A comparative analysis between antibiotic allergy labels and non-antibiotic allergy labels in liver transplant recipients

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Introduction

Antibiotic allergy labels (AALs) are associated with suboptimal prescribing and inferior clinical outcomes in hospitalised patients, especially in the immunocompromised.1,2 The prevalence and type of AALs in liver transplant recipients (LTR), and subsequent effects on the choice of antibiotic prophylaxis strategies and treatment remains ill defined. We report on AALs and their impact on a cohort of LTR.

Methods

• This was a retrospective matched cohort study, conducted over a 5-year period (2010 – 2015) at Austin Health – a tertiary hospital with a liver transplant centre in Melbourne, Victoria.
• We used a departmental liver transplant database to identify LTR with an AAL (AA group) and an equal number of matched controls (LTR without an AAL; NAA group) were randomly selected for comparison.
• AA were defined as Type A adverse drug reactions (ADRs), non immune mediated, Type B ADRs (immune mediated) or unknown.3
• Baseline demographics, transplant history and infection-related admission data was collected
• Antibiotics administered during liver transplant and subsequent infection-related admissions were recorded: agent(s) and duration.
• Readmission, ICU-admission, multidrug resistance (MDR) organisms isolation, Clostridium difficile infection (CDI) and mortality rate were captured.

Results – Baseline demographics

Table 1. Baseline demographics of AA and NAA cohorts

<table>
<thead>
<tr>
<th>Baseline demographics</th>
<th>Antibiotic allergy (AA) N= 51; n (%)</th>
<th>No Antibiotic allergy (NAA) N= 52; n (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR)</td>
<td>55 (17-60)</td>
<td>55 (45 – 75.75)</td>
<td>0.58</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, median (IQR)</td>
<td>5 (4-7)</td>
<td>6.5 (5-9)</td>
<td>0.15</td>
</tr>
<tr>
<td>Sex, male</td>
<td>23 (45)</td>
<td>39 (75)</td>
<td>0.003</td>
</tr>
<tr>
<td>Number of transplants, (&gt;1 transplant)</td>
<td>5 (10)</td>
<td>3 (6)</td>
<td>0.49</td>
</tr>
<tr>
<td>Rejection history (&gt; 1 episode)</td>
<td>16 (31)</td>
<td>13 (25)</td>
<td>0.51</td>
</tr>
<tr>
<td>Infection related ICU admission</td>
<td>5 (8)</td>
<td>5 (8)</td>
<td>1</td>
</tr>
<tr>
<td>Total number of infective diagnosis</td>
<td>130</td>
<td>103</td>
<td>0.01</td>
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<tr>
<td>Common infective syndrome</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bilary-oesopha/cholangitis</td>
<td>5 (4)</td>
<td>6 (6)</td>
<td></td>
</tr>
<tr>
<td>Bacteremia / sepsis not specified</td>
<td>10 (8)</td>
<td>13 (13)</td>
<td></td>
</tr>
<tr>
<td>Clostridium difficile infection</td>
<td>9 (15)</td>
<td>4 (3)</td>
<td></td>
</tr>
<tr>
<td>Intra-abdominal infection</td>
<td>3 (2)</td>
<td>8 (8)</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4 (3)</td>
<td>8 (8)</td>
<td></td>
</tr>
<tr>
<td>Liver transplant prophylaxis</td>
<td>49 (98)</td>
<td>52 (100)</td>
<td></td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>2 (4)</td>
<td>2 (2)</td>
<td>1</td>
</tr>
<tr>
<td>Length of stay, median (IQR)</td>
<td>12 (6 – 22)</td>
<td>13 (8-29.75)</td>
<td>0.20</td>
</tr>
<tr>
<td>Mortality, 60 day (all cause)</td>
<td>6 (12)</td>
<td>4 (8)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Results – Antibiotic usage

1. Higher cephalosporin use in AA versus NAA group
   (107/354 [30%] courses vs. 75/328 [23%] courses, p=0.03)
2. Higher glycopeptid use in AA versus NA group
   (78/354 [22%] courses vs. 76/328 [23%] courses, p=0.08)
3. Lower penicillin use in AA versus NA group
   (26/354 [7%] vs. 36/328 [11%], p=0.14)

4. Multidrug resistance (MDR) organisms and CDI in AA group
   ↑ trend in cases of MDR gram-negative isolation (4 [8%] vs. 1 [2%]) and CDI (9 [18%] vs. 3 [6%], p= 0.07)

Results – Trimethoprim-sulfamethoxazole allergy

Trimethoprim-sulfamethoxazole (TMP-SMX) Allergy

• Sixteen (31%) LTR had a TMP-SMX ADR history noted, 11 (68%) Type B (7 [43%] delayed, 4 [25%] immediate), 2 (13%) Type A and 3 (19%) unknown.

   TMP-SMX as therapy
   • There was reduced TMP-SMX use as a proportion of total antibiotic courses in the AA group (p vs. 9/328[3%], p=0.001).
   • TMP-SMX as Pneumocystis jiroveci pneumonia (PIP) prophylaxis
     • Aerosolised Pentamidine (AP) was employed in 56% (9/16) of patients with a TMP-SMX ADR history immediately post-transplant, in 77% (7/9) the TMP-SMX ADR was a Type B reaction.
     • 4 patients switched to AP during the PIP prophylactic period due to ADRs.
     • 1 patient received dapsone, without ADR.
     • Sixty percent (10/16) of TMP-SMX ADR patients were toxoplasmosis IgG-positive, of which 80% (8/10) received no directed toxoplasmosis prophylaxis.

Results – Antibiotic allergy labels in LTR

Fig. 2. Proportion of antibiotic allergy labels per antibiotic class (n = 77)

Conclusions

• A high antibiotic allergy (AA) label prevalence in liver transplant recipients (LTR) was identified
• A higher rate of cephalosporin and glycopeptide use was noted in LTR with antibiotic allergy (AA)
• Almost one in four patients had a Type A ADR amendable to pharmacist-led ‘de-labeling’
• TMP-SMX could be more readily employed for PIP prophylaxis with re-challenge or desensitisation strategies
• Antibiotic allergy ‘de-labeling’, especially pre-transplantation, may effectively reduce AAL prevalence, improve antibiotic prescribing and clinical outcomes.

References


Figure 1: Description of antibiotic allergy labels for liver transplant cohort (2010-2015)

51 (16%) LTR had ≥ 1 antibiotic allergy label (AAL)

Type A 23% (18/77)
Type B 66% (51/77)
Unknown 23% (18/77)

66% (31/47) GIT upset
6% (3/51) SCAR**
55% (28/51) MPE*
35% (18/51) Anaphylaxis#
4% (2/51) Other

** Severe cutaneous adverse drug reactions, * Maculopapular exanthema, # Anaphylaxis, urticaria, angioedema

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References

** Severe cutaneous adverse drug reactions, * Maculopapular exanthema, # Anaphylaxis, urticaria, angioedema