A review of vancomycin therapeutic drug monitoring recommendations in Scotland

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Sir,

Confusion continues regarding the therapeutic monitoring of vancomycin. Most clinicians would agree that the analysis of peak concentrations is of limited value due to both the pharmacodynamic (time-dependency) and pharmacokinetic (multiexponential decline) properties of vancomycin. However, there is still a lack of uniformity with respect to trough concentrations. The historical recommendation of 5–10 mg/L was based on efficacy data from in vitro experiments, protein-binding information and early concerns about nephrotoxicity. However, recent evidence suggests that nephrotoxicity is rare with vancomycin monotherapy and that trough concentrations ≥15 mg/L may be safe and even desirable. Despite a lack of definitive evidence correlating greater clinical efficacy with higher vancomycin concentrations,1,2 there has been a trend towards recommending higher trough concentrations of vancomycin. This reflects a greater awareness of the need for adequate penetration into target tissues and concerns about vancomycin treatment failure in infections caused by methicillin-resistant Staphylococcus aureus (MRSA) strains that display heteroresistance to glycopeptides. Consequently, recent guidelines have recommended vancomycin trough concentrations of 10–15 mg/L for endocarditis and meningitis, and continuous infusions of vancomycin with target concentrations of 15–25 mg/L are increasingly being used, particularly in intensive care. The British National Formulary (BNF) now recommends aiming for vancomycin trough concentrations of 10–15 mg/L, rather than 5–10 mg/L. However, although the focus has changed to concerns about underdosing rather than toxicity, there has been little consideration of how this might influence dosage requirements. This audit examined current practice within Scotland with respect to vancomycin dosing and monitoring.

Seventeen microbiology laboratories serving all 14 NHS Health Boards within Scotland were contacted in October 2007, and a consultant microbiologist or clinical scientist was invited to answer the following questions: (i) What are the current targets for vancomycin trough concentrations reported by your laboratory? (ii) Do you measure peak concentrations? (iii) Are there plans to change the current targets for vancomycin monitoring and if so, to what? and (iv) If you have changed your monitoring recommendations, have you or do you plan to change your vancomycin dosing recommendations?

All 17 microbiology laboratories responded. Vancomycin concentrations are monitored during therapy within all 14 NHS Boards in Scotland. The analysis of peak vancomycin concentrations was discouraged in 13 laboratories, undertaken sometimes in 3 and routinely in 1. There was a wide range of recommended trough concentrations (Table 1). Of the six laboratories that recommended an upper limit of 10 mg/L, four accepted concentrations up to 15 or 20 mg/L for severe infections and were preparing to change their routinely recommended ranges upwards. Two laboratories did not report a lower limit for trough concentrations. Most laboratories recommending an upper limit of 15 mg/L had made this increase within the last 1–2 years. None of the laboratories with higher trough ranges had made changes to their dosing recommendations, although some had plans to address this.

Our results indicate that recommendations for vancomycin therapy in Scotland are in a state of flux. Laboratories have been moving away from target trough concentrations of 5–10 mg/L towards a variety of higher targets, up to and exceeding 15 mg/L. However, when changing recommendations for vancomycin trough concentrations, it would seem appropriate to consider whether dosage guidelines are in place to achieve these ranges. Current BNF dosage recommendations are 1000 mg twice daily, halved in patients over 65 years of age. However, to achieve these higher troughs, our clinical experience indicates that total daily doses of 2500–3000 mg (sometimes higher) are required by patients with normal renal function. The potential for underdosing these patients is of concern, especially in the first few days of therapy before vancomycin concentration results are available. A recent pharmacokinetic analysis suggested that up to a third of patients on standard doses of vancomycin could be receiving insufficient treatment and our own observations support this.

Table 1. Vancomycin trough concentration ranges recommended within Scottish microbiology laboratories

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<thead>
<tr>
<th>Vancomycin trough concentration (mg/L)</th>
<th>No. of laboratories</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10</td>
<td>1</td>
</tr>
<tr>
<td>5–10</td>
<td>5</td>
</tr>
<tr>
<td>5–15</td>
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<td>15–25</td>
<td>5</td>
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<td>10–15</td>
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Many clinicians (and microbiologists) remain cautious when dosing vancomycin, due to concerns regarding toxicity. In contrast, measurement of vancomycin concentrations should primarily focus on maintaining clinically effective values, especially for severe infections, less susceptible organisms and when the source of infection involves an area where vancomycin tissue penetration is poor. Trough concentrations of 5 mg/L are potentially subtherapeutic and could increase the risk of resistance developing.3

It is likely that our findings in Scotland reflect what is happening more widely in the UK and elsewhere. It is remarkable that, given the current concerns about MRSA, there remains such uncertainty and variation in how the principal antibiotic for its treatment is administered and monitored. Recent guidelines for the prophylaxis and treatment of MRSA infections in the UK suggest that vancomycin trough concentrations up to 15–20 mg/L are safe, but stop short of recommending an optimum range and the dosing strategy to achieve this.3 Although the situation has improved with recent guidelines, there remains an ongoing need for clearer guidance on dosing and monitoring of vancomycin if a consistent and effective approach to treating infections with this antibiotic is to be achieved.

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References