ARTICLE DETAILS

TITLE (PROVISIONAL) | INVESTIGATION OF SURFACTANT PROTEIN D AND INTERLEUKIN-6 LEVELS IN BLUNT CHEST TRAUMA PATIENTS WITH MULTIPLE RIB FRACTURES AND PULMONARY CONTUSIONS: A CROSS-SECTIONAL STUDY IN BLACK SEA REGION OF TURKEY

AUTHORS | Kurt, Aysel; Turut, Hasan; Acipayam, Ahmet; Kirbas, Aynur; Yuce, Suleyman; Cumhur Cure, Medine; Cure, Erkan

GENERAL COMMENTS

This is a study of IL-6 and SP-D levels is serial plasma from a cohort of blunt chest trauma patients with rib fractures and pulmonary contusions. The authors found that plasma IL-6 and SP-D levels were elevated in subjects with rib fractures or pulmonary contusion compared to healthy controls at several time points.

1. The definitions of the 2 main groups are very confusing. One group, “RFs” is listed as having 2 or more rib fractures, while the second group, “PC” is described as having rib fracture with or without pulmonary contusions. Was this second group supposed to be defined as “pulmonary contusions with or without rib fracture”? Otherwise, there could presumably be patients with rib fractures but without pulmonary contusions in the PC group, which would seem to overlap with the RF group. Alternatively, all the blunt chest trauma patients could be combined into one group and compared to both healthy subjects and a non-chest trauma control group.

2. There is no mention of how pulmonary contusion was diagnosed.

3. The control group was comprised of age/gender matched healthy controls. Although this does provide some useful comparisons, it would be more interesting to include a comparison group of trauma patients with a similar overall severity of injury, but without chest trauma to assess the effect of chest trauma on these biomarkers. As is, it is difficult to ascertain whether the observed effects are due to chest trauma or are reflective of overall injury severity (Okeny et al, BMC Emerg Med, 2015).

4. Although intubated patients were excluded, the data was not adjusted for key clinical variables, particularly severity of illness scores relevant to trauma, such as the injury severity score (ISS). Furthermore, was there any association between these biomarkers...
5. How were smoking status and other comorbidities assessed in this cohort?

6. What was the rationale for using Mann Whitney U vs. Student’s t test based on sample size? The use of these tests should be determined by the distribution of the data rather than the sample size as is done here.

7. The data analysis consists of multiple univariate analyses. This is extended into studying subgroups including smokers/nonsmokers, those with comorbidities, and the presence of complications (Table 4). This should be performed as a multivariate regression analysis assessing these factors rather than how the analysis is presently performed.

8. The authors state that the goal of the study is to assess whether SP-D or IL-6 were “useful parameters” in these subpopulations. However, there is no assessment made of an association between these biomarkers and clinical variables or outcomes. Such analyses should be performed or the goals of this study must be restated.

9. The authors should take advantage of the serial testing (a strength of this study) and assess whether changes in biomarkers over time were associated with key clinical variables or outcomes.

10. The correlation analyses in Table 5 and Figure 3 do not add anything meaningful to this study and should be removed.
Was SP-D clinically different from IL-6 after BLC?

Page 9, line 11. SP-D level reflects systemic inflammation and SP-D is released from many tissues, such as alveolar type II cells, bladder, stomach and intestinal mucosa. In RFs cases, SP-D might be induced from local reaction? Which cells secret SP-D in RFs?

Page 10, line 10. Both SP-A and SP-D can enhance phagocytosis and regulate TNF-alpha secretion (Nature Rev Immmol 2005 Wright JR)

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Mithat Gunaydin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ondokuz Mayis University, Faculty of Medicine, Department of Pediatric Surgery</td>
<td></td>
</tr>
<tr>
<td>samsun-turkey</td>
<td></td>
</tr>
</tbody>
</table>

| REVIEW RETURNED | 08-Jun-2016 |

<table>
<thead>
<tr>
<th>GENERAL COMMENTS</th>
<th>This is beautilful study. I suggest that the following be added to the references.</th>
</tr>
</thead>
</table>

The reviewer also provided a files in addition to these comments. Please contact the publisher for full details.

