Cystatin C as a Marker for Detection of Early Renal Failure in Diabetes Type 2 Patients

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Abstract

The epidemiological studies have show dramatic increase and prevalence of end stage renal disease in patients with type 2 diabetes therefore early markers of diabetic nephropathy need to be identified (1). During the treatment of patients at the Clinic of endocrinology, diabetes mellitus and metabolic diseases in Sarajevo, we observed a necessity of application of new markers in assessment of early renal failure. Serum cystatin C level is another marker of renal function. Cystatin C is freely filtered at the level of the glomerulus and virtually all is re– absorbed and metabolized by the proximal tubular cells. Serum cystatin C is a screening test and an early indicator and predictor of the development of renal failure. Aim of the study: To estimate correlation among cystatin C, serum creatinine and albuminuria in diabetes type 2 patients for assessment of early renal failure. Serum cystatin C as a screening test has to be considered in the treatment of diabetes type 2 patients for assessment of early renal failure.

KEY WORDS: diabetes mellitus, early marker, renal disease, cystatin C, creatinine

Introduction

The epidemiological studies have show dramatic increase and prevalence of end stage renal disease in patients with type 2 diabetes therefore early markers of diabetic nephropathy need to be identified (1). In the last 50 years, serum urea and serum creatinine estimation has become the most commonly used serum markers of renal function. Urea concentration in the blood can vary with diet, hepatic function and numerous disease states. Serum creatinine is also insensitive for detecting small decreases in glomerular filtration rate, because of the nonlinear relationship between plasma concentration and glomerular filtration rate. (2) Patients with newly diagnosed type 2 diabetes quite often have albuminuria. The reason is probably that such patients may have had diabetes for several years, thus already showing evidence of long-term diabetic complications. Screening for albuminuria is important aim

in the newly diagnosed type 2 diabetes, not only because of better prognosis for the kidney but there is also a better prognosis for survival with more effective treatment. Micro albuminuria is considered to be a risk factor for diabetic nephropathy and progressive renal insufficiency but recent investigations have raised questions about its predictive value owing to its variability for the underlying renal pathology (3). Serum cystatin C level is another marker of renal function, because it is thought to be produced at a constant rate by most nucleated cells. Cystatin C is a protease inhibitor with a molecular weight of 13 kD and a constant formation rate. It is filtered free by the healthy kidney, reabsorbed by the tubules and degraded. The serum concentration depends exclusively on the glomerular filtration rate of the kidney. Among the non – invasive diagnostic methods, cystatin C has the highest sensitivity to detect a reduced glomerular filtration rate. Cystatin C production has been reported to be not affected by age, sex, inflammations, consumptive diseases, or muscle mass. Cystatin C is freely filtered at the level of the glomerulus and virtually all is re – absorbed and metabolized by the proximal tubular cells. A recent meta – analysis concluded that serum cystatin C level is superior marker of renal function compared with serum creatinine level. Serum cystatin C level alone is a better predictor of creatinine clearance than serum creatinine level (4, 7, 8). Low molecular weight proteins have been suggested to replace serum creatinine. Serum or plasma cystatin C may be a better marker for glomerular filtration rate than serum creatinine (5). Cystatin C offers an advantage over creatinine because of its age and gender independence (6, 9).

Objectives

To estimate correlation among cystatin C, serum creatinine and albuminuria in diabetes type 2 patients for assessment of early renal failure.

Patients and Methods

This study was randomized and conducted in Clinic of Endocrinology, Diabetes Mellitus and Metabolic Diseases, University Clinical Center of Sarajevo. A total of 49 subjects with type 2 diabetes were screened in our study, during 6 months. We compared cystatin C, in patients with type 2 diabetes with abnormal urine albumin excretion rate versus normo albuminuric patients with type 2 diabetes for assessment of early renal failure. Patients were divided in two groups according to urine albumin excretion rate (group A with abnormal versus group B with normal albumin urine excretion rate). We followed duration of diabetes mellitus, sex distribution, fasting blood glycaemia (3,1 – 6,1 mmol/l), HbA1c, urine albumin secretion (after 8 h of rest, from an overnight timed urine sample, urine was sterile, in non-ketotic patients), cystatin C (0,50 – 0,96 mg/l), serum creatinine (45 – 115 μmol/l).

