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STIMULATION OF KIDNEYS' ADAPTIVE CAPABILITIES IN PATIENTS WITH UROLITHIASIS

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Inflammatory changes in the kidney that occurred in the early postoperative period due to surgical trauma, deterioration of microcirculation, hypoxia, are significant risk factors for the development of renal function violation. The aim of this work is to study the effect of the combined drug "Uriclar" (Asfarma-Ros) on the kidneys' adaptive capability in the early postoperative period as a response to operative trauma of patients with complicated urolithiasis. The effect of surgical intervention – percutaneous puncture nephrolithotripsy on the blood content of proteins of the acute phase of inflammation and cystatin C was studied. The results of examination of 35 patients (20 – the main group and 15 – the control group) were analyzed. The median age was 51 ± 8.4 years. 20 patients of the main group began receiving Uriclar 2 capsules (430 mg) twice a day for 5 days before surgery and continued it for 1 month after surgery. Patients from the control group in the pre- and postoperative periods didn't receive Uriclar. The median age was 51 ± 8.4 years. There was a statistically significant increase in the level of cystatin C and changes in biochemical markers in the patients of the main group only that indicates the presence of adaptogenic effect of Uriclar. Thus, the inclusion of a combined drug Uriclar in a complex treatment of patients with urolithiasis allows disturbed biological and adaptive functions of the kidneys to be corrected in the early postoperative period.

Keywords: urolithiasis; electrophoregram in patients with urolithiasis; Uriclar; nephrolithotripsy.

СТИМУЛЯЦИЯ АДАПТАЦИОННЫХ ВОЗМОЖНОСТЕЙ ПОЧЕК У БОЛЬНЫХ МОЧЕКАМЕННОЙ БОЛЕЗНЬЮ

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Воспалительные изменения в почке, возникшие в раннем послеоперационном периоде на фоне операционной травмы, ухудшения процессов микроциркуляции, гипоксии, являются значимым фактором нарушения ее функции. Цель настоящей работы — изучение влияния комбинированного препарата Уриклар™ на адаптационные возможности почек в раннем послеоперационном периоде в ответ на операционную травму у пациентов с мочекаменной болезнью. Изучено влияние оперативного вмешательства — чрескожной пункционной нефролитотрипсии на содержание в крови белков острой фазы воспаления и цистатина С. Выполнен анализ результатов обследования 35 пациентов (20 — основная группа и 15 — контрольная). Средний возраст больных составил 51 ± 8,4 года. Пациенты основной группы начинали прием Уриклара по 2 капсулы (430 мг) два раза в день за 5 дней до операции и продолжали его в течение 1 мес. после операции. Пациенты из контрольной группы в до- и послеоперационном периоде Уриклар не принимали. У пациентов основной группы, в отличие от контрольной, после операции не было отмечено статистически значимого повышения уровня цистатина С и изменения содержания биохимических маркеров электрофореграммы, что свидетельствует о наличии адаптогенного эффекта Уриклара. Таким образом, включение комбинированного препарата Уриклар в комплексное лечение больных мочекаменной болезнью позволяет корректировать нарушенные биологические и адаптационные функции почек в раннем послеоперационном периоде.

Ключевые слова: мочекаменная болезнь; Уриклар™; адаптация; нефролитотрипсия.

Percutaneous puncture nephrolithotripsy (PPNLT) is the current standard of treatment for large kidney stones [1]. Despite the conventional perioperative antibiotic prophylaxis, according to various authors, the incidence of acute pyelonephritis in the postoperative period is 87.5% [2], systemic inflammatory response syndrome 27.4%, and urosepsis 7.9% [3, 4]. Infectious and inflammatory complications increase the duration of hospital stay of patients and the subsequent rehabilitation period and increase the cost of treatment. The most common postoperative complications of PPNLT besides pyelonephritis and problems caused by residual stones include febrile fever (in up to 32.1% of cases) [5].

