Reviewer's report

Title: Causative Agent Distribution and Antibiotic Therapy Assessment among Adult Patients with Community Acquired Pneumonia in Chinese Urban population

Version: 1 Date: 3 December 2008

Reviewer: Patrick GP Charles

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Major compulsory revisions:

1. Greater mention should be given to missed data. The numbers of patients who had viral testing was small (only 184/610 or 30.2%). In addition, blood cultures were only obtained in only 141/610 or 23.1%. Why were blood cultures not obtained in all patients? Restricting them only to patients with fevers is a major limitation of the study. Given that this was the case, it is a pity that pneumococcal urinary antigen testing was not performed. Given that over half the patients were pre-treated before enrolment, the rate of pneumococcal infections may be grossly underestimated.

2. Greater mention should be given to the limitations of the viral testing using serological methods only. In particular, serological testing for adenovirus and RSV has major limitations in both sensitivity and specificity. It is a pity that in such a large study, the PCR was not used as this would have likely given a more accurate picture. In addition, Chlamydia serology suffers from similar problems and is frequently misleading. In some of the studies done elsewhere that showed very high rates of chlamydial infections e.g. up to 46%, the authors accepted single high titres of antibodies to Chlamydia, thus overestimating the real rate of chlamydial infections.

3. Urinary antigen testing for legionellosis would also have been useful as serological testing for it also has limitations, particularly when the convalescent sample was taken at 2 – 4 weeks, too early for many patients with Legionella infections to show evidence of seroconversion.

4. Break points for penicillin non-susceptibility to penicillin have changed for patients with non-CNS infections.

Current cut-offs are:

- Susceptible MIC ≤ 2 mcg/ml
- Intermediate MIC = 4 mcg/ml
- Resistant MIC ≥ 8 mcg/ml

Thus, the levels of penicillin non-susceptibility are even lower than the 22.2% stated. There were in fact no penicillin-resistant isolates found.
5. Inadequate information is given about sputum testing. In the methods, it says on page 8, line 8: “Regular sputum testing was done with most (590/610) patients enrolled in the study.”

Does this mean that more than one sample was taken? Were patients diagnosed by sputum cultures on samples taken a day or more after their admission?

What proportion of sputum samples were obtained before antibiotics? Organisms such as Klebsiella pneumoniae or E. coli are more commonly cultured after antibiotics are given and may not be the cause of the pneumonia.

What was the required correlation between sputum Gram stain and culture results? Sputum that shows mixed flora on Gram stain but cultures a Gram-negative organism is likely to be indicative of a misleading culture result.

Minor essential revisions:

On page 13, paragraph 3, line 2, there is a formatting error: “In patients with Class # disease …”

Discretionary revisions:

1. While I agree with the most of the recommendations for therapy that are given at the end of the article (i.e. beta-lactam monotherapy if mild disease and beta-lactam plus macrolide if moderate to severe), I think it would be prudent to discourage use of fluoroquinolones for CAP patients in China. Rates of TB, including drug-resistant TB are high and treatment of CAP with fluoroquinolones is likely to worsen that situation. Treating CAP with fluoroquinolones has also been shown to lead to worse outcomes, including higher mortality, when the diagnosis ends up being TB rather than standard CAP. Further, the authors highlight the relatively high rates of fluoroquinolone-resistance in their pneumococcal isolates and the very high rates of fluoroquinolone-resistance in Gram-negative organisms in China is well documented.

2. Tables 2 & 3 could probably be simplified. The lists of very small number of patients with 2, 3 or 4 pathogens found is too detailed and could be collated into groups.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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.