Thrombocytopenia occurred in 3% of the patients who received linezolid in clinical trials. Gerson et al.³ extracting data from two prospective studies, compared the risk of thrombocytopenia (platelet count < 150 x 10³ cells/μL) between linezolid and vancomycin in 862 patients with nosocomial pneumonia. Thrombocytopenia occurred in 2.8% in the linezolid group and in 3.6% in the vancomycin group. However, these percentages have been considered underrated by other authors. In two post-marketing studies, the linezolid-associated thrombocytopenia rate was about 47% in both cases and a platelet count lower than 100 x 10³ cells/μL occurred in 32% and 19% of the patients, respectively.²,⁶ Our incidence of thrombocytopenia, considering

### Table 1. Patient characteristics at admission to the intensive care unit and at the beginning of linezolid treatment

<table>
<thead>
<tr>
<th>Mean</th>
<th>Age (years)</th>
<th>Simplified Acute Physiologic Score II</th>
</tr>
</thead>
<tbody>
<tr>
<td>63.4 (95%CI 58.9–67.9)</td>
<td>54.9 (95%CI 47.9–62.0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory values at the beginning of linezolid treatment</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>platelet count (10⁹ cells/μL)</td>
<td>326.4 (95%CI 227.1–375.7)</td>
</tr>
<tr>
<td>albumin (g/100 mL)</td>
<td>2.4 (95%CI 2.2–2.6)</td>
</tr>
<tr>
<td>creatinine (mg/100 mL)</td>
<td>1.5 (95%CI 1.1–1.9)</td>
</tr>
<tr>
<td>blood urea nitrogen (mg/100 mL)</td>
<td>40.4 (95%CI 29.5–51.3)</td>
</tr>
<tr>
<td>calculated glomerular filtration rate (mL/min/1.73 m²)</td>
<td>64.4 (95%CI 52.2–76.5)</td>
</tr>
</tbody>
</table>

### References


### Correspondence

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2. Statistical tests used were Mann–Whitney U-test for quantitative independent variables, and χ² and Fisher exact tests for dichotomous variables. Patients were mainly male (51.1%) and admitted to the intensive care unit (ICU) due to medical (21/49, 42.9%), surgical (27/49, 55.1%) and trauma (1/49, 2.0%) causes. The rest of patient characteristics are shown in Table 1. The mean duration of linezolid treatment lasted 14.4 days (95% CI 11.9–17.0, range 3–41). Thrombocytopenia was detected in 12 patients (24.5%). Through a univariate analysis, three factors were related to thrombocytopenia: Simplified Acute Physiologic Score II, pre-treatment albumin and pre-treatment platelet count. Through a multivariate analysis, only the pre-treatment platelet count remained as an independent factor related to thrombocytopenia (P = 0.034) and to platelet decrease (P < 0.001). There were significant differences between the thrombocytopenic group and the non-thrombocytopenic group in mean initial pre-treatment platelet count [240.7 ± 10³ cells/μL (95%CI 160.3 ± 10³ to 321 ± 10³) versus 354.2 ± 10³ cells/μL (95% CI 295.3 ± 10³ to 413.0 ± 10³), P = 0.021] and in the mean platelet drop [–161.2 ± 10³ cells/μL (95%CI –240.1 ± 10³ to –82.3 ± 10³) versus –52.6 ± 10³ cells/μL (95% CI –111.5 ± 10³ to 6.4 ± 10³), P = 0.023]. Patients with a pre-treatment platelet count of 240.7 ± 10³ cells/μL or less had more incidence of thrombocytopenia (8/18, 44.4%) than those with higher pre-treatment values (4/31, 12.9%, P = 0.018), odds ratio: 5.4 (95% CI 1.3–21.95). When all patients were considered, crude mortality rate, ICU and hospital length of stay did not differ between patients who developed thrombocytopenia and those who did not (P = 0.504, P = 0.321 and P = 0.732, respectively). When only survivors were considered (18/49, 36.7%), patients who developed thrombocytopenia had a longer ICU length of stay (87.3 days (95%CI 11.9–17.0) versus 35.4 days (95%CI 16.7–50.0), P = 0.025). Economic outcomes were not assessed.

