EUROPEAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH AND MANAGEMENT STUDIES

VOLUME03 ISSUE06
DOI: https://doi.org/10.55640/eijmrms-03-06-31 Pages: 151-156

THE ROLE OF LIPOCALIN-2 ASSOCIATED WITH NEUTROPHIL GELATINASE (NGAL) IN THE DEVELOPMENT OF ACUTE NEPHROLOGICAL PATHOLOGY IN CHILDREN AGAINST THE BACKGROUND OF COVID-19

Ismoilova Z.A.
Assistant Of Pediatrics And HN Department Of Urgench Branch Of TMA, Uzbekistan

Ahmedjanova N.I.
D.M.S. Associate Professor, Head Of Pediatrics Department, Samarkand State Medical University, Uzbekistan

ABOUT ARTICLE

Key words: NGAL in urine, acute pyelonephritis, acute interstitial nephritis, COVID-19, children, Ingavirin.

Received: 09.06.2023
Accepted: 14.06.2023
Published: 19.06.2023

Abstract: We studied the features of the course of acute pyelonephritis and acute tubulointerstitial nephritis on the background of Covid-19 in children living in the region. Khorezm in modern conditions constituting the general epidemiological situation, etiology and clinical manifestations of renal pathology in children. Determination of NGAL in urine is an accessible and noninvasive method for early detection of renal parenchyma affection, for improving the quality of differential diagnosis and choosing the tactics of management of patients with microbial-inflammatory diseases of the urinary system.

INTRODUCTION

Increasing efforts are being made to elucidate the specific mechanisms of intrinsic renal pathophysiology following acute COVID-19 infection. Determining these mechanisms can be challenging due to ethical limitations associated with routine kidney biopsy in children and the current lack of an accurate noninvasive diagnostic test [3,4].

Because of the nonspecificity of clinical symptoms, laboratory and instrumental methods of investigation are of great importance in the diagnosis of inflammatory diseases of the urinary system. Minimally invasive methods with high sensitivity should be preferred in the examination of children with suspected urinary tract infection. Difficulties in differential diagnosis of urinary tract infection and

pyelonephritis force the search for new markers to help establish the correct diagnosis and timely conduct the necessary therapy. The development and search for new biomarkers in urine to verify bacterial inflammation in the renal tissue, which can further lead to the development of tubulointerstitial fibrosis, is an important task in pediatric nephrology. Recently, new potential biomarkers of bacterial inflammation have been proposed, including interleukins, enzymes, prostaglandins, lipocalin-2 associated with neutrophil gelatinase (NGAL), and several others. A.E. Eremeeva in the nephrology department of G.N. Speransky Children's Clinical Hospital No.9 examined 30 children with inflammatory diseases of the urinary system. The author determined that the level of NGAL in the urine of children with active microbial inflammatory process in the renal tissue was significantly higher than that of children in the group with urinary tract infection, as well as in the group of children with acute pyelonephritis a direct correlation of moderate strength ($r=0,72$; $p<0,05$) between the level of NGAL excretion and the value of leukocytosis, as well as the level of CRP in the blood was established ($r=0,67$; $p<0,05$). These data indicate the need for further study of the significance of increased NGAL excretion as one of the diagnostic markers of renal parenchymal damage [1-2].

The aim of the study was to investigate the clinical and diagnostic significance of the determination of lipocalin-2 associated with neutrophil gelatinase (NGAL) in the urine of children with acute renal pathology developed against the background of Covid-19.

Object and subject of the study. We studied 132 children, including 65 children with AP, of which 30 with AP without history of Covid-19 and 35 with AP against Covid-19, as well as 67 patients with acute TIN, of which 35 with OTIN without history of Covid-19 and 32 with aTIN against Covid-19, aged from 4 to 18 years. Depending on the methods of treatment, the patients were divided into two groups: Group 1 consisted of 20 patients with AP and 17 children with aTIN who had a history of Covid-19, who received conventional methods of treatment; Group 2 consisted of 15 patients with AP and 15 patients with aTIN who had Covid-19 in the anamnesis and received complex therapy. One of the components of the basic therapy was etiotropic treatment.

