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Research Article

ACUTE AND DISEASE WITH GLOMERULONEPHRITIS CYTOKINE BALANCE IN SICK PATIENTS

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ABSTRACT

Glomerular kidney damage - glomerulonephritis (GN) is one of the serious medical and economic problems. Often, GN is the main cause of end-stage chronic renal failure, which is incompatible with life and requires renal replacement therapy (dialysis, donor kidney transplantation) [2]. According to the course of the disease, there is an acute form of GN (the duration of the disease is less than one year) and chronic (the duration of the disease is more than one year). In clinical practice, there are often difficulties in timely differentiation of chronic GN and acute GN exacerbation, in particular, in the urinary (hidden) form of the disease, due to the lack of clear criteria for their diagnosis.

KEYWORDS

Chronic glomerulonephritis, cytokine balance, children.

INTRODUCTION

Glomerular kidney damage - glomerulonephritis (GN) is one of the serious medical and economic problems. Often, GN is the main cause of end-stage chronic renal failure, which is incompatible with life and requires

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renal replacement therapy (dialysis, donor kidney transplantation) [2]. According to the course of the disease, there is an acute form of GN (the duration of the disease is less than one year) and chronic (the duration of the disease is more than one year). In clinical practice, there are often difficulties in timely differentiation of chronic GN and acute GN exacerbation, in particular, in the urinary (hidden) form of the disease, due to the lack of clear criteria for their diagnosis.

There are works dedicated to the study of biomarkers of glomerulonephritis chronicity [1, 3, 7]. At the same time, the role of pro- and anti-inflammatory cytokines in maintaining the inflammatory process in glomerulonephritis of various clinical courses has not yet been determined. In relation to the above, the aim of this study was to investigate the circulating levels of cytokines in patients with acute and chronic GN.

METHODS

This study included 55 patients with GN aged 10 to 18 years who were treated in the nephrology department at Children's City Hospital No. 1 in Samarkand. At the beginning of the disease, 10 patients (acute GN), with exacerbation of chronic GN - 45 patients were studied. Diagnostic nephrobiopsy was performed in 34 patients, mesangioproliferative variant of GN was detected in 21 cases, membranoproliferative variant in 6 cases, membranous in 6 cases, and GN with minimal changes in 1 case. There are 24 girls and 31 boys among those who passed the examination. Groups of patients with acute GN and chronic GN were representative of patients with different morphological variants of the disease and representative of the functional status of the patients' kidneys. In addition to the generally accepted studies (general clinical blood and urine tests, biochemical studies - creatinine, urea, bilirubin, transaminases, hemostasiogram, proteinogram, C-reactive protein, glomerular filtration rate, tubular reabsorption, ultrasound examination of the kidneys), concentration. The main cytokines circulating in the blood were identified - interleukin-1b (IL-1b), interleukin-2 (IL-2), interleukin-10 (IL-10), interferon-y (IFN-y) and IL-1b receptor antagonist - Ra -IL-1b. The object of the study was venous blood serum. Blood tests were performed twice - at admission to inpatient treatment (on days 2-3) and at the end of the period of inpatient treatment (on days 12-14). The following parameters of descriptive statistics were determined: arithmetic mean (M), standard deviation (SD). When comparing two samples, Student's t-test (p) was used to assess the significance of differences. In the case of asymmetric distribution of the set of indicator values in the groups, the median (Me) was calculated, the limits of variation of the study population were from 5% to 95% (P5 - P95), and the reliability of the differences was non-parametric Mann-Whitney tests for independent groups. (pm-w) and was evaluated using Wilcoxon (pw) for conjugated groups [4]. The reliability of the relationship between two series of observations was evaluated based on the calculation of the Spearman

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rank correlation coefficient (rs), the reliability of the coefficients was considered acceptable when prs<0.05. The values of the laboratory parameters obtained during the study were compared with the reference values, which were the results of the examination of 25 practically healthy people. Research results and discussion. The results of the study show that patients with GN, regardless of the nature of the clinical course of the disease - acute or chronic, produce both pro-inflammatory cytokines (IL-1b, IL-2) and anti-inflammatory cytokines. is released. - IL-10 and Ra-IL-1b. The object of research was venous blood serum. Blood tests were performed twice - at admission to inpatient treatment (on 2-3 days) and at the end of the inpatient treatment period (on 12-14 days).

