emergency Clinical Hospital of Constanta County. Eligible participants from group A had type 2 diabetes and a clinical diagnosis of DKD, with at least 300 mg/dl of urinary albumin excretion (or ≥500 mg/dl of proteinuria) and patients from group B, with a similar degree of CKD, nondiabetics (primary disease: hypertensive nephroangiosclerosis or chronic glomerular disease). All participants were 18 years or older. Potential participants who were expected to survive fewer than 3

years, those with advanced renal failure (defined as stage 4 or 5 CKD, with creatinine clearance of <29 mL/min or on dialysis), those awaiting imminent dialysis, those with rapidly progressive disease or under immunosuppressive therapy, and pregnant women or those unwilling to practice effective contraception, were not eligible for the trial.

Baseline assessments for trial participants included medical history, physical examination, laboratory analyses (glycemia, urea, creatinine, uric acid, hemogram, lipidic profile, HbA1c, creatinine clearance), ECG, imagistic evaluation (abdominal ultrasound, echocardiography, CT scans) and current medications. Participants follow-up was achieved with clinic visits every 3 months for up to 5 years or during hospitalisations for comorbidities. The primary outcome measure was progression of nephropathy, which was assessed by change in glomerular filtration rate (GFR). GFR was estimated by the 4-variable Modification of Diet in Renal Disease (MDRD) formula.

Table 1. Demographic characteristics of studied groups

	Group A n= 70	Group B n= 70
Age (years)	57±12	52±11
Urban/rural	63/7	58/12
Serum creatinine (mg/dl)	3.3±1.8	3.1±1.6
UAER(mg/24 hrs)	1386(385-3674)	526 (458–603)
Smokers/nonsmokers	38/32	52/18
Romanian/other nat.	44/26	51/19
Haemoglobin (g/dl)	9.1±2.0	10.2±2.3
HbA1c	7.6±1.8	

Results. Discussions

After analysing all data, in association with dynamical evaluation of eGFR the following results have been obtained:

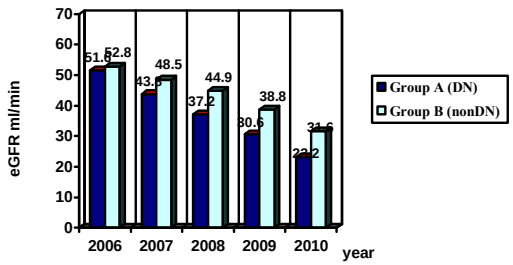

Fig. 1. eGFR evolution in studied groups

It is obvious that the decline of renal function was more rapid in the group A (DKD group) with ~7,5ml/min/year, in comparison with those from nondiabetics ~5.8 ml/min/year, starting from the same degree of moderate CKD.

This decline of renal function occurred, despite the fact that diabetic patients had a better referral to nephrologists (56%), compared to non-diabetics (24%). The main explanation is the constant and proper professional cooperation between diabetologists and nephrologists in our hospital.

Renoprotective therapy was properly recommended to both diabetic and non-diabetic patients, either by general practitioners, or by specialists - diabetologists or nephrologists (>70% in diabetics and >52% in non-diabetics).

It can be noticed that 98% of diabetic patients and 56% of non-diabetics are receiving antihypertensive renoprotective therapy (ACEI's, ARB's or combinations of both drugs). Significant statistical differences were noticed for vitamins and peripheral vasodilators, usually more prescribed/ indicated in diabetics.

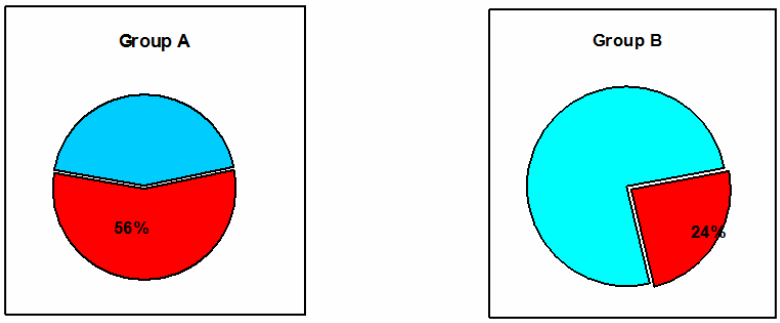

Fig. 2. Quarterly referral to nephrologists

Table nr. 2- Renoprotective therapy

Medication	Group A		Group B		
	Nr. pts	(%)	Nr. pts	(%)	*p*
ACEI's	38	54.3	25	35.7	0.056
ARB's	17	24.3	9	12.9	0.032
ACEI's+ ARB's	13	18.7	5	7.2	< 0,005
Statins	54	77.1	42	60	< 0.005
Antiplatelet agents	52	74.3	43	61.4	0.032
Vitamins (B complex ±E)	16	22.8	3	4.2	<0.001
Pentoxifylline	39	55.7	4	5.7	<0.001

