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# Optimization of Remote Shock-Wave Lithotripsy on the State of Renal Parenchyma in Patients with Nephrolithiasis

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**Annotation:** Complex approaches to assessing the state of the renal parenchyma after remote shock wave lithotripsy in patients with nephrolithiasis are considered. The aim of the study was to evaluate the damage to the renal parenchyma in patients with nephrolithiasis during extracorporeal shock wave lithotripsy. It was found that if it is necessary to conduct repeated sessions of Remote shock wave lithotripsy, there is an increase in the damaging effect of the shock wave on the renal parenchyma, which may be accompanied by adverse consequences both in the early and in the long-term postoperative period with the development of nephrosclerosis and a decrease in renal functions.

**Keywords:** urolithiasis, extracorporeal shock wave lithotripsy, markers of renal damage, lipocalin-2.

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**Relevance.** Urolithiasis is one of the most common urological diseases and ranks second after inflammatory nonspecific diseases of the kidneys and urinary tract, and occurs in at least 3% of the population. In the Republic of Uzbekistan, the absolute number of registered patients with urolithiasis from 2017 to 2020. increased by 25.8%. In about 25% of cases, stones must be removed [1]. Remote lithotripsy is the treatment of choice in patients with ICD. However, in addition to crushing the calculus, it also has a traumatic effect on the kidney parenchyma, which often leads to severe inflammatory changes.

The incidence of urolithiasis (Urolithiasis) in the world ranges from 3 to 5% and continues to progressively increase [6]. Currently, extracorporeal shock wave lithotripsy (ESWL) continues to hold the leading position in the formation of a treatment strategy in patients with urolithiasis. Despite the fact that extracorporeal shock wave lithotripsy is a non-invasive treatment that is well tolerated by patients and is accompanied by a low percentage of complications, it has been proven that a shock wave, regardless of the nature of the generator, causes a significant number of side effects [2]. The introduction into clinical practice of new informative criteria for assessing damage to the renal parenchyma could serve as an objective basis for regulating the parameters of wave action and optimize the timing of repeated procedures in the course of surgical treatment of nephrolithiasis by remote lithotripsy. One of these criteria can be diffusion-weighted magnetic resonance imaging (DWI MRI) [3]. With various damaging effects on the cell, a cascade of pathological reactions develops. One of the parameters that can be used to assess the degree of tissue damage is the diffusion of water molecules in the extracellular space.

Power of destructive effect Extracorporeal shock wave lithotripsy (ESWL) is usually very high. In this case, the risk of damage to the renal parenchyma increases if the effect is directed at calculi located in the kidney [7].

Currently, a search is underway for new urinary markers that should have high sensitivity and specificity both for the early diagnosis of acute kidney injury and for assessing its severity. Determination of the level of cystatin-C is recognized by the world medical community as the most accurate endogenous marker of glomerular filtration rate (GFR). Despite the fact that, normally, cystatin-C is freely excreted by glomerular filtration, and then undergoes complete tubular reabsorption and catabolization (without secretion), if tubular functions are impaired, the concentration of its indicators in urine can increase 200 times, especially in acute kidney damage [eight].

Lipocalin-2 (NGAL) is a component of the acute phase of the inflammatory response, the main functions of which include stimulating the proliferation of damaged cells and counteracting bacterial infections [4,5].

At present, the question of the damaging effect of a shock wave on the state of the renal parenchyma with long-term consequences remains controversial. In connection with the above, it seems expedient to search for new methods for determining the damaging effect of shock waves on the renal parenchyma.

Objective: to conduct a comprehensive assessment of biochemical markers of renal parenchyma damage in patients with nephrolithiasis during ESWL.

**Material and methods.** In the period from 2017 to 2020. we examined 90 patients with urolithiasis, who were treated at the Urology Department of the Bukhara Regional Multidisciplinary Medical Center. All patients were diagnosed with urolithiasis at the prehospital stage, surgical treatment was carried out in the hospital in the amount of ESWL and, along with traditional methods of examination and treatment, a number of specific biological markers of renal damage (lipocalin-2, cystatin-C) were determined. The first group consisted of 45 patients with nephrolithiasis who underwent one session of ESWL, and the clinical efficacy was 100%. The density of stones in patients of this group varied from 800 to 1200 HU, the number of impulses per session was 2000-2500. The second group consisted of 45 patients who underwent 2 or more ESWL sessions, while the calculus density was 1200-1580 HU, the number of impulses per session was 2500-3000.

The control group for comparing the results of the studied patients with nephrolithiasis consisted of 32 people aged 25 to 39 years, who had no complaints, a history and, according to the results of clinical and laboratory studies, there were no data for urolithiasis.

Inclusion criteria for the study: patients with a verified diagnosis of urolithiasis, subject to surgical treatment in the amount of ESWL, calculus size from 0.6 to 2.0 cm, patients' age from 25 to 60 years, no impairment of renal excretory function, urine passage, active inflammatory process, voluntary informed consent of the patient to participate in the study.

Exclusion criteria from the study: age of patients younger than 25 and older than 60 years, calculus size less than 0.6 cm and more than 2.0 cm, signs of impaired renal excretory function, signs of acute calculous pyelonephritis, impossibility to perform ESWL, indications for open surgery or PPNL, decreased kidney function by 50% or more, bacteriuria 10<sup>5</sup> CFU or more, patient refusal to participate in the study. All patients of the main group and the comparison group received surgical treatment in the amount of ESWL using a Sonolith I-syl device manufactured by EDAP (France).

