UDC 616.613-007.63 https://doi.org/10.33619/2414-2948/40/07

STUDYING OF THE SYSTEM IL-1 AND G-CSF IN HYDRONEPHROSIS AS A PERSPECTIVE OF CREATING NEW DIAGNOSTIC TEST SYSTEMS

©Vechkanova N., *SPIN-code: 4986-0472, ORCID: 0000-0001-8563-9759, Ph.D., National Research Mordovia State University, Saransk, Russia, vechkanova-med@gmail.com*
©Stepanov N., *SPIN-code: 5786-4753, ORCID: 0000-0002-8293-9753, National Research Mordovia State University, Saransk, Russia, jedi777jedi@mail.ru*
©Mashnin I., *National Research Mordovia State University, Saransk, Russia, igor.ssmei@mail.ru*
©Duvayarov Z., *National Research Mordovia State University, Saransk, Russia, duvayarov@mail.ru*
©Selkin V., *National Research Mordovia State University, Saransk, Russia, vlasel95@gmail.com*

ИЗУЧЕНИЕ СИСТЕМЫ IL-1 И G-CSF ПРИ ГИДРОНЕФРОЗЕ КАК ПЕРСПЕКТИВА СОЗДАНИЯ НОВЫХ ДИАГНОСТИЧЕСКИХ ТЕСТОВЫХ СИСТЕМ

©Вечканова Н. А., *SPIN-код: 4986-0472, ORCID: 0000-0001-8563-9759, канд. биол. наук., Национальный исследовательский Мордовский государственный университет им. Н. П. Огарева, г. Саранск, Россия, vechkanova-med@gmail.com*
©Степанов Н. Ю., *SPIN-код: 5786-4753, ORCID: 0000-0002-8293-9753, Национальный исследовательский Мордовский государственный университет им. Н. П. Огарева, г. Саранск, Россия, jedi777jedi@mail.ru*
©Машнин И. В., *Национальный исследовательский Мордовский государственный университет им. Н. П. Огарева, г. Саранск, Россия, igor.ssmei@mail.ru*
©Дуваяров З. А., *Национальный исследовательский Мордовский государственный университет им. Н. П. Огарева, г. Саранск, Россия, duvayarov@mail.ru*
©Селькин В. В., *Национальный исследовательский Мордовский государственный университет им. Н. П. Огарева, г. Саранск, Россия, vlasel95@gmail.com*

Abstract. Hydronephrosis refers to diseases of the urinary system, which are characterized by high prevalence. Moreover, this pathology of all obstructive uropathies, leading to a decrease in the function of the renal parenchyma, accounts for up to 15% of cases. Therefore, the search for various markers involved in the development and progression of kidney damage is particularly relevant, since in the literature there are very contradictory data. Our article presents the results of a survey of 40 patients with established and confirmed diagnosis of stage I hydronephrosis (according to the classification of N. A. Lopatkin), and 20 completely healthy people (control group). All patients initially and at the end of the study determined the levels of cytokines: IL-1a, IL-1b, IL-1ra and G-CSF. We found that patients with hydronephrosis had higher rates of pro-inflammatory components of the IL-1β system: IL-1β — 104.42 (75% CI [111.8–151.4]) pg/ml, which was significantly higher than in the control group 3.7 times. In patients with hydronephrosis, there is an increase in the levels of IL-1β, IL-1a, and G-CSF against the background of a decrease in IL-1ra. The study of the IL-1 and G-CSF systems in dynamics during hydronephrosis is a very promising direction, opening up enormous opportunities in creating effective diagnostic markers of hydronephrosis in the very early stages of the formation of this pathology. Thus, analysis of the literature indicates that damage to the renal tissue in obstructive uropathies is an extremely complex process, and the initiation of fibrogenesis processes with partial inhibition of resorption leads to remodelling of connective tissue and progression of nephrosclerosis.