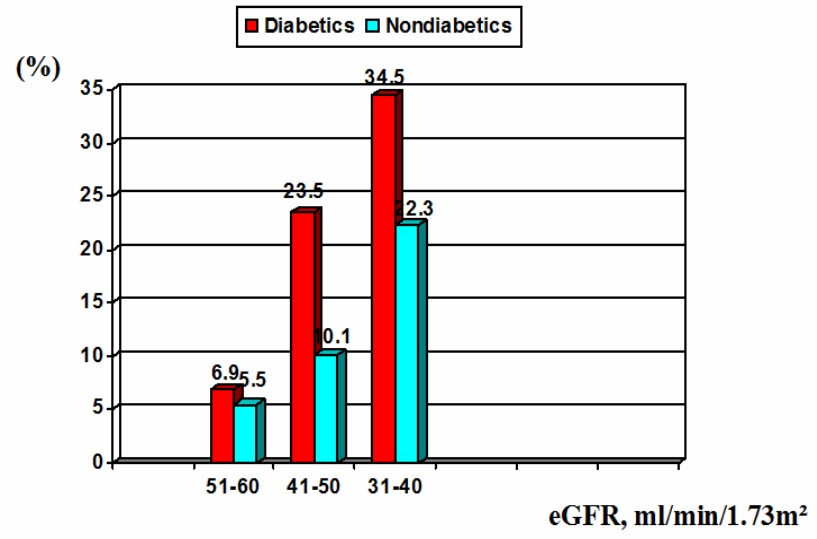

Fig. 3. Prevalence of anemia in moderate CKD

Anemia of the diabetic CKD patients is more severe than in non-diabetic patients with the same level of GFR deterioration; the main cause of this difference is an earlier and more severe erythropoietin (EPO) deficiency in diabetic patients. Prevalence of anemia was 34,5% in patients with eGFR 31-40 ml/min/1.73 sqm, that means pre-dialysis

patients. Because the severity of anemia at the beginning of dialysis is a risk factor for early mortality in diabetic patients, the control of renal anemia in those patients, is mandatory and includes a proper management of iron deficit and the use of human recombinant erythropoietin.

During our study, despite the moderate degree of CKD, almost 7% of diabetic patients needed initiation of renal replacement therapy, in comparison with 5.7% in non-diabetic patients.

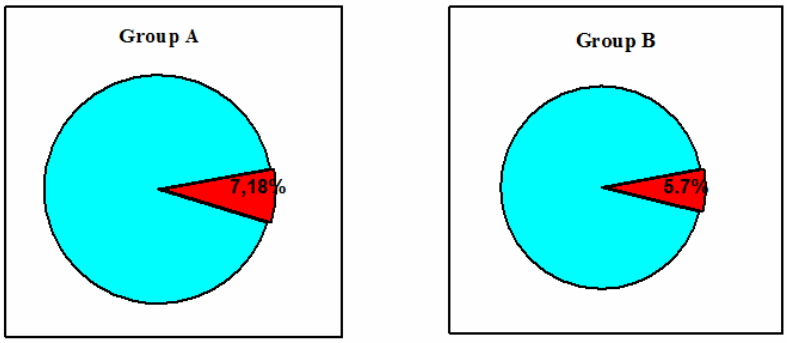

Fig. 4. Dialysis initiation

Table 3. Comorbidities in our study groups

	Group A		Group B		
	No. pts	(%)	No. pts	(%)	*p*
Ischemic heart disease	40	57	23	32.9	0.002
Arterial HT	63	90	58	75.8	0.021
Heart failure	21	30	14	20	0.030
Peripheral vascular disease	11	15.5	10	13.9	0.056
COPD	8	11.1	9	12.7	0.122

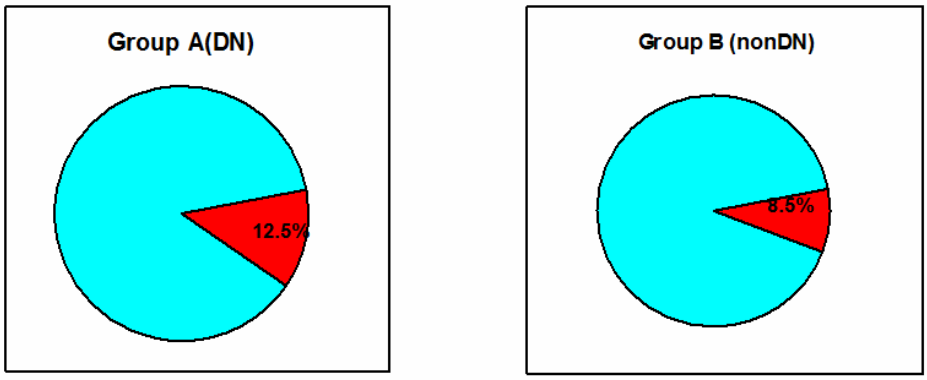

Fig. 5. Mortality ~ 10 %

The most frequent comorbidities were detected in diabetics: ischaemic heart disease (57% vs 33% in non-diabetics), arterial HT (90% vs 76%), congestive heart failure (28%

vs 12%), explaining the increased mortality in DKD group (12.5% vs 8.5).

Due to the well-known increased cardiovascular risk of diabetic patients, mortality occurred in 12.5% in this group, in comparison with non-diabetic group (8.5%).

Conclusions

The decline of GFR was about 6.8±3.8 ml/min/year for the diabetic patients and about 5.9±2.9 ml/min/year for the non-diabetics. CKD progression was more severe in males, smokers, Turkish patients and in patients with severe proteinuria/anemia.

The quarterly referral to nephrologists was better for diabetics (56% vs 24%).

Anemia was more severe and frequent in diabetics, affecting ~35% of the patients with eGFR 31-40 ml/min/1.73 sqm and requiring higher iron supplements and EPO doses.

The most frequent comorbidities were detected in diabetics: ischaemic heart disease (57% vs 33%, p=0.002), arterial HT (90% vs 76%, p<0.032), congestive heart failure (28% vs 12%, p=0.03), explaining the increased mortality in DKD group (12.5% vs 8.5% in group B).

Renoprotective therapy is still insufficiently used (<80% in diabetics and <60% non-diabetics) and metabolic control hard to achieve in patients with moderate CKD. The increasing referral of this special group of patients to nephrologists and diabetologists, makes their monitoring a permanent challenge.

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