RESEARCH METHODS

NGAL level was measured in the morning urine using enzyme immunoassay (BioVendor Laboratory Medicine kit) according to the manufacturer's instructions. The study was performed on an automated microplate photometer. Urinary NGAL levels were expressed in nanograms per 1 ml, with a detection limit of <0.1 ng/ml. To standardize the index, creatinine level in each urine portion was determined and NGAL level in urine was converted to 1 mg of creatinine.

Results of the study. Plasma NGAL was found to be freely filtered by the glomeruli, but then reabsorbed to a large extent in the proximal tubules due to endocytosis. For this reason, the "renal" pool of NGAL synthesized in the kidneys predominates in the urine; this pool of NGAL does not enter the circulatory system but is completely excreted in the urine.

It has been shown that when the proximal tubules are damaged, there is a rapid increase in NGAL-encoding mRNA synthesis in the ascending knee of the Genle loop and in the collecting tubules. Its main functions are to counteract bacterial infections and stimulate the proliferation of damaged cells,

primarily epithelial cells. Urinary NGAL levels in children in Group 2 were significantly higher than those in the comparison group (110.73±8.37 and 65.66±3.54 ng per 1mg creatinine, respectively; p<0.001) (Table 1).

Table 1

NGAL scores in AP patients depending on the presence of Covid-19

Indicator	In healthy	Before treatment	
		1 group (n=30)	2 group (n=35)
NGAL, (ng/ml)	4,2±1,8	65,66±3,54 p<0,001	110,73±8,37 p<0,001

Note: p - statistical difference between the values before treatment and healthy children.

Thus, the concentration of NGAL in the urine of children with AP developed against the background of Covid-19 was significantly higher than in children from the comparison group (p<0.001).Analyzing the results of this study, we found that the concentration of NGAL in the urine directly correlated with the degree of renal parenchyma damage, which proves the development of the most significant damage to the renal tissue in children exposed to coronavirus infection.

In the group of children with AP a direct correlation of moderate strength (r=0,65; p<0,05) between the level of excretion of NGAL and the value of leukocytosis, as well as a strong direct correlation (r=0,75; p<0,05) between the level of NGAL in the urine and the degree of damage of the renal parenchyma according to the results of dynamic nephroscintigraphy were established.

Table 2

NGAL score in aTIN patients depending on the presence of Covid-19

Indicator	In healthy	Before treatment	
		1 group (n=35)	2 group (n=32)
NGAL, (ng/ml)	4,2±1,8	18,76±2,54 p<0,001	89,73±5,43 p<0,001

Note: p is the statistical difference between the pre-treatment and healthy children.

Thus, increased NGAL excretion was combined only with the presence of urinary tract infection and positive urine culture, whereas against the background of renal parenchymal ischemia-reperfusion characteristic of aTIN a less pronounced increase in NGAL in urine was noted.

Thus, against the background of proximal tubule lesions under the influence of coronovirus there is an accelerated growth of NGAL-forming mRNA synthesis in the ascending part of the Genle loop and in the collecting tubules. Its main function is resistance to bacterial agents and activation of proliferation of the affected cells, especially epithelial cells.

At the same time, application of Ingavirin in children resulted in 11-fold decrease of NGAL level in the urine, making 10,46±1,3 ng/ml, whereas in Group 1 children this index decreased only 5-fold to 20,78±1,2 ng/ml (p1<0,001; p2<0,001).

Table 3

NGAL index in urine of AP patients depending on applied treatment methods

Indicator	Before treatment	After treatment	
		1 group (n=17)	2 group (n=15)
NGAL, (ng/ml)	110,73±8,37	20,78±1,2 p_1<0,001	10,46±1,3 p_1<0,001, p_2<0,001

Note: p1-validity of differences between the parameters before treatment and after therapy; p2-comparison of the courses of complex and conventional treatment.

High efficacy of combined therapy was observed according to the dynamics of cytokine levels in serum and urine in all children with AP against the background of Covid-19.

Thus, in Group 2 children against the background of Ingavirin application, there was an authentic decrease of NGAL in children by 12 times and it was 7,46±1,3 ng/ml (p1<0,001, p2<0,001), while with the conventional treatment there was only 5 times decrease (16,78±4,2; p1<0,001) (Table 4).

