Risk factors for colistin-resistant Enterobacteriaceae in a low endemicity setting for carbapenem-resistance – a matched case-control study

Andrea C. Büchler¹, MD, Christian Gehringer², MD, Andreas F. Widmer¹, MD MSc, Adrian Egli³, MD PhD, Sarah Tschudin-Sutter¹, MD MSc

¹Division of Infectious Diseases & Hospital Epidemiology, ²Division of Clinical Microbiology, University Hospital Basel, University of Basel, Switzerland
³Applied Microbiology Research, Department of Biomedicine, University of Basel, Switzerland 4Department of Clinical Research, University Hospital Basel, University of Basel, Switzerland

Introduction and Purpose

• Colistin-resistant Enterobacteriaceae are an emerging problem worldwide, especially because of the global spread of carbapenem-resistant Enterobacteriaceae resulting in increased use of this antibiotic of last resort.
• In November 2015, a new plasmid-related colistin-resistance mechanism called mcr-1 has been described, enabling horizontal gene transfer between bacteria of the same and different species (1), facilitating further spread.
• Carbapenem-resistance in Switzerland is still low, therefore use of colistin is still rare (0.01 defined daily doses [DDD]/1000 inhabitants/day in outpatient settings and 0.3 DDD/100 bed-days in hospitals (2)).
• However, colistin is used widely in veterinary medicine and it is hypothesized, that there might be a connection between colistin-resistant bacteria in animals and humans (1).
• The goal of this study was to assess clinical risk factors for colistin-resistant *E. coli* and *K. pneumoniae* in a low endemicity setting for carbapenem-resistant Enterobacteriaceae.

Methods

• Retrospective screening of samples for colistin-resistant *E. coli* and *K. pneumoniae* isolated from any clinical sample submitted to the microbiology laboratory from 01/2011 – 11/2015. Electronic and/or paper chart review for data collection.
• For each case patient, three controls with detection of a colistin-susceptible strain of the identical genus of Enterobacteriaceae was selected. Matching was performed according to site of isolation, ward type and date of isolation (Fig. 1).
• Patient’s baseline characteristics and comorbidities were compared by applying the Mann-Whitney U test or Fisher’s exact test.

Results

• Forty-two cases (33 with colistin-resistant *E. coli* and 9 with colistin-resistant *K. pneumoniae*) and 126 matched controls were identified.
• Age, gender and underlying diseases did not differ between cases and controls (Tab. 1).
• Susceptibility rates to quinolones, fosfomycin and tobramycin differed significantly between cases and controls (Fig. 2).
• Prior exposure to carbapenems as well as hospitalization and stay abroad were associated with colistin-resistance (Fig. 3).
• Only prior exposure to carbapenems was associated with colistin-resistance in multivariable analysis (OR 5.00, 95%CI 1.19-20.92, p=0.028).

Figure 1: Flowchart; FPS = Felix Platter Hospital

Figure 2: Antibiotic susceptibility testing of cases (light) and controls (dark).
P-values: *=0.010, **=<0.001, *’=0.011

Table 1: Demographics and underlying diseases

<table>
<thead>
<tr>
<th>Underlying disease</th>
<th>Cases (n=42)</th>
<th>Controls (n=126)</th>
<th>OR*6957</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charlson Comorbidity Index</td>
<td>2 (4.8%)</td>
<td>3 (2.4%)</td>
<td>0.831</td>
<td></td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1 (2.4%)</td>
<td>0 (0%)</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (57.1%)</td>
<td>48 (38.1%)</td>
<td>1.61</td>
<td>0.94-2.87</td>
</tr>
<tr>
<td>Cancer</td>
<td>7 (16.7%)</td>
<td>22 (17.5%)</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>4 (9.5%)</td>
<td>11 (8.7%)</td>
<td>1.05</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>10 (23.8%)</td>
<td>17 (13.5%)</td>
<td>1.08</td>
<td></td>
</tr>
<tr>
<td>Renal disease</td>
<td>13 (30.9%)</td>
<td>19 (15.1%)</td>
<td>1.81</td>
<td>1.01-3.25</td>
</tr>
<tr>
<td>Aids</td>
<td>2 (4.8%)</td>
<td>2 (1.6%)</td>
<td>2.67</td>
<td>0.96-7.48</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
<td>1 (2.4%)</td>
<td>0 (0%)</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>5 (11.9%)</td>
<td>8 (6.4%)</td>
<td>1.67</td>
<td>0.83-3.35</td>
</tr>
</tbody>
</table>

Figure 3: Risk factors for colistin-resistance, OR and 95% CI in a logarithmic scale (x-axis)

Conclusions

• In a low-endemicity setting for carbapenem-resistance with common use of colistin in animal production, prior exposure to carbapenems was the only risk factor for colonization or infection with colistin-resistant *E. coli* or *K. pneumoniae*.
• Prior exposure to colistin was low and not related to detection of colistin-resistance.
• Colistin-resistance mainly occurred in absence of concurrent carbapenem-resistance. The higher rate of quinolone-, fosfomycin- and tobramycin-resistance needs to be evaluated.

References

(2) Swiss Antibiotic Resistance Report 2016. FOPH publication number: 2016-OEG-3