Author's response to reviews

Title: A Cross-sectional Study of Alterations of Serum Biomarkers Associated with Lung Ventilation Function Impairment in Coal Workers

Authors:

Jimin Zou (jiminzou@126.com)
Baojun Yuan (ybj25999@163.com)
Xianhong Liang (hh_liang@hotmail.com)
Dongmei Wang (wdm7252196@sina.com)
Chao Li (li_chao0296@sina.com.cn)
Xianming Carroll (mingming30@yahoo.com)
Sandra Leeper-Woodford (leeper_sk@mercer.edu)

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Version: 2 Date: July 28, 2011
Author's response to reviews: see over
Response to reviewer’s report, reviewer Ilker Ates

Major Compulsory Revisions

General
1. The reviewer is correct. We are very grateful for the thoughtful suggestions. We have invited a native English speaker to correct the 2nd version of the manuscript.
2. Corrected accordingly.
3. A new table (Table 1) has been added to describe the detailed demographic data of the study population in the Method section. Lung function parameters were also given in Fig.1, using histogram instead of arithmetical averages. This study focused on the relationship between alterations of lung function parameters and serum biomarkers. Regarding arithmetical averages or medians of some serum biomarkers, we have reported on those in our previous studies (References 20-24).

Minor Essential Revisions
We thank the reviewer for the very helpful suggestions. We followed most of the reviewer’s suggestions.

Abstract:
1) - 3) Corrected.

Background:
1) - 8) Corrected.

Methods:
1) - 3) Subject section has been rewritten according to reviewer’s suggestions.
4) Has been moved to the results section.
5) - 8) Corrected accordingly.

Results:
1) - 5) Corrected.

QUESTION:
After scrutinizing the original data and repeated statistical analysis, we found that the result is the same - a trend towards significant but not significant.
1) - 4) Corrected.
1) -14) Corrected.

QUESTION:
The necessary changes have been made in the second paragraph.
1) - 2) Corrected accordingly.
QUESTIONS:
1) Lung function parameters were given in Fig.1, using histogram instead of arithmetical averages. Fig.1 shows that FEV₁ levels are decreased in the patients with CWP, Fig.2 shows the decrease of FEV₁ is correlated with a decrease of IL-18R in these coal workers with CWP.
2) The “Authors instruction” of the magazine limited the numbers of figures and tables; the multiple stepwise analyses is more powerful than linear correlation analysis; FEV₁ values have a significant relationship with IL-18R levels in both statistical analysis, others only have significance in linear correlation analysis.

Discussion:
1) - 35) Corrected.

Conclusion:
1) - 2) Corrected.

Acknowledgment:
1) Corrected.

Figure legends:
Re-arranged according to suggestions.

Tables:
1) - 2) Corrected according to suggestions.
Response to reviewer’s report, reviewer Antonio Mutti

Major

Title
The reviewer is correct. We are thankful for the very helpful comment and have changed the title in the revised manuscript.

Introduction
- We have made the necessary changes according to the reviewer’s suggestions.

Methods
- We checked the subjects smoking habits according to their regular physical examinations from the medical records, which included their smoking habit, drinking habit, and medical history.

- The diagnostic criteria of pneumoconiosis GBZ70-2002 (Reference 26)
  ● Category 1: few small opacities present, distribution to at least two areas of lung.
  ● Category 2: numerous small opacities present, distribution to more than four areas of lung.
  ● Category 3: a large opacity present, its size not less than 20mm x 10mm.
  ● Asymptomatic miners: chest radiograph without pneumoconiosis appearances.
  ● Group 0+: chest radiograph with uncertain pneumoconiosis like appearances, however not enough to be diagnosed as pneumoconiosis category 1.

In addition, the 34 miners with CWP were all Category 1. Category 2 or higher grades of CWP is rare and uncommon, especially in nonsmokers.

- Percent of predicted values >80%
  - FEV1/FVC% >70%

- Only designated worker with CWP could be measured. ‘CO diffusion’ was not included in the mine worker’s routine medical examination due to financial reasons.

We have not discussed ‘lung volume’ in this study because there is not enough clinical value in the observation of these coal miners.

Results
- We have corrected in the revised manuscript.
  - Respecting that some serum biomarkers descriptions have been reported in our previous study (see reference 20-24), we focused on the relationships between the alterations of lung function parameters and serum biomarkers in this study.

Minor
Conclusion
- Corrected accordingly.
Response to reviewer’s report, reviewer Jean-Baptist du Prel

General Comments
We thank you very much for the suggestions which are valuable in improving the quality of the manuscript. We have made the necessary changes in the revised manuscript according to your instructions.

Minor Essential Revisions
In the revised manuscript (Methods part), we have explained the details of the recruitment. We will pay more attention to this issue in future studies.

We did not have a sample size calculation. We selected all of the workers with CWP and all matched miners with minimal symptoms (group 0+) according the eligibility criteria from the region and in the time interval. Regarding the tendency of statistical significance of some associations, we have added this possibility in the revised manuscript (Discussion section).

The information in this manuscript was a complete case analysis after discarding missing data. According to the eligibility criteria, 40 miners with CWP, 20 miners with minimal symptoms (group 0+), and 25 asymptomatic miners were selected. The total number of the subjects was 85. After the missing data had been excluded, 69 subjects completed the study.

Missing data and causes have been presented below:
- 6 subjects: inappropriate cooperation in lung function test (2 CWP, 4 Group 0+).
- 8 subjects: the volume of the sample was not sufficient for determination of all serum biomarkers (3 CWP, 5 Group 0+).
- 2 subjects: sample haemolysis (1 CWP, 1 asymptomatic miner).

Eligibility criteria:
1. All subjects recruited were non-smokers.
2. All subjects were ages 40 to 75 years old based on the common age range of CWP.
3. All subjects were working under similar mine environment conditions.
4. All subjects had normal liver and kidney function, and no coronary artery disease, hypertension, diabetes mellitus or autoimmune disease.
5. All subjects had no recent or current infection.

Concerning the distribution of the variable and Person’s correlation, we have modified the Method section according to your instruction.

Concerning the grammar mistakes and spelling errors, we have corrected all of them in the revised manuscript.

We made statistical tests for differences between groups to avoid selection bias. The “potential determinants” have been deleted as the “independent variable”.