Identification of Solid Organ Transplant Antimicrobial Stewardship Opportunities in Pediatric Liver Transplant Patients

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Background

• Through the prospective audit with feedback program, post-operative antimicrobial use for pediatric liver transplant was observed to extend beyond the recommended 24 hours for surgical site infection (SSI) prophylaxis.
• Bacterial infections in the immediate post-transplant period represent significant risk in pediatric liver transplant recipients, including SSI which occurs at a rate of 10–37%.
• Predominant pathogens: Gram-negative organisms, Enterococci, S. aureus, CoNS, Candida spp.

Objectives

• To describe postoperative antimicrobial utilization in pediatric liver transplant patients.
• To investigate prolonged postoperative antimicrobial use.
• To identify ASP opportunities that will reduce unnecessary antibiotic exposure while maintaining low rates of infectious complications.

Methods

Study Cohort

• All patients with liver transplant at LPCHS during study period (January through September 2017)
• Data collection: Duration of antimicrobials ordered within 24 hours of post-operative, microbiologic data pre and post-transplant (within 30 days), presence of fever, ID consult within 14 days of transplant, donor positive information, mass transference protocol (MTP)

Study Endpoints

• Compare identified factors associated with prolonged postoperative antimicrobial use (>48 hours): post-op fever, MTP, etc.
• Incidence of postoperative microbiologic positive infections

Liver Transplant Postop Order Set

• 3rd gen cephalosporin + ampicillin
• Piperacillin/tazobactam

Characteristics of Patients with Liver Transplant

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>N = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) ± SD</td>
<td>4.2 ± 5.3</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>20 (52)</td>
</tr>
<tr>
<td>Multi-organ transplant (%)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Mean length of stay (days) ± SD</td>
<td>42 ± 60</td>
</tr>
<tr>
<td>Mean length of stay-post-transplant (days) ± SD</td>
<td>27 ± 35</td>
</tr>
<tr>
<td>ID consult (%)</td>
<td>6 (16)</td>
</tr>
</tbody>
</table>

* Multi-organ transplant (n = 4); combined liver and kidney (n = 3), and combined heart and liver (n = 1).

Figure 1. Incidence of Antimicrobial Use Based on Post-Op Duration

Figure 2. Duration of Antimicrobials by Post-Op Duration

Results

Figure 3. Microbiological Characteristics of Patients with Liver Transplant

<table>
<thead>
<tr>
<th>Culture proven infection</th>
<th>N = 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPT treated PTT*</td>
<td>35</td>
</tr>
<tr>
<td>Remote h/o infection PTT**</td>
<td>35</td>
</tr>
<tr>
<td>Culture proven infection post-op ***</td>
<td>25</td>
</tr>
</tbody>
</table>

* PPT: Prior to transplant
** None of the patients experienced recurrence or post-operative infection.
*** Remote history of infection: Enterobacter (piperacillin/tazobactam susceptible), Serratia, and Candida (n = 1), and E. coli (multidrug resistant, n = 1). Both patients developed post-op proven bacterial infection: urine culture with Enterococcus on post-op day (POD) 8, and peritoneal fluid culture with E. coli (resistant to piperacillin/tazobactam and piperacillin/oral fluoroquinolone) on POD15, respectively.

As stated above and one patient with C. stauaniana isolated from blood and peritoneal fluid cultures POD4.

Figure 4. Identified Factors for Antibiotic Use Stratified by 48 hours Postop

<table>
<thead>
<tr>
<th>Fever within 14 d after post-op</th>
<th>MTP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>16</td>
<td>7</td>
</tr>
</tbody>
</table>

* Allos < 48 hr (n = 9)
  - Gram-negative antibiotic (Abs)
  - Vancomycin
  - Cefazolin

Discussion

• Antimicrobial use beyond 48 hours post-transplant was common; however, culture-proven infection was not.
• Fever in the immediate post-op period occurred in half of the patients and was not associated with culture proven bacterial infection.
• MTP did not appear to be high risk for post-transplant infections and does not warrant prolonged gram-negative antibiotic courses.
• Since no resistant Gram-positive organisms were identified post-transplant, vancomycin is not required as prophylaxis or empiric therapy and can be reserved for culture proven infections.
• Anti-fungal therapy is not required as prophylaxis or empiric therapy since only one fungal infection was identified post-transplant and treated accordingly.
• Appropriately treated pre-transplant infections do not warrant prolonged post-transplant antibiotics and only appear to induce resistance.
• Non-sterile cultures, such as ETT aspirations do not warrant prolonged post-transplant antibiotics.
• Fungal infections identified in the post-transplant period should prompt an ID consult.

Conclusions

• The majority of children received post-transplant antibiotics beyond 48 hours which was not attributable to fevers or positive cultures.
• The indications for post-transplant antibiotics beyond 48 hours were not clinically relevant or identifiable by chart review.
• Identified ASP opportunities include shortening post-op antibiotics to 48 hours, eliminating vancomycin, restricting antifungals to MTP only, and limiting MTP antimicrobials to 5 days.

Future Initiatives

• Order set revision based on revised algorithm (see below)
• Follow patients undergoing liver transplant for adherence to new recommendations and clinical outcomes (i.e., infectious complications).