**VERSION 1 – AUTHOR RESPONSE**

1. RF group included only patients with rib fractures. All the patients included in the pulmonary contusion group had pulmonary contusion. We observed that the sentence written previously to be expressed mistakenly. It was corrected. We did not combine RF and PC groups because even though SP-D and IL-6 levels of PC group statistically were not significant they were higher.

2. We added how we diagnosed pulmonary contusion to the method section.

3. Even though we agree with opinion Reviewer’s opinion, our study is the first study that investigated serum surfactant protein D and interleukin 6 levels of BCT patients. We believe that in future more detailed studies would be performed. As the most patients with multiple trauma have chest trauma, it is difficult to find a multiple trauma patients without chest trauma (without any chest trauma). As one of our groups included only patients with rib fractures and the other group included patients with pulmonary contusion, we may found a result similar to that suggested by the Reviewer. Thus, the SP-D level of the pulmonary contusion group even though statistically insignificant it was higher than RF group.

4. ISS scores were calculated. We added the observations of the relation of ISS scores and the biomarkers to findings and discussion sections.

5. We evaluated smoking and comorbidities using Multivariate stepwise regression analysis.

6. According to suggestions of the Reviewer; as the entire groups were homogenous we repeated the statistics using student T test. Variable p values were added.
7. We evaluated smoking and comorbidities using Multivariate stepwise regression analysis. We found that Smoking and co-morbidity to have no relations with hospitalization duration, ISS scores and the development of complication. Regression analysis was added to the article as table 4. The old table 4 was changed to table 5.

8. The relations of hospitalization duration, ISS scores and the development of complications with SP-6 and IL-6 levels were evaluated using Multivariate regression analysis. As there were no intubated patient or mortality, they were not evaluated in this study.

9. In literature the results of the studies investigated IL-6 levels and our findings have shown that except the 1st day these markers to be not helpful in following up the patients. However, the measurement of these markers for more intervals for following up the patients may be investigated. Our study is a pilot study and more detailed studies are needed to investigate these findings.

10. Table 5 and figure 3 that were related to correlation analysis were removed from the study.

Sincerely

ANSWERS TO THE REVIEWER 2:
1. We added the information regarding IL-6 to the introduction.
2. We added the ethical institution name and the approval number.
3. We investigated blunt chest trauma patients with or without pulmonary contusion. This study is a pilot study and pulmonary contusion patients without systemic trauma may be investigated in the future. There is a need for new studies in this subject.

Sincerely

ANSWERS TO THE REVIEWER 3:
1. We added the information regarding IL-6 to the introduction.
2. We added the ethical institution name and the approval number.
3. We investigated blunt chest trauma patients with or without pulmonary contusion. This study is a pilot study and pulmonary contusion patients without systemic trauma may be investigated in the future. There is a need for new studies in this subject.

Sincerely

ANSWERS TO THE REVIEWER 4:
In our article, we made the citations to the related articles.

Sincerely

VERSION 2 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Vivian Cury</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Universidade de São Paulo - Brazil</td>
</tr>
</tbody>
</table>

| REVIEW RETURNED | 28-Aug-2016 |

| GENERAL COMMENTS | This is a organized study and well-presented manuscript, which is publishable in the BMJ Open. |
Investigation of surfactant protein-D and interleukin-6 levels in patients with blunt chest trauma with multiple rib fractures and pulmonary contusions: a cross-sectional study in Black Sea Region of Turkey

Aysel Kurt, Hasan Turut, Ahmet Acipayam, Aynur Kirbas, Suleyman Yuce, Medine Cumhur Cure and Erkan Cure

*BMJ Open* 2016 6:
doi: 10.1136/bmjopen-2016-011797

Updated information and services can be found at:
http://bmjopen.bmj.com/content/6/10/e011797

These include:

**References**

This article cites 38 articles, 3 of which you can access for free at:
http://bmjopen.bmj.com/content/6/10/e011797#BIBL

**Open Access**

This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**

Articles on similar topics can be found in the following collections

Respiratory medicine (351)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/