Reviewer’s report

Title: Empiric guideline-recommended weight-based vancomycin dosing and mortality in methicillin-resistant Staphylococcus aureus bacteremia: a retrospective cohort study

Version: 1 Date: 12 February 2012

Reviewer: Dale Fisher

Reviewer’s report:

This study represents a great deal of work but this manuscript overstates the findings. I believe it is publishable (somewhere, if not BMC ID) but should be in a much abbreviated form eg a brief report or a letter so that many of the meaningless results are omitted.

1. This is a large study which does not show any difference in mortality with 2 different approaches to initial dosing. It however goes another step and implies potential dangers of “excessive” dosing. I think this is a step too far in this negative study.

Methods

2. "Guideline recommended weight-based dosing was defined as at least 30 mg/kg/day in the first 24 hours (at least 15 mg/kg/day for patients with a creatinine clearance of 30-50 ml/min)."

Why is this so? Surely in the first 24 hours we want an adequate dose given. Renal impairment would influence subsequent dose intervals.

3. Charlson Comorbidity index can be made at any time and need not be emphasised as calculated on the first day of the bacteraemia.

4. Line 7 of definitions……what is meant by “initial” hospital stay?

5. “Nephrotoxicity” is applied too loosely. An increase in creatinine could be due to concurrent drugs, hypotension, contrast. There is an implication in the manuscript that all raised creatinines are due to vancomycin and whether or not this is deliberate it should be clarified. In the results section the rate is 23% but it doesn’t break it down to a relationship with dosing.

6. In Statistical analysis, the first sentence is mostly unnecessary, especially the reference to extensive clinical experience.

Results:

7. Under results/patients it is stated that non survivors were more likely to have adjustment for renal failure. Is this because more patients had renal failure or because more adjustments were made; either way it suggests that these patients may have taken longer to reach adequate trough levels.
8. Too many results are expressed which is a distraction. Especially in univariate analysis which includes illogical findings such as mortality was associated with high vancomycin levels.

9. It is not clear when the vancomycin levels were taken. The time to reach therapeutic levels is important obviously.

Discussion and conclusions

10. I think the implications of the conclusions are dangerous.

"Clinicians should critically evaluate vancomycin trough concentrations and kidney function to help minimize this risk in patients receiving guideline-recommended weight-based vancomycin regimens."

Simply because this study did not show reduced mortality is not a reason to suggest acceptance of suboptimal dosing or even to implicate the weight based dosing as dangerous. This study is actually a negative study and does not prove anything one way or the other.

11. The limitations of the work are clearly stated

The writing:

12. Should remove reference to this being the first study. At best it is the first published study….or the authors know of no other work addressing this question

13. At times the writing is a little repetitive or clumsy eg last para of introduction. The first sentence in methods uses the word “identified” twice and “hospital” 4 times.

14. Under study definitions the first sentence is unnecessary.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.