The statistics of the obtained result were determined by the following parameters: arithmetic mean (M), standard deviation (SD). When comparing two samples, Student's t-test (p) was used to assess the significance of differences. In the case of asymmetric distribution of the set of indicator values in the groups, the median (Me) was calculated, the limits of variation of the study population were from 5% to 95% (P5 - P95), and the reliability of the differences was non-parametric Mann-Whitney tests for independent groups. (pm-w) and was evaluated using Wilcoxon (pw) for conjugated groups [4]. The reliability of the relationship between two series of observations was evaluated based on the calculation of the Spearman

rank correlation coefficient (rs), the reliability of the coefficients was considered acceptable when prs<0.05. The values of the laboratory parameters obtained during the study were compared with the values of the results of the examination of 25 practically healthy people.

RESULTS

The results of the study show that in patients with GN, regardless of the nature of the clinical course of the disease - acute or chronic, both pro-inflammatory cytokines (IL-1b, IL-2) and anti-inflammatory cytokines are produced. Released - IL-10 and Ra-IL-1b. An exception is the pro-inflammatory cytokine IFN-γ, which has regulatory functions, and their values are at the reference level.

During GN, the increase in the production of pro-inflammatory cytokines is explained by the development of inflammatory changes in the glomeruli as a result of infiltration by lymphocytes, monocytes and the increase of resident glomerular cells [5]. An increase in the production of anti-inflammatory cytokines - IL-10 and Ra-IL-1b, which occurs in parallel with an increase in the level of pro-inflammatory cytokines, can be considered as an autoregulatory reaction aimed at suppressing the increase in production, inflammation to suppress the production of pro-inflammatory cytokines [6].

Cytokine profile of patients with GN revealed some features depending on the clinical course of the disease. Thus, the average amount of Ra-IL-1b in

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patients with exacerbation of chronic GN is 2.6 times lower than the corresponding value in patients with acute GN, and IFN-γ in the last stage of inpatient treatment with acute GN was 1.6 times higher than that of the group of sick patients. Despite the fact that the average amount of IL-1β in patients with chronic GN was 4.7 times lower than the corresponding value in patients with acute GN, the difference between the level of production of this cytokine in the compared groups of patients was statistically not important.

Comparison of cytokine levels before and after treatment using the Wilcoxon test revealed certain dynamics of cytokine production levels during treatment in patients with acute GN, with a decrease in the initial high levels of IL-1β, Rα-IL-1β and IL-2 appeared. The level of IFNγ was also significantly decreased ($p_w<0.05$), its baseline level was not different from the corresponding reference values. No significant dynamics in the production of cytokines were observed during treatment in patients with chronic GN.

In connection with the known situation about the mutual dependence of the production of individual cytokines, we investigated the correlation relationship between the levels of the studied cytokines. In healthy people, only one correlation was established between the indicators of cytokine status - a negative correlation of the levels of anti-inflammatory cytokines - IL-10 and Ra-IL-1b ($r_s = -0.76$; $p_{rs} = 0.030$). Being With the development of glomerular kidney damage, the total number of connections increased significantly. Cytokine profile of patients with chronic GN including pro-inflammatory cytokine IL-1β and its receptor antagonist, pro-inflammatory cytokines IL-2 and IFNγ, pro-inflammatory cytokine IFNγ and pro-inflammatory cytokine IL-10 baseline characterized by the existence of a direct relationship between internal levels. Relationships established at the end of treatment were also observed. In addition, by the end of treatment, a new correlation was found between IL-2 and IL-10 levels. The correlations found in patients with chronic GN suggest the interaction of pro-inflammatory and anti-inflammatory cytokine production.

This, the results of the correlation analysis show that there is a correlation between only pro-inflammatory cytokines in healthy individuals. The relationships identified in the acute form of GN reflect the interdependence of the production of pro-inflammatory cytokines. A close relationship between the levels of pro-inflammatory and anti-inflammatory cytokine production during the period of exacerbation of chronic GN is revealed. In addition, by the end of chronic GN exacerbation relief, the number of such connections increases, in patients with acute GN, by the end of inpatient treatment, no correlation is found in the level of studied cytokines.

