

NECESSITY OF ANTIBACTERIAL PROPHYLAXIS IN THE TREATMENT OF RENO-URETERAL LITHIASIS BY EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY. A PROSPECTIVE DESCRIPTIVE STUDY

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ABSTRACT

Introduction. Due to the increase in the incidence of reno-ureteral lithiasis worldwide from 1% to 15%, varying according to age, sex, race, and geographical location, extracorporeal shock wave lithotripsy remains the method of choice in the treatment of reno-ureteral lithiasis. The need for antibacterial prophylaxis is required only in well-defined cases, uroculture with antibacterial sensitivity being crucial in order to reduce the infectious complications.

The objective of the study was to evaluate the need for antibiotic administration and to detect risk factors for the development of post-ESWL bacteriuria.

Material and methods. Between 05 Nov 2018 – 10 Dec 2019, a group of 120 patients with the diagnosis of reno-ureteral lithiasis was selected, who underwent ESWL treatment in Department of Urology and Surgical Nephrology from Republican Clinical Hospital „Timofei Mosneaga“. In all 120 patients, urine sample was taken before and after ESWL. In all patients included in the study, uroculture with antibiogram was performed.

RÉSUMÉ

La nécessité d'une prophylaxie antibactérienne dans le traitement de la lithiase réno-urétérale par lithotripsie extracorporelle par ondes de choc. Une étude descriptive prospective

Introduction. En raison de l'augmentation de l'incidence de la lithiase réno-urétérale dans le monde de 1% à 15%, variant selon l'âge, le sexe, la race et la situation géographique, la lithotripsie extracorporelle par ondes de choc reste la méthode de choix dans le traitement de la lithiase réno-urétérale. La nécessité d'une prophylaxie antibactérienne est exigée seulement dans des cas bien définis et l'uroculture avec une sensibilité antibactérienne est décisive afin de réduire les complications infectieuses.

L'objectif de l'étude a été l'évaluation de la nécessité d'une administration d'antibiotiques et de détecter les facteurs de risque pour le développement d'une bactériurie post-ESWL.

Matériel et méthodes. Du 5 novembre 2018 au 10 décembre 2019, un groupe de 120 patients avec une lithiase réno-urétérale, qui ont subi un traitement

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Results. The uroculture results obtained before ESWL were positive in 25 (20.84%) patients without any clinical symptoms and absence of leukocytes in the general urine analysis more than 10 per high power field. At the same time, the number of positive urine culture after ESWL increased significantly in 47 patients.

Conclusions. Antibiotic prophylaxis is not justified in the absence of definite risk factors such as positive urine culture before ESWL, JJ stent or nephrostome and a history of infectious reno-ureteral lithiasis or recurrent urinary tract infections.

Keywords: ESWL, reno-ureteral lithiasis, antibacterial therapy.

par ESWL au Département d'urologie et de néphrologie chirurgicale de l'Hôpital Clinique Républicain «Timofei Mosneaga» a été sélectionné. Un échantillon d'urine a été prélevé avant et après ESWL chez tous les patients, soit 120 cas. Egalement, une uroculture avec un antibiogramme a été réalisée pour tous les patients inclus à l'étude.

Résultats. Les résultats d'uroculture obtenus avant ESWL ont montré des résultats positifs chez 25 (20,84%) patients sans aucun symptôme clinique et l'absence de leucocytes dans l'analyse d'urine générale en nombre de plus de 10 leucocytes par champ visuel du microscope avec puissance élevée. Dans le même temps, le nombre de cultures positives d'urine après ESWL a augmenté significativement chez 47 (39,17) patients.

Conclusions. La prophylaxie antibiotique n'est pas justifiée dans l'absence du facteur de risque défini par une culture positive d'urine avant ESWL, un stent JJ ou une néphrostomie et des antécédents de lithiase réno-urétérale infectieuse ou infections récurrentes des voies urinaires.

Mots-clés: ESWL, lithiase réno-urétérale, thérapie antibactérienne.