Table 4

Urinary NGAL index in patients with aTIN depending on the treatment methods used

Indicator	Before treatment	After treatment	
		1 group (n=17)	2 group (n=15)
NGAL, (ng/ml)	89,73±5,43	16,78±4,2 P_1<0,001	7,46±1,3 P_1<0,001, P_2<0,001

Note: p1-validity of differences between the parameters before and after treatment of patients with aTIN; p2-validity when comparing the courses of complex and traditional treatment of patients with aTIN.

The results of the study indicate that the method of combined use of the drug "Ingavirin" in the complex treatment of group 2 patients leads to a stable and complete correction of the level of NGAL in the urine, observed in aTIN against the background of Covid-19 in children.

CONCLUSIONS

In our study, we determined that the level of NGAL in the urine depends on the degree of damage to the renal parenchyma. A positive correlation between NGAL excretion and such acute phase indices as leukocytosis level in children with acute pyelonephritis and acute tubulointerstitial nephritis against Covid-19 has been established, which allows to use NGAL excretion level as a marker of acute disease. The data obtained indicate the need for further study of the significance of increased NGAL excretion as one of the diagnostic markers of renal parenchymal damage. The proposed method of combined treatment (and "Ingavirin") leads to faster recovery of filtration-reabsorption, ammonioacidogenetic and osmoregulatory functions of the kidneys and promotes normalization of NGAL in the urine.

REFERENCES

1. A.V. Eremeeva, V.V. Dlin, A.A. Korsunsky, S.B. Orekhova. Clinical and diagnostic significance of determination of lipocalin-2 associated with neutrophil gelatinase in urine of children with microbial inflammatory diseases of the kidneys and urinary tract. RUSSIAN BULLETIN OF PERINATOLOGY AND PEDIATRICS. 2015,6,60-65.
2. 2.Yilmaz A., Sevketoglu E., Gedikbasi A. et al. Early prediction of urinary tract infection with urinary neutrophil gelatinase associated lipocalin. Pediatr Nephrol 2009; 24: 12: e2387-92.
3. Kim B.H., Yu N., Kim H.R. et al. Evaluation of the optimal neutrophil gelatinase-associated lipocalin value as a screening biomarker for urinary tract infections in children. Ann Lab
4. Med 2014; 34: e354-359.
5. Karavanaki K., Haliotis F.A., Haliotis F.A. DMSA scintigraphy in febrile urinary tract infections could be omitted in children with low procalcitonin levels. Infectious Diseases in Clinical Practice 2007; 15: 6: e377-381.
6. 5.Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z,et al. Epidemiology of COVID-19 among children in China. Pediatrics. 2020;145(6):
7. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 infection in children. N Engl.
8. J Med. 2020;382(17):1663-5.
9. Xu Y, Li X, Zhu B, Liang H, Fang C, Gong Y,et al. Characteristics of pediatric SARS-CoV-2
10. infection and potential evidence for persistent fecal viral shedding. Nat Med. 2020;26(4):502-5
11. 8.Godfred-Cato, S.; Bryant, B.; Leung, J.; Oster, M.E.; Conklin, L.; Abrams, J.; Roguski, K.; Wallace, B.; Prezzato, E.; Koumans, E.H.;et al. COVID-19–associated multisystem inflammatory syndrome in children—United States, March–July 2020. MMWR Morb.Mortal. Wkly. Rep. 2020, 69, 1074–1080. [CrossRef] [PubMed]
12. González-Dambrauskas, S.; Vásquez-Hoyos, P.; Camporesi, A.; Díaz-Rubio, F.; Piñeres-Olave, B.E.; Fernández-Sarmiento, J.;
13. Gertz, S.; Harwayne-Gidansky, I.; Pietroboni, P.; Shein, S.L.; et al. PediatriccriticalcareandCOVID-19. Pediatrics2020, 146, e20201766. [CrossRef] [PubMed]

14. Mishra J., Ma Q., Prada A. et al. Identification of neutrophil gelatinase–associated lipocalin as a novel early urinary biomarker for ischemic renal injury. Clin J Am Soc Nephrol 2003; 14: e2534–2543.

15. Коровина Н.А. Пиелонефрит. Диагностика и лечение нефропатий у детей. Под ред. М.С. Игнатовой, Н.А. Коровиной. М: ГЭОТАР-Медиа 2007; 164–199. (Korovina N.A. Pyelonephritis. Diagnosis and treatment of nephropathy in children. M.S. Ignatova, N.A. Korovina (eds). M: GJEOTAR-Media 2007; 164–199.)