THE THERAPEUTIC APPROACH IN FEBRILE LITHIASIC RENAL COLIC-SINGLE CENTER EXPERIENCE

Lăpușan Carmen, Crișan Nicolae, Cucu Vlad, Coman Ioan

Department of Urology, Cluj-Napoca Clinical Hospital, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca

Address for correspondence:
Lăpușan Carmen, MD
11 Tăbăcarilor St., PO 400139, Cluj-Napoca, Cluj
Tel: 0745-316717
Email: carmenlapusan@yahoo.com

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Abstract

Introduction: One of the most frequent urologic pathologies is represented by the febrile renal colic with an evolutionary potential to sepsis, in which case, concurrently with the specific therapy of resuscitation, urinary diversion is considered to be obligatory.

Objective: The aim of this study is to evaluate the clinical and bioumoral parameters, in order to establish possible predictive values for the necessity of the urinary diversion in patients with febrile renal colic of lithiasic origin.

Materials and Methods: The present trial is a prospective one and it includes all of the patients with renoureteral lithiasis and febrile colic (above 38°C) who have come at the ED of the Municipal Hospital in Cluj, between 2010 and 2012. The diagnosis and treatment protocols are standardized. The clinical parameters considered for the evaluation are the following: age, sex, urosepsis stage, diabetes, active neoplasia, size and location of the renal calculus, degree of hydronephrosis, urinary diversion.

Results: 142 patients were admitted for febrile renal colic (above 38°C) through lithiasic obstruction between 2010-2012. The decision to perform urinary drainage was significantly associated with the location and size of the calculus (p<0.0001), the degree of hydronephrosis (p<0.0001) and the severity of urosepsis (p<0.0001).

Conclusions: The febrile colic remains a urological emergency. The remission of the septic phenomena during the first hours from the initiation of the resuscitation therapy could be followed by the spontaneous passage of the calculus, particularly if it is located distally and has small size.

Keywords: infected ureteral lithiasis, febrile renal colic, urinary diversion

Introduction

The high incidence of urosepsis is encountered both in the urology departments and intensive care units, knowing that evolution and prognosis of septic patient depend on early diagnosis and rapid treatment setting [1-3]. The urosepsis diagnosis is based on clinical, laboratory and imagistic criteria, but optimal time for the urologic intervention is still only relatively defined [1,2,4]. One of the most common urologic pathology is the febrile renal colic, potentially evolving to sepsis, situation where specific therapy of resuscitation is considered mandatory, concomitant with emergency diversion of the urinary tract [1,4,5]. Recent studies have indicated a continuing increase in the incidence of the infected urolithiasis; practically, its value has doubled in the past ten years. The same upward trend has been observed in the association of urolithiasis with sepsis,
but mortality rate has remained unchanged (0.2 to 0.25%) [6]. Currently, there is a set of nonspecific criteria that determines indication for urinary drainage in patients with renal colic: fever over 38°C, leukocytosis with neutrophilia and persistent pain despite adequate analgesia. There are specific situations in which the positive evolution of the patient with febrile lithiasic colic was demonstrated, also in the absence of invasive procedures involving the diversion of the superior urinary tract [2,7,8].

**Objectives**

The aim of this study is to evaluate the clinical and biohumoral parameters, both independently and in association, in order to establish possible predictive values for the necessity of the urinary diversion in patients with febrile renal colic of lithiasic origin. We also offer comparative evaluation of the isolated pathogens and their susceptibility to antibiotics.

**Materials and Methods**

The present trial is a prospective one and it includes all of the patients with renoureteral lithiasis and febrile colic (above 38°C) who have come at the First Emergency Department of the Municipal Hospital in Cluj-Napoca, between the 1st of April 2010 and the 31st of December 2012. The diagnosis protocol is standardized and it includes the following steps: medical history, objective examination, ultrasound exam, simple renovesical radiography and/or computed tomography, laboratory tests (glycemia, renal and hepatic function, hemoleucogram, coagulogram, urinalysis, and urine culture). The biologic samples were collected by qualified personnel and then analyzed in the accredited laboratory of the hospital.

The clinical parameters considered for the evaluation are the following: age, sex, urosepsis stage, diabetes, active neoplasia, size and location of the renal calculus, degree of hydronephrosis, urologic procedures concerning the urinary tract.

The clinical and biohumoral parameters were dynamically analyzed (on arrival, after 12h, 24h and 48h) but also in correlation with the time of urinary diversion, if this ever occurred. These parameters are: body temperature, pulse, blood pressure, the number of leukocytes and the percent of neutrophils, urine analysis and culture, renal function and last but not least, the urosepsis stage.

Moreover, the urinary drainage method was noted (spontaneous passage, ureteral stent JJ or nephrostomy) as well as, the type of the germs responsible for the septic condition and their sensibility towards antibiotics.

