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Q3 Correlation study of podocyte injury and kidney function in patients with acute kidney injury

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ABSTRACT

Objective: To investigate the correlation between the podocyte injury indexes in urine such as nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2-associated protein (CD2AP) and the kidney function in patients with acute kidney injury (AKI).

Methods: A total of 120 severe postsurgical patients treated in the Intensive Care Unit of our hospital from May 2012 to October 2015 were selected and divided into AKI group (n = 38) and non-AKI group (n = 82) according to the diagnostic criteria of AKI. After admission to the Intensive Care Unit for 24 h, their blood samples were collected to detect the contents of serum creatinine (Scr), serum urea (SUrea), β2-microglobulin (β2-MG) and cystatin C (Cys-C), and urine samples were collected to detect the contents of kidney injury molecule-1 (KIM-1), liver-type fatty acid binding protein (L-FABP), Netrin-1, nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP.

Results: For patients in AKI group, the contents of Scr, SUrea, β2-MG and Cys-C in their blood samples and the contents of KIM-1, L-FABP, Netrin-1, nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP in their urine samples were both significantly higher than those in non-AKI group. The contents of nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP in urine samples and contents of Scr, SUrea, β2-MG, Cys-C and neutrophil gelatinase associated lipocalin in blood samples were positively correlated with the contents of KIM-1, L-FABP, and Netrin-1 in urine.

Conclusions: Contents of podocyte injury molecules in urine of patients with acute kidney injury such as nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP raised remarkably and the changes were consistent with the changes of kidney function indexes in the blood and urine samples.

1. Introduction

Acute kidney injury (AKI) is a common severe clinical disease with a high fatality rate caused by multiple factors which involves various subjects. The common primary pathogenesis causing AKI are severe infection, massive haemorrhage, major surgery or major trauma[1,2]. According to the RIFLE, the severity degree of AKI can be divided into risk stage, injury stage and failure stage, and the prognosis conditions can be divided into loss stage, terminal stage and kidney disease stage[3,4]. Although the severity degree of AKI condition can be accurately confirmed and the prognosis can be estimated according to the RIFLE, the diagnosis of the disease mainly depends on the contents of serum creatinine (Scr) and serum urea (SUrea) and the changes of urinary volume, which is of great difficulty for early diagnosis[5]. In recent years, more and more clinical scholars have realized that the vital factor for causing an extremely high fatality rate of AKI is the lack of reliable markers for diagnosis[6].

Glomerular podocyte is a highly differentiated somatic cell. Podocytes connect each other through transmembrane protein and intermediate filament protein and then participate in the formation of the selective filtration barrier of glomerular capillary wall. In the process of AKI, when the podocyte, the last defense for glomerular filtration barrier, is injured, the function of glomerular filtration could be destroyed along with the presence of proteinuria[7–9]. Nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2-associated protein (CD2AP)

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The study protocol was performed according to the Helsinki declaration and approved by the ethic committee of Suining Central Hospital. Informed written consent was obtained from patients.

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are important protein molecules connected podocytes. Podocyte injury can result in the excretion of the above protein molecules in urine. Therefore, the degree of podocyte injury can be demonstrated by detecting the contents of nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP in urine[10–12]. At present, whether the podocyte injury is involved with the pathophysiologic process of AKI and the relations between the marker molecules of podocyte injury and the changes of kidney function of AKI are not yet precisely reported. In the following study, we analyzed the correlation between podocyte injury and kidney function in patients with AKI.

2. Materials and methods

2.1. Study subjects

A total of 120 cases of severe postsurgical patients treated in the Intensive Care Unit (ICU) of our hospital from May 2012 to October 2015 were selected as study subjects after obtaining an approval from the hospital ethics committee. They were divided into AKI group ($n = 38$) and non-AKI group ($n = 82$) according to the diagnostic standards recommended by the Kidney Disease Improving Global Outcomes (2012). The selected standards were as follow: (1) The kidney function deteriorated within 48 h, and the increased absolute value of Scr had exceeded 26.4 mmol/L or increased more than 50% compared with the basal value or the urine volume was less than 0.5 mL/kg per hour, which lasted for more than 6 h; (2) Clinical data were completed and the clinical samples such as blood and urine samples were collected; (3) Patients with a history of chronic renal disease, kidney surgery and any access to nephrotoxic drugs, incomplete laboratory data and unsaved clinical samples were excluded.

