Vancomycin Therapeutic Drug Monitoring in Non-Pregnant Adults

Key Messages

- Vancomycin therapeutic drug monitoring (TDM) that targets steady-state trough concentrations of **10 to 15 mg/L** is recommended
- Vancomycin trough concentrations between 15 and 20 mg/L are no longer recommended due to increased risk of acute kidney injury (AKI) and lack of clinical benefit
- Trough-based vancomycin TDM should only be performed when clinically necessary (see Appendix 1)

The Background

- The 2020 American Society of Health-System Pharmacists, Infectious Diseases Society of America, Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists vancomycin TDM guidelines recommend AUC:MIC-based vancomycin monitoring and dosage adjustments for serious methicillin-resistant *Staphylococcus aureus* (MRSA) infections; however, evidence to support this method is lacking.

The Rationale

- Published studies on AUC:MIC-based vancomycin TDM are mainly retrospective and derived from patients managed with trough-based monitoring. Correlation of AUC:MIC with clinical outcomes has not been consistently demonstrated.
- Determination of AUC differs between studies, which makes it difficult to interpret and determine ideal AUC:MIC targets. AUC:MIC monitoring requires additional resources, since it involves further training, specialized software and additional serum concentration testing. Prospective well-designed trials are required to evaluate whether there is any association between AUC:MIC monitoring and clinical outcomes.
- Clinical studies have shown correlations between AUC and trough concentrations, so there may not be any benefit with AUC-based monitoring.
- Previous recommendations for a vancomycin trough range of 15 to 20 mg/L in serious MRSA infections were not supported by high quality evidence.
- There is no clear evidence that better clinical outcomes are associated with higher trough concentrations (i.e. 15 to 20 mg/L) even for serious Gram positive infections, including methicillin-resistant *Staphylococcus aureus* bacteremia, endocarditis or other deep-seated infections.
- As clinical benefit is unclear with a vancomycin trough range of 15 to 20 mg/L and there appears to be an increased risk of AKI, a target range of 10 to 15 mg/L for serious infections would be appropriate.
  Note: For hemodialysis and peritoneal dialysis patients, the optimal range for vancomycin serum concentrations is unclear. Local institutions target pre-dialysis concentrations of 10-20 mg/L based on limited data and because AKI with higher doses is less concerning in the setting of limited residual renal function.
- Overall, trough concentration monitoring appears effective, does not require additional training, and can be achieved with less serum concentration testing.

The Solution

- A target vancomycin trough concentration range of **10 to 15 mg/L** for adults is recommended
- Target vancomycin trough concentrations between 15-20 mg/L are not recommended (except in dialysis patients since risk/benefit remains unclear).
- Alternate monitoring (e.g., AUC:MIC-based vancomycin TDM) is **NOT** routinely recommended as standard of practice.

Appendix 1: When to Order Vancomycin Trough Concentrations

Order vancomycin troughs only if the patient meets the following criteria:

1) Vancomycin treatment duration is greater than 7 days, where baseline and ongoing TDM may be indicated (e.g. MRSA bacteremia, infective endocarditis, osteomyelitis, septic arthritis)

OR

2) Vancomycin treatment duration is greater than 72 hours **WITH** one or more of the following:
   - Patient receiving aggressive dosing (where trough concentration is anticipated to target 15 mg/L)
   - Renal function unstable, serum creatinine increased by 30 µmol/L or 1.5 times baseline
   - Patient on dialysis (hemodialysis or peritoneal dialysis)
   - Patient receiving concurrent nephrotoxic or ototoxic drug
   - Patient with altered volume of distribution or clearance, including:
     - Age 65 years or greater
     - Hypermetabolic (e.g. burn patient, cystic fibrosis)
     - Low body weight / muscle mass or frail
     - Obese (125% of ideal body weight or greater)
     - Septic shock
   - Patient not responding to therapy

Notes:
- Avoid ordering unnecessary vancomycin troughs, particularly when vancomycin is not likely to be continued (i.e. when vancomycin is started empirically, but discontinued once returning cultures do not support ongoing use)
- Vancomycin troughs are unlikely to be of benefit when a validated vancomycin dosing nomogram is used, where the above risk factors are absent, and when therapy is less than 7 days in duration

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