The decision of performing the urinary diversion was taken in conformity with the recommendations featured in the current EAU guidelines: fever above 38°C, leukocytosis with neutrophilia and the persistence of pain for more than 24 hours in the context of using the adequate analgesation. The antibiotherapy and the complementary therapy were both applied in a standardized way, pursuant to the current guidelines, depending on the urosepsis stage, the type of suspected infection (community acquired or nosocomial) and previous antibiotic treatments. The method of choice for urinary drainage in the context of infected renoureteral lithiasis, used in our clinic is the internal ureteral drainage in analgosedation and in case of failure, the ultrasound-guided percutaneous nephrostomy in local anesthesia.

The patients for whom the standard protocol of diagnosis and treatment was not pursued for different reasons were excluded from the study; so were those found in the situation in which the lithiasic origin of the episode was not established.

Numerical data were either continuous or discrete. Discrete variables were characterized through frequencies (number and percent). Continuous values were presented as means ± standard deviation (SD). Comparison between groups was performed using the Student’s t-test for continuous variables with normal distribution and the χ² test for categorical variables. The differences between categories, in case of more than two categories, were tested using Kruskal-Wallis or ANOVA method. P values < 0.05 were considered statistically significant. The MedCalc® 9.3.9.0.software was used for the analysis of statistical data.

**Results**

142 patients were hospitalized for febrile renal colic (above 38°C) through lithiasic obstruction between 2010-2012, 99 (66.9%) of them being women and the other 47 (33.1%) men. The age median was 51. The characteristics of the patients at the time of hospitalization are summarized in Table I.

A number of 56 patients (40%) presented a calculus under 4 mm and for 84 patients (60%) the dimension was over 4 mm. Approximately a third of the patients (32.4%) eliminated the lithiasic fragment spontaneously, as for the rest of them a urinary diversion procedure was necessary, as it follows: in 82 of the cases (57.7 %) a ureteral stent JJ was insert endoscopic and in 14 of the cases (9.9%) a percutaneous nephrostomy was performed.
The decision to perform urinary drainage was significantly associated with the location and size of the calculus (p<0.0001), the degree of hydronephrosis (p<0.0001), the severity of urosepsis (p<0.0001), the value of seric creatinine (p=0.0037) and with the positive results of the urine culture (p=0.0087). 46 cases of spontaneous passage of the calculus were registered, the majority of them presenting small size (41 cases - 89.13%) and distal location (40 cases - 86.95%), Figure 1.

Considering the stage of urosepsis, the majority of the patients presented SIRS, only 31 patients (21.83%) presented urosepsis out of which 2 cases featured severe urosepsis. The persistence of fever, leukocytosis and hydronephrosis after 12 hours of hospitalization represented the criteria for the decision of performing the emergency urinary diversion in most of the cases. The urinary diversion was performed in the first 6 hours of arrival for the patients admitted with clinical symptoms of urosepsis and severe urosepsis. For the patients with SIRS the urinary drainage was performed at an average of 24 hours (12-48 hours) since admission. There were no cases of decease registered.

Two patients required ureterolithotomy open surgery and pyelolithotomy respectively, performed in emergency due to complications arising after a failed
attempt of ureteral stenting. The curative surgery was scheduled and performed 14-21 days after the remission of the septic process for the 94 cases which underwent ureteral stent or nephrostomy diversion.

The location of calculi was significantly associated with the degree of hydronephrosis (p=0.0001). The degree of pyelocalicial dilatation was of major importance for the lumbar calculi, then for the iliac, juxtavezical and pyelic ones, Figure 2.

In cases of calculi with a diameter greater than 4 mm, their size were significantly associated with the presence of leukocytes in urine (p=0.02) and positive urine culture (p=0.04), but also with the presence of hydronephrosis degree II (p=0.001).

Although by the time of admission, infection was suspected in 99 patients (69.7%), objectification through the urine culture of the germs involved in the occurrence of the septic process was done in 64 of the cases (45.07%). Out of those, in 49 of the cases (76.56%) Gram negative germs were involved the most frequent was E.Coli in 35 of the cases (71.42%). Within the analyzed group, there were 10 cases of extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae and 13 cases of multiresistant germs. The ascending trend of these infections during those three years can be observed. The bacteriologic results which were obtained are presented in Table II.

There was no statistically significant correlation between procedure and sex or age within the analyzed group.

The duration of hospitalization was significantly correlated with the size of the calculus (p<0.001), the location of the calculus (p=0.001) but also with the degree of hydronephrosis (p<0.001) and the type of procedure (p<0.0001).

**Discussion**

In the absence of a real marker, the diagnosis of urosepsis can only be done by considering nonspecific clinical criteria, some of these being caused either by urosepsis or the acute pain felt in renal colic. The febrile colic represents a urologic emergency but the optimal time and the type of urinary deviation have not been defined yet [1,2,4]. The urinary drainage for the septic patient should be performed in the least invasive manner [1,2,4]. Recently, in patients with renoureteral lithiasis and infection, Sammon et al evaluated the 28.5% patients who need a urinary diversion on the first day of hospitalization and the fact that 70.1% out of them were women [6]. The results recently published by Yamamoto et al, on a group of 98 patients with obstructive PNA for whom a urinary drainage was performed, indicate an average of 3 days (0-38) from the beginning of the condition until the time of the urologic surgery [10]. The choice regarding urinary drainage (stent or nephrostomy) is still controversial; the ureteral JJ drainage is preferred in the USA and EAU [9,11] while in the U.K the percutaneous nephrostomy is performed in case of ureteral obstruction accompanied by urosepsis [12].

Sammon et al have recently emphasized the fact that the incidence of urinary lithiasis is higher in men but lithiasis associated with infection is more frequent in women considering that its value has doubled between 1999-2009. The same study indicates the fact that emergency diversion is more frequent in women who are more prone to develop urosepsis than men; the mortality was similar [6].

Regarding the treatment methods of the ureteral calculi depending on location and size, several studies show an increased rate (up to 80%) of the spontaneous passage for the calculi under 4 mm located in the distal ureter while the spontaneous elimination of the proximal ureteral calculi with the same size occurs in maximum 50% of the cases without specifying the time until expulsion. Though, these percentages decrease with the increasing dimension of the ureteral calculi [11-15]. In the context of associated urosepsis, in most cases, drainage of the urinary tract, by performing invasive procedures with all the risks that they imply, can’t be delayed by waiting for the spontaneous passage of the calculus, even if its dimensions are small. Within the analyzed group, there were 14 cases in which a stent was fixed for calculi under 4mm.

<table>
<thead>
<tr>
<th>Year/germ</th>
<th>2010 (37 pac/16 inf.)</th>
<th>2011 (44 pac/17 inf)</th>
<th>2012 (61 pac/31 inf)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram neg. total</td>
<td>11</td>
<td>15</td>
<td>23</td>
</tr>
<tr>
<td>G- multiresistent</td>
<td>–</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>G- ESBL</td>
<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Gram poz. total</td>
<td>5</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>G+ multiresistent</td>
<td>1</td>
<td>–</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table II. Bacteriologic results, urine culture**

Lăpuşan et al
Angulo et al, in their prospective study on 110 patients with renal colic secondary to upper urinary calculi concluded that determination of CRP in patients with renal colic due to urolithiasis provides an objective and useful parameter for deciding placement of urinary stent, which is even more valuable than leukocytosis or seric creatinine level [16].

In terms of bacteriological results, emphasizing the pathogenic agent in urine culture was possible only in 45.07% of the cases, a lower percentage than the one for urosepsis in general [1,3]. One of the explanations is the existence of a complete urinary obstruction, as the overlying purulent stasis could not be objectified after the drainage since the patient was already taking antibiotics [4].

Schmudermaier M et al in their 6 years study concluded that there is a significant increase in resistance development for standard antibiotics in E. Coli urinary tract infections but no increase in ESBL resistance [17]. In 2010, Hoban et al. find that the increasing resistance in Gram-negative bacilli isolated from hospital-acquired infections worldwide has complicated empirical antimicrobial selection for these infections [18,19]. In 2008, Souli et al. in 2008 find that there is an increasing isolation of organisms with resistance to beta-lactam/ beta-lactamase inhibitor combinations as well as carbapenem-resistant Enterobacteriaceae [19,20].

The limitations of this study are drawn by the establishment of the threshold of 4mm for the calculi for which a spontaneous passage is expected, although in the medical literature, spontaneous eliminations for the 5-7 mm up to 1 cm calculi are quoted. Within the analyzed group, there were 6 patients with calculi of over 4 mm that were spontaneously eliminated. Another limitation of the study is the fact that the data obtained from patients with febrile colic is not compared with the data obtained from patients with renal colic and infection, but without the clinical signs of sepsis.

**Conclusions**

In the absence of a real marker for the urosepsis, the febrile colic remains a urological emergency in the context of which alongside the resuscitation procedure a drainage of the urinary tract is required. The remission of the septic phenomena during the first hours from the initiation of the resuscitation therapy could be followed by the spontaneous passage of the calculus, particularly if it is localized distally and has small size. These situations require careful monitoring and urinary drainage if the clinical and bioumoral parameters urge for it. The increasing incidence of the multiresistant microbes requires the review of local protocols for antibiotherapy in concordance with the susceptibility of isolated microbes.

**References**