INTRODUCTION

Due to an increased incidence of reno-ureteral lithiasis worldwide, from 1% to 15%, varying according to age, sex, race, and geographical location^{1,2}, extracorporeal shock wave lithotripsy remains the method of choice in the treatment of reno-ureteral lithiasis. Infected calculi or infectious lithiasis are those calculi which are formed as a result of urinary infection^{3,4}. The driving force of the struvite calculus is urine infection with urease-producing bacteria, the microorganisms of the group Klebsiella, Staphylococci, Mycoplasma, Proteus, Pseudomonas being most commonly encountered. This is due to the high concentration of ammonia derived from microorganisms producing in an alkaline urine pH. Infected calculi occur most commonly in patients prone to frequent urinary tract infections (UTIs), with a higher rate in women than in men, the ratio being 2: 1^{5,6}. Nanobacteria are also involved in the development of lithiasis and their pathogenicity is still investigated⁷. Microorganisms, being 10-100 times smaller than normal bacteria, they can be involved in the formation of crystals and the matrix for the subsequent formation of calculi. Therefore, the risk of post-extracorporeal shock wave lithotripsy (ESWL) infectious complications is correlated with the release of these microorganisms from the calculus during

treatment. Endotoxins are another presumed factor involved in the pathogenesis of urinary tract infection and lithiasis⁸. High levels of endotoxins are detected both in infected calculi (struvite and carbonate apatite) and in non-infected calculi. It is considered that high concentrations of endotoxins (lipopolysaccharides) are released into the systemic circulation during lithotripsy treatment, resulting in a systemic inflammatory response syndrome (SIRS), which can lead to sepsis^{8,9}. A positive culture for Proteus, Pseudomonas, Klebsiella, Staphylococcus aureus and Staphylococcus epidermidis could be considered a determining factor in the etiology of struvite calculus formation. This will also justify the antibacterial treatment before initiating any therapeutic procedure for calculus fragmentation^{10,11}. It is also proven that in patients with negative urocultures before ESWL the risk of developing post-operative infectious complications without the administration of antibiotics is 14%¹².

The administration of prophylactic antibacterial drugs remains a controversial issue in patients with sterile urine undergoing ESWL treatment¹³⁻¹⁵. The European Urology Association (EUA) and the recommendations of the American Association of Urology (AAU) have proposed different protocols for prophylaxis of developing post-ESWL infectious complications¹⁶. According to the AAU recommendations,

Table 1. Demographic information on patients.

Age (years)	Frequency	Per cent (%)
18- 35	35	29.17
36-59	53	44.16
60-79	32	26.67
Total	120	100
Sex		
Male	73	60.83
Female	47	39.17
Total	50	100
Calculus localization		
Kidney	67	55.84
Left side	32/67	47.76
Right side	24/67	35.82
Bilaterally	11/67	16.42
Ureter	53	44.16
Total	120	100
Calculus size		
< 1 cm	74	61.67
> 1 cm	46	38.33
Total	120	100
History of UTI		
Yes	34	28.3
No	86	71.66
Total	120	100
History of surgery caused by lithiasis		
Yes	27	22.5
No	93	77.5
Total	120	100

prophylactic antibiotic therapy is required in a single dose 24 – 48 hours before ESWL¹⁵⁻¹⁷. At the same time, in patients with urinary stents or in the presence of possible infected calculi it is necessary to administer antibiotics for 5 days after ESWL¹⁷.

THE OBJECTIVE OF THE STUDY

To assess the need for antibiotic administration and to detect risk factors for the development of post-ESWL bacteriuria.

MATERIAL AND METHODS

Between 05 Nov 2018 – 10 Dec 2019, a group of 120 patients with the diagnosis of reno-ureteral lithiasis was selected, who underwent ESWL treatment in Department of Urology and Surgical Nephrology from Republican Clinical Hospital „Timofei Mosneaga“, Chisinau, Republic of Moldova. The patients' urine sample was taken before and after ESWL. In all patients included in the study, uro-culture with antibiogram was performed. Statistical analysis was performed with Epi-Info 7 and Excel. Statistical significance was evaluated using Fisher's

Table 2. Results of urine culture test before ESWL.

Urine culture results before ESWL	Frequency	Percentage (%)
Negative urine culture	95	79,16
Positive urine culture	25	20,84
Escherichia coli	4	3,33
Enterococcus faecalis	2	1,66
Klebsiella pneumoniae	13	9,16
Proteus mirabilis	4	3,33
Staphylococcus aureus	2	1,66
Streptococcus agalac.	2	1,66
Total	120	100

Table 3. Results of urine culture test after ESWL.

Urine culture results after ESWL	Frequency	Percentage (%)
Negative urine culture	73	60.83
Positive urine culture	47	39.17
Escherichia coli	15	12.5
Enterococcus faecalis	4	3.33
Klebsiella pneumoniae	16	13.34
Proteus mirabilis	4	3.34
Staphylococcus aureus	5	4.16
Streptococcus agalac.	3	2.5
Total	120	100

exact test, with $p < 0.05$ considered statistically significant. The study was approved by the Research Ethics Committee decision no. 49/40 of May 10, 2016 of „Nicolae Testemitanu“ State University of Medicine and Pharmacy, Chisinau, Republic of Moldova.

