Value of the combined examination of Cys-C and HbA1c for diagnosis of early renal injury in pediatric diabetes

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Abstract. The objective of the present study was to evaluate the combined application of measuring cystatin C (Cys-C) and hemoglobin A1c (HbA1c) levels for early renal injury in pediatric patients with type 2 diabetes. A total of 130 children with type 2 diabetes admitted to our hospital from May 2013 to July 2015 were selected. Patients were divided according to whether there was complication of renal injury. In group A (n=65), the patients had renal injury and in group B (n=65), the patients did not have renal injury. The levels of Cys-C and HbA1c in the two groups were examined. The results showed that the levels of Cys-C and HbA1c of patients in group A were significantly higher than those in group B (P<0.05), and the positive rate of the combined examination of Cys-C and HbA1c in group A was 92.3%, and was higher than that of the individual examinations of either Cys-C or HbA1c (P<0.05). The Spearman's correlation coefficient analysis was applied to group B and showed that Cys-C was positively correlated with HbA1c (r=0.842, P<0.05). From analysis of the receiver operating characteristic curves, the combined examination of Cys-C and HbA1c surpassed the individual examinations of Cys-C or HbA1c in sensitivity and specificity (P<0.05). In conclusion, the positive detection rate of early renal injury was significantly increased by the combined examination of Cys-C and HbA1c in pediatric patients with type 2 diabetes, which is beneficial for early identification and diagnosis of this diseases and is worthy of clinical application.

Introduction

In recent years, with the rising incidence of obesity, hypertension, and other pediatric diseases, the number of children with type 2 diabetes has been gradually increasing (1). As a relatively common complication of type 2 diabetes, diabetic nephropathy (DN) usually shows inconspicuous clinical symptoms in the early stage (2). However, when DN appears in clinic, most

patients have already entered the middle or advanced stage of the disease, which is irreversible (3). Therefore, early identification and diagnosis is beneficial for the prognosis of these patients.

At present, examination of indexes such as urine protein and creatinine are the most commonly used clinical methods for the diagnosis of early renal injury in diabetes (4-7). However, these indexes have a relatively low sensitivity and specificity for the diagnosis of diabetic renal injury. Therefore, the optimal treatment time for patients is easily missed. Cystatin C (Cys-C) and hemoglobin A1c (HbA1c) are important markers of renal injury (8-10).

The aim of the present study was to assess the application value of the combined examination of Cys-C and HbA1c in the diagnosis of early renal injury in pediatric patients with type 2 diabetes.

Patients and methods

Patients. A total of 130 children with type 2 diabetes who were admitted to our hospital from May 2013 to July 2015 were selected. The age range of the 70 males and 60 females was 7-13 years, with a mean age of 10.5±1.4 years. All the patients met the diagnostic criteria of type 2 diabetes (11), and those with other diseases of major organs such as of the heart were excluded. Patients were divided according to whether there was complication of renal injury. In group A (n=65), patients had renal injury and in group B (n=65), patients did not have renal injury. The general parameters of the two groups were compared and are shown in Table I.

Methods. Patients were required to fast, after which venous blood (3 ml) was drawn in the morning from the two groups. The blood was centrifuged at 2,000 x g for 5 min to collect serum. The serum levels of Cys-C were measured with a fully automatic biochemical analyzer (Shanghai Kehua Instrument Co., Ltd., Shanghai, China) with the emulsion turbidimetric method. The concentration of HbA1c was measured with an HbA1c detector (Beijing Wiconda Technology Co., Ltd., Beijing, China) with high performance liquid chromatography. The rate of positive diagnosis was determined as: Cys-C >1.1 mg/l, HbA1c ≥6.5%.

Statistical analysis. SPSS 20.0 software (IBM SPSS, Armonk, NY, USA) was used for data analysis. A χ^2 test was used

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Table I. Comparison of general parameters of the two groups (mean ± SD).

