Reviewer's report

Title: Clinical presentation and predictors of outcome in patients with severe acute exacerbation of chronic obstructive pulmonary disease requiring admission to intensive care unit

Version: Date: 25 August 2006

Reviewer: Angshu Bhowmik

Reviewer's report:

General

This paper from a tertiary respiratory unit in India is a welcome addition to the literature on the subject of COPD as detailed data from India on exacerbations of COPD and their management have previously been lacking. The authors describe the presenting features of 116 patients with severe exacerbations of COPD who required admission to the intensive care unit. The pathophysiological features and laboratory values are described in some detail. Finally, a regression analysis has been performed to identify predictors of mortality in these patients.

While data from India is necessary in order to obtain a global picture of the burden and management of COPD, this paper does not purport to be an epidemiological study. The description of management of severe exacerbations of COPD is interesting only insofar as it shows that a tertiary referral hospital in India can provide care equivalent to the best practice seen in the United Kingdom. The main message of importance is the analysis of factors predicting death in this setting.

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

1. Abstract:
   a. Hypercapnia has been mentioned as a predictor of death, but the p value for this parameter in the multiple regression is only 0.083 whereas a cut-off of 0.05 has been selected.
   b. In the Conclusions, it has been stated that metabolic abnormalities render the diagnosis of AE-COPD difficult and contribute to mortality, but it is unclear which metabolic abnormalities are referred to here. Table 4a suggests that they are hypoalbuminaemia and elevated transaminases.
   c. The relationship between past or active PTB, AE-COPD (acute exacerbations of COPD) and smoking has been highlighted, but the data presented in this paper do not seem to justify this conclusion. The authors have not shown that the prevalence of PTB in this population of patients with COPD admitted with AE is any higher than that in the general population. Nor have they shown data to suggest that it is COPD patients with PTB who are more likely to suffer AE than COPD patients who do not have PTB. While it has been shown that smoking is related to PTB and smoking is related to COPD, it is purely speculative to infer that there is a complex interplay between the three. This may merely be an epiphenomenon rather than the PTB somehow leading to worsening of COPD. If the latter is, in fact, the case, the data presented here is not adequate to show this. Perhaps the analysis has not been described in sufficient detail to make the relationship apparent.

2. Introduction: The introduction states that all the patients included in the study were managed on an intensive care unit. However, in the "Materials and Methods" paragraph 6, it is stated that after initial stabilisation in the ER, the patients were managed in the ICU, Acute Medical Care Unit and Medical Wards. This needs clarification.

3. Materials and Methods: Some additional detail about the statistical analysis should be provided. “To determine the various predictors of death…” was a correlation performed? Was a correction used to allow for the use of multiple correlations?

4. Results:
   a. The first paragraph of the results seems to largely duplicate the data presented in table 1.
   b. I note that the definition of AE-COPD requires the presence of increased sputum purulence as well as increased sputum quantity, but the two features seem to have been combined into one in Table 2 without
further clarification.
c. “Chest radiographs revealed infiltrates….” Does this mean pneumonia was present? In this case, should these patients have been analysed as “pneumonia” rather than exacerbations of COPD? This should be clarified.
d. Tuberculosis: I am confused about the inclusion of patients with active tuberculosis in this study. Several diseases such as bronchiectasis and interstitial lung disease have been excluded, as has been the case in other published work on the subject, so it is unclear why tuberculosis has been left in. The authors should justify this inclusion rigorously as it is unjustifiable in the manuscript as it stands. As mentioned in my comments about the abstract, the data has not been analysed in sufficient detail with adequate numbers of control subjects in order to reach the conclusion that the co-existence of PTB and COPD is anything other than an epiphenomenon in a locality where both diseases are highly prevalent.

5. Discussion:
a. Paragraph 1: it is “traditional” to emphasise the important results, or the contribution made by the paper to what is known on this subject, in the first paragraph of the discussion.
b. paragraph 2 lines 5 – 8: “…dyselectrolytemia, uremia and hepatic function derangements” – I presume the authors mean Table 3 rather than Table 2. But there is no data/analysis showing if there is a relationship between these metabolic abnormalities and altered sensorium.
c. Paragraph 6: The authors have not considered the updated 2004 ATS/ERS position paper on the diagnosis and treatment of patients with COPD nor the BTS-NICE guidelines of 2004. This paragraph is therefore completely out of date.
d. Paragraph 8 (conclusions): I cannot see where the authors have shown that the presence of co-morbidities makes the diagnosis of AE-COPD difficult although I agree that the inclusion of PTB into the analysis has probably confounded the results. The data presented does not justify the conclusion that “Correction of metabolic abnormalities such as dyselectrolytemia and … antimicrobial treatment…help in reducing the mortality.”

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

1. Reference 6 is quoted in support of the statement that there is an increasing tendency to abuse tobacco in India but this does not seem to be correct.

2. Materials and methods: paragraph 2, line 7: “…that is not fully reversible”. I presume reversibility testing was done for all patients. However, data on baseline or exacerbation spirometry (accepting that spirometry might not always be possible at exacerbation) as well as reversibility data has not been presented and should be included so that the reader may obtain a definite impression about the severity of COPD in the patients described.

3. The description of the investigation and management of the patients is too long and parts of it could easily be omitted (e.g. methods of ECG, arterial blood gas analysis, details of oxygen and bronchodilator therapy etc.) (Incidentally, the dose of nebulised ipratropium 0.5 mg every 15 minutes seems quite high).

4. SI units should be used for all quantities (e.g. PaO2, bilirubin, albumin, etc).

5. Earlier in the methods, it is mentioned that the tobacco content of 4 bidis is equivalent to one cigarette when calculating pack-years of smoking. Apparently contradicting this, in the first paragraph of the discussion, it is stated that bidi smoking causes 2 – 3 times more tar and nicotine inhalation than conventional cigarettes. Has this been taken in to account in the methods?

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Discretionary Revisions (which the author can choose to ignore)

1 In the introduction line 2 – 4, the authors mention that there is great variation in death rates due to COPD, but co-morbidities and access to medical care do not seem feature in the list of possible causes for this.

2 Introduction para 2, line 2: the statement “Following an acute exacerbation, …patients experience … decrease in their quality of life” should be referenced.
3 Introduction para 2 last line: this statement should show some example references.

4 It would be interesting to know which domestic fuels were the culprits in the development of COPD in the female subjects.

5 Description of Statistical analysis: Further description of the regression model might be useful.

6 Increased sputum purulence and quantity were essential features to make the diagnosis of AE-COPD so I presume that sputum culture was requested for all patients. A detailed analysis of all organisms grown would be of great interest rather than the brief summary which has been included.

7 Arterial blood gas data would also be interesting.

8 Discussion: paragraph 2, line 2 – 5: “The observation that a considerable number of patients ….” This sentence does not add anything new or useful to the paper.

9 There are many typographical, grammatical and syntactical errors which I would be happy to point out in detail should the editors require me to do so. (e.g. Table 4a "presence of new infiltrates..." duplicated in columns 1 and 2)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No

Declaration of competing interests:

I have received honoraria from AstraZeneca, GlaxoSmithKline and Boehringer-Ingelheim for lectures, and received unrestricted travel grants for attending conferences from all three companies in the past.