RESULTS

Of the 120 patients included in the study, 73 patients were men (60.83%) and 47 (39.17%) were women, mean age 43 ± 15 years, ratio men:women 1.9:1. The following comorbidities were found: 10 (20%) patients – high blood pressure, 5 (10%) patients – diabetes mellitus. Of the 120 patients included in the study, there were 67 (55.84%) patients with renal calculi, of which 11 (16.41%) patients with bilateral kidney calculi; 53 patients from 120 (44.16%) had calculi located in the upper, middle, and lower ureter. All patients were subjected to ESWL for calculi treatment, of which 15/120 (12.5%) patients were placed a double JJ stent before ESWL. The calculi size ranged from 0.6 cm to 2 cm (± 0.48 cm) (Table 1).

The uro-culture results before ESWL were positive in 25 (20.84%) patients without any clinical symptoms and the absence of leukocytes in the general urine analysis more than 10 per high power field (Table 2).

At the same time, the number of positive urine cultures after ESWL increased significantly in 47 patients (Table 3).

The *Proteus* microorganism was positive in patients both with a history of urinary tract infection and surgery.

DISCUSSION

There is obviously controversy regarding the need for pre- and post-ESWL antibacterial prophylaxis, which is also highlighted by the differences in the AAU and EAU recommendations^{14,18-19}. The AAU good practice statement on antimicrobial prophylaxis for minimally invasive interventions including ESWL states that antibiotic prophylaxis is indicated in all patients, with a single dose of antibiotic administered over 24 hours after ESWL^{20,21-22}. This recommendation is based on a meta-analysis by Salem and Sharma evaluating 8 randomized clinical trials and 6 clinical studies^{16,17}. The meta-analysis of these authors demonstrated a reduction in the median probability of developing post-ESWL - UTIs, from 5.7% without antibacterial treatment up to 2.1% in patients with antibiotic treatment^{16,17}. Alternatively, the EAU guidelines for urological infections recommend only prophylaxis in cases of „stent, due to increased bacterial load (e.g., JJ stent, nephrostome, or infectious calculi)¹⁸.

An unique prospective cohort study of 120 patients with pre- and post-ESWL urocultures, without antibacterial prophylaxis, analyzed the risk factors which could be linked to a positive urine culture²¹. Factors considered were sex, age, diabetes, hypertension and history of previous surgery (including JJ stent, or nephrostome), personal history of UTIs, calculi size, chemical structure, or location^{2,7,9,12}. It was found that in patients with a history of UTIs and surgery or the presence of JJ stent administration of antibiotic after ESWL is statistically significant justified, according to the statistical analysis of the study ($p=0.04$). These studies support the EAU recommendations that routine prophylaxis for ESWL patients with sterile urinary cultures is not required¹⁸⁻²⁰. However, patients with a history of UTI and previous surgical intervention (ureteral stent or nephrostome) are recommended to follow antibacterial prophylaxis before ESWL¹⁸⁻²⁰. In this prospective study, it was shown that sex, age, calculus size are risk factors for the development of UTI. Moreover, this study has demonstrated that the presence of JJ stent or nephrostome before ESWL is a risk factor for bacteriuria after ESWL^{18,19,21}. At the same time, the need for universal antibiotic prophylaxis prior to ESWL is not recommended because the development of UTI is low in patients with negative urinary cultures^{16,21,22}. This shows that antibiotics are not required in these patients, having no benefit in reducing infectious

complications and presenting an increased risk of bacterial resistance and side effects²⁰⁻²².

CONCLUSIONS

Antibacterial prophylaxis is not justified in the absence of definite risk factors, such as positive urine culture before ESWL, JJ stent or nephrostome and a history of infectious calculi or recurrent UTIs. The unjustified administration of antibacterials has no benefits and may present some risks of increased bacterial resistance and side effects.

Author Contributions:

Conceptualization, A.B. and E.C.; methodology, A.B.; software, A.B; validation, E.C. and A.B.; formal analysis, E.C.; investigation, A.B.; resources, A.B; data curation, E.C. and A.B.; writing—original draft preparation, A.B.; writing—review and editing, A.B, E.C.; visualization, E.C. and A.B.; supervision, E.C.; project administration, E.C. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article“

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study“

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