Inflammatory changes in the kidney because of hypoxia and microcirculatory disorders during the early postoperative period are significant factors causing a deterioration in its function [6]. Pathological structural changes in the kidneys, including nephron malfunction, affect the regulation of renal function in homeostasis and water-electrolyte metabolism. These factors, as well as the inflammatory complications, prolong patients' hospital stay, increase the cost of treatment, and extend the rehabilitation period. Therefore, it is imperative to prevent postoperative inflammatory processes in the kidneys in patients burdened with a history of urolithiasis. The use of herbal remedies in the complex treatment of urological patients can improve treatment efficiency [7]. The legal status of biologically active additives for the prevention of nutritional-dependent conditions and diseases, per the requirements of medical science, is regulated by the Russian Federation through orders and guidelines [8]. BAA parapharmaceuticals normalize or improve the functional activity of organs and systems within the physiological boundaries, as well as affect the body's ability to adapt to adverse conditions. These aspects support their extensive use as adjunctive therapy for various diseases. In Russia, herbal remedies account for approximately 40% of the total number of drugs used in practical medicine [9]. According to I.V. Kazanskaya (2015), the advantages of herbal remedies over synthetic drugs are their higher bioavailability, good tolerance, very rare and mild side effects [7]. Notably, phytotherapy has been used since a long time for the treatment of urolithiasis because essential oils and terpenes can positively affect the renal functions (blood circulation, diuresis), as well as the smooth muscles of the pelvis and ureter [9].

The aim of this work is to study the effect of the combined drug "Uriclar" (Asfarma-Ros) on the kidneys' adaptive capability in the early postoperative period as a response to surgical trauma of patients with complicated urolithiasis.

MATERIALS AND METHODS

The effect of PPNLT in patients burdened with urolithiasis was assessed by evaluating the blood levels of proteins of the acute phase of inflammation and cystatin C.

The study included 35 patients, 20 in the main group, and 15 in the control group. Patients of both groups were comparable regarding diagnosis, age, and sex characteristics. The average age of patients was 51 ± 8.4 years. All patients participated in the study voluntarily and signed informed consent. The study included patients over 18 years of age with a complicated urolithiasis history (previously operated, with recurrent stones, with calculous pyelonephritis), who were scheduled to undergo PPNLT. The sizes of calculi of the pyelocaliceal system of the kidney ranged from 10 to 80 mm. All patients underwent standard studies (X-ray, ultrasound, and laboratory tests) with urea and blood creatinine levels assessment, urine culture for flora, and sensitivity to antibiotics. The levels of blood proteins and cystatin C were determined 5 days before the surgery with the help of electrophoresis. The intergroup difference in preparation for surgery was that 5 days before the surgery, patients of the main group started to receive a combined product with herbal components, Uriclar 2 capsules (430 mg) twice per day [10]. In the postoperative period, they continued taking it for up to one month. The rest of the treatment did not differ between groups. Per the Russian Urology Society [11] recommendations, all patients received antibacterial prophylaxis. For this purpose, patients underwent urine culture for flora, and a broad-spectrum antibiotic (typically third-generation cephalosporin) or a drug based on the antibiotic sensitivity of urine culture flora was administered to them 1 hour before the surgery. PPNLT was performed on the Karl Storz equipment using a 26Ch nephroscope and a 10Ch rigid ureteroscope. The renal casing Amplac 28Ch was used for work, which helped to prevent increased pressure in the pyelocaliceal system during the surgery. The surgery was completed with a nephrostomy. The time of surgical intervention ranged from 20 to 150 minutes. In the postoperative period, patients of the main and control

groups were prescribed antibacterial drugs, antihistamines (Suprastin), NSAIDs (Ketonal), and antihemorrhagic drugs (sodium ethamsylate). Repeated blood tests for patients of both groups were performed in the postoperative period on days 3 or 4. All patients underwent thermometry daily twice a day.

The effect of surgical injury on kidneys was evaluated using the level of blood proteins, which indirectly indicates the severity of the body's inflammatory response. The study focused on markers of structural and functional damage to the kidneys, namely cystatin C and β2-microglobulin. Cystatin C is a cysteine protease inhibitor, a non-glycosylated total protein with a low molecular weight (13.4 kDa). Its level may indicate the preclinical phase of renal dysfunction. In addition, it is recognized as a reliable and sensitive marker of glomerular filtration rate (GFR) compared with serum creatinine, and its serum clearance is independent of the patient's sex and age characteristics. Cystatin C is known to be formed in the body at a constant rate in all nuclear cells, is filtered freely in the renal glomeruli, and is almost completely reabsorbed and destroyed in the renal tubules [12].

A blood test for cystatin C was performed with the Huma Star 600 biochemistry analyzer by using an immunoturbidimetric method. Serum protein electrophoresis was performed using a Capillaris 2Flex Piercing capillary electrophoresis system manufactured by Sebia. This method enables the separation of proteins into six fractions based on their physical properties (one albumin and five globulin fractions). Proteins with a certain biological function, a certain clinical diagnostic value migrate into each fraction. Electrophoresis of blood serum proteins is one of the best screening tools because it provides a more effective approach to identify pathophysiological conditions, as this method is based on the fact that the protein functions are incredibly diverse and changes in their concentrations in biological fluids can indicate even minor functional disorders of the body systems [13].