Аннотация. Гидронефроз относится к заболеваниям мочевыделительной системы, которые характеризуются высокой распространенностью. Причем на данную патологию из всех обструктивных уропатий, приводящих к снижению функции почечной паренхимы, приходится до 15% случаев. Поэтому поиск различных маркеров, участвующих в развитии и прогрессировании поражении почек особенно актуален, так как в литературных источниках встречаются весьма противоречивые данные. В нашей статье приведены результаты обследования 40 больных с установленным и подтвержденным диагнозом гидронефроз I стадии (по классификации Н. А. Лопаткина), и 20 совершенно здоровых людей (контрольная группа). У всех пациентов исходно и в конце исследования определялись показатели уровня цитокинов: IL-1a, IL-1b, IL-1ra и G-CSF. Нами было выявлено, что у больных с гидронефрозом зафиксированы достоверно более высокие уровни IL-1β: IL-1β — 104,42 (75% ДИ [111,8–151,4]) пг/мл, в сравнении с группой контроля. У пациентов с гидронефрозом происходит повышение уровней IL-1β, IL-1a, и G-CSF на фоне снижения IL-1ra. Изучение системы G-CSF и IL-1 при гидронефрозе является весьма перспективным направлением, открывающим колоссальные возможности в создании эффективных диагностических маркеров гидронефроза на самых ранних этапах формирования данной патологии. Таким образом, подводя итог проделанной нами работы, можно отметить, что повреждение почечной ткани в следствие обструктивных уропатий является крайне мультикомпонентным процессом и инициация начальных этапов фиброгенеза с ингибированием процессов резорбции в конечном итоге может привести к прогрессированию нефросклероза.

Keywords: hydronephrosis, obstructive uropathy, IL-1, G-CSF.

Ключевые слова: гидронефроз, обструктивные уропатии, IL-1, G-CSF.

Hydronephrosis is a very common disease [1, p. 233]. In children, hydronephrosis occurs 2.5 times more often in boys. In the age group from 20 to 45 years [2, p. 1345], this pathology is 1.5 times more common in women than in men [11, p. 64].

Perhaps the most key reason for the physiology of urodynamics in up to 25% of cases of hydronephrosis [4, p. 792] is the various forms of the renal vessels intersecting with the urinary tract in the vesicoureteral region [7, p. 42; 9, p. 610]. It is a proven fact that nephrosclerosis is formed in 30-65% of patients with impaired urodynamics [10, p. 701].

Increased knowledge of the mechanisms of damage to the kidneys during obstruction of the urinary tract causes an increased interest in the problem of diagnosis and treatment of uropathies [5, p. 479]. However, diagnostic methods [3, p. 350; 8, p. 170], which are used for diagnostics at the present time, make it possible to identify this pathology already in the later stages. Therefore, the search for various markers involved in the development and progression of kidney damage is particularly relevant, since in the literature there are very contradictory data.

Materials and methods

The results of the examination of 40 patients with established and confirmed diagnosis of stage I hydronephrosis (according to the classification of N.A. Lopatkin), and 20 completely healthy people (control group) are presented. In order to confirm the diagnosis was a comprehensive examination. All patients initially and at the end of the study determined the levels of cytokines: IL-1a, IL-1b, IL-1ra and G-CSF. The number of IL-1a, IL-1b, IL-1ra and G-CSF. The enzyme

immunoassay method was determined in the urine using test systems of the Immunoscrin-RNL_url. The company on an ABBOT "AxSYM" automated immunoassay system.

For statistical processing used the software package Statistica 7.0. The normal distribution of the indicators was determined using the Kolmogorov-Smirnov single-sample criterion, which justified the use of the Mann-Whitney criterion. The obtained data are presented in the form of a median (Me) and interquartile range - the 25th and 75th percentiles (C25% -C75%).

Results and discussion

The proven fact is that an imbalance in the formation of immunological molecules and receptors to them leads to irreversible changes in cells, tissues, organs, which leads to a violation of their functions.

In hydronephrosis, as in the other pathological process, localized expression of cytokines, chemokines, cell adhesion molecules, damaged parenchymal and endothelial cells initiate the migration of leukocytes to the lesion site. Due to an imbalance in the expression of pro-inflammatory cytokines, which, under physiological conditions, being in a harmonious state with anti-inflammatory cytokines have a protective effect. We found that patients with hydronephrosis had higher rates of pro-inflammatory components of the IL-1β system: IL-1β — 104.42 (75% CI [111.8-151.4]) pg/ml, which was significantly higher than in the control group 3.7 times ($p < 0.001$), IL-1 a — 99.82 (75% CI [91.1-135.87]) pg/ml, which is 2.6 times higher than the control ($p < 0.001$). At the same time, IL-1ra, being the physiological buffer of the system, was reduced by 1, 9 times and amounted to 281.3 (75% CI [227-380]) pg/ml, and the indicators of the G-CSF system — 170.42 (75% CI [155.45-545.45]) pg/ml. During the study, the following indicators of the IL-1 family in the control group were identified: IL-1β — 28.33 (75% CI [24.13 -45.54]) pg/ml; IL-1a - 38.63 (75% CI [29, 22-69, 79]) pg/ml; IL-1ra — 534.3 (75% CI [485.12-711.65]) pg/ml. The IL-1 a/ratio (IL-1β + IL-1a) in the group with patients suffering from Hydronephrosis decreased 3.7 times and is 99.3 (75% CI [90.43-309]) pg/ml, the control 367.47 (75% CI [307.3-708.6]), $p < 0.001$.