2.2. Study methods

2.2.1. Methods for collecting clinical samples

After admission to ICU for 24 h, 5 mL of peripheral venous blood of patients of the two groups was collected and left for standing and blood was coagulated for 30 min at room temperature. Then the samples were placed in the centrifugal machine and centrifuged at 12000 r/min for 20 min, and the serum was separated, transferred into a cleaning EP tube (1.5 mL), numbered and preserved in the refrigerator at −80 °C. Five milliliters of cleaning middle urine specimens of those patients were collected simultaneously, transferred into cleaning EP tubes (1.5 m/L) and also numbered and then preserved in the refrigerator at −80 °C, respectively.

2.2.2. Detection methods for clinical indexes

Fully automatic biochemical analyzer was used to detect Scr and SUrea. ELISA was used to detect the contents of β2-microglobulin (β2-MG) and cystatin C (Cys-C) in serum and the contents of kidney injury molecule-1 (KIM-1), liver-type fatty acid binding protein (L-FABP), Netrin-1, nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP in urine. All the operation sequences were strictly carried out in accordance with the instruction of test kits.

2.2.3. Statistical methods

Software SPSS version 19.0 was used for the input and analysis of data. Measurement data were expressed by mean ± SD. And *t*-test was used for the analysis between two groups. Enumeration data were expressed by frequency forms and analyzed by *Chi*-square test. Correlation between two variables was tested by the Pearson's correlation analysis. Difference was considered as statistically significance when $P < 0.05$.

3. Results

3.1. General data of two groups' subjects

Out of the 38 patients in AKI group, 24 cases were males and 14 were females in AKI group with ages of (48.4 ± 7.2) years and body mass index (BMI) of (23.12 ± 2.97) kg/m^2. Among them, there were 5 cases of hypertension (13.16%), 4 cases of diabetes (10.53%) and 14 cases with smoking history (36.84%) in this group, and the contents of triglyceride was (1.58 ± 0.19) mmol/L and cholesterol was (4.09 ± 0.62) mmol/L. In non-AKI group, there were 52 males and 30 females with age of (49.1 ± 6.9) years and BMI of (23.06 ± 3.14) kg/m^2. Among them, there were eleven cases of hypertension (13.41%), 9 cases of diabetes (10.98%) and 32 cases of smoking history (39.02%). The contents of triglyceride and cholesterol were (1.61 ± 0.20) mmol/L and (4.14 ± 0.67) mmol/L, respectively. According to statistical analysis, the gender, age, BMI, case numbers of hypertension, diabetes, smoking history and the contents of triglyceride and cholesterol in AKI group had no significant differences with those in non-AKI group ($P > 0.05$).

3.2. Indexes of kidney function of two groups' subjects

The kidney function indexes of patients in AKI group such as Scr, SUrea, β2-MG, Cys-C, KIM-1, L-FABP and Netrin-1 were analyzed as follow. Contents of Scr [(216.48 ± 32.57) *vs.* (82.32 ± 10.14) μmol/L], SUrea [(18.85 ± 2.28) *vs.* (7.14 ± 0.93) mmol/L], β2-MG [(5.82 ± 0.74) *vs.* (1.09 ± 0.14) μg/mL] and Cys-C [(3.57 ± 0.41) *vs.* (1.15 ± 0.18) μg/mL] in blood samples and contents of KIM-1 [(2.59 ± 0.41) *vs.* (1.14 ± 0.18) ng/mL], L-FABP [(22.68 ± 4.28) *vs.* (10.49 ± 1.64) ng/mL] and Netrin-1 [(8.59 ± 1.05) *vs.* (3.62 ± 0.49) pg/mL] in urine samples of patients in AKI group were all significantly higher than those of non-AKI group. Differences of contents of Scr, SUrea, β2-MG and Cys-C in blood samples and differences of contents of KIM-1, L-FABP and Netrin-1 in urine samples in two groups were considered statistically significant ($P < 0.05$).

3.3. Indexes of podocyte injury of two groups' subjects

The podocyte injury indexes of two groups' patients in urine including nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP were analyzed. The contents of nephrin [(9.48 ± 1.17) *vs.* (4.16 ± 0.67) ng/mL], desmin [(7.35 ± 0.87) *vs.* (3.24 ± 0.45) ng/mL], P-cadherin [(204.52 ± 31.67) *vs.* (94.45 ± 11.37) pg/mL], podocin [(15.27 ± 2.25) *vs.* (6.48 ± 0.93) ng/mL], podocalyxin [(6.74 ± 0.85) *vs.* (3.42 ± 0.45) ng/mL] and CD2AP [(189.34 ± 22.62) *vs.* (67.86 ± 8.53) pg/mL] in urine of patients in AKI group were all significantly higher than those of non-AKI group. Differences of the contents of nephrin, desmin, P-cadherin, podocin, podocalyxin and CD2AP in urine of two groups' patients were considered statistically significant ($P < 0.05$).

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