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Optimization Of Remote Shock Wave Lithotripsy for Renal Parenchyma in Patients With Nephrolithiasis

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ABSTRACT.

Background: Urolithiasis, a prevalent condition affecting at least 3% of the population, presents significant challenges globally. In the Republic of Uzbekistan, the incidence of urolithiasis has risen by 25.8% from 2017 to 2020. While external lithotripsy remains a preferred treatment, it can induce traumatic effects on kidney parenchyma, leading to inflammatory changes. The search for less invasive treatments with fewer complications is ongoing.

Methods: This study examined 90 urolithiasis patients treated between 2017 and 2020 at the Bukhara Regional Multidisciplinary Medical Center. Patients underwent extracorporeal shock wave lithotripsy (ESWL), and specific kidney damage markers (lipocalin-2, cystatin-C) were evaluated alongside conventional assessments. Patients were divided into two groups based on the number of ESWL sessions. A control group of 32 individuals without urolithiasis was also included.

Results: Initial serum creatinine, glomerular filtration rate (GFR), lipocalin-2, and cystatin-C levels were within normal ranges for all urolithiasis patients before ESWL. Significant increases in lipocalin-2 and cystatin-C levels in serum and urine were observed post-ESWL, particularly after multiple sessions. While markers decreased in the first group over time, they remained elevated in the second group, indicating persistent renal parenchymal damage.

Conclusion:

Assessment of lipocalin-2 and cystatin-C levels in serum and urine proves promising for non-invasive monitoring of renal parenchyma status, aiding treatment effectiveness evaluation and timely intervention. Repeated ESWL sessions exacerbate renal parenchymal damage, emphasizing the need for optimized patient management and nephroprotective therapies. These findings highlight the importance of refining treatment approaches to minimize adverse outcomes in urolithiasis patients undergoing ESWL.

KEYWORDS: urolithiasis, extracorporeal shock wave lithotripsy, markers of kidney damage, lipocalin-2.

INTRODUCTION

Urolithiasis is one of the most common urological diseases and ranks second after inflammatory non-specific 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, 5-12, 50]. External lithotripsy is the method of choice in the treatment of patients with urolithiasis disease. However, in addition to crushing the calculus, it also has a traumatic effect on the kidney parenchyma, which often leads to severe inflammatory changes [5, 12, 32-41, 52].

The incidence of urolithiasis in the world is from 3 to 5% and continues to grow progressively [2]. Currently, extracorporeal shock wave lithotripsy (ESWL) continues to hold a leading position in the formation of a treatment strategy in patients with urolithiasis. Despite the fact that external shock wave lithotripsy is a non-invasive treatment method that is well tolerated by patients and is accompanied by a low percentage of complications, it has been proven that the shock wave, regardless of the nature of the generator, causes a significant number of side effects [3-7, 19, 25-31, 48]. 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 during the surgical treatment of nephrolithiasis by remote lithotripsy. Diffusion-weighted magnetic resonance imaging (DW MRI) can serve as one of such criteria [4, 15-22, 18, 34, 51]. With various damaging effects on the cell, a cascade of pathological reactions develops. One of the parameters by which the degree of tissue damage can be assessed is the diffusion of water molecules in the extracellular space [9, 17, 21, 32-40].

The destructive power of external shock wave lithotripsy (ESWLT) is usually very high. At the same time, the risk of damage to the renal parenchyma increases if the impact is directed to stones located in the kidney [5, 18-22, 42-49, 53].

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 disturbed, the concentration of its indicators in the urine can increase 200 times, especially in acute kidney injury [6, 18-23, 34, 39].

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 [7, 18-26, 30-34, 48].

At present, the question of the damaging effect of a shock wave on the state of the renal parenchyma with long-term consequences remains debatable. In connection with the foregoing, it seems appropriate to search for new methods to determine the damaging effects of shock waves on the kidney parenchyma [8-16, 27, 33-36, 48-51].

Purpose of the study: to conduct a comprehensive assessment of biochemical markers of renal parenchyma damage in patients with nephrolithiasis during ESWLT.

MATERIAL AND METHODS.

Between 2017 and 2020 we examined 90 patients with urolithiasis treated in the

Department of Urology of the Bukhara Regional Multidisciplinary Medical Center. All patients were diagnosed with urolithiasis at the prehospital stage, surgical treatment was performed in the hospital in the scope of ESWLT, and along with traditional methods of examination and treatment, a number of specific biological markers of kidney damage (lipocalin-2, cystatin-C) were determined. The first group consisted of 45 patients with nefolithiasis who underwent one session of ESWLT, while the clinical efficacy was 100%. The density of stones in patients of this group varied from 800 to 1200 HU, the number of pulses per session was 2000-2500. The second group consisted of 45 patients who underwent 2 or more sessions of ESWLT, while the density of calculi was 1200-1580 HU, the number of impulses per session was 25003000.

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, had no history of urolithiasis and, according to the results of clinical and laboratory studies, no data for urolithiasis.