The most reliable inducers of the apoptosis process in obstructive uropathies are cytokines of the IL-1 family. In turn, G-CSF is a polypeptide cytokine whose main functions are associated with the stimulation of growth and differentiation of hematopoietic cells, such as granulocytes, macrophages and eosinophils, and the stimulation of neutrophil chemotaxis. According to one hypothesis, G-CSF provides nephroprotection.

From the results of our study, it is clear that with hydronephrosis, a significant increase in IL-1β occurs. When IL-1β receptors bind to the ligand, activation of the signalling pathway triggers the immune mechanisms of action on the cellular apparatus. As a result, colossal damage to the receptor apparatus of the cell occurs when interacting with the JAK codon of IL-1β, the intracellular signalling pathway is ruptured and, as a result, the sclerosis of the renal parenchyma develops. At the same time, there is a significant increase in the number of pro-inflammatory cytokines that ensure apoptosis. In turn, the IL-1 receptor complex contains an a-chain consisting of a single IL-1 receptor complex of the ST2 family, and IL1-RAcP, a protein required for the IL-1 receptor and a common P-chain for IL-1 receptors, since both molecules have a Toll/IL-1R (TIR) domain [4, p. 793] necessary for transmitting the signal inside the cell [6, p. 904].

Thus, analysis of the literature indicates that damage to the renal tissue in obstructive uropathies is an extremely complex process, and the initiation of fibrogenesis processes with partial inhibition of resorption leads to remodelling of connective tissue and progression of nephrosclerosis.

The signs of sclerosing processes of the renal parenchyma, detected at early stages, allow a more rational approach to the issue of renoprotective therapy and thereby slow down or prevent further progression of renal scarring, as well as open new directions and treatment options for patients with urinary tract obstruction.

Findings

1. In patients with hydronephrosis, there is an increase in the levels of IL-1β, IL-1a, and G-CSF against the background of a decrease in IL-1ra.

2. The study of the IL-1 and G-CSF systems in dynamics during hydronephrosis is a very promising direction, opening up enormous opportunities in creating effective diagnostic markers of hydronephrosis in the very early stages of the formation of this pathology.

References:

1. Aron, B., Tessler, A., & Morales, P. (1973). Angiography in hydronephrosis. *Urology, 2*(3), 231-236.

2. Krajewski, W., Wojciechowska, J., Dembowski, J., Zdrojowy, R., & Szydełko, T. (2017). Hydronephrosis in the course of ureteropelvic junction obstruction: An underestimated problem? Current opinions on the pathogenesis, diagnosis and treatment. *Advances in clinical and experimental medicine: official organ Wroclaw Medical University, 26*(5), 857-864.

3. Carlström, M. (2019). Hydronephrosis and risk of later development of hypertension. *Acta Paediatrica, 108*(1), 50-57.

4. Faure, A., London, K., & Smith, G. H. (2016). Early mercaptoacetyltriglycine (MAG-3) diuretic renography results after pyeloplasty. *BJU international, 118*(5), 790-796.

5. Fernbach, S. K. (2013). Ultrasound grading of hydronephrosis: introduction to the system used by the Society for Fetal Urology. *Pediatr Radiol, 23* (6), 478-480.

6. Harber, M. (2015). Hydronephrosis. *Practical Nephrology*, 114 (12), 901-915.

7. Fernbach, S. K., Maizels, M., & Conway, J. J. (1993). Ultrasound grading of hydronephrosis: introduction to the system used by the Society for Fetal Urology. *Pediatric radiology, 23*(6), 478-480.

