Surfactant protein-A levels in patients with acute respiratory distress syndrome

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Background & objectives: The decrease in surfactant protein-A (SP-A level) has recently been implicated in the pathophysiology of acute respiratory distress syndrome (ARDS). Mechanical ventilation is the main modality of treatment of ARDS. But information on the SP-A levels after mechanical ventilation is scanty. We therefore studied the effect of mechanical ventilation on SP-A levels in patients with ARDS.

Methods: In a prospective, observational study conducted in the Respiratory Intensive Care Unit of a tertiary care hospital in north India, 13 patients with ARDS requiring mechanical ventilation were included. SP-A levels in the bronchial aspirates were serially estimated by ELISA at the start of mechanical ventilation and after 24 and after 48 h.

Results: The SP-A level at the start of mechanical ventilation was 3.06±2.56 µg/ml. The levels gradually increased to 3.99±2.39 and 6.64±2.72 µg/ml, at 24 and 48 h respectively, and this increase was statistically significant (P<0.05). Patients having an infectious etiology had lower SP-A levels compared to those with non-infections causes. Neither the initial SP-A level nor the increase in SP-A level correlated with the improvement in lung function or duration of ventilation.

Interpretation & conclusion: The present study showed a progressive increase in the SP-A levels in patients with ARDS on mechanical ventilation. Further studies are required to confirm that the increase in SP-A levels may be one of the contributors for recovery in ARDS.

Key words Acute lung injury - ARDS - bronchial aspirates - mechanical ventilation - PEEP - pneumonia - pneumocytes - surfactant protein-A

Acute respiratory distress syndrome (ARDS) is a common clinical condition and has a high mortality rate despite advances in intensive care. The underlying pathophysiology of acute lung injury and ARDS is the consequence of an unregulated over-expression of the usual systemic inflammatory responses to infection and/or injury, which involves both the alveolar epithelium and the pulmonary capillary endothelium. Besides a chain of events and a plethora of biochemical changes that take place in ARDS, surfactant may be affected in several other ways. The alterations in surfactant composition contribute to the disturbances of fluid balance seen in ARDS.

Mechanical ventilation with positive end expiratory pressure (PEEP) is the accepted mode of therapy for ARDS. This serves to increase lung volume, which in turn opens collapsed alveoli and decreases lung shunting. Surfactant protein-A
(SP-A) is the most abundant protein in the alveoli, constituting about 50 per cent of the total surfactant protein. It has the dual function of maintenance of surface-active properties of surfactant and immunomodulation. Since SP-A has important properties of keeping the surface tension low in the alveoli and is altered in ARDS contributing to its pathophysiology, it is important to observe the effect of mechanical ventilation on SP-A levels. Changes in the surfactant constituents have been observed after ventilation especially in animal models but information on humans is scanty. In the present study, we have serially measured the SP-A levels in bronchial aspirates in ventilated patients of ARDS to find out the effect of mechanical ventilation on SP-A levels.

Material & Methods

Twenty two patients with the diagnosis of ARDS during June 1998 to October 1999 were admitted in the Respiratory Intensive Care Unit of the Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, a tertiary care hospital in north India. Five patients died within 48 h and were excluded from the study. Four patients were excluded because of the requirement of high oxygen concentration making it relatively harmful to obtain aspirates. Thirteen consecutive patients fulfilling the inclusion criteria were studied. The Institute’s Ethics Committee approved the study.

Inclusion criteria: The patients satisfied the criteria for definition of ARDS which include acute onset of respiratory failure due to exposure to endogenous or exogenous agents, rapid development of diffuse bilateral interstitial or alveolar infiltrates on chest X-ray, absence of clinical evidence of cardiogenic pulmonary oedema, and severe hypoxaemia characterized by a ratio less than 200 of arterial oxygen concentration to inspired oxygen concentration (PaO₂/FiO₂). Three samples of bronchial aspirates were taken for each patient: within 30 min after starting mechanical ventilation - 0 h, after 24 h, while on ventilator, and after 48 h, while still on ventilator. Ventilatory parameters like respiratory rate, inspired oxygen concentration, tidal volume, positive end expiratory pressure and static lung volume was automatically calculated by the ventilator (Puritan Bennett 7200 series, USA).