Mathematical data processing was performed using the statistical package Statistica v13. The Kolmogorov-Smirnov method was used to check the normality of data in the groups. The significance of differences in the content of biochemical markers between the compared patient groups was analyzed using the nonparametric Wilcoxon method for independent samples.

RESULTS

Table 1 presents the blood protein levels of patients of the compared groups before and after surgery.

Cystatin C level analysis

In patients of the main group, who received Uriclar, the average cystatin C index before the surgery was 1.44 ± 1.7 mg/L (0.9 to 3.31 mg/L), and after the surgery, it was 1.13 ± 0.66 mg/L (0.8 to 1.74 mg/L). Only one patient had an increase in this level from 1.13 to 1.74 mg/L after the surgery, whereas in others, a decrease was registered. The average values varied within the reference interval. The average level of cystatin C is known to be 0.77 ml/L [10]. Notably, in people over the age of 50, the normal cystatin C values are 0.74–1.55 mg/L. In one patient of the main group who had a maximum cystatin C index initially, chronic renal failure of the latent stage was determined, and the creatinine level was noted to be increased to 140 μmol/L. In the control group, preoperatively, cystatin C levels ranged from 0.85 to 1.76 mg/L (on average, 1.22 ± 0.64 mg/L), and after the surgery, it ranged

Table 1 / Таблица 1

Proteins blood level of patients in the main and control groups before and after surgery, $M \pm m$ ($n = 35$)
Содержание белков в крови пациентов основной и контрольной групп до и после операции, $M \pm m$ ($n = 35$)

Biochemical markers	Main group ($n = 20$)		p	Control group ($n = 15$)		p
	before surgery	after surgery		before surgery	after surgery	
Cystatin C, mg/L	1.44 ± 1.7	1.13 ± 0.66	**0.01108**	1.22 ± 0.64	1.17 ± 0.65	0.08532
Albumin, %	56.82 ± 8.27	56.42 ± 7.21	0.61551	56.42 ± 9.05	53.9 ± 9.68	**0.00506**
Globulin α1, %	5.29 ± 2.12	5.17 ± 1.2	0.34637	5.08 ± 1.34	6.28 ± 1.48	**0.00089**
Globulin α2, %	11.12 ± 4.49	11.98 ± 1.62	0.09954	10 ± 2.89	11.0 ± 3.25	**0.00428**
Globulin β1, %	5.83 ± 1.55	5.88 ± 1.55	0.80173	5.86 ± 0.91	6.24 ± 0.63	**0.00314**
Globulin β2, %	4.86 ± 1.83	5.0 ± 2.03	0.31517	5.31 ± 1.41	5.81 ± 1.48	**0.00065**
Total protein, g/l	71.43 ± 13	69.8 ± 7.77	0.22204	71.76 ± 7.91	67.14 ± 11	0.07962

Note. Statistically significant differences are emboldened ($p < 0,05$).

from 0.86 to 1.84 mg/L (on average, 1.17 ± 0.65 mg/L) (Fig. 1, *a*). In two patients with preoperative levels of 1.76 and 1.45 mg/L and initially having azotemia (serum creatinine was 155 and 135 μmol/L respectively with a norm of 110–115 μmol/L), an increase was observed in cystatin C levels to 1.84 and 1.55 mg/L, respectively.

Data analysis performed using the Wilcoxon test indicated that the cystatin C level in the group of patients treated with Uriclar stabilized at approximately the same level after surgery in all patients ($p \leq 0.05$) (Fig. 1, *a*).

Electropherogram analysis

The term "total protein" refers to the concentration of all plasma proteins. The average total blood protein level in the groups is presented in Table 1. It was revealed that the protein level in the group of patients who did not take Uriclar tended to decrease in the postoperative period, and remained the same in the group of patients taking the drug in the postoperative period, but the concentration dispersion in the group was much smaller (Fig. 1, *b*). All changes occurred within the reference total protein level for healthy adults (65 to 80 g/L). In our study, the total protein level values in the main group were 71.4 and 69.8 g/L, and in the control group were 71.7 and 67.1 g/L.