In connection with the differences in the levels of Rα-IL-1β and IFNγ detected in patients with acute and chronic GN, it is noteworthy that these cytokines correlate with the indicators of a set of standard

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laboratory tests for GN (4 -table). Baseline values of Rα-IL-1β were positively correlated with peripheral blood neutrophil leukocyte levels and negatively correlated with urine specific gravity. At the end of hospital treatment, IFNγ levels were positively related to serum creatinine levels.

Cytokines	Laboratory indicators	Rs	Prs
IL-1b (1)	Serum urea (2)	0,35	0,016
	Specific gravity of urine (1)	-0,33	0,027
Ra-IL-1b (1)	neutrophils% (1)	0,45	0,009
	neutrophils abs (1)	0,37	0,037
	neutrophils abs (2)	0,43	0,015
IFNy	Serum creatinine(2)	0,35	0,047

Table 1. Statistically significant correlation between indicators of cytokine status and standard laboratory tests in patients with GNNote: (1) - indicator values on days 2-3 and (2) - on days 12-14 of hospital treatment; abs. – absolute value (in 1 l).

In view of the established correlation of the cytokine system, some features of laboratory results of GN can be explained by different types of clinical course.

In patients with chronic GN, the content of neutrophil cells is lower than in patients with acute GN. This fact may be related to the low initial level of Rα-IL-1β in the chronic course of GN, which is positively related to the amount of neutrophils in the blood.

Table 2. Statistically significant differences in laboratory parameters in patients with different clinical course of GN

Note: (1) - indicator values on days 2-3 and (2) - on days 12-14 of hospital treatment; abs. – absolute value (in 1 l).

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Previously, we tried to find immuno-hematological markers that distinguish the exacerbation of chronic GN from the onset of the disease [1]. We found that the absolute number of neutrophils and the relative number of eosinophils determined before treatment of a patient with GN can be used to distinguish the nature of the clinical course of GN. Contrary to expectations, immunological indicators were not suitable for use as diagnostic criteria to determine the nature of the clinical course of GN: we could not find differences in innate and adaptive immune response indicators in groups of patients with acute and chronic diseases

In patients with GN, a different situation occurs according to the results of the study of the cytokine profile: the exacerbation of chronic GN is distinguished from the onset of GN by a smaller increase in the level of anti-inflammatory cytokine - Pa-IL-1b, the characteristics of which are 5- 95 percentile interval from 111 to 3915 pg/ml (in patients with acute GN - from 395 to 2942 pg/ml) and high levels of pro-inflammatory cytokine - IFNγ are distributed, at the end of treatment from 26.7 With changes up to 412.4 pg / ml (in patients with acute GN - from 24.1 to 45 pg / ml). Therefore, determination of the levels of Rα-IL-1β and IFN-γ can be used to distinguish between acute and chronic GN: a baseline Rα-IL-1β level below 395 pg/ml in a patient with GN is concentration increases the probability of diagnosis in favor of chronic GN with the presence of other symptoms of chronic GN. In this case, if the level of IFN-γ is higher than 45 pg / ml, the diagnosis of chronic GN can be confirmed by the 14th day of hospital treatment.

CONCLUSION

1. Differences in the cytokine profile in patients with GN were determined depending on the clinical course of the disease.

2. In the acute period of GN, a direct correlation was found in the levels of production of pro-inflammatory cytokines, which disappear until the end of hospital treatment. The chronic course of GN is characterized by the presence of interdependence in the production of pro-inflammatory and anti-inflammatory cytokines.

3. Cytokine profile of patients with exacerbation of chronic GN is characterized by low initial level of circulating Pa-IL-1b and high level of IFN-γ by the end of the inpatient treatment course.

4. The initial concentration of Ra-IL-1b at hospitalization of a patient with GN below 395 pg / ml increases the probability of diagnosis in favor of chronic GN.

