Reviewer’s report

Title: In vitro evaluation of antibiotics combinations for empirical therapy of suspected methicillin resistant Staphylococcus aureus severe infections

Version: 1 Date: 5 June 2007

Reviewer: Fortino Solorzano

Reviewer’s report:

1. Is the question posed by the authors new and well defined?
The question is not new and has been studied previously by many authors. Principal contribution is the in vitro evaluation of triple combinations. However, antibiotic selection, were not limited to those with activity versus staphylococcal infections, and some of them are mainly used in gram-negative infections. Last paragraph of background section mentions "...which are suggested for empirical combinations in the hospital setting when MRSA aethiology is suspected". Reference quoted for this sentence is from the American Thoracic Society, in relation to the recommended empirical treatment of nosocomial pneumonia. Authors did not delineate properly the concept of empirical therapy and etiology of severe infections in the background. Perhaps they are considering aerobic gram-negative bacilli as well as MRSA when making their proposal, but the text is not clear.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
Methods are not described in detail, neither the references support them. The checkerboard technique allows the calculation of FIC index for double combinations, but not for triple combinations. It is convenient that the authors describe how they evaluated the triple combination antibiotics by this, and how the FIC Index was calculated. Why the authors decided to test only five MRSA strains for the Time-kill assays and what selection criteria were applied? Were all the assays performed once, or in duplicate for reproducibility evaluation? For Time-kill curves only used the Synergy definition. Authors not considered bactericidal, antagonism or indifference activity definitions?

3. Are the data sound and well controlled?
It were not described the controls used for experiments. Tables including in the manuscript could improve the information, specially table 2,3,4.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Data in Tables are a summary of FIC Index interpretation. FIC Index values should be more specific.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
Many of the data obtained by the authors are not discussed, majority of discussion is based in medical literature, moreover, conclusions are not supported by the data.

6. Do the title and abstract accurately convey what has been found?
Title and abstract suggest that antibiotics with anti-staphylococcal activity were evaluated, however, some of them had predominant activity against gram-negative bacilli.

7. Is the writing acceptable?
Yes.

- Major Compulsory Revisions

Methods in the study are required in detail. Techniques for the calculation of the FIC index in the triple combinations are essential. It is convenient to describe the criteria for selection of MRSA strains that were included in the Time-kill curves, with definitions for all the possible results. Methods for mutational frequency are required.
Minor Essential Revisions
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