Total and LDL cholesterol are associated with glomerular filtration rate in normoalbuminuric type 1 diabetic patients

Tomislav Bulum, Ingrid Prkačin, Lea Duvnjak
Merkur University Hospital, University of Zagreb, School of Medicine, Zagreb, Croatia

INTRODUCTION

Patients with type 1 diabetes have a 20-50% probability of developing end-stage renal disease. In type 1 diabetic patients many studies have identified poor glycemic control as a most important risk factor for progression of diabetic kidney disease. Dyslipidemia has also been associated with the development and progression of nephropathy, and with mesangial, tubulointerstitial, and glomerular changes in the kidney. Little is known about the relationship between lipids and change in renal function among individuals with normal renal function, because most studies have focused on the progression of established renal disease. The objective of this study, therefore, was to evaluate the associations of serum lipids, including total, LDL, HDL, VLDL cholesterol and triglyceride levels with estimated glomerular filtration rate (eGFR) in normoalbuminuric type 1 diabetic patients.

SUBJECTS AND METHODS

Study included 313 normoalbuminuric type 1 diabetic patients with normal or mild decrease (eGFR > 60 ml/min per 1.73 m2) renal function and before any interventions with statins, ACE inhibitors or angiotensin II receptor blockers. Urinary albumin excretion rate was measured from at least two 24-h urine samples and determined as the mean of 24-h urine collections. Data on serum creatinine levels, age, sex and race were used to calculate the eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

RESULTS

The average age was approximately 34 years, most were not overweight and 51% of subjects were female. Mean/median values of BMI (24 kg/m2), waist to hip ratio (WHR) (0.81), systolic and diastolic blood pressure (122/78 mmHg), fasting glucose (5.7 mmol/L), HDL cholesterol (1.7 mmol/L), and triglycerides (1.07 mmol/L) were within the normal range for patients with diabetes with slightly elevated levels of HbA1c (7.4%), total (5.0 mmol/L) and LDL cholesterol (2.8 mmol/L). eGFR was significantly associated with duration of diabetes, fasting glucose, daily insulin dose, HbA1c, total, LDL, and HDL cholesterol, with duration of diabetes, total and HDL cholesterol showing the strongest correlation (r=-0.29, -0.21, and -0.21, respectively, for all $p<0.05$). Stratifying serum lipids for degree of eGFR, levels of total, LDL and HDL cholesterol were inversely related to eGFR, but trends were significant only for total (5.1 vs 4.6 mmol/L, p=0.02) and LDL cholesterol (2.9 vs 2.4 mmol/L, p=0.006). In logistic regression analysis, after adjustment for age, sex and duration of diabetes, serum lipids were not associated with eGFR in our normoalbuminuric subjects (Table 1).

Table 1: Multivariate logistic regression analysis of serum lipids with development of lower eGFR

INDEPENDENT VARIABLE	MODEL A	MODEL B
Total cholesterol	0.65 (0.50-0.84)*	1.01 (0.73-1.38)
LDL cholesterol	0.60 (0.44-0.82)*	0.93 (0.64-1.35)
HDL cholesterol	0.49 (0.28-0.87)*	0.96 (0.46-1.99)
VLDL cholesterol	1.53 (0.71-3.29)	1.52 (0.60-3.83)
Triglycerides	1.20 (0.85-1.70)	1.20 (0.79-1.82)

Data are OR (95% CI) from separate models. Model A crude; model B adjusted for age, sex and duration of diabetes.
*P < 0.05.

DISCUSSION

Serum lipids may play a significant independent role in the development of diabetic nephropathy and decline in renal function and progression of albuminuria. In a number of studies, an increase in total and LDL cholesterol levels has been found to be a risk factor for nephropathy in type 1 diabetes. Our patients with mild impaired renal function display an atherogenic lipid profile with high total cholesterol and LDL cholesterol. Our results are in accordance with previous study showing that in normoalbuminuric type 1 diabetic patients progression of nephropathy was linked to LDL cholesterol. Circulating lipoproteins play a direct role in the pathogenesis of glomerulosclerosis and tubulointerstitial changes. Animal models suggest that dyslipidemia plays an important role not only in the progression of chronic renal disease but also in its development. In addition, a decline in renal function has been reported to be associated with advanced glomerular lesions even in normoalbuminuric type 1 diabetic patients with reduced GFR. We observed an increased frequency of patients with LDL-cholesterol over 2.6 mmol/L, target recommended by international guidelines for LDL cholesterol, in parallel with decreasing in eGFR. Our study included patients before any interventions with statins, ACE inhibitors or angiotensin II receptor blockers that may allows purer physiological examination of the association between GFR and serum lipids because ACE-inhibitors can elevate serum creatinine and statins lower serum lipids.

In conclusion, we have detected an association between eGFR and lipid abnormalities in type 1 diabetes in early stages. The study was conducted in patients with no therapeutic intervention. This may suggest that lipid abnormalities may play a role in the pathogenesis of renal impairment in type 1 diabetic patients.

50ERA-EDTA
285--MP
Diabetes - clinical studies
Ingrid Prka&269;in
DOI: 10.3252/pso.eu.50era.2013
Poster presented at: ERA-EDTA 50th Congress Istanbul Turkey May 15-21, 2013
PosterSessionOnline.com