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Original Article

The significance of the hemalexin C1q, RBP, and urinary NAG levels in the diagnosis and prognosis of children with purpura nephritis

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Abstract: Purpose: To investigate the significance of the hemalexin C1q, retinal-binding-protein (RBP), and urinary N-acety1-β-D-glucosaminidase (NAG) levels in the diagnosis and prognosis of children with purpura nephritis. Methods: A total of 130 children with purpura nephritis admitted to our hospital from January 2017 to December 2019 were recruited as the study cohort, including 43 children with purpura nephritis as the observation group, 51 children with purpura nephritis as the control group, and 36 healthy children undergoing physical examinations at the same time period as the healthy group. The basic data of the three groups of children were compared, and the hemalexin C1q, RBP, and urinary NAG levels were observed. The children were divided into a good prognosis group and a poor prognosis group according to the observation group's follow-up data. The significance of the hemalexin C1q, RBP, and urinary NAG levels for the diagnosis and prognosis of children with purpura nephritis was investigated by comparing the hemalexin C1q, RBP, and urinary NAG levels in these two groups. Results: The hemalexin C1q, RBP, and urinary NAG levels in the observation group, the control group, and the healthy group were significantly reduced, and the differences were statistically significant ($P < 0.05$). The hemalexin C1q, RBP, and urinary NAG levels of the children in the good prognosis group were significantly lower than they were in the poor prognosis group ($P < 0.05$). Conclusion: The hemalexin C1q, RBP, and urinary NAG levels in the diagnosis and prognosis of children with purpura nephritis have a definite value and can be used as effective predictors for the prognosis of children with purpura nephritis.

Keywords: Hemalexin C1q, RBP, measuring NAG in the urine, pediatric purpura nephritis, diagnostic significance, prognostic impact

Introduction

Purpura nephritis, also known as Henoch-Schönlein purpura nephritis, is a renal damaging disease caused by Henoch-Schönlein purpura. The incidence of renal damage in patients with purpura nephritis ranges from 10%-100%. It occurs frequently in children and is usually accompanied by skin purpura, painful swollen joints, abdominal pain, hemafecia, hematuria, and proteinuria. The symptoms are more common within one month after the skin purpura appear, and some patients also show asymptomatic abnormal urine [1, 2].

The clinical features and pathological types of purpura nephritis are diversified. Due to a wide variety of immunosuppressants, there is still a lack of a unified standard for Henoch-Schönlein purpura nephritis in clinical treatment [3, 4].

Studies have shown that about 10%-20% of children with purpura nephritis have a chronic renal insufficiency. On account of this, the clinical diagnosis and treatment of patients with Henoch-Schönlein purpura nephritis should be carried out as early as possible to ensure a desirable prognosis [5, 6].

In this study, patients with purpura nephritis, allergic purpura, and healthy children were recruited as the study cohort for this clinical study to explore the significance of the hemalexin C1q, retinal-binding-protein (RBP), and uri-

nary N-acety1-β-D-glucosaminidase (NAG) levels in the diagnosis and prognosis of children with purpura nephritis.

Materials and methods

General information

Children with purpura nephritis who were admitted to our hospital from January 2017 to December 2019 were enrolled in the study, 43 of them with purpura nephritis as the observation group, 51 of them with purpura nephritis as the control group, and 36 healthy children undergoing physical examinations at the same time period as the healthy group. There were 22 boys and 21 girls in the observation group, their average age was (8.26 ± 3.19) years old, their body mass index (BMI) was 3-13 kg/m^2, with an average of (6.58 ± 2.19) kg/m^2. There were 29 boys and 22 girls in the control group, their average age was (8.56 ± 3.22) years old, their BMI was 3-13 kg/m^2, and they had an average of (6.52 ± 3.11) kg/m^2. There were 14 boys and 22 girls in the healthy group, the average age was (8.79 ± 2.51) years old, their BMI was 2-13 kg/m^2, with an average of (6.69 ± 3.92) kg/m^2. The comparison of the general information among these three groups was not of statistical significance (P > 0.05).

Inclusion criteria

① Patients who met the diagnostic criteria for purpura nephritis. ② Patients who were confirmed to have purpura nephritis through a laboratory examination and a doctor's diagnosis. ③ Patients under 18 years old. ④ Patients with no other causes of renal injury. ⑤ Patients with no immune system diseases. ⑥ Patients who had complete clinical data.