REFERENCES

1. Alchinbaev M. K., Sultonova B. G., Karabaeva A. J. Surunkali pielonefrit bilan og'rigan bemorlarda funktsional buyrak zaxirasi. // Nefrologiya. - 2001. 5-jild, 2-son. 71-74 betlar.
2. Yesayan A.M., Buyrakning to'qima renin-angiotensin tizimi. nefroproteksiyaning yangi strategiyasi / / nefrologiya.- 2002. 6-jild, 3-son.10-14 betlar

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3. Kartamisheva N. N., Chumakova O. V., Kucherenko A. G. Surunkali pielonefrit va surunkali interstitsial nefritning rivojlanish omillari / / pediatriya. G. N. Speranskiy Tomonidan 2004 Yil. №5.50-53 betlar.
4. Muhin N. A., Balkarov I. M., Moiseev S. V. va boshqalar. Surunkali progressiv nefropatiyalar va zamonaviy insonning turmush tarzi / / ter. arx. -- 2004.-№9.5 10 sahifa.
5. Ni A. N., Luchaninova V. N., Popova V. V., Simeshina O. V. Bolalardagi dismetabolik bilan nefropatiyalarning gomeostatik buyrak funktsiyalarining tuzilishi / / nefrologiya.-2004.8-jild, 2-son.-C. 68-72.
6. Rogov V. A., Kutirina I. M., Tareyeva I. E. va boshqalar. Nefrotik sindromda buyraklarning funktsional zaxirasi / / ter. arx. - qaniydi? 1996.-No6.-C. 55-58.
7. Smirnov A. V., Yesayan A. M., Kayukov I. G. Surunkali buyrak kasalligi: yakdillik birligi yo'lida //nefrologiya.-2002.6-jild, 4-son.11-17 betlar.
8. Ишкабулова Г.Д., Холмурадова З.Э. Фосфолипидная структура и состояние перекисного окисления липидов эритроцитарных мембран у новорожденных от матерей с гестозом, сочетанным хроническим пиелонефритом. //Журнал Биомедицины и практики .2022.-№3 –С71-77.
9. Epstein M. Aldosterone as a mediator of progressive renal disease: Pathogenetic and clinical implications ||Am, J. Kidney Dis.-2001; 237:677-688.
10. Mazzali M., Hyghes J.; Kin Y. et. al. Elevated uric-acid increases blood pressure in the rat by a novel crystalindependent mechanism Hypertension.-2001; 38: 1101-1106.
11. Ishkabulova G. D. et al. MODERN METHODS FOR ASSESSING THE COURSE, TREATMENT, AND PROGNOSIS OF CHRONIC RENAL FAILURE IN CHILDREN //British Medical Journal. – 2023. – Т. 3. – №. 1.
12. Yuryeva E. A., Dlin V. V. “Nefrologiya diagnostik qo'llanmasi,".-2002.-95c.
13. Ишкабулова Г. Д., Холмурадова З. Э. Homiladorlik surunkali pielonefrit va gestoz bilan kechgan onalardan tug'ilgan chaqaloqlarda fosfolipid tuzilishi va eritrotsit membranalarining lipid peroksidlanish holati //Журнал Биомедицины и Практики. – 2022. – Т. 7. – №. 3.
14. Ishkabulova G.D.,Kholmuradova Z.E. Functional state of the kidneys in Newborn born From Mothers With Pre-Eklampsia // World Bulletin of Public Health (WBPH).-2022 Semtember, -c75-78
15. Comparative assessment on the effect of different methods of corrective therapy on lipid metabolismand homeostatic renal function. ISHKABULOVA G.J.1, KHAIDAROVA K.R.1, KUDRATOVA G.N.1, KHOLMURADOVA Z.E.1 Department of Pediatrics, Faculty of Therapeutics,

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16. Ergashevna K. Z., Ramizovna K. K., Botirbekovna I. Y. Obesity and the Functional State of the Cardiovascular System in Children //Eurasian Medical Research Periodical. – 2022. – Т. 8. – С. 48-51.
17. Jonhurozovna I. G., Ergashevna K. Z. CLINICAL SIGNIFICANCE OF FUNCTIONAL RESERVING OF THE KIDNEYS IN DISMETABOLIC NEPHROPATHY AND CHILDREN //Archive of Conferences. – 2021. – Т. 17. – №. 1. – С. 60-65.