Comparison of Metronidazole q12h to q8h in Combination with Other Antibiotics on the Clinical Outcome and Readmission Rate of Patients with Appendicitis and Diverticulitis

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Background & Objectives

Background: Pharmacokinetic, pharmacodynamic and limited published data support metronidazole 500 mg administered in a twice daily (q12h) regimen. As part of an Antimicrobial Stewardship Program (ASP) initiative, we started promoting metronidazole q12h in March 2015 during weekly rounds with the General Surgery teams in our 1100-bed tertiary-care institution.

Objectives: To determine 1) if more patients were prescribed metronidazole q12h compared to q8h after the intervention; 2) if metronidazole q12h differed from q8h in patients with appendicitis or diverticulitis, regarding clinical outcomes and 30-day readmission rates.

Methodology

Retrospective chart review of General Surgery patients with:

- Appendicitis: Aug.1/14 to Jan. 30/15 (pre-intervention), and Aug.1/15 to Apr.30/16 (post-intervention)
- Diverticulitis: June 1/14 to Jan.30/15 (pre-intervention), and June 1/15 to Jan.30/16 (post-intervention).

Definition of Resolution:

- Appendicitis: no reported complications in the 30 days post-admission or at the follow-up visit, if before 30 days.
- Diverticulitis: no reported complications in the 30 days post-admission. Patients without complications during their stay, with documented instructions to return to the hospital for any clinical deterioration and without a subsequent visit were considered to have had resolution.

Results & Discussion

125/508 patients with appendicitis and 62/202 patients with diverticulitis were included. The main reasons for exclusion were: receipt of ≤ 1 dose of metronidazole, multiple dosing frequencies during the same admission, or prior admission already included.

There was no statistically significant difference at baseline in the number of patients with abscesses or perforation between the q12h and q8h groups for either condition, or with a history of diverticulitis in that group. 80% of appendicitis case were treated surgically and 92% of diverticulitis cases were managed conservatively.

The number of patients prescribed metronidazole q12h increased significantly after the intervention (Figure 1). Resolution rates (Figure 2) and readmission rates (Table 1) did not differ between patients prescribed metronidazole q12h and q8h for appendicitis and diverticulitis.

Figure 1- Comparison of Regimens in the Pre- and Post-Intervention Periods

Figure 2- Resolution Rate by Dosing Frequency and Condition

Table 1 - 30-Day Readmission Rate

<table>
<thead>
<tr>
<th></th>
<th>Appendicitis</th>
<th>Diverticulitis</th>
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</thead>
<tbody>
<tr>
<td>q12h</td>
<td>4/46 (9%)</td>
<td>0/23 (0%)</td>
</tr>
<tr>
<td>q8h</td>
<td>3/79 (4%)</td>
<td>2/39 (5%)</td>
</tr>
<tr>
<td>p</td>
<td>0.421</td>
<td>0.526</td>
</tr>
</tbody>
</table>

The study limitations include: retrospective design, number of cases, variation in other antibiotics & duration of therapy.

Conclusion

The number of patients prescribed metronidazole q12h over q8h increased after our ASP initiative, and resolution and readmission rates did not differ between the two groups. These findings support that q12h is an appropriate dosing frequency for metronidazole when used in regimens for appendicitis and diverticulitis. This may minimize the risk for missed doses, adverse events and cost.