The study was approved by the ethics committee of the hospital, and the children and their family numbers knew the purpose and process of the research and signed the informed consent forms.

Exclusion criteria

① Patients also suffering from congenital heart disease. ② Patients with blood diseases and liver diseases, etc. ③ Patients who recently used glucocorticoid drugs for treatment. ④ Patients with liver or kidney dysfunction.

Methods

Measuring the hemalexin C1q and RBP levels: 5 ml fasting venous blood was collected from the three groups in the morning. After conventional centrifugation (5000 r/min) for 15 min, the supernatant was obtained and stored at a low temperature. The C1q level in the three groups was measured using the immunoturbidimetric method, and the kits we used were produced by Shanghai Beijia Biochemical Reagent Co., LTD.

5 ml fresh urine was collected from three groups, and the supernatant was collected using conventional centrifugation and stored at -20°C for testing. The urine RBP and NAG levels were measured using double antibody enzyme-linked immunosorbent assays, and the kits we used were provided by Shanghai Sun Biotechnology Co., LTD.

Follow-up prognostic analysis: By analyzing the follow-up prognosis data of the children in the observation group, the prognostic grading standards were established as follows: no renal damage = grade A, mild urinary abnormality = grade B, and active nephropathy = grade C. Grades A and B were set as the good prognosis group, and grade C as the poor prognosis group. According to the follow-up data, 26 of the patients had a good prognosis, and 17 of the patients had a poor prognosis.

Statistical methods

The experimental data were statistically analyzed and processed using SPSS 20.0 software. The measurement data were expressed as (x ± s) and tested using t-tests, and the enumeration data were tested using x^2 tests and expressed as [n (%)]. When P < 0.05, a difference had statistical significance. GraphPad Prism 8 software was used to plot the graphics.

Results

Comparison of the hemalexin C1q levels among the three groups

The hemalexin C1q levels in the observation group, the control group, and the healthy group were significantly reduced, and the differences were statistically significant (P < 0.05), as shown in **Figure 1A**.