Regarding the level of the main fraction of the electropherogram, albumin did not change in patients receiving Uriclar and was 56.82% and 56.42% before and after surgery, respectively. In the control group of patients, the level of albumin decreased insignificantly from 56.4% to 53.9% (with a norm of 55.8–66.1% g/L for the laboratory technique used by us). Albumin belongs to a group of proteins that respond negatively to inflammation. A decrease in the level of albumin, which is the main transport protein, is associated with an amino acid deficiency and an increase in IL-6 synthesis in response to the acute phase of inflammation. In this study, significant changes in the level of albumin in patients of the main group, in response to surgical trauma, were not recorded. A slight decrease in albumin synthesis within normal limits (51–61 or 35–52 g/L) [13] was registered in nine pa-

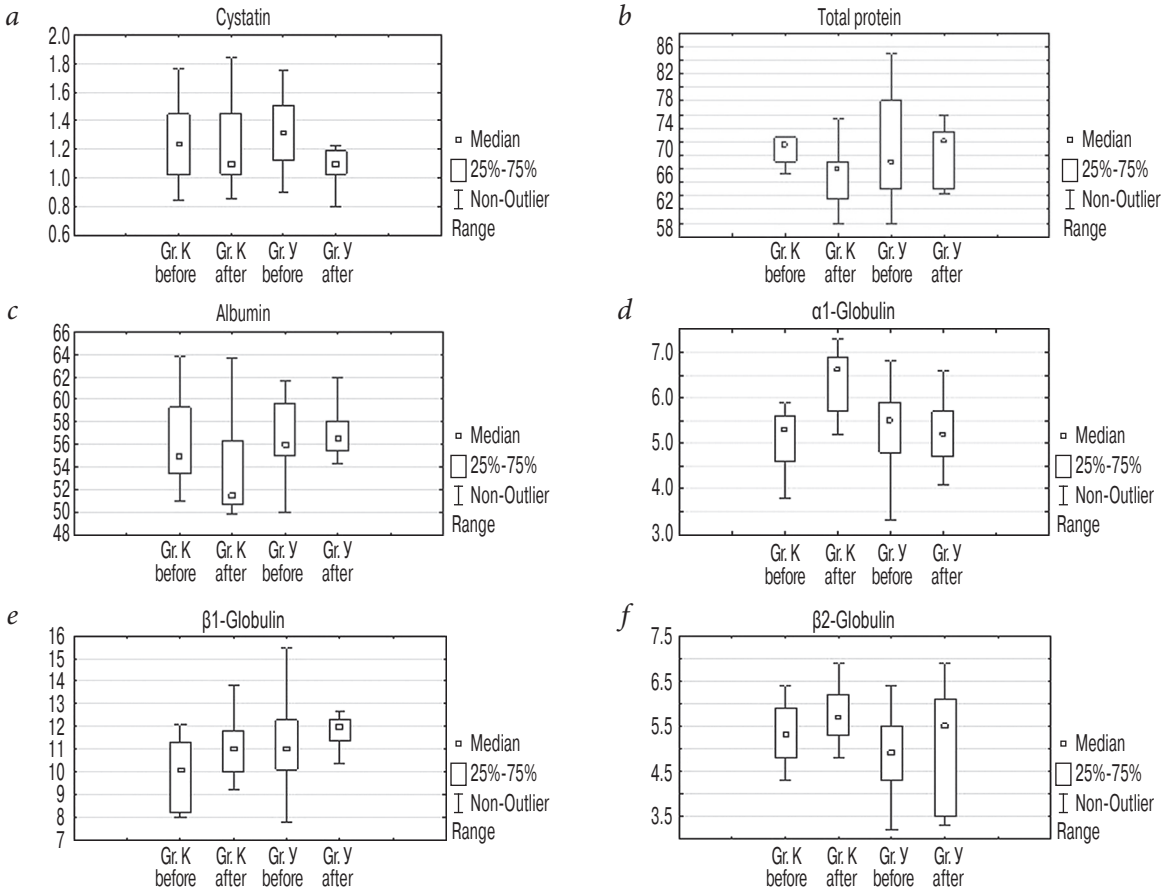

Fig. 1. Distribution of cystatin C (*a*) and electrophoregram indices (*b*–*f*) in patients of the main (group У) and control (group К) groups before and after surgery

Рис. 1. Распределение цистатина С (*a*) и показателей электрофореграммы (*b*–*f*) у пациентов основной (гр. У) и контрольной (гр. К) групп до и после операции

tients (45%, 9/20). An increase in albumin is typically associated with dehydration. In the control group, a decrease in this indicator was detected in 13 patients, which amounted to 86.6% (13/15). Thus, the blood albumin of the control group of patients decreased on average, whereas in the patients of the main group, it stabilized at approximately the same level (Fig. 1, *c*).

