The effect of non-invasive sequential ventilation treatment based on the use of an invasive ventilator on the arterial blood gas and inflammatory stress reaction in patients with severe pneumonia with respiratory failure

Jianfeng Gong¹*, Xiang Yang¹, Jingfen Xiang², Huali Zhou³, Weiliang Wu¹

1 Department of Critical Care Medicine, The Sixth Affiliated Hospital of Guangzhou Medical University, Qingyuan People's Hospital, 511500 Qingyuan, Guangdong, China
2 Department of Emergency, The Sixth Affiliated Hospital of Guangzhou Medical University, Qingyuan People's Hospital, 511500 Qingyuan, Guangdong, China
3 Department of Plastic and Cosmetic Surgery, The Sixth Affiliated Hospital of Guangzhou Medical University, Qingyuan People's Hospital, 511500 Qingyuan, Guangdong, China

*Correspondence
jfgong@163.com
(Jianfeng Gong)

Abstract
To investigate the impact of non-invasive sequential ventilation treatment based on the use of an invasive ventilator on the arterial blood gas and inflammatory stress reaction in patients with severe pneumonia with respiratory failure. Ninety patients with severe pneumonia and respiratory failure were equally separated into two groups via a random number table: a conventional treatment group (subjected to invasive mechanical ventilation) and a study group (subjected to invasive mechanical ventilation and non-invasive sequential ventilation treatment). We compared the two groups with respect to several key parameters before and after treatment, including mechanical ventilation time, invasive ventilation time, intensive care unit (ICU) stay, hospital stay, blood gas analysis indicators and the levels of inflammatory factors in the serum. We also compared the two groups with regard to complications. Mechanical ventilation time, invasive ventilation time, ICU stay and hospital stay in the study group were significantly shorter than that in the conventional treatment group (p < 0.05). Arterial Oxygen Saturation (SaO₂), Partial Pressure of Oxygen (PaO₂) and pH in the study group after intervention were significantly higher than those in the conventional treatment group after intervention (p < 0.05). Following intervention, white blood cell (WBC), serum c-reactive protein (CRP) and serum interleukin-6 (IL-6) were significantly lower than those in the conventional treatment group (p < 0.05). The total incidence of complications in the study group was markedly lower than in the conventional treatment group. Non-invasive sequential ventilation therapy based on an invasive ventilator had a significant treatment impact on patients with severe pneumonia and respiratory failure. This treatment effectively reduced the average treatment time, improved blood gas analysis indicators and reduced inflammatory stress, thus reducing the incidence of complications.

Keywords
Severe pneumonia; Respiratory failure; Invasive mechanical ventilation; Non-invasive sequential ventilation; Blood gas analysis; Inflammatory factor

1. Introduction
Severe pneumonia is a common type of inflammatory lung disease in clinical practice that is associated with a mortality rate as high as 30–50%. The occurrence of this condition is prone to cause multiple organ dysfunction, faintness, shock and other complications that are serious and even life-threatening [1, 2]. As a common complication of severe pneumonia, respiratory failure can increase the difficulty of treatment and can exert significant effects on the therapeutic effect [3]. The occurrence of this disease predominantly affects the pulmonary function of patients, thus resulting in carbon dioxide retention and a reduced arterial partial pressure of oxygen, ultimately leading to an increased risk of death [4]. Therefore, the timely and effective improvement of pulmonary ventilation function and correction of the hypoxic state is the key to controlling the disease and reducing mortality. Invasive mechanical ventilation is emerging as one of the most commonly used tools in clinical practice; this regimen has been shown to effectively restore pulmonary ventilation as well as oxygenation capacity, reduce carbon dioxide retention and lower mortality [5, 6]. However, some studies have suggested that as invasive mechanical ventilation reduces mortality, it is also prone to cause malnutrition, oropharyngeal gastrointestinal dysfunction, ventilator dependence and ventilator-associated pneumonia (VAP) due to the
significant trauma involved in the treatment and the long-term period of treatment, thus leading to poor patient tolerance and weaning difficulties [7, 8]. Non-invasive sequential ventilation treatment is a novel treatment developed on the foundation of traditional invasive ventilation therapy, and its use can effectively reduce the treatment time required by invasive mechanical ventilation and reduce the occurrence of adverse complications caused by prolonged invasive ventilation [9]. In the current study, we investigated the impact of non-invasive sequential ventilation treatment based on the use of an invasive ventilator on the arterial blood gas and inflammatory stress reaction in patients with severe pneumonia with respiratory failure.