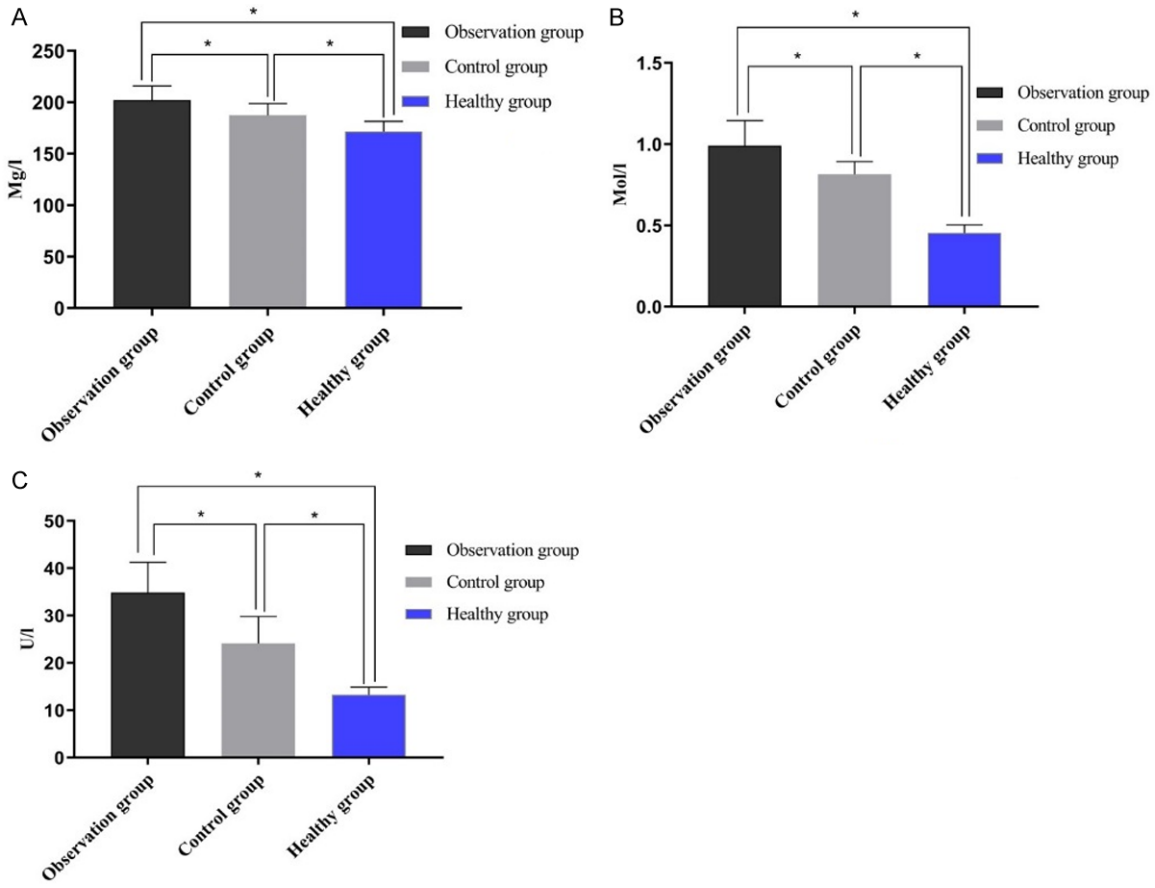

Figure 1. A comparison of the hemalexin C1q, RBP, and urinary NAG levels among the three groups ($\bar{x}$ ± s). Note: A. The abscissa represents the observation group, the control group, and the healthy group, and the ordinate represents the hemalexin C1q levels, mg/l; The hemalexin C1q level in the observation group was (192.34 ± 19.55) mg/l. The hemalexin C1q level in the control group was (179.35 ± 16.24) mg/l. The hemalexin C1q level in the healthy group was (164.33 ± 14.34) mg/l. There was a significant difference in the hemalexin C1q levels between the observation group and the control group (T=3.5194, *P=0.001). There was a significant difference in the hemalexin C1q levels between the control group and the healthy group (T=4.119, *P=0.002). There was a significant difference in the hemalexin C1q levels between the observation group and the healthy group (T=3.4923, *P=0.001). B. The abscissa represents the observation group, the control group, and the healthy group, and the ordinate represents the RBP level, mol/l. The RBP level in the observation group was (0.88 ± 0.22) mol/l. The RBP level in the control group was (0.76 ± 0.11) mol/l. The RBP level in the healthy group was (0.42 ± 0.07) mol/l. There was a significant difference in the RBP levels between the observation group and the control group (t=3.4230, *P=0.0009). There was a significant difference in the RBP levels between the control group and the healthy group (t=16.3416, *P=0.0008). There was a significant difference in the RBP levels between the observation group and the healthy group (t=12.0348, *P=0.0007). C. The abscissa represents the observation group, the control group, and the healthy group, the ordinate represents the level of urinary NAG, u/l. The urinary NAG level in the observation group was (30.28 ± 9.12) u/l. The urinary NAG level in the control group was (20.05 ± 8.10) u/l. The urinary NAG level in the healthy group was (12.14 ± 2.30) u/l. There was a significant difference in the urinary NAG levels between the observation group and the control group (t=5.7585, *P=0007). There was a significant difference in the urinary NAG levels between the control group and the healthy group (t=5.6908, *P=0009). There was a significant difference in the urinary NAG levels between the observation group and the healthy group (t=11.6177, *P=0004).

Comparison of the RBP levels among the three groups

The RBP levels in the observation group, the control group, and the healthy group were significantly reduced, and the differences were statistically significant (P < 0.05), as shown in **Figure 1B**.

Comparison of the urinary NAG levels among the three groups

The urinary NAG levels in the observation group, the control group, and the healthy group were significantly reduced, and the differences were statistically significant (P < 0.05), as shown in **Figure 1C**.

Comparison of the hemalexin C1q , RBP, and urinary NAG levels in the children with Henoch-Schönlein purpura nephritis with different prognoses

According to our data, 26 of the patients had good prognoses and 17 of the patients had poor prognoses. The hemalexin C1q, RBP, and urinary NAG levels in the good prognosis children with purpura nephritis were lower than the corresponding levels in the poor prognosis children, and the differences were statistically significant ($P < 0.05$). The hemalexin C1q levels in the good prognosis group were lower than they were in the poor prognosis group, and the differences were statistically significant ($P < 0.05$), as shown in **Figure 2A**.

Comparison of the RBP levels in the two prognosis groups

The RBP levels in the good prognosis group were significantly lower than they were in the poor prognosis group ($P < 0.05$), as shown in **Figure 2B**.

