Reviewer's report

Title: Severe Pneumococcal Community-acquired Pneumonia: Prognosis in Patients Treated by Beta-Lactam and Quinolone

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Reviewer: Fracesca Montagnani

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In this manuscript David Olive et al. performed a retrospective study in 70 patients admitted to an ICU for severe community acquired pneumococcal pneumonia and treated with a combination therapy of beta-lactam plus fluoroquinolone. The study aims to determine risks factors for mortality in this patient setting, focusing on the outcome effect of different types of fluoroquinolones. Beside to septic shock at ICU admission and older age, use of ofloxacin or ciprofloxacin rather than levofloxacin has been identified has an independent risk factor for mortality. Materials and methods are well described, results are interesting and the manuscript is well written, however some issues need to be addressed before acceptance.

MAJOR COMPULSORY REVISIONS:

1. Material and Methods. Patients. (page 4) Definition of CAP: “We excluded patients coming from nursing homes or hospitalized within 30 days”: if the authors are going to exclude Health care-associated CAP, 90 days should be used (Ref. Niederman MS. Hospital-acquired pneumonia, health care-associated pneumonia, ventilator-associated pneumonia, and ventilator-associated tracheobronchitis: definitions and challenges in trial design. Clin Infect Dis. 2010 Aug 1;51 Suppl 1:S12-7.)

2. Appropriate drug dosage (page 5): please refer to international literature or reference book your definition of “appropriate”, in particular regarding pro kilo dosage of beta-lactams and levofloxacin dosage (500 mg/12h is an “evidence based” dosage in clinical practice to treat severe infections, however current CAP guidelines reported 750 mg OD). Please discuss your choices.

3. Table 1:
   a. Please specify that age was measured in years
   b. Please show also percentages for male sex and PSI 4/5
   c. Please report in table 1 the #-lactams used in the two groups and the p value for between group comparison. A difference in #-lactams used could influence the results.

4. Apparently in group B a higher proportion of patients received a third generation cephalosporin as #-lactam. Is there a significant between group difference? Theoretically an in vivo higher activity of cephalosporin in comparison to amoxicillin-clavulanic acid could contribute to the differences observed in
mortality. The authors should comment in the discussion if this difference could influence the results.

5. Was the antibiotic therapy modified after results of cultures? In how many patients and which antibiotic were used? This could be reported to better interpret the results.

6. The phrase “all underlying diseases...in this analysis” appears unclear. According to table 3 Chronic heart failure appeared associated to mortality, while cephalosporin and bacteremia were not: please clarify. Moreover, mechanical ventilation is not reported in table 3: please report.

7. Table 3: Please show also percentages for male sex, PSI 4/5, patients in group A

8. Why sepsis-related complications and HA-LRT superinfections were not included in the multivariate model? Their development could be strictly related to the empirical antibiotic therapy used. If authors believe that these complications could be mainly related to factors other than antibiotic therapy (for example invasive procedures), why did they not excluded patients with these complications from the analysis?

9. Discussion “Finally, some important prognostic parameters such as the time elapsed between admission and the first dose of antibiotic were not taken into account in our study.”: Why? It is a fundamental information to be inserted in statistical analysis. If not available, it should be discussed more accurately.

MINOR ESSENTIAL REVISIONS:

10. Results: “we identified 70 patients treated by a #-lactam combined with a fluoroquinolone, including 53 men and 17 women. The mean age was 63.8 ± 16.8 yrs. S. pneumoniae was identified in blood cultures in 25 patients. For 18 patients infection was polymicrobial.” AND “Thirty-eight patients were classified as Group A. #-lactams combined with ofloxacin (n=33) or ciprofloxacin (n=5) were amoxicillin ± clavulanic acid (n=16), a third generation cephalosporin (n=20), and piperacillin-tazobactam (n=2). Thirty-two patients were classified as Group B. #-lactams combined with levofloxacin were amoxicillin ± clavulanic acid (n=5), a third generation cephalosporin (n=26), and piperacillin-tazobactam (n=1)”: please report percentages

11. Global revisions of English language is desirable: e.g. risks factors "of" mortality, treated "by", but the difference "is" not statistically significant, etc..

Level of interest: An article of importance in its field

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

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