Evaluation of Enterobacteriaceae Resistance to Broad-spectrum Cephalosporins in Patients with Infection following open heart surgery in Shahid Madani Hospital

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Abstract

Background: Increase in bacterial resistance to broad spectrum antibiotics constitutes a major challenge in medicine. Enterobacteriaceae are among the important causes of nosocomial infections and mortality. This study was performed to evaluate the enterobacteriaceae resistance rate to broad spectrum Cephalosporins in Shahid Madani Heart Center and to determine the optimal antibiotic regimen for such cases.

Methods: In a cross-sectional descriptive study, 100 patients from heart surgery wards who were diagnosed with enterobacteriaceae infection in Shahid Madani hospital in 2009 were enrolled. After determination of bacteria type in microbiology laboratory by standard methods, the resistance of bacteria to cephalosporins were evaluated by disc diffusion agar method.

Results: Resistance rate of enterobacteriaceae for ceftriaxone, ceftazidime, cefixime, cefotaxime, ceftizoxime and cefepine were 33%, 38%, 29%, 20%, 3% and 5% respectively. Among the third generation cephalosporins, ceftizoxime with a 3% resistance rate was found to be the most effective and ceftazidime with 38% resistance rate the least effective. Ninety four percent of enterobactriaceae were sensitive to cefepime, a fourth generation cephalosporin.

Conclusion: This study shows that third and fourth generation cephalosporin are more effective than first generations in the treatment of enterobacteriaceae infection among open heart surgery patients. A higher rate of resistance was reported in this study compared to the previous studies.


Keywords: Enterobactriaceae ˝ Cephalosporins ˝ Bacterial resistancy
**Introduction**

Cephalosporins are β-lactam antibiotics that have important role in bacterial infections treatment. Mechanism of action of this group similar to other β-lactam antibiotics is destruction of bacterial walls. Cephalosporins are divided into 4 generations based on spectrum of their antimicrobial activities. Enterobacteriaceae constitute a group of gram-negative bacilli that include more than 100 species of bacteria which form normal flora of human’s and animal’s intestinal tract. Gram-negative organisms especially Enterobacteriaceae are among the chief pathogens involved in the community acquired and nosocomial infections. In gram-negative bacilli, β-lactamase enzyme is the chief element contributing to the bacterial resistance to β-lactam antibiotics. Important species of Enterobacteriaceae include E.coli, Klebsiella spp., Enterobacter spp., Proteus spp., Salmonella spp. and Shigella spp. Some risk factors have been proposed to explain the increase in bacterial resistance such as prolonged hospitalizations and irregular prescriptions of antibiotics. Recent studies demonstrate that increase in the prescriptions of third and fourth generations of cephalosporin is a very important risk factor for increasing the resistance of Enterobacteriaceae which produce extended spectrum β-lactamase (ESBLs). Nosocomial infections constitute an important challenge and result in prolonged hospitalizations and excessive cost. Unfortunately nowadays many outpatient and nosocomial infections are treated empirically before culture results become available. Accordingly, the present study was designed to evaluate the susceptibility pattern of Enterobacteriaceae to broad spectrum cephalosporin in Shahid Madani Heart Center and determine the optimal antibiotic regimen in such cases.

**Methods**

This study was performed in Shahid Madani Heart Center, a university-affiliated hospital located in Tabriz, Iran, that includes cardiology and heart surgery wards, CCU, cardiac surgery ICU and angiography units. In a cross-sectional descriptive study, 100 patients from heart surgery wards who were diagnosed to be infected by enterobactriaceae in 2009 were enrolled. After determination of bacteria type in the microbiology laboratory by standard methods, the resistance of bacteria to cephalosporins were evaluated through disc diffusion method. Antibiotics that were evaluated in this study were cefazolin, cephalaxin, cephalothin, cefuroxime, cefotaxime, ceftazidime, cefixime, cefotaxime, ceftizoxime and cefepepine. Patient data were collected using their medical records. SPSS (version 16) software was used for statistical analysis.

**Results**

In the present study, urinary tract infection was found to be the most common infection (82%) and E.coli the most common organism (65%). Other organisms were Klebsiella spp. (15%), Enterobacter spp. (12%), Proteus spp. (4%) and Citrobacter spp. (4%). The male (26%) to female (74%) ratio was 1:3. Data regarding source of infection is summarized in table 1.