Comparison of the urinary NAG levels between the two prognosis groups

The urinary NAG levels in the good prognosis group were significantly lower than they were in the poor prognosis group, and the differences were statistically significant ($P < 0.05$), as shown in **Figure 2C**.

Discussion

Purpura nephritis is a secondary glomerulopathy with a high incidence in childhood. Its pathogenesis is associated with humoral immunity and cellular immunity and so on. Most cytokines and inflammatory mediators are also involved in the pathogenesis of this disease. Its pathological changes are the key to glomerular mesangial proliferative lesions, which are often accompanied by segmental glomerular capillary loop necrosis and crescent formation and other manifestations of vasculitis [7, 8]. Most children with Henoch-Schönlein purpura nephritis usually have renal damage within 6 months after the onset of the disease. According to the medical literature, the number of children with purpura nephritis progressing to end-stage nephropathy reaches 14.9%-21%. The early detection and diagnosis of purpura nephritis is of great significance in determining the prognosis.

More clinicians pay attention to the development of the renal function indicators in the early stage, and some studies have shown that renal tubular injuries in patients with purpura nephritis generally occur earlier than glomerular injuries. The Study by Yel, et al. [11] suggested that measuring the urinary RBP and other renal tubular marker protein levels is conducive to the early detection of purpura nephritis.

Hemalexin C1q is an important starting molecule to open the classic pathway of complement. It can combine with a variety of ligands to clear the apoptotic cells, remove retroviruses and cell adhesion, and regulate the immune processes of the dendritic cells and B cells. Prior studies showed that hemalexin C1q plays a positive role in the diagnosis of purpura nephritis, but its specific mechanism remains poorly understood, or there is a certain relationship between hemalexin C1q and immune globulin deposition in glomeruli, which leads to an imbalance of the immune function [12, 13].

RBP is a low molecular protein, and its main function is to transport retinol from the liver to the epithelial cells. After its filtration from the glomerulus, RBP is easily reabsorbed by the convoluted tubules. If the renal tubule function is abnormal, the RBP reabsorption is impaired, so its excretion in the urine will increase. Additionally, it is not easily destroyed in the acidic environment. It is stable and helpful in the evaluation of nephropathy [14, 15]. We found that it is of pivotal importance in the diagnosis and prognosis of Henoch-Schönlein purpura nephritis.

NAG, a glycoprotein, is a common lysosomal hydrolase in cells, and it generally exists in the lysosomes of cells contained in proximal convoluted tubules [16, 17].

Under normal conditions, the serum NAG in the body cannot pass through the glomerular filtration membrane. When the kidney is damaged, the lysosome in the renal proximal convoluted tubular cells will be ruptured, NAG will be released, and the urine NAG level will increase significantly, effectively reflecting the body's kidney injury [18, 19]. This study showed that NAG can provide information for the diagnosis and evaluation of purpura nephritis.