Thrombocytopenia occurred in 3% of the patients who received linezolid in clinical trials. Gerson et al.,³ extracting data from previous clinical trials, analysed anaemia, thrombocytopenia (<75% of baseline value) and neutropenia from 2046 linezolid-treated patients versus 2001 comparator (vancomycin, ceftriaxone, cefpodoxime, clarithromycin, or oxacillin-dicloxacillin)-treated patients. The overall rate was 2.9% in the linezolid group and 1.5% in the comparator group. Nasraway et al.,³ extracting data from two prospective studies, compared the risk of thrombocytopenia (platelet count < 150 x 10³ cells/μL) between linezolid and vancomycin in 862 patients with nosocomial pneumonia. Thrombocytopenia occurred in 2.8% in the linezolid group and in 3.6% in the vancomycin group. However, these percentages have been considered underrated by other authors. In two post-marketing studies, the linezolid-associated thrombocytopenia rate was about 47% in both cases and a platelet count lower than 100 x 10³ cells/μL occurred in 32% and 19% of the patients, respectively.²,⁶ Our incidence of thrombocytopenia, considering
the same definition, was in this range. Two factors have to be taken into account for this high rate. Our patients were not selected as those enrolled in clinical trials and, in addition, were critical patients with high severity scores, and had increased risk of developing thrombocytopenia.

Gerson et al. stated that thrombocytopenia and/or anaemia occurred most often in patients with underlying haematological abnormalities or lower haematological baseline values. That statement seems to be supported by the results of the Senneville et al. study for red blood cells in patients with osteomyelitis and by our study for platelets in critical patients.

Outcomes in patients with linezolid-associated haematological disturbances have not been generally assessed in the published studies and, therefore, it is unknown whether these disturbances caused prolonged hospital stay or higher mortality rate. In our study, thrombocytopenia did not increase mortality rate or hospital stay when considering all patients. However, survivors who developed linezolid-associated thrombocytopenia more that doubled their ICU length of stay compared with patients who did not.

Patients on linezolid therapy with lower pre-treatment haematological values are at risk not only to develop anaemia, as Senneville et al. concluded, but also they are at risk to develop thrombocytopenia. Patients with short treatments, especially in severe conditions, are also at risk to develop thrombocytopenia.

References


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Duration of antibiotic treatment: are even numbers odd?

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Keywords: antibiotic treatment, treatment duration

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Sir,

The optimal duration of antibiotic treatment of infections is still controversial. While medical textbooks mainly offer advice for extended treatment duration such as 10 days, 14 days, 4 weeks, 6 weeks or 12 months,1–5 in clinical practice antibiotic treatment is frequently given for shorter durations (≤7 days). To see whether our hunch was right that ‘even’ numbers of treatment days in this setting are ‘odd’, we prospectively studied the choice, indication and duration of antibiotic treatment of 50 intensive care unit patients, receiving a total of 150 antibiotic courses.

The average number of treatment courses per patient was three, with a range of 1–11; resulting in a total of 1172 treatment days. Amoxicillin/clavulanic acid and ceftazidime were the antibiotics most commonly used. Treatment was given for an uneven number of days to 17 of 18 patients (94.4%) treated with amoxicillin/clavulanic acid and 18 of 25 patients (72%) treated with ceftazidime. Fever of unknown origin (FUO) was the most common reason for starting treatment empirically (Table 1). Of 30 antibiotic courses given for this indication, 21 (70%) were given for an uneven number of days. Overall, 95 (64.0%) of the 149 treatment courses were discontinued after an uneven number of treatment days. When separating short (≤7 days) from long (>7 days) treatment courses, antibiotics were given for an uneven number of days in 89 (92.7%) and 7 (7.3%) of the 110 short and 40 long cases, respectively. By chance, about 28% of the antibiotics should have been stopped during the weekend, but actually less than 10% were stopped on Saturday and Sunday, while 24%, or 1.7 time the expected per day chance, about 28% of the antibiotics should have been stopped during the weekend, but actually less than 10% were stopped on Saturday and Sunday, while 24%, or 1.7 time the expected per day rate, were stopped on Monday.

Duration of antibiotic treatment frequently remains a mystery. While textbooks commonly tell us to treat patients for an even number of days,1–5 we obviously favour an uneven number of treatment days, especially for short courses. Does this reflect a

Table 1. Indication for antibiotic treatment

<table>
<thead>
<tr>
<th>Reason</th>
<th>Days</th>
<th>Even</th>
<th>Uneven</th>
<th>Ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>21</td>
<td>0</td>
<td>3</td>
<td>3.00</td>
</tr>
<tr>
<td>FUO</td>
<td>2–14</td>
<td>9</td>
<td>21</td>
<td>2.33</td>
</tr>
<tr>
<td>Respiratory tract infection</td>
<td>2–16</td>
<td>19</td>
<td>41</td>
<td>2.16</td>
</tr>
<tr>
<td>Sepsis/CRI</td>
<td>2–28</td>
<td>13</td>
<td>25</td>
<td>1.92</td>
</tr>
<tr>
<td>Other infections</td>
<td>5–42</td>
<td>13</td>
<td>4</td>
<td>0.31</td>
</tr>
</tbody>
</table>

*Uneven/Even, a ratio >1 indicates a preference for uneven treatment duration (in the case of an empty field 0.1 was used for the calculation; for fields with only one observation the ratio was not calculated).

FUO, fever of unknown origin; CRI, catheter-related infection.