Reviewer's report

Title: Risk factor for mortality in patients with Pseudomonas aeruginosa bacteremia; Impact of combination antimicrobial therapy

Version: 1
Date: 23 November 2013
Reviewer: David Chien Lye

Reviewer's report:

The authors studied 3 years of Pseudomonas aeruginosa bacteremia at a tertiary hospital and reported that severity of illness was independently associated with 14-day mortality. They performed stratified analysis and reported that in neutropenic patients combination antibiotic was associated with survival.

The study was undermined by retrospective analysis, and the inclusion of aminoglycoside as appropriate antibiotic.

Major compulsory revisions

1. Explain why 30-day mortality was not chosen as primary outcome. If good justification cannot be provided, re-analysis using 28 or 30 day mortality should be done.

2. Sites of infections were defined using the very old CDC 1988 criteria. Please revise using the 2011 criteria available on CDC Atlanta website. Attached for the authors.

3. Please explain and justify input variables for multivariable logistic regression analysis. Non-survivors had more neutropenia, higher APACHE score, more septic shock, more device use (CVC, IDC and MV), more pneumonia. It appears that the authors selected age, neutropenia, MV, CVC, APACHE score, septic shock, carbapenem resistance, pneumonia, inappropriate empiric and targeted antibiotic for logistic regression. Combination antibiotic which is a key finding should be included.

4. There were 234 patients. 145 had appropriate empiric antibiotic and 183 had appropriate targetted therapy. Please clarify why 51 patients did not have appropriate targetted therapy. Only 25 died early.

5. Please review and include in manuscript the following essential studies. Essentially both BMJ meta-analysis by Paul et al are on RCT's while Safdar et al is on observational studies. The authors must be able to evaluate strength of evidence.

(a) BMJ 2003;326:1111 on combination antibiotic for febrile neutropenia which showed no benefit of combination antibiotic in Pseudomonas infections.

(b) Lancet ID 2005;5:192 which highlighted the flaw in reference 19.

6. The authors should refrain from self-fulfilling prophecy by stating that more patients who survived received combination therapy empirically (17.4% vs.
12.8%) and in targetted therapy (19.5% vs. 10.3%) even though they stated that the difference was not statistically significant. With small numbers such small difference in proportion was not uncommon!

(7) Please repeat analysis by removing aminoglycoside as appropriate. Please see Lancet ID 2005;5:192 above about the influence of this confounder.

Minor essential revisions

(1) Provide reference for claim in lines 3-6 of paragraph 2 of Introduction on combination antibiotic being more effective, synergistic or additive and preventing resistance, as well as in Discussion.

(2) In abstract 145 patients (61.9%) received appropriate empiric therapy. In manuscript, 145 patients (53.4%) were reported. Please check data.

(3) Line 9 paragraph 2 of results was repetitive. Please delete.

(4) Please check P value for time in hospital before bacteraemia, 42 vs. 9.7 days. Likely skewed data so instead of mean, they should use median and repeat analysis.

(5) Please replace "lesser" with "less".

(6) Please correct spelling for APACHE not APCHE.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

No conflicting interests to all questions above.