Bronchial aspirate were obtained by aseptic technique using a sterile suction catheter each time. The secretions were collected in a mucous trap and carried to the laboratory for analysis. The SP-A level in the samples was estimated by the ELISA immunoassay method.

Wilcoxon signed rank test was used to compare the changes of SP-A levels with mechanical ventilation. Non-parametric Mann-Whitney U test was used to compare initial SP-A levels in patients with that of normal controls. To study relationship between variables, Spearman’s rho test was used to know whether changes in SP-A were dependent on changes in other variables. P value < 0.05 was taken as significant.

Results & Discussion

The age of the 13 patients (6 males, 7 females) ranged from 15 to 60 yr with a mean of 25.7±13.04 yr. The risk factors for ARDS observed in the patients were sepsis in 7 (53.8%), malaria in 2 (15.3%), trauma/fat embolism in 2 (15.3%), and alveolar haemorrhage and near drowning in 1 (7.69%) each. Of the 7 patients with sepsis, 6 had pneumonia as the precipitating factor. Thus ARDS in 9 patients was due to infectious causes and in 4 non-infectious causes. The mean duration of artificial ventilation was 8.1±7.9 (range 3 to 30 days) days and respiratory care unit stay (range 6 to 44 days) was 12.9±11.13 days.

The SP-A level in lung aspirate at 0 h was 3.06±2.56 µg/ml (Table I). This was lower than the normal SP-A level (5.36±2.3 µgm/ml) found in bronchial lavage fluid of patients with normal chest X-ray in another study at our center though the decrease was not statistically significant. The SP-A level increased to 3.99±2.39 µg/ml at 24 h and, to 6.64±2.72 µg/ml at 48 h, the difference between these two levels being significant (P<0.05).

Although FiO₂ given decreased and SP-A level increased from 0 to 48 h; these changes did not
Table I. Change of parameters and surfactant protein-A with ventilation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Before ventilation</th>
<th>After ventilation (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.48±0.05</td>
<td>0.64±0.2*</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>48±13</td>
<td>87±27.1*</td>
</tr>
<tr>
<td>PaO₂/FiO₂</td>
<td>100.31±24</td>
<td>148±63.7*</td>
</tr>
<tr>
<td>RR (p/min)</td>
<td>44.77±3.9</td>
<td>22±7.12*</td>
</tr>
<tr>
<td>VT (l)</td>
<td>--</td>
<td>0.44±0.06</td>
</tr>
<tr>
<td>PEEP (mmHg)</td>
<td>--</td>
<td>4.15±2.25</td>
</tr>
<tr>
<td>Compliance (ml/cm H₂O)</td>
<td>--</td>
<td>23±5.59</td>
</tr>
<tr>
<td>SP-A level (µg/ml)</td>
<td>--</td>
<td>3.06±2.56</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n=13); FiO₂, inspired oxygen concentration; PEEP, positive end expiratory pressure; PaO₂, partial pressure of arterial oxygen; RR, respiratory rate; VT, tidal volume

*compared to before ventilation, **compare to 0 h, ***compared to 24 h

Table II. Comparison of parameters in patients with ARDS due to infectious causes and non infectious causes