Globulin group

α1-Antitrypsin and acidic α1-glycoprotein migrate into the zone of protein fractions of α1-globulins of electropherogram. It is known that bacterial infection is the most powerful inducer of increasing the level of α1-antitrypsin of this protein, therefore, in the postoperative period, an increase in acidic α1-glycoprotein even in the presence of an acute phase response to surgical trauma is an indicator of local infection [13]. The most significant effect of α1-antitrypsin is the suppression of leukocyte esterase activity. α1-Antitrypsin is a protein of the acute phase of inflammation, which level increase is also registered with tissue injuries after about 48 hours. Its production in the liver increases under the influence of tumor necrosis factor, IL-1, IL-6, that is, this group of proteins is positive in relation to the inflammatory process activity [13]. In our study, an increase in α1-globulin was registered only in patients of the control group (Fig. 1, *d*, Table 1), while in patients of the main group, an increase in α1-globulin was not registered. An analysis of the significance of differences using the Wilcoxon test indicates that the α1-globulin level in the postoperative period in patients of the main group stabilized at approximately the initial level (Fig. 1, *d*).

The level of α2-globulin in the patients of the control group increased insignificantly, and in the main group, the values were stabilized in all patients at approximately the initial level (see Table 1). The level of proteins migrating to the α2-zone (haptoglobin and α2-macroglobulin) is known to increase insignificantly during acute inflammation. In the acute phase response, they perform a protective function, forming complexes with proteins released during cell decay [13].

Analysis of the fraction of β-globulins

It was revealed that the level of β1- and β2-globulin in patients who did not take Uriclar (control group) increased in the postoperative period. By contrast, in patients taking the drug in the pre- and postoperative period, the levels remained at the baseline, albeit with a significant increase in the concentration range (Fig. 1, *e*, *f*, Table 1). Transferrin; the complement components, C3 and C4; and lipoprotein are known to dominate the β-globulin fraction. C3 synthesis occurs in the liver, macrophages, fibroblasts, and accelerates in the acute phase of inflammation (activator is IL-6). The C3 complement is crucial in the case of bacterial infections. Furthermore, C4 is a protein of the acute phase of inflammation, and an increase in its concentration is observed during inflammation [13].

Thus, when analyzing the level of biochemical markers, it was observed that in patients who did not receive Uriclar in the pre- and postoperative period, a statistically significant difference in the level of biochemical markers, except for cystatin C was observed (see Table 1). This finding indicates that the body of patients of this group, specifically the kidneys, reacted to the surgical damage by producing proteins of the acute phase of inflammation. In patients taking Uriclar (main group), the difference in the level of biochemical markers during these periods, except for cystatin C, was statistically insignificant (see Table 1). This finding indicates the effect of this drug on the postoperative condition of the corresponding body systems in terms of compensation or adaptation to the surgical impact.

An example of electropherograms of patients of the main and control groups is presented in Figure 2.

Thermometry results

Fever was recorded in 50% (n = 10) patients of the main group and in 66.6% (n = 10) of the control group. Moreover, an increase in body temperature to febrile values was registered in 3 (15%) patients of the main group and in 4 (26.6%) of the control group, which required optimization of antibacterial therapy and detoxification treatment.

DISCUSSION

At a time when an endoscopic approach to the treatment of urolithiasis became predominant, the level of molecular markers of renal dysfunction is garnering significance. It is generally recognized that the determination of GFR values is necessary for diagnosis and monitoring of renal dysfunction [14–16]. Notably, creatinine and cystatin C are almost entirely filtered by glomeruli; therefore, an increase in their serum levels indicates a decrease in GFR, and the level of cystatin C can indicate a "preclinical" phase of renal dysfunction [10].

