Reviewer’s report

Title: Effectiveness of azithromycin in aspiration pneumonia: a prospective cohort study

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Reviewer: Barbara Jones

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In this small prospective observational cohort study, the authors report that in a subset of patients hospitalized with aspiration pneumonia, 36 patients who were treated with azithromycin had no difference in mortality or antibiotic success, and significantly lower hospital costs, than 81 patients treated with ampicillin/sulbactam. The authors conclude that azithromycin thus may be used safely to treat hospitalized aspiration pneumonia patients.

This is an important paper, as it calls into question the empiric antibiotic selection decision in patients with aspiration pneumonia, in whom – likely – the majority of patient would see clinical resolution without broad antibiotic coverage. The aim – to compare clinical outcomes in patients receiving azithromycin versus those receiving ampicillin/sulbactam – is well defined. The data appear sound. However, I have two major methodological concerns that I feel should preclude the authors’ conclusion.

- With a total N of only 127, the study is underpowered to demonstrate non-inferiority.
- The study was not randomized, raising concern for confounding by indication. The authors declare that the two groups had similar severity at baseline (measured by A-DROP and CURB-65 scores), however the numbers are too small to truly state this, and unmeasured clinical factors other than the elements of the A-DROP and CURB-65 likely contributed to the antibiotic selection decision.

Major compulsory revisions.

- The conclusion should be changed to “in this small prospective non-randomized observational study, we found no statistically significant differences in mortality or antibiotic failure in patients receiving azithromycin compared to ampicillin/sulbactam.”
- The authors should state more clearly how “antibiotic success” was defined by the clinicians.
- The Figure demonstrating the differences in time to resolution of fever, which is a major component to the objective measurement of clinical stability, is interesting and should be highlighted more. This suggests that time to clinical stability was different for the two groups. This should be added as a measured clinical outcome.
- Were there any patients during the study period who received both azithromycin and ampicillin/sulbactam? If so, these patients should be included in the study. ATS/IDSA guidelines would recommend combination therapy with both an anti-streptococcal beta-lactam and a macrolide for any patients with community-onset pneumonia, regardless of aspiration risk.

- State more clearly the inclusion criteria, ie, how “aspiration pneumonia” was defined. Was this based upon a reported history of aspiration by the patient? Actual documentation of oropharyngeal dysfunction? If the latter, were these test performed prior to the hospitalization or after the initial presentation?

- Add a power analysis in the statistical methods for all primary outcomes of interest (mortality and antibiotic success).

Minor, essential

- Add a description of A-DROP and CURB-65. Were the data elements contributing to these severity measurements consistently collected? Was there any missing data? If so, how was this treated?

Minor, discretionary

- It would be interesting to see a severity-adjusted comparison in clinical outcomes between the two groups using logistic regression and the two severity scores (A-DROP and CURB-65).

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests in relation to this paper.