Patients underwent determination of the level of specific biological markers in blood serum and urine by enzyme-linked immunosorbent assay using commercial reagent kits at the preoperative stage, on days 1, 5-7 (in patients of the second group after repeated sessions of ESWL) and one month later. The following kits were used: for the determination of lipocalin-2 (NGAL) Human Lipocalin-2 / NGAL ELISA, BioVendor (Czech Republic); for the determination of cystatin-C Human Cystatin-C ELISA, BioVendor (Czech Republic).

Statistical analysis of the obtained data was carried out using Statistica 7.0, SPSS 17 packages, as well as statistical functions MS Excel'2003. The calculation of descriptive statistics and statistical analysis of the data obtained were carried out in accordance with the scale of measurement of the trait and the type of its distribution. To identify significant differences in normally distributed indicators presented in an interval scale, the Student's t test was used. Differences were considered significant at a significance level of  $p < 0.05$ .

**Results and discussion.** From the data presented in table. 1 and 2, it can be seen that in patients with nephrolithiasis, the baseline values of serum creatinine, GFR, lipocalin-2 (NGAL), and cystatin-C in serum and urine were within the normal range, which confirms stable and satisfactory renal function in both groups. before ESWL.

Serum content of markers of renal damage ( $M \pm m$ )

**Table 1**

Indicators cytokine profile	First group (n = 45)				Second group (n = 45)				Contr ol group (n = 32)
	Before treartme nt	First day after surgery	5-7 days after surgery	First month after surgery	Before treartme nt	First day after surgery	5-7 days after surger	First month after surgery	
Creatinine mkmol/l	94,47± 3,74	97,57± 4,1	96,65± 3,97	92,02± 3,5	97,29± 4,5	99,47± 4,7	101,14± 4,9	94,77± 4,3	88,63± 6,08
Glomerular filtration rate(Cockrof t-Gault)	102,34± 11,8	103,36±1 3,05	102,79± 1 2,11	104,81±14, 0 3	103,4± 12,9	105,72± 1 2,1	107,18± 1 2,4	104,18± 1 1,28	109,09 ± 10,63
NGAL, НГ/МЛ	55,91± 2,84*	86,69± 5,84*#	66,27± 4,67*	53,74± 1,86*	58,93± 4,68*	124,8± 7,45*#	102,47± 8,34*#	65,51± 5,4*	40,18± 0,69
Cystatin-C, НГ/МЛ	1050,7± 29,6	1327,78± 4 5,7*	1201,92 ± 36,98*	1141,83±3 1, 42	1021,98 ± 22,07	1421,09 ± 43,93 *#	1388,78 ± 37,05 *#	1290,73 ± 24,55*	923,19 ± 14,47

\* Significance of differences with the indicators of the control group,  $p < 0.05$ .

Significance of differences with the initial data of the group,  $p < 0.05$ .

When analyzing the serum creatinine level and glomerular filtration rate among the patients of the main group and the comparison group on the 1st, 5th and 7th postoperative days, as well as one month after the ESWL, no significant differences were found among the patients of the 1st and 2nd groups with the control group ( $p > 0.05$ ).

On the 1st day after the ESWL session, there was a significant increase in the level of lipocalin-2 and cytatine-C in serum and urine in both groups, which was due to the damaging effect of the shock wave ( $p < 0.05$ ), however, in the second group, these changes had more pronounced character.

Subsequently, on days 5-7 after ESWLT, among the patients of the first group, there was a tendency towards a decrease in the values of the level of the studied markers of renal damage, while among the patients of the second group the level of indicators remained at the same level.

A month later, among the patients of the first group, normalization of the level of cystatin-C and lipocalin-2 in blood serum and urine was noted, the levels of which were comparable to the values of the control group ( $p > 0.05$ ). In patients of the second group, the level of markers of renal parenchyma damage remained above normal values.

Thus, during repeated sessions of ESWL, the degree of damaging effect of the shock wave increases, which leads to the development of persistent functional disorders of the renal parenchyma. The rapid increase in the level of cystatin-C after lithotripsy is evidence of an acute inflammatory reaction of the kidney to shock wave action [6,7]. The increase in the level of cystatin-C in the postoperative period is a reflection of the violation of tubular functions. The increased synthesis of lipocalin in blood serum and urine during ESWL indicates that it is involved, on the one hand, in the process of apoptosis, and on the other, in an increase in the survival rate of damaged cellular structures [8]. When these processes are disturbed against the background of repeated ESWLT sessions, lipocalin over-synthesis occurs, which is characteristic of damaged tissues.

Renal damage in patients with KSD is realized mainly due to the tubulointerstitial component [9] and can be reversible in patients with a short history of the disease, no signs of nephrosclerosis and severe urinary tract obstruction.

The resulting difference is indicative of deeper impairments arising on the background of a repeated ESWL session.

**Conclusion.** The use of determining the level of markers of renal tissue damage lipocalin-2 and cystatin-C in blood serum and urine is a promising method for non-invasive assessment of the state of the renal parenchyma in dynamics, reflecting the effectiveness of the therapeutic measures and contributing to the timely correction of the revealed disorders.

If there is a need for repeated sessions of ESWL, there is an increase in the damaging effect of the shock wave on the renal parenchyma, which can be accompanied by adverse consequences both in the early and in the long-term postoperative period with the development of nephrosclerosis and a decrease in renal functions.

The results obtained in the course of the study dictate the need to optimize the management of patients who are subject to surgical treatment by the ESWL method, and the development of nephroprotective therapy.

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