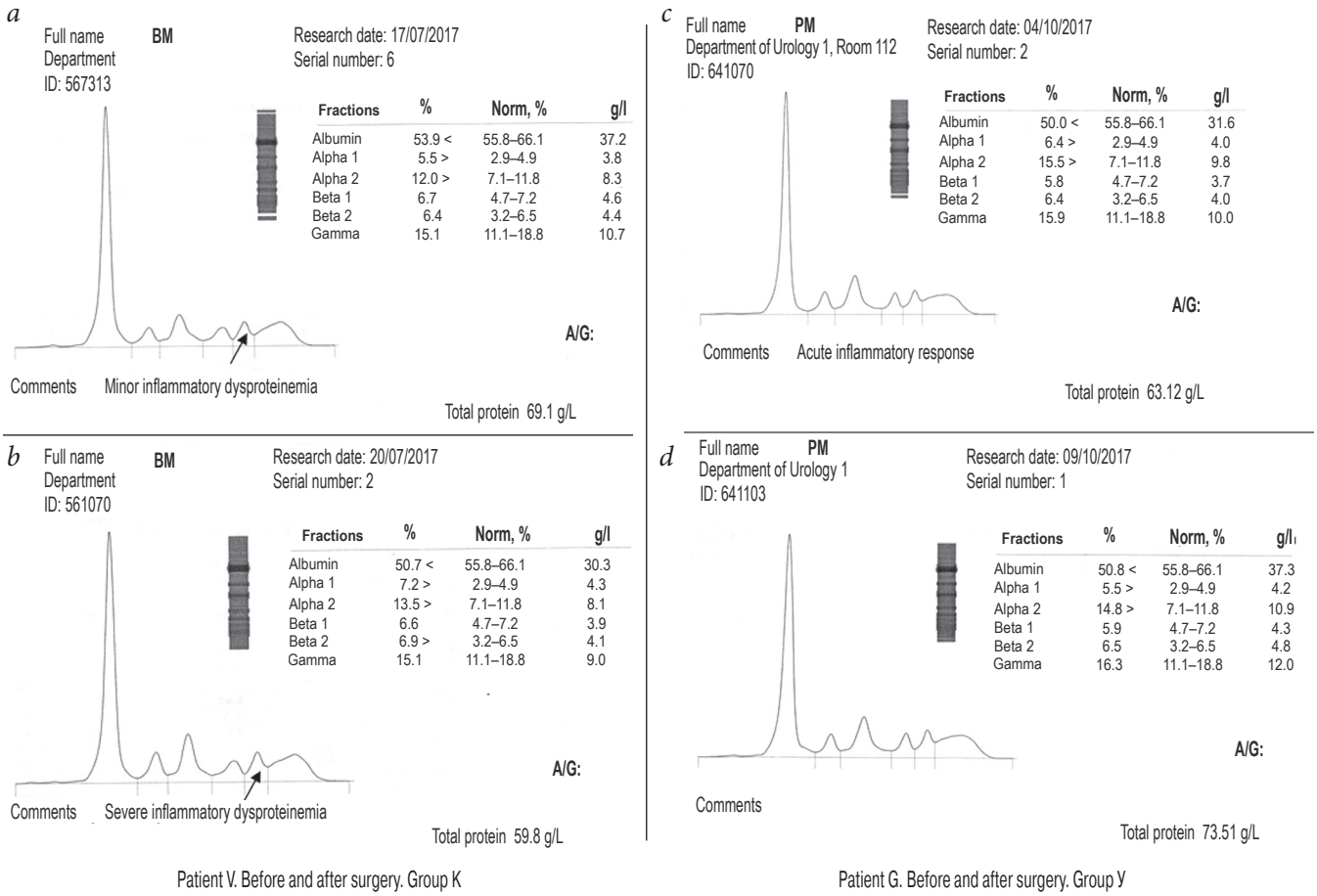

Fig. 2. Electrophoregrams of patients in the control group – group K (*a*, *b*) and the main group – group У (*c*, *d*) before and after surgery. The peak of the β2-globulin fraction is indicated by the arrow (*a*, *b*)
Рис. 2. Электрофореграммы пациентов контрольной группы — гр. К (*a*, *b*) и основной группы — гр. У (*c*, *d*) до и после операции. Пик фракции β2-глобулина указан стрелкой (*a*, *b*)

In our study, it was revealed that PPNLT is a factor that can cause a generalized response of the body to surgical trauma. Nevertheless, the use of the drug Uriclar during the preoperative period stabilized cystatin C in the postoperative period, thereby causing no pronounced damage to the renal parenchyma, as evidenced by unchanged GFR value.

Uriclar is a drug that contains a combination of herbal components, such as flavonoids, essential oils, tannins, carotenoids, phytoncides, and organic acids, as well as a citrate complex, which helps maintain the functions of the urinary system. The flavonoids from dry extracts of plant components are involved in the body's metabolic processes, help decrease the smooth muscle tone, and exhibit antimicrobial and anti-inflammatory properties. Nowadays, Uriclar is widely used in clinical practice, primarily for the treatment and metaphylaxis of urolithiasis [17].