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>E.coli</th>
<th>Klebsiella spp</th>
<th>Enterobacter spp</th>
<th>Citrobacter spp</th>
<th>Proteus spp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>65</td>
<td>8</td>
<td>5</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Blood</td>
<td>-</td>
<td>2</td>
<td>6</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Secretions</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Wound</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tissue</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>15</td>
<td>12</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Mean sensitivity rate of enterobactriaceae to first generation Cephalosporins (Cefazolin, Cephalothin, Cephalexin) that was evaluated in this study was 38.3% ± 3.77% and mean resistance rate was 50.3% ± 9.55%. Cefuroxime was the only second generation cephalosporin that was evaluated in this study. Sixty two percent of enterobacteriaceae were resistant, 11% of them were partially sensitive and 27% of them were completely resistant to it. Five third generation cephalosporins (Ceftriaxone, Cefixime, Cefotaxime, Ceftazidime and Ceftizoxime) were studied. Mean sensitivity rate of enterobactriaceae to this group was 65.8% ± 10.48% and the mean rate of complete resistance...
was 24.6% ± 10.48%. Among third generation Cephalosporins, ceftizoxime with 3% resistance was found to be the most effective and ceftazidime with 38% resistance the least effective one. Ninety four percent of enterobacteriaceae were completely sensitive to cefepime- a fourth generation cephaplorin. Rate of partial resistance was 16% for cefotaxime, 13% for ceftriaxone, 11% for cefuroxime and 9% for cefixime. Susceptibility of enterobacteriaceae to cephaplorins is summerized in figure 1.

![Fig 1- Susceptibility pattern of enterobactriaceae to Cephalosporins](image)

**Discussion**

The increase in the rate of antimicrobial resistance constitutes a major challenge. In this study, urinary tract infection was the most common infection (82%) and E.coli was the most common organism (65%). Similar results have been reported in previous studies. In a study from Latin America hospitals, E.coli (60.3%) was the most common organism that lead to urinary tract infection. Klebsiella spp. (11.5%) and Enterobacter spp. (7.4%) accounted for the remaining cases.

Similarly, in the present study, E.coli (63%) was the most common pathogen identified in urinary tract infection. Klebsiella spp. (8%) and Enterobacter spp. (5%) constituted the remaining cases. Mean resistance rate of E.coli was 49.7% ± 3.4% for first and 23.66% ± 12.16% for third generation cephaplorins. In a study that was performed in France in 1996, these figures were reported to be 7% for the first and 0.8% for the third generation cephaplorin. Results demonstrate that resistance to both groups have increased. In a study performed in 2002, enterobacteriaceae resistance to ceftriaxone, cefotaxime and cefepime were reported 2%, 7.2% and 0.7%. In our study these rates were 33% for ceftriaxone, 20% for cefotaxime and 5% for cefepime. These results point that resistance rate to these antibiotics in our study is higher than John et al study. In another study that was performed in USA in 2001, 90% of enterobacteriaceae were sensitive and 10% of them were resistant to ceftazidime. In the present study 57% of enterobactriaceae were sensitive, 5% of them were partially resistant and 38% of them were completely resistant to ceftazidime and the most effective antibiotics was cefepime. Since the antibiotic susceptibility issue has been put forward, susceptibility profiles of common nosocomial pathogens are used in choosing the appropriate antibiotic regimen and also control of nosocomial infections. In comparison to previous studies, the resistance rate of enterobacteriaceae to Cephalosporins were significantly higher in the present study; yet similar to them, third and fourth generation Cephalosporins were more effective than first and second generations. Rate of partial-resistance was 16% for cefotaxime, 13% for ceftriaxone, 11% for cefuroxime and 9% for cefixime. This result demonstrates that resistance rate of enterobacteriaceae to these Cephalosporins is increasing. Increase in bacterial resistance especially enterobactreiaceae to antibiotics is one of the major challenges in medicine. Thus necessary actions should be taken in this regard. Antibiotic exposure is one of the most important risk factors for emerging antibacterial resistance among hospital pathogens. Among various factors that influence antibiotic consumption, the physician/patient relationship plays a key role. Irregular prescriptions of antibiotics must be avoided and prescription of appropriate antibiotics is necessary. Finally, patients must be advised to finish the course of treatment completely. Therefore it is important to perform antibiotics surveillance programs in order to implement appropriate empirical therapy and infectious control practices.
**Limitations**

Some limitations of this study deserve to be mentioned. It was conducted in patients who had undergone open heart surgery in a single center. Adequate antibiotic disc for second and fourth generation cephalosporins were lacking.

**Acknowledgement**

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**References**