<table>
<thead>
<tr>
<th></th>
<th>Infectious group (n=9)</th>
<th>Non infectious group (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>28.3±4.14</td>
<td>19.75±5.18</td>
</tr>
<tr>
<td>PaO₂/FiO₂ before ventilation</td>
<td>105.7±25.4</td>
<td>88±20.06</td>
</tr>
<tr>
<td>Respiratory rate (p/min)</td>
<td>49.56±12.61</td>
<td>34±11.54</td>
</tr>
<tr>
<td>Compliance at 0h (ml/cm H₂O)</td>
<td>21.46±4.9</td>
<td>26.25±6.84</td>
</tr>
<tr>
<td>Duration of ventilation (days)</td>
<td>6.0±2.51</td>
<td>13±14.73</td>
</tr>
<tr>
<td>Duration of stay (days)</td>
<td>10.75±6.47</td>
<td>17.25±17.87</td>
</tr>
<tr>
<td>SP-A level at 0h (µg/ml)</td>
<td>2.11±1.36*</td>
<td>5.19±3.53</td>
</tr>
<tr>
<td>SP-A level at 24 h (µg/ml)</td>
<td>3.14±2.34*</td>
<td>5.9±1.08</td>
</tr>
<tr>
<td>SP-A level at 48 h (µg/ml)</td>
<td>6.1±2.00</td>
<td>7.86±4.00</td>
</tr>
</tbody>
</table>

Values are mean±SD

*significant compared to non infectious group (P<0.05)

correlate (r=-0.154; P>0.05). There was no correlation between the improvement in PaO₂/FiO₂ ratio and increase in SP-A levels (r=-0.148; P>0.05); increase in SP-A level and the period of artificial ventilation (r=0.004; P>0.05). No correlation was found between SP-A levels and the duration of mechanical ventilation in patients with infectious causes (r=-0.209, P>0.05) and non-infectious causes (r=-0.4, P>0.05). There was no correlation between the initial SP-A level and the corresponding PaO₂/FiO₂ ratio (r=0.055, P>0.05) or the lung compliance (r=0.17, P>0.05).

Parameters like age, PaO₂/FiO₂ ratio, respiratory rate, compliance, duration of ventilation and respiratory care unit stay were comparable in the infectious and non-infectious groups. SP-A levels at 0 and 24 h were significantly (P<0.05) lower in the infectious group compared to non-infectious group but became comparable at 48 h (Table II).

Decrease in SP-A levels in bronchoalveolar lavage fluid is a consistent finding in patients with ARDS. The decrease in SP-A may be due to decreased synthesis because of damage to the alveolar type II pneumocytes and increased degradation by neutrophil mediators. There is also...
a qualitative defect in surfactant protein-A, which is due to inhibition by the leaking serum proteins.

SP-A levels increased significantly 48 h after mechanical ventilation. An earlier study had also shown that artificial ventilation increases SP-A synthesis in preterm lamb lung. Studies in children with ARDS showed that SP-A levels did not change significantly with ventilation.

There was no relation of initial SP-A level with the duration of ventilation, PaO$_2$/FiO$_2$ ratio or the lung compliance in this study. Duration of mechanical ventilation depends on many other factors like the basic disease, the severity of disease, multiorgan dysfunction etc., which were not assessed in the present study.

In some studies reduction of SP-A levels has been shown to be correlated with severity of ARDS, which was not found in the present study. This could be because the severe cases of ARDS who died within 48 h were excluded from the study. It has been found that the SP-A levels remained low in patients with severe lung injury, and in those with moderate lung injury the levels of SP-A that were initially low increased to more than control values after mechanical ventilation.

The present study shows that the SP-A level increases after mechanical ventilation and this increase is not correlated with the severity of lung injury. Exposure to increased oxygen concentration has been found to stimulate the secretion of surfactant proteins by type II pneumocytes. The increase in SP-A level could be due to increased oxygen concentration during mechanical ventilation. Increase in SP-A may also be related to recovery of functioning of type II pneumocytes when the initial insult subsides. In an earlier study the phospholipid abnormalities found in the surfactant in ARDS normalized over a period of time and this could be responsible for improvement in PaO$_2$/FiO$_2$ ratio.

Thus, the present study revealed a progressive increase in the SP-A level with mechanical ventilation in ARDS. Further studies may be required to confirm that the increase in SP-A levels may be one of the contributors for recovery in ARDS.

References


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