A change in the level of blood serum proteins is associated with pathological conditions of the body, particularly an acute inflammatory response [18]. Proteins of the acute phase are plasma proteins that are formed mainly in the liver and exert both direct and indirect bactericidal or bacteriostatic effects, as well as act as chemoattractive agents, nonspecific opsonins, and alteration inhibitors. Furthermore, the study of blood plasma protein fractions helped to identify changes in the qualitative and quantitative composition of individual proteins and their fractions in blood plasma at a normal level of total protein in the pre- and postoperative periods.

A comparative analysis of the changes in time of the electropherogram indicators in the main and control groups helps to deduce that because of the intake of Uriclar during the preoperative period, the fluctuations in the level of biochemical markers of the acute phase of inflammation were statistically insignificant. By contrast, in the group of patients who did not receive the drug, differences in biomarker levels were statistically significant. Parapharmaceutical drugs are, as a rule, minor (that is, containing small amounts) components of food that provide regulation (weakening or strengthening) within the physiological boundaries of the functional activity of organs and

systems, as well as positively influence the body's ability to adapt to adverse conditions [8]. This fact was confirmed by the smaller number of temperature reactions after surgery in the group of patients taking Uriclar compared with the control group (50% and 66.6%, respectively). Nonetheless, it should be borne in mind that a temperature increase is possibly a response to the action of not only pyrogens produced in the body by macrophages and neutrophils under the influence of infectious processes, but also non-infectious pyrogens, such as IL-1, IL-6, TNF, γINF, which are components of the acute phase inflammatory response.

CONCLUSIONS

The study results suggest that Uriclar exhibits a significant adaptogenic effect, helping to manage the nonspecific inflammatory process in the kidneys in response to surgical trauma. The inclusion of a combined drug Uriclar in a complex treatment of patients with urolithiasis can help to regulate impaired biological and adaptive functions of the kidneys in the early postoperative period.

REFERENCES

1. Türk C, Neisius A, Petrik A, et al. EAU Guidelines on urolithiasis [Electronic resource]. European Association of Urology; 2017. 84 p. Available from: https://uroweb.org/wp-content/uploads/EAU-Guidelines-on-Urolithiasis_2017_10-05V2.pdf.
2. Толордава Э.Р. Роль бактериальных биопленок в этиопатогенезе мочекаменной болезни: Автореф. дис. … канд. биол. наук. – М., 2014. – 27 с. [Tolordava ER. Rol' bakterial'nyi bioplenok v etiopatogeneze mochekamennoi bolezni. [dissertation abstract] Moscow; 2014. 27 p. (In Russ.)]. Доступно по: https://dlib.rsl.ru/viewer/01005545003#?page=1. Ссылка активна на 02.06.2019.
3. Liu YQ, Lu J, Hao YC, et al. [Predicting model based on risk factors for urosepsis after percutaneous nephrolithotomy. (In Chinese)]. *Beijing Da Xue Xue Bao Yi Xue Ban*. 2018;50(3):507-513.
4. Koras O, Bozkurt IH, Yonguc T, et al. Risk factors for postoperative infectious complications following percutaneous nephrolithotomy: a prospective clinical study. *Urolithiasis.* 2015;43(1):55-60. https://doi.org/10.1007/s00240-014-0730-8.
5. Yang T, Liu S, Hu J, et al. T. The evaluation of risk factors for postoperative infectious complications after percutaneous nephrolithotomy. *Biomed Res Int*. 2017;2017:4832051. https://doi.org/10.1155/2017/4832051.
6. Патент РФ на изобретение RU № 2253366. Татевосян А.С., Осипов А.А., Опольский А.Б., Татевосян Т.С. Способ консервативного лечения мочекаменной болезни и предупреждения рецидивного образования камней почек. [Patent RUS № 2253366. Tatevosyan AS, Osipov AA, Opolskiy AB, Tatevosyan TS. Conservative method for treating the cases of urolithiasis and preventing recurrent calculus formation. (In Russ.)]. Доступно по: http://www.freepatent.ru/patents/2253366. Ссылка активна на 16.05.2019.
7. Казанская И.В. Фитопрепараты в детской уронефрологии // Вестник Российского общества урологов. – 2015. – № 2. – С. 18. [Kazanskaya IV. Fitopreparaty v detskoi uronefrologii. *Vestnik Rossiyskogo obshchestva urologov*. 2015;(2):18. (In Russ.)]
8. Постановление Правительства РФ № 917 от 10.08.1998 «О Концепции государственной политики в области здорового питания населения Российской Федерации на период до 2005 года». – М., 1998. [Decree of the Government of the Russian Federation № 917 "O Kontseptsii gosudarstvennoy politiki v oblasti zdorovogo pitaniya naseleniya Rossiyskoy Federatsii na period do 2005 goda"; dated 2014 August 10. Moscow; 1998. (In Russ.)]. Доступно по: http://www.consultant.ru/cons/CGI/online.cgi?req=doc;base=EXP;n=259367;dst=100010#03399473135018607. Ссылка активна на 02.06.2019.
9. Гуденко Ю.А., Казанская И.В., Лобжанидзе З.Д. Применение препарата Роватинекс в детской урологии // Экспериментальная и клиническая урология. 2013. – № 3. – С. 61–65. [Gudenko YaA, Kazanskaya IV, Lobyanidze ZB. Rovatinex usage in pediatric urology. *Experimental and clinical urology*. 2013;(3):61-65. (In Russ.)]
10. Справочник лекарств [электронный ресурс]. Уриклар. Инструкция по применению. [Spravochnik lekarstv [Elektronnyi resurs]. Uriklar. Instruktsiya po primeneniyu. (In Russ.)]. Доступно по: http://instrukciya-otzyvy.ru/1588-uriklar-po-primeneniyu-analogi-kapsuly-tabletki-kamni-v-pochkah-profilaktika-sostav.html. Ссылка активна на 02.06.2019.
11. Урология. Российские клинические рекомендации / Под ред. Аляева Ю.Г., Глыбочко П.В., Пушкаря Д.Ю. – М.: Медфорум, 2017. – 544 с. [Urologiya. Rossiiskie klinicheskie rekomendatsii. Ed. by Alyaev YuG, Glybochko PV, Pushkar' DYu. Moscow: Medforum; 2017. 544 p. (In Russ.)]
12. Вельков В.В. Цистатин С — новые возможности и новые задачи для лабораторной дигностики [электронный ресурс]. – М.: ЗАО «Диакон», 2011. – 73 с. [Velkov VV. Cystatin C: The new opportunities and new goals for laboratory diagnostics [Elektronnyi resurs]. Moscow: ZAO "DIAKON"; 2011. 73 p. (In Russ.)]. Доступно по: http://www.diakonlab.ru/files/Docs/SciArticles/Cystatin_C_Rev_Site(2).pdf. Ссылка активна на 02.06.2019.
13. Клиническая лабораторная диагностика: национальное руководство. В 2 т. Т. 1 / Под ред. В.Д. Долгова, В.В. Меньшикова. – М.: ГЭОТАР-Медиа, 2012. – 928 с. [Klinicheskaya laboratornaya diagnostika: natsional'noe rukovodstvo. V 2 t. Vol. 1. Ed. by V.D. Dolgov, V.V. Men'shikov. Moscow: GEOTAR-Media; 2012. 928 p. (In Russ.)]

14. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39(2 Suppl 1):S1-266.
15. Grubb A, Björk J, Lindström V, et al. A cystatin C-based formula without anthropometric variables estimates glomerular filtration rate better than creatinine clearance using the cockcroft-gault formula. *Scand J Clin Lab Invest*. 2005;65(2):153-162. https://doi.org/10.1080/00365510510013596.
16. Тарасенко А.И., Пушкарев А.М., Ракипов И.Г., и др. Биомаркеры повреждения почек при контактной уретеролитотрипсии // Урология. – 2017. – № 5. – С. 75–79. [Tarasenko AI, Pushkarev AM, Rakipov IG, et al. Biomarkers of renal injury in contact ureteral lithotripsy. *Urologiia*. 2017;(5):75-79. (In Russ.)]. https://doi.org/10.18565/urology.2017.5.75-79.
17. Шестаев А.Ю., Протощак В.В., Паронников М.В., Киселев А.О. Комбинированный (цитратный и растительный) препарат Уриклар в дистанционной литотрипсии и метафилактике мочекаменной болезни // Урологические ведомости. – 2018. – Т. 8. – № 1. – С. 19–25. [Shestaev AYu, Protoshchak VV, Paronnikov MV, Kiselev AO. Combined (citrate and herbal) drug Uriklar in extracorporeal shock wave lithotripsy and metaphylaxis of urolithiasis. *Urologicheskie vedomosti*. 2018;8(1):19-25. (In Russ.)]. https://doi.org/10.17816/uroved8119-25.
18. Шевченко О.П., Долгов В.В., Олиференко Г.А. Электрофорез в клинической лаборатории. – М.: Реафарм, 2006. – 160 с. [Shevchenko OP, Dolgov VV, Oliferenko GA. Elektroforez v klinicheskoi laboratorii. Moscow: Reafarm; 2006. 160 p. (In Russ.)]

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