Results

A total of 49 patients with type 2 diabetes (27 men and 22 women) , mean aged 54,76 (S.D. = 5,55), with a known duration of diabetes of 4,73 (S.D. = 1,44), were consecutively screened in our study. Mean fasting blood glycaemia was 7.02 mmol/l (S.D. = 1,35), and mean HbA1c 6,81% (S.D. = 1,44). Patients were divided in two groups according to urine albumin excretion rate (group with abnormal versus group with normal albumin urine excretion rate). In our study 14 patients were with normal albumin urine excretion rate and 35 patients were with abnormal albumin urine excretion rate. Mean cystatin C in a group with normal albumin urine excretion rate was 0,55 mg/l (S.D. = 0,14). Mean cystatin C in a group with abnormal albumin urine excretion rate was 1,03 mg/l (S.D. = 0,25). Mean serum creatinine level in normal albumin urine group was 79 μmol/l (S.D. =7), and in a group with abnormal albumin urine was 86 μ mol/l (S.D. =14). The values of mean serum creatinine in both observed groups were within the referent range (45 – 115 μ mol)/L, thus it could not be used as relevant indicator for early renal impairment. The value of mean serum cystatin C in abnormal albumin urine group in comparison with normal albumin urine group was higher and indicated statistically significant difference ($p < 0,01$), which was proven with F – Test Two – Sample for Variances F (P (F< = f) 0,01183 (Table 1.) and t-Test: Two-Sample Assuming Unequal Variances T (P (T< = t) 6,3846 E – 11 (Table 2). In this connection cystatin C could be used as a marker for early renal impairment.

Discussion

Early detection of renal function failure is vital in treatment of patients with diabetes type 2. During the treatment of patients at the Clinic of Endocrinology, diabetes mellitus and metabolic diseases in Sarajevo, we observed a necessity of application of new markers in assessment of early renal failure, considering that the values of serum urea and creatinine have not indicated a sufficient and reliable correlation with early renal failure. The values of the above mentioned parameters have been also

F-TEST TWO-SAMPLE FOR VARIANCES	VARIABLE 1	VARIABLE 2
Mean	1,031142857	0,551428571
Variance	0,061122185	0,01829011
Observations	35	14
Df	34	13
F	3,341816164	
P(F<=f) one-tail	0,011831619	
F Critical one-tail	2,361136227	

TABLE 1. Serum cystatin C in abnormal albumin urine group in comparison with normal albumin urine group

T-TEST: TWO-SAMPLE ASSUMING UNEQUAL VARIANCES	VARIABLE 1	VARIABLE 2
Mean	1,031142857	0,551428571
Variance	0,061122185	0,01829011
Observations	35	14
Hypothesized Mean Difference	0	
df	42	
t Stat	8,682295713	
P(T<=t) one-tail	3,19233E-11	
t Critical one-tail	1,681952358	
P(T<=t) two-tail	6,38466E-11	
t Critical two-tail	2,018081679	

TABLE 2. Serum cystatin C in abnormal albumin urine group in comparison with normal albumin urine group

affected by other diseases. Patients with type 2 diabetes quite often have albuminuria. The reason is probably two-hold, first of all, such patients may have had diabetes for several years, thus already showing evidence of long-term diabetic complications. Another important issue is that patients with type 2 diabetes exhibit features of the so-called metabolic syndrome which include some elevation of blood pressure. Elevated blood pressure is an important risk factor for albuminuria (3). Albuminuria is not absolutely indicator of renal failure. Serum cystatin C level together with albuminuria is useful marker for early diagnosis of renal disease. Serum cystatin C level alone is a better predictor of creatinine clearance than serum creatinine level (4). This study was focused at the group of patients with fairly regulated glycaemia who had sterile urine samples. The group consisted of two subgroups one with abnormal urine albumin excretion rate versus group with normal urine albumin excretion rate. We found that serum creatinine level was not significantly different between groups. Serum cystatin C level was higher in patients with albuminuria than in normal albuminuric patients.

Conclusion

Serum cystatin C as a screening test and as an early indicator and predictor of the development of renal failure has to be considered in the treatment of patients with diabetes type 2.

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