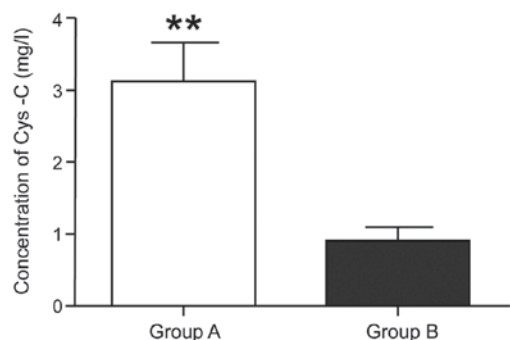| Groups	n	Gender (case) Male	Female	Age (years)	BMI (kg/m^2)
Group A	65	36	29	10.8±1.2	23.8±1.7
Group B	65	34	31	10.3±0.9	24.1±1.9
P-value		>0.05	>0.05	>0.05	>0.05

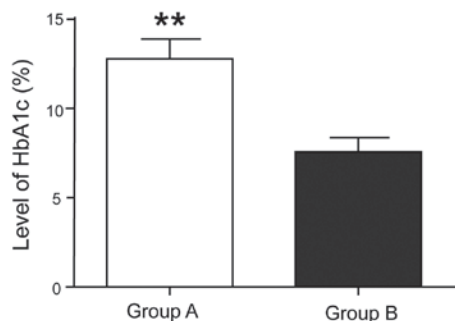Figure 1. Concentration of cystatin C (Cys-C) in the two groups. **P<0.05 compared to that of group B.

Figure 2. Level of hemoglobin A1c (HbA1c) in the two groups. **P<0.05 compared to that of group B.

for comparisons of enumeration data between the groups. Measurement data are presented as mean ± standard deviation. A t-test was used for comparisons between groups, and an F-test was used for comparisons between the groups. The Spearman's correlation coefficient was used for the analysis of each parameter. P<0.05 was considered statistically significant. The specificity and sensitivity of the diagnosis were analyzed with the receiver operating characteristic (ROC) curve of the combined examination of Cys-C and HbA1c, as well as the ROC curves of the individual examinations of the two indexes.

Results

Comparisons of the levels of Cys-C and HbA1c in patients of the two groups. The levels of Cys-C and HbA1c in patients of group A were significantly higher than those in group B (P<0.05) (Figs. 1 and 2).

Table II. Comparisons of the positive rate of combined examination of Cys-C and HbA1c and the individual examinations of the patients in group A.

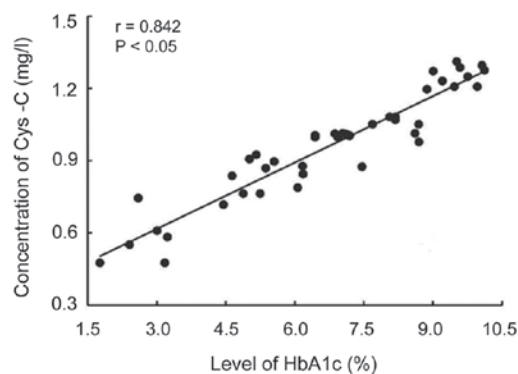| Classification	n	Positive	Negative	Positive rate (%)
Individual examination of Cys-C	65	47	18	72.3
Individual examination of HbA1c	65	50	15	76.9
Combined examination of Cys-C and HbA1c	65	60	5	92.3
P-value				<0.05

Cys-C, cystatin C; HbA1c, hemoglobin A1c.

Figure 3. Correlation analysis of cystatin C (Cys-C) with hemoglobin A1c (HbA1c).
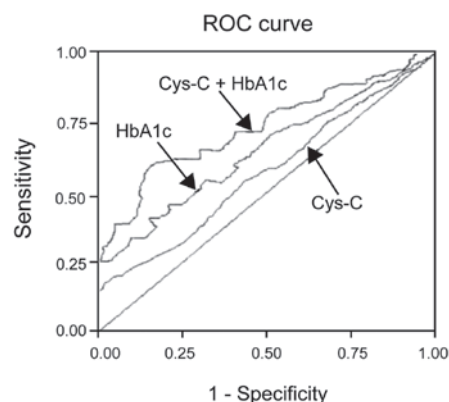

Figure 4. Receiver operating characteristic (ROC) curve of cystatin C (Cys-C), hemoglobin A1c (HbA1c) and a combination of Cys-C and HbA1c.