2. Materials and methods

2.1 General information

The subjects of this study were patients with severe pneumonia and respiratory failure who were admitted to our hospital between March 2020 and May 2022. All subjects needed to meet specific inclusion criteria, as follows: (1) patient had severe pneumonia with respiratory failure, as confirmed by clinical laboratory tests, etiological diagnosis and imaging examination results [10, 11]; (2) arterial blood gas outcomes demonstrated that mechanical ventilation was required, and (3) the patient had a complete clinical dataset and provided informed consent, voluntarily joined the study, and cooperated fully with therapists. Patients with the following conditions were excluded: the acute onset of severe coma, severe lung or thoracic damage due to external force factors, mental disorders, acute and chronic infectious diseases, autoimmune diseases, cardiogenic shock, gastrointestinal bleeding and other serious cardiovascular and cerebrovascular or organ dysfunction, shock occurring before the onset of the disease or death occurred during treatment. Ninety patients were equally separated into two groups with a random number table: a conventional treatment group and a study group. There were 45 subjects in each group, and the general baseline data of the 90 subjects is shown in Table 1. The mean age, gender ratio and mean disease duration of the subjects did not differ significantly between the two groups (p > 0.05). The study was conducted in accordance with the standards of the hospital ethics committee with appropriate permission.

2.2 Study methods

The subjects in both groups received conventional symptomatic and supportive treatment for severe pneumonia with respiratory failure, including expectorant and anti-asthmatic treatment, the maintenance of water and electrolyte balance and anti-infection strategies. On this basis, invasive mechanical ventilation was provided by a PB840 invasive ventilator (Shanghai Siou Medical Equipment Co., Ltd., Shanghai, China). The parameter settings were as follows: a positive end breathing pressure ventilation of 4–5 cmH₂O, a respiratory ratio of 1.2:0.1, a tidal volume of 5–13 mL/kg, an adjusted PSV of 5–10 cmH₂O, a ventilation frequency of 20 times/min, and a trigger sensitivity of 5 L/min. The treatment mode started with synchronized intermittent mandatory ventilation (SIMV) in the assisted/controlled mode; this was then changed to the pressure support ventilation (PSV) after the patient’s condition was stable; we then monitored the patient’s status over time. The pulmonary infection control window (PIC window) represented the time at which the PSV had fallen to 10–12 cmH₂O, the pulmonary infiltration image was noticeably reduced, and the serological white blood cell count was lower than 10 × 10⁹/L with a body temperature below 38 °C. The patients in the conventional treatment group continued to receive the original invasive mechanical ventilation therapy; we adjusted the PSV to 5–10 cmH₂O and the positive end-expiratory pressure ventilation (PEEP) to 4–5 cmH₂O. Extubation was performed after the patient’s condition was stable. Upon the occurrence of the PIC window, the subjects in the study group were converted or underwent a spontaneous breathing trial (SBT). The tracheal intubation was removed and changed to non-invasive sequential ventilation therapy for successful patients. If SBT failed, invasive ventilation was performed first and then changed to non-invasive intervention following successful SBT. The specific manipulation involved selection of the ventilation mouth and nose mask and adjustment to S/T mode. Various parameters were set: the respiratory rate was set to 14–20 times/min, the inspired oxygen concentration was set to 40%, and the initial parameter of inspired air pressure regulation was set to 6–8 cmH₂O. The pressure was then gradually increased according to the actual situation of the patient involved, but not higher than 25 cmH₂O. The initial parameter of expiratory pressure was 3–6 cmH₂O, such that the oxygen saturation was >90%. The frequency and duration of use was controlled by the nursing staff in light of the patient’s condition for the first three days. Then, after the condition stabilized, the specific ventilator parameters were adjusted, during which time the doctor’s advice was followed strictly until weaning. Subjects in both groups were continuously treated for one course of treatment; that is, 5 to 10 days.