8. Rickard, M., Lorenzo, A. J., Braga, L. H., & Munoz, C. (2017). Parenchyma-to-hydronephrosis area ratio is a promising outcome measure to quantify upper tract changes in infants with high-grade prenatal hydronephrosis. *Urology, 104,* 166-171.

9. Taylor, A. T. (2014). Radionuclides in nephrourology, part 1: radiopharmaceuticals, quality control, and quantitative indices. *Journal of Nuclear Medicine, 55*(4), 608-615.

10. Van Batavia, J. P., & Tasian, G. E. (2016). Clinical effectiveness in the diagnosis and acute management of pediatric nephrolithiasis. *International Journal of Surgery, 36,* 698-704.

11. Van Dervoort, K., Lasky, S., Sethna, C., Frank, R., Vento, S., Choi-Rosen, J., ... & Trachtman, H. (2009). Hydronephrosis in infants and children: natural history and risk factors for persistence in children followed by a medical service. *Clinical medicine. Pediatrics, 3,* CMPed-S3584.

Список литературы:

1. Aron B., Tessler A., Morales P. Angiography in hydronephrosis // Urology. 1973. V. 2. №. 3. P. 231-236.

2. Krajewski W. Wojciechowska J., Dembowski J., Zdrojowy R., Szydełko T. Hydronephrosis in the course of ureteropelvic junction obstruction: An underestimated problem? Current opinions

on the pathogenesis, diagnosis and treatment // Advances in clinical and experimental medicine: official organ Wroclaw Medical University. 2017. V. 26. №. 5. P. 857-864.

3. Carlström M. Hydronephrosis and risk of later development of hypertension // Acta Paediatrica. 2019. V. 108. №. 1. P. 50-57.

4. Faure A., London K., Smith G. H. H. Early mercaptoacetyltriglycine (MAG-3) diuretic renography results after pyeloplasty // BJU international. 2016. V. 118. №. 5. P. 790-796.

5. Fernbach S. K. Ultrasound grading of hydronephrosis: introduction to the system used by the Society for Fetal Urology // Pediatr Radiol. 2013. V. 23. №6, P. 478-480.

6. Harber M. Hydronephrosis // Practical Nephrology. 2015. V. 114. №12. P. 901-915.

7. Fernbach S. K., Maizels M., Conway J. J. Ultrasound grading of hydronephrosis: introduction to the system used by the Society for Fetal Urology // Pediatric radiology. 1993. V. 23. №6. P. 478-480.

8. Rickard M., Lorenzo A. J., Braga L. H., Munoz C. Parenchyma-to-hydronephrosis area ratio is a promising outcome measure to quantify upper tract changes in infants with high-grade prenatal hydronephrosis // Urology. 2017. V. 104. P. 166-171.

9. Taylor A. T. Radionuclides in nephrourology, part 1: radiopharmaceuticals, quality control, and quantitative indices // Journal of Nuclear Medicine. 2014. V. 55. №. 4. P. 608-615.

10. Van Batavia J. P., Tasian G. E. Clinical effectiveness in the diagnosis and acute management of pediatric nephrolithiasis // International Journal of Surgery. 2016. V. 36. P. 698-704.

11. Van Dervoort K., Lasky S., Sethna C., Frank R., Vento S., Choi-Rosen J., Trachtman H. et al. Hydronephrosis in infants and children: natural history and risk factors for persistence in children followed by a medical service // Clinical medicine. Pediatrics. 2009. V. 3. P. CMPed. S3584.

Работа поступила
в редакцию 17.02.2019 г.

Принята к публикации
21.02.2019 г.

Cite as (APA):
Vechkanova N., Stepanov N., Mashnin I., Duvayarov Z., & Selkin V. (2019). Studying the system IL-1 and G-CSF in hydronephrosis as a perspective of creating new diagnostic test systems. *Bulletin of Science and Practice, 5*(3), 64-68. https://doi.org/10.33619/2414-2948/40/07.

Ссылка для цитирования:
Vechkanova N., Stepanov N., Mashnin I., Duvayarov Z., Selkin V. Studying of the system IL-1 and G-CSF in hydronephrosis as a perspective of creating new diagnostic test systems // Бюллетень науки и практики. 2019. Т. 5. №3. С. 64-68. https://doi.org/10.33619/2414-2948/40/07.