Abstract

Disproportionality Analysis of Safety with Nafcillin and Oxacillin with the FDA Adverse Event Reporting System (FAERS)

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Background

• Oxacillin and nafcillin are among the drugs of choice for severe and invasive MSSA infections
• While alternative agents such as cefazolin are associated with improved safety compared to these, comparative safety data between individual antistaphylococcal penicillins is limited
• A recent single center study found nafcillin was associated with and has shown possible improved safety with compared to oxacillin among adults with regards to hypokalemia and acute kidney injury

Objective

• This study aimed to determine the relative adverse events (AEs) reporting for these agents among the FDA Adverse Event Reporting System (FAERS) database.

Methods

• AE reports for oxacillin and nafcillin from FAERS, a voluntary and publicly available FDA database, were included from Q1/2004 through Q4/2017
• Only medications indicated as primary or secondary suspected cause were included, removing concomitant and interacting
• Duplicate cases were removed by retaining only the most recent update
• Common indications for nafcillin and oxacillin patients were also examined
• AEs were searched using Medical Dictionary of Regulatory Activity (MedDRA) terminology
• MedDRA preferred terms were used along with lower level terms

Methods (Continued)

• Safety terms included AEs related to acute renal failure (ARF), rash, hypokalemia, hepatotoxicity, thrombocytopenia, and neutropenia
• Relative signals for adverse effects were observed through performing disproportionality analysis of safety events for nafcillin and oxacillin
• Measures of association for safety evaluated included reporting odds ratio (ROR) and proportion reporting ratio (PRR) (Figure 1)
• All analyses were performed in SAS 9.4 (SAS Institute, Cary, NC)

Table 1. Antibiotic Indications

<table>
<thead>
<tr>
<th>Indication</th>
<th>Nafcillin No. (%)</th>
<th>Oxacillin No. (%)</th>
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<tbody>
<tr>
<td>Bacteremia</td>
<td>17 (15.7)</td>
<td>26 (23.6)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>4 (4)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Staphylococcal infection</td>
<td>11 (10.2)</td>
<td>20 (18.2)</td>
</tr>
<tr>
<td>Device related infection</td>
<td>3 (2.8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other or missing</td>
<td>63 (58.3)</td>
<td>49 (44.5)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>10 (9.3)</td>
<td>1 (1.0)</td>
</tr>
</tbody>
</table>

Patients often with multiple indications listed

Results

• A total of 8,043,167 unique adverse effect drug reports were identified, nafcillin and oxacillin were noted for 153 and 134 reports, respectively.
• The majority of indications were noted for bacteremia and Staphylococcal infections (Table 1).
• Reports of ARF were more common with nafcillin (PRR 16.9, 95% CI 13.5 – 21.5) than oxacillin (PRR 4.8, 95% CI 2.9 – 8.1).
• Hypokalemia was more common with nafcillin than oxacillin (PRR 14.0, 95% CI 6.8 – 28.8 vs 1.1, 95% CI 0.7 – 18.1).

Conclusions

• Oxacillin may be associated with overall improved safety compared to nafcillin based on reporting signals from FAERS. Our results support previous limited observational data. With the likely equal efficacy of these agents, clinicians may want to consider prescribing oxacillin over nafcillin if indicated for an invasive MSSA infection. However, given the limitations of reporting systems, further evaluation is warranted.

Figure 1. Disproportionality Analysis

Figure 2. Reporting Odds Ratios of AEs with Nafcillin and Oxacillin

Figure 2. Reporting Odds Ratios of AEs with Nafcillin and Oxacillin

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References