Criteria for inclusion in the study: patients with a verified diagnosis of urolithiasis subject to surgical treatment in the scope of ESWLT, calculus size from 0.6 to 2.0 cm, age of patients from 25 to 60 years, no impaired renal excretory function, urine passage, active inflammatory process, voluntary informed consent of the patient to participate in the study.

Criteria for exclusion 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, inability to perform ESWL, indications for open surgery or PCNL, decrease in kidney function by 50% or more, bacteriuria 105 CFU or more, refusal of the patient to participate in the study. All patients of the main group and the comparison group received surgical treatment in the scope of ESWLT using the Sonolith I-sys device manufactured by EDAP (France).

Patients were determined the level of specific biological markers in blood serum and urine by enzyme immunoassay using commercial kits of reagents at the preoperative stage, on days 1, 5-7 (in patients of the second group after repeated sessions of ESWLT) and a 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 performed using the Statistica 7.0, SPSS 17 packages, as well as MS Excel'2003 statistical functions. 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. Student's t-test was used to identify significant differences in normally distributed indicators presented on an interval scale. Differences were considered significant at $p<0.05$.

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 normal values, which confirms stable and satisfactory kidney function in both groups. before ESWLT.

Table 1. The content of markers of kidney damage in blood serum (M±m)

Cytokine profile	First group (n=45)	Second group (n=45)	Control group

indicators	before treatment	1 day after surgery	5-7 days after surgery	1 month	before treatment	1 day after surgery	5-7 days after surgery	1 month	(n=32)
Creatinine µmol/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
GFR (Cockroft-Gault)	102,34 ± 11,8	103,36± 13, 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, ng/ml	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-S, ng/ml	1050,7 ± 29,6	1327,78 ±4 5,7*	1201,92 ± 36,98*	1141,83 ±31, 42	1021,98 ± 22,07	1421,09 ± 43,93 *#	1388,78 ± 37,05 *#	1290,7 3± 24,55*	923,19± 14,47

* Reliability of differences with the indicators of the control group, $p < 0,05$.

\# Significance of differences with the initial data of the group, $p < 0,05$.

Table 2. The content of markers of kidney damage in the urine (M±m)

Cytokine profile indicators	First group (n=45)				Second group (n=45)				Control group (n=32)
	before treatment	1 day after surgery	5-7 days after surgery	1 month	before treatment	1 day after surgery	5-7 days after surgery	1 month	
NGAL, ng/ml	6,37±1,8 9 *	60,84± 6,74*#	64,5± 6,7*#	4,26± 2,4*	7,12± 1,81 *	77,95± 6,61*#	86,05± 7,45*#	12,55± 0,94*	0,00±0,0 0
Cystatin-S, ng/ml	9,3±3,6	49,7± 4,45*#	36,95±3, 2 8*#	6,08±2, 0	10,18± 1,64	68,7± 5,71*#	57, 84±5,52* #	18,08±2, 6 *	7,46±1,7 9

* Reliability 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 level of creatinine in the blood serum and the glomerular filtration rate among the patients of the main group and the comparison group on the 1st, 5th-7th postoperative days, and also one month after the ESWLT, no significant differences were found among the patients of the first and second groups with the control group ($p>0,05$).

On the 1st day after the ESWLT session, there was a significant increase in the level of lipocalin-2 and citin-C in the blood 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 patients of the first group, there was a tendency to decrease in the values of the studied markers of renal damage, while at the same time, among 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 the blood serum and urine was noted, the levels of which were comparable with the values of the control group ($p>0.05$). In patients of the second group, the level of markers of damage to the renal parenchyma remained above normal values.

Thus, during repeated sessions of ESWLT, the degree of damaging effects of the shock wave increases, which leads to the development of persistent functional disorders of the renal parenchyma. A rapid increase in the level of cystatin-C after lithotripsy is evidence of an acute inflammatory response of the kidney to shock wave exposure [6,7]. An increase in the level of cystatin-C in the postoperative period is a reflection of a violation of tubular functions. Increased synthesis of lipocalin in blood serum and urine during ESWLT indicates that it is involved, on the one hand, in the process of apoptosis, and, on the other hand, in increasing the survival of damaged cell structures [8]. If these processes are disturbed against the background of repeated sessions of ESWLT, there is an oversynthesis of lipocalin, which is characteristic of damaged tissues.

Renal damage in patients with KSD is realized mainly due to the tubulointerstitial component [9] and may be reversible in patients with a short history of the disease, no signs of nephrosclerosis and severe urinary tract obstruction. The resulting difference indicates deeper disorders that occur against the background of a repeated ESWLT session.

CONCLUSION

The use of determining the level of markers of damage to the renal tissue 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 ongoing therapeutic measures and contributing to the timely correction of identified disorders.

If it becomes necessary to conduct repeated ESWLT sessions, there is an increase in the damaging effect of the shock wave on the renal parenchyma, which may be accompanied by adverse effects both in the early and late postoperative period with the development of nephrosclerosis, a decrease in renal functions. The results obtained in the course of the study dictate the need to optimize the management of patients subject to surgical treatment by ESWLT, the development of nephroprotective therapy.

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