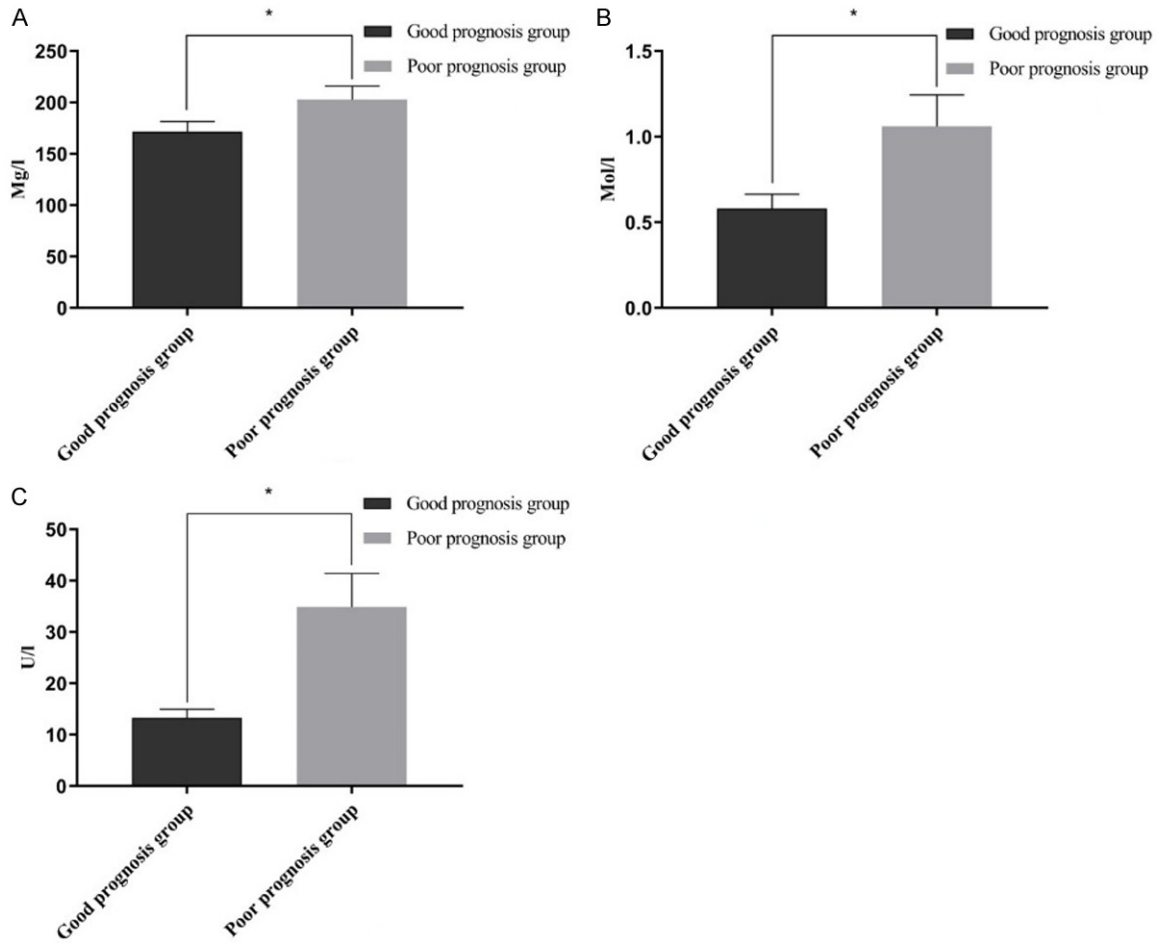

Figure 2. A comparison of the hemalexin C1q , RBP, and urinary NAG levels between the two prognosis groups ($\bar{x}$ ± s). Note: A. The abscissa represents the good prognosis group and the poor prognosis group, the ordinate represents the hemalexin C1q levels, mg/l. The hemalexin C1q level in the good prognosis group was (164.33 ± 14.35) mg/l. The hemalexin C1q level in the poor prognosis group was (193.43 ± 18.60) mg/l. There was a significant difference in the hemalexin C1q levels between the good prognosis group and the poor prognosis group (t=5.7939, *P=0008). B. The abscissa represents the good prognosis group and the poor prognosis group, the ordinate represents the RBP levels, mol/l. The RBP level in the good prognosis group was (0.52 ± 0.12) mol/l. The RBP level in the poor prognosis group was (0.93 ± 0.26) mol/l. There was a significant difference in the RBP levels between the good prognosis group and poor prognosis group (t=6.9463, *P=0001). C. The abscissa represents the good prognosis and poor prognosis groups, the ordinate represents the urinary NAG levels, u/l. The urinary NAG level in the good prognosis group was (12.15 ± 2.34) u/l. The urinary NAG level in the poor prognosis group was (30.31 ± 9.20) u/l. There was a significant difference in the urinary NAG levels between the good prognosis group and the poor prognosis group (t=9.4927, *P=0002).

A previous study [20] confirmed that hemalexin C1q and urinary NAG have high diagnostic values in the determination of nephropathy. This study preliminarily showed that the hemalexin C1q, RBP, and urinary NAG levels in the observation group, the control group, and the healthy group all decreased significantly, which means that the hemalexin C1q, RBP, and urinary NAG levels in the purpuric nephritis patients were on the rise, indicating that hemalexin C1q, RBP, and urinary NAG have a certain diagnostic value in purpura nephritis, and they can improve the purpura nephritis early diagnosis rate.

We also observed that the hemalexin C1q, RBP, and urinary NAG levels in children with purpura nephritis in the good prognosis group were lower than they were in the poor prognosis group, a finding that contributes to the prognosis evaluation of children with purpura nephritis. Due to the small sample size and the short-term follow-up, the present trial may yield some bias.

In conclusion, hemalexin C1q, RBP, and urinary NAG demonstrate a definite value in the diagnosis and the prognosis of children with Henoch-Schönlein purpura nephritis.

Disclosure of conflict of interest

None.

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