2.3 Study contents

Various indicators were analyzed and compared between the two groups, including mechanical ventilation time, invasive ventilation time, ICU stay and hospital stay. We also compared a range of indicators before and after intervention, including blood gas analysis indicators, such as Arterial Oxygen Saturation (SaO₂), Partial Pressure of Oxygen (PaO₂), arterial carbon dioxide partial pressure (PaCO₂) and pH; and serum inflammatory factors, such as white blood cell (WBC), C-reactive protein (CRP) and the levels of interleukin-6 (IL-6) levels. The incidence of complications during treatment were also statistically analyzed. The diagnostic criteria for VAP were as follows: the patient’s body temperature was >37.5 °C, purulent secretions were produced in the respiratory tract, moist rales were heard in the lungs, there were infiltration shadows in the lungs, and pathogenic bacteria were cultured from bronchial secretions.

2.4 Statistical analysis

Raw data were tabulated and analyzed by Statistical Product and Service Solutions (SPSS, IBM Corporation, Chicago, IL,
USA) version 23.0. The independent sample t test was utilized for measurement data in line with sample means such as time-related, blood gas analysis and inflammatory factor levels. The Chi-squared test was used to analyze numerical data. p < 0.05 denoted statistical significance.

3. Results

3.1 A comparison of time indicators between groups

Compared with the conventional treatment group, time indicators such as mechanical ventilation time, invasive ventilation time, ICU time along with hospital stay were significantly shorter in the study group (p < 0.05); the outcomes were detailed in Table 2.

3.2 A comparison of blood gas indicators between groups

The four blood gas parameters did not differ significantly between the two groups prior to intervention (t = 1.146, 0.142, 0.212, 0.054; p = 0.255, 0.888, 0.832, 0.957). In comparison with the index levels before intervention in the same group, SaO2, PaO2 and pH were raised to different extents after intervention, while PaCO2 was reduced substantially. SaO2, PaO2 and pH in the study group were significantly higher while PaCO2 was significantly lower than the conventional treatment group after intervention (p < 0.05). The outcomes are shown in Table 3.

3.3 A comparison of serological indicators between groups

WBC, CRP and IL-6 levels in the conventional treatment group and the study group were not significantly different prior to intervention (t = 1.789, 1.238, 0.172; p = 0.077, 0.219, 0.864). However, these three factors were reduced to different extents in both groups after intervention when compared to before intervention. However, WBC, CRP and IL-6 in the intervention group were significantly lower than the conventional treatment group after treatment (p < 0.05). Outcomes are shown in Table 4.

3.4 The incidence of complications

Of the 45 patients in the conventional treatment group, five experienced pneumothorax, four experienced VAP, and six experienced oropharyngeal gastrointestinal discomfort; the total complication rate was 8.89%; this was which was significantly lower than the conventional treatment group (p < 0.05), as shown in Table 5.

4. Discussion

Among the numerous complications of severe pneumonia, the incidence of respiratory failure is 30–70%. Furthermore, this complication causes the disease to progress rapidly with a poor diagnosis [12, 13]. Ventilation and assisted respiration are effective approaches to improve the respiratory condition of patients. Therefore, mechanical ventilation is considered as an effective protocol for treatment [14]. Nevertheless, invasive mechanical ventilation is highly efficient at restoring respiratory function and improving body dysfunction in patients. However, weaning can be difficult, and various complications can occur, thus limiting the use of traditional invasive mechanical ventilation therapy [15, 16]. Non-invasive sequential ventilation treatments are simple to perform and cause less trauma to the body. Some studies have indicated that this type of therapy has little effect on the gastrointestinal tract and can effectively correct body hypoxia [17, 18]. However, research has also proven that mechanical ventilation alone can be insufficient in terms of secretion drainage compensation, thus creating a limitation of its single application [19, 20]. Non-invasive sequential ventilation therapy is based on the use of an invasive mechanical ventilator. After improving the pathological state of respiratory failure in patients, the mechanical ventilator is changed to a ventilator with a mask or nasal mask. Previous studies discovered that invasive-non-invasive mechanical ventilation therapy can effectively reduce treatment time and can promote disease recovery [21–23].