Comparisons of the positive rate of combined examination of Cys-C and HbA1c and the individual examinations of the patients in group A. The positive rate of the combined examination of Cys-C and HbA1c in group A was 92.3%, and was

higher than that of the individual examinations of either Cys-C or HbA1c (P<0.05) (Table II).

Correlation analysis. The Spearman's correlation coefficient analysis was applied to group B and showed that Cys-C was positively correlated with HbA1c (r=0.842, P<0.05) (Fig. 3).

Analysis of the ROC curves. From the analysis of the ROC curves, the combined examination of Cys-C and HbA1c surpassed the individual examinations of Cys-C and HbA1c in sensitivity and specificity (P<0.05) (Fig. 4).

Discussion

The blood glucose level in patients with diabetes, induced by the disorder of insulin secretion, is maintained at relatively high levels over long periods of time, which makes it easy for chronic renal and vascular injuries to occur (12-14). In the early stage, the onset of DN is relatively inconspicuous, without typical clinical symptoms, and the pathogenesis is relatively complex. Previous reports showed that the occurrence of DN was intimately correlated with long-term hyperglycemia and factors such as abnormalities of hemodynamics and metabolism of glucose and adipose tissue (15-17).

Cys-C is a dicysteine proteinase inhibitor, which is filtered by the glomerulus because of its relatively small molecular weight and the positive charge it acquires in the presence of physiological pH. It is also absorbed and degraded in the proximal convoluted tubule of the kidney, and is thus absent in vascular circulation (18). As discussed above, glomerular filtration is intimately correlated with the level of Cys-C in blood. If there is dysfunction of glomerular filtration, the levels of Cys-C in blood will also be abnormal. Therefore, the concentration of Cys-C in blood can be used as a measure of function of glomerular filtration. HbA1c is glycated hemoglobin, and its formation is irreversible. HbA1c is positively correlated with blood glucose, and reflects the mean level of blood glucose in the body in the past 8-12 weeks with relative accuracy (19,20).

The present findings showed that the levels of Cys-C and HbA1c of patients in group A were significantly higher than those in group B (P<0.05). This suggested that the abnormality of Cys-C and HbA1c in patients with type 2 diabetes reflects, to some degree, the extent of renal injury. Further analysis showed that the positive rate of the combined examination of Cys-C and HbA1c in group A was 92.3%, which was higher than that of the individual examinations of either Cys-C or HbA1c (P<0.05).

The Spearman's correlation coefficient analysis was applied to group B and showed that Cys-C was positively correlated with HbA1c (r=0.842, P<0.05). The result suggested that Cys-C increased with the increase of HbA1c, which indicated that the combined examination of Cys-C and HbA1c can more accurately estimate early renal injury in type 2 diabetes.

From the analysis of the ROC curves, the combined examination of Cys-C and HbA1c surpassed the individual examinations of Cys-C and HbA1c in sensitivity and specificity (P<0.05). The result suggested that the application of combined examination of Cys-C and HbA1c in pediatric patients with type 2 diabetes can increase the detection rate of early renal injury, with higher sensitivity than the individual examinations of Cys-C and HbA1c, thus reducing the rate of misdiagnosis.

In conclusion, changes of glomerular filtration can be reflected by the levels of Cys-C and HbA1c. The combined examination of the two can enhance the positive detection rate of early renal injury in children with type 2 diabetes more efficiently, and diagnose the disease as early as possible, which allows for the optimal chance for patients to receive interventional treatment as early as possible. The combined measurement of Cys-C and HbA1c is worthy of clinical application.

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