Reviewer's report

Title: Cloxacillin versus Vancomycin for Presumed Late-Onset Sepsis in the Neonatal Intensive Care Unit and the Impact upon Outcome of Coagulase Negative Staphylococcal Bacteremia: A Retrospective Cohort Study

Version: 2 Date: 14 March 2005

Reviewer: David Isaacs

Reviewer's report:

General
This paper deals with an important topic, the use of cloxacillin or vancomycin in the empiric treatment of late-onset neonatal sepsis

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The definition of what constitutes true coagulase negative sepsis, as opposed to contaminated blood cultures, is given in the Discussion but not the Methods. A formal definition of CONS sepsis needs to be explicitly stated in the Methods section: e.g. clinical sepsis, one positive blood culture, pure growth (I presume it was considered a contaminant if 2 strains of CONS were isolated from the 1 bottle), and must grow within 48 hours. The authors should then state that blood cultures which grew CONS but did not meet these criteria were considered contaminants.

There is also no definition of what constitutes a death from sepsis. The single death they describe sounds as if it was caused by CONS sepsis, yet the authors state in the Abstract "One death during period 2 was possibly related to CONS sepsis.." Did the study protocol state in advance that death caused by sepsis would be distinguished from death possibly caused by sepsis?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The authors state in the first sentence of the Discussion that this is the largest study aimed primarily at comparing outcomes in neonates with CONS sepsis. As it was a retrospective study, like the studies they discuss from Karlowicz and Matrai-Kovalsis (references 10 and 11), I do not think the authors can validly claim the largest study. This is especially pertinent because their study was probably under-powered to detect non-inferiority.

I do not understand why the authors chose a 1% difference in mortality as being the statistical margin of non-inferiority. They mention the Wilson score method, but since one of 37 babies died from CONS sepsis when cloxacillin was used and none of 45 when vancomycin was used, there is a statistical increase in mortality. Yet a difference of one death in either arm should not reach statistical significance, unless the sample size is too small. Surely the mortality difference should be calculated on the basis of the sample size. It would help if a statistician was able to advise.

Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes

Declaration of competing interests:
I declare that I have no competing interests