Alberta Health Services Pharmacy Services

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Antimicrobial Stewardship Backgrounder

Update on Vancomycin Monitoring

(For dosing recommendations, refer to Bugs & Drugs)

BOTTOM LINE:

1. AUC:MIC-based vancomycin monitoring/dosage adjustment is **not** recommended in AHS.
2. AHS endorses vancomycin trough based monitoring with recommended steady-state target vancomycin trough range of 10-20 mg/L.
3. Order vancomycin trough levels only when necessary and at appropriate time.

1. AUC:MIC-based monitoring

- Area under the curve (AUC) to minimum inhibitory concentration (MIC) ratio (AUC:MIC) - based vancomycin monitoring and dosage adjustment has been recently endorsed in the United States (US).(1,2)
- However this method is not considered ready for routine use in AHS for numerous reasons, including:
  - Published literature is not consistently in support of the use of AUC:MIC based monitoring.(3–7)
    - Some retrospective studies have shown that the AUC:MIC ratio can identify patients at higher risk of clinical failure in some types of infections.(8–14) Other similar studies however, have not found a statistically significant relationship between AUC:MIC and outcome.(15–19) More study is required to determine if prospective monitoring by AUC:MIC is associated with improved patient outcomes.
  - MIC:
    - MIC, the denominator of the ratio, is reported in doubling dilution concentrations and the acceptable precision of MIC is +/- one dilution, therefore AUC:MIC does not have high precision.(20,21)
    - Published research on AUC:MIC has primarily used the broth microdilution method for MIC determination, which produces results markedly different than methods used in Alberta microbiology laboratories.(9,10,20)
    - The assumption of an MIC of 1 mg/L for all *S. aureus* isolates for the purpose of monitoring (as recommended in the US guidelines) is unfounded since studies supporting AUC:MIC-based monitoring used actual MIC as the denominator.(8–11,14,19)
  - There are different methods for determining AUC, which have significant variability. Therefore, appropriate AUC:MIC target ratios are difficult to establish without standardized methods.(22,23)
  - AUC:MIC monitoring is more resource intensive, requiring specialized training.(24) Some AUC estimation methods require two blood level draws. Trough level monitoring is more intuitive, requires less training/ education, and requires fewer levels, leading to greater patient comfort, acceptability, and convenience.
  - Calculations are frequently associated with medical errors and the increasing complexity of these in the AUC:MIC-based method of monitoring may add to this risk.(25,26)
  - AHS consensus meetings were held and participants were surveyed, and the majority preferred to continue trough-based monitoring.
  - Correlation between AUC and trough has shown inconsistent results from computer simulation versus patient data. Clinical studies frequently demonstrate high correlation (R^2>0.8) between AUC and trough, indicating minimal potential for improvement by use of AUC-based monitoring.(27–31,35)

2. Recommended target vancomycin trough range is now 10-20 mg/L

- The previously recommended range of 15-20 mg/L for select serious infections was not based on high quality evidence, but rather on expert opinion.(32)
- Trough levels of 15-20mg/L are associated with higher rates of nephrotoxicity.(33,34)
- In an AHS sample of 200 patients with MRSA bacteremia treated with vancomycin, the trough level associated with an AUC of 400 was approximately 12.5 mg/L.(35)
- Therefore, the AHS Antimicrobial Stewardship Committee recommends a vancomycin target trough range of 10-20mg/L, with careful clinician assessment of the risk and benefits of targeting the higher end of this range in select patients.

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3. Ordering of vancomycin trough levels

- Order only if patient meets inclusion criteria:
  - deteriorating/unstable renal function (increase in baseline Scr of ≥ 40 µmol/L, or 50% of baseline)
  - morbidly obese patients [≥ 190% IBW or BMI ≥ 40kg/m^2]
  - patients with anticipated therapy ≥ 7 days
  - patients who are severely ill (i.e. sepsis)
  - patients with altered volume of distribution or clearance of vancomycin (e.g. cystic fibrosis, pediatrics, elderly > 60 years, cancer, burns > 20% BSA)
  - selected dialysis patients [e.g. high flux and continuous hemodialysis/filtration (CAVH, CVVH, CVVHDF)].

- Trough levels drawn before steady-state is reached are not recommended as they often lead to increased vancomycin dosages and potentially supra-therapeutic levels and toxicity. Use the Bugs & Drugs Vancomycin SS calculator to estimate patient-specific time to steady state.
- Schedule levels during daytime hours; usually no need to do in evening/overnight or on weekends.
- Vancomycin trough levels should be deferred until after culture & susceptibility results are available and it is confirmed that ongoing vancomycin therapy is needed.

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