In addition, we investigated a range of time-related indicators, blood gas analysis indicators, inflammatory factor levels and complications during the treatment of patients. We found that mechanical ventilation time, invasive ventilation time, ICU stay and hospital stay in the study group were significantly shorter in the intervention group when compared to the conventional treatment group, thus indicating that non-invasive sequential ventilation therapy based on the use of an invasive ventilator can effectively shorten the mechanical ventilation time. This regimen was also shown to be conducive to the recovery of the disease, as confirmed by hospital stay data; these results were consistent with some previous reports [24, 25]. Because non-invasive sequential ventilation therapy can ensure the stability of ventilation after invasive mechanical ventilation therapy; this strategy can improve a patient’s respiratory failure symptoms, and parameters can be gradually adjusted according to the patient’s actual condition to ensure
### TABLE 2. A comparison of time indicators between groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Mechanical ventilation time</th>
<th>Invasive ventilation time</th>
<th>ICU time</th>
<th>Hospital stays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional treatment group</td>
<td>45</td>
<td>18.48 ± 3.18</td>
<td>14.06 ± 3.81</td>
<td>26.45 ± 2.55</td>
<td>31.43 ± 4.50</td>
</tr>
<tr>
<td>Study group</td>
<td>45</td>
<td>11.72 ± 2.64</td>
<td>8.04 ± 2.09</td>
<td>16.13 ± 2.54</td>
<td>21.06 ± 2.56</td>
</tr>
<tr>
<td>( t ) value</td>
<td></td>
<td>10.976</td>
<td>9.298</td>
<td>19.252</td>
<td>13.433</td>
</tr>
<tr>
<td>( p ) value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ICU: intensive care unit.

### TABLE 3. A comparison of blood gas indicators between groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Time</th>
<th>( \text{SaO}_2 ) (%)</th>
<th>( \text{PaO}_2 ) (mmHg)</th>
<th>( \text{PaCO}_2 ) (mmHg)</th>
<th>( \text{pH} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional treatment group</td>
<td>45</td>
<td>Pre-intervention</td>
<td>72.53 ± 3.96</td>
<td>49.36 ± 6.64</td>
<td>72.27 ± 4.12</td>
<td>7.22 ± 0.10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post Intervention</td>
<td>84.60 ± 5.41</td>
<td>74.33 ± 5.25</td>
<td>48.46 ± 4.59</td>
<td>7.33 ± 0.07</td>
</tr>
<tr>
<td>Study group</td>
<td>45</td>
<td>Pre-intervention</td>
<td>73.51 ± 4.15</td>
<td>49.54 ± 5.28</td>
<td>72.07 ± 5.02</td>
<td>7.23 ± 0.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post Intervention</td>
<td>90.77 ± 6.40</td>
<td>80.88 ± 6.78</td>
<td>45.58 ± 4.10</td>
<td>7.41 ± 0.05</td>
</tr>
<tr>
<td>( t ) value</td>
<td></td>
<td>5.941</td>
<td>5.124</td>
<td>3.133</td>
<td>6.515</td>
<td></td>
</tr>
<tr>
<td>( p ) value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Note: Statistics in the table indicate a comparison between both groups after intervention. \( \text{SaO}_2 \): Arterial Oxygen Saturation; \( \text{PaO}_2 \): Partial Pressure of Oxygen; \( \text{PaCO}_2 \): partial pressure of carbon dioxide in artery.

### TABLE 4. A Comparison of serological indicators between groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Time</th>
<th>WBC (10^9/L)</th>
<th>CRP (mg/L)</th>
<th>IL-6 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional treatment