Original Article

DOES C-REACTIVE PROTEIN HAVE A VALUE IN EARLY DETECTION OF INFECTION AFTER EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY?

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Abstract
Introduction: Extracorporeal shock wave lithotripsy (ESWL) has produced a great revolution in the treatment of the urolithiasis. Bacteriemia, bacteriuria, and septic shock are the documented complaints for which early diagnosis and treatment can be vital. C-reactive protein (CRP), an acute phase reactant, serves as a marker of the infection before other measures. In this study, we measured the CRP value in the early detection of bacteriemia and bacteriuria after ESWL.
Methods: In 2005, we sought patients who had urolithiasis and were candidates for ESWL, and we recruited such patients for this study. The inclusion criteria were sterile urine and a negative CRP test. The patients who participated in the study were requested to undergo laboratory tests on the third and seventh days after ESWL. After the resulting data were entered into the SPSS-11.5 data analysis software, the analyses were done with Chi squared test.

Results: Among the studied subjects, 29 out of 97 (29.9%) had a positive CRP test and 16 (15.2%) had positive urine cultures. There was no significant statistical relationship between the CRP tests and the urine cultures (P value > 0.05). On the third day, the relationship between CRP and erythrocyte sedimentation rate (ESR) was significant (P value < 0.001). The positive predictive values of CRP were 0.087 and 0.214, and the negative predictive values were 0.87 and 0.963. The sensitivity and specificity of CRP were 18.2% and 74.1% (first stage), respectively, and 60% and 82.5% (second stage), respectively.

Conclusions: We were unable to determine what the diagnostic value of CRP should be in the early detection of infection after ESWL. Additional studies are needed to provide greater insight into this issue.

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Keywords: CRP, ESWL, Bacteriemia, Bacteriuria

INTRODUCTION

Nephrolithiasis is one of the most common problems in the urinary tract that results in patients seeking medical care. Extracorporeal Shock Wave Lithotripsy (ESWL) is very effective in treatment of nephrolithiasis, and this technique is widely used. The main idea upon which ESWL is based was initially developed as a hypothesis in Russia in 1950. Wide application of this method began about 1980. At the present time, ESWL is the choice therapy in 80-90% of nephrolithiasis cases (3-4), and there has been a significant decrease in open surgery due to the availability of this technique (1-2).

Despite the non-invasive nature of the method, some complications may occur, such as gross hematuria, nausea and vomiting, abdominal pain, urinary retention, perirenal hematoma, and pancreatitis. In addition, there may be infectious complications, including bacteriuria, bacteriemia, and septic shock. Bacteriuria and bacteriemia are diagnosed by cultures that take 48-72 hours develop, and early diagnosis and treatment can be vital for the patient (5).

CRP is considered as a comparable diagnostic method to urine or blood cultures (6). This marker is an acute phase reactant in the serum that can show the level of tissue damage after inflammation stimulators (7-8). Serial measuring of the CRP level is considered to be effective for the evaluation of the patient’s response to the therapies. Early detection of bacteriuria and bacteriemia after ESWL and before preparing the cultures and early empiric therapy can be valuable for the patient (9).

This study was designed to evaluate the diagnostic value of the CRP test for the rapid diagnosis of bacteriuria and bacteriemia after ESWL in Gorgan, Iran.

MATERIALS AND METHODS

This study was conducted in 2005 in Gorgan, Iran, and all patients with nephrolithiasis who were candidates for ESWL were included by simple random sampling without substitution.
Ultrasonography was done for all the potential participants, and those with sterile urine and negative CRP values were included. Then, they were asked to give samples on the third and seventh days after ESWL so that test could be conducted for Complete Blood Culture, CRP, Urine Analysis, Urine Culture, and Blood Culture. Diphasic Castaneda medium was used for the blood cultures. Negative cultures were those without any colony count or cloudiness after three weeks. For urine cultures, 100 λ of mid-stream urine was cultured in Eosin-Methylene Blue and Blood Agar, and, after 24-48 hours, it was read, and the bacteria count was determined. In positive U/C samples, the strain and genus of the bacteria were determined. The quantitative CRP test was done with the Omega kit, and a concentration greater than 0.6 mg/100 ml was considered positive. Data were entered into the SPSS-11.5 software, and the χ2 test was used for analysis. A P value less than 0.05 was considered significant.

RESULTS

In this cross-sectional study, 97 cases were included with mean (± SD) age of 42.1 ± 14.23 years. The male to female ratio was 1.4 to 1. The locations of the renal stones were as follows: 56 cases in the right kidney (57.7%) and 41 cases in the left kidney (42.3%). The mean (± SD) size of the stone was 13.12 ± 6.06 cm. Mean (± SD) duration of electromagnetic waves were 39.8 ± 9.72 minutes, and the voltage was 5260 ± 9.72 Joule. The average waves used for these patients were 2944.12 ± 327.45 Joule. The CRP was reported positive in 26 cases (26.8%) in the third day and in 14 cases (15.2%) in the seventh day after ESWL, while 11 were positive on both the third and seventh days, and only three new positive cases were seen on the seventh day. Totally, 29 out of 97 (29.9%) were CRP positive and 16 (15.2%) had positive urine cultures, while 11 cases revealed positive U/C on the third day and five on the seventh day after ESWL. For the blood cultures, only one positive case was identified, and this occurred on the seventh day (Table 1.).

<table>
<thead>
<tr>
<th>Urine culture</th>
<th>CRP</th>
<th>Negative</th>
<th>Positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-</td>
<td>60</td>
<td>74.1</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>21</td>
<td>25.9</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>81</td>
<td>100</td>
<td>11</td>
</tr>
<tr>
<td><strong>P-value:</strong></td>
<td></td>
<td>Not significant</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1. The relationship between CRP results after ESWL and the urine culture of that time

The specificity and sensitivity of CRP in diagnosing urinary infections were 18.2% and 74.1%, respectively, in the first test and 60% and 82.5%, respectively, in the second test. No significant relationship was seen between CRP and the cultures (P value > 0.05).

No significant relationship was reported between CRP and other variables, such as age, sex, and size and location of the renal stone (P value > 0.05). The mean ESR level...
on the third day was 23.7 in cases in which CRP was positive and 13.7 in the cases in which CRP was negative (P value < 0.001), but no significant relationship was observed in the seventh day (P value > 0.05). The most common microorganism found in this study was E. coli (Table 2).

### Table 2. Distribution of microorganism in urine culture positive cases after ESWL

<table>
<thead>
<tr>
<th>Type</th>
<th>Number of positive cases of U/C in the first time</th>
<th>Number of positive cases of U/C in the second time</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Staph Aureous</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>5</td>
</tr>
</tbody>
</table>

**DISCUSSION**

In the present study, 12.5% of all urine cultures were positive after the patients’ nephrolithiasis was treated with ESWL, which is in accordance to other studies, such as a study in Turkey in which 13.3% of the urine cultures were positive (10). However, in some other reports from Turkey, the incidence of positive urine cultures was much lower, i.e., about 5.1% (11). Also, in another multi-centre project in Turkey, 5% of sterile urine cases became positive after ESWL (12). This difference could be explained by the different rate of infectious stones in these regions, which could affect the rate of infection after nephrolithiasis.

Positive blood cultures were very low in the present study (1.5%), and this is comparable to the results of a similar study in Turkey in which positive blood cultures were 4% (10). CRP positive cases were 29.9% in our study, and no significant relationship was reported between CRP and cultures. Wolff et al. showed no significant increase in the titer of CRP after nephrolithiasis in 150 cases (13). In another study by Yilmaz et al. in Turkey, a meaningful relationship was seen between the two variables (10). Yen et al. concluded that high titers of CRP in pediatric patients under 15 years of age could indicate a high risk for pyelonephritis (14). In the present study, a significant relationship was observed between CRP and ESR on the third day but not on the seventh day. This could have resulted from the fact that ESR changes much more slowly than CRP (15). CRP results showed no relationships with the other variables, such as age, sex, size and location of the stone, and the number of shock waves used to treat nephrolithiasis. This finding was similar to the findings of other related studies (11).

Bacteriuria showed no significant relationship with the number of stones or their location and size in the present results, and this finding was also similar to the findings of other studies (13). In the present research, the most prevalent microorganism was E. coli both in the third and seventh days. In other studies in Turkey and Taiwan, a similar pattern was observed (10, 14).

Regarding the sensitivity and specificity of CRP observed in our results, Pullian et al. reported that it was 79% and 91% in babies of ages one and 36 months, respectively (16). Biggi et al. reported these values to be
about 64% and 69% in children with their first urinary tract infection with a technetium dimercapto-succinic acid (DMSA) scan positive (17).

It could be that the differences in the ages of the subjects and the location or type of the renal stone affect the results of such studies. It has been shown that positive CRP is more related to pyelonephritis (14), so the location of the renal stone could play a role. It may be suggested that CRP should be measured in the early diagnosis of the infections, especially if there is strong clinical suspicion or if risk factors exist. Another key determinant is whether the titer is equal to or greater than 12 (18). Thus, serial measuring of CRP titer could be helpful in early detection of infection in patients who have undergone an invasive or non-invasive diagnostic or therapeutic procedure (19-20).

CONCLUSION

Those According to the results obtained in this study, the role of CRP in detecting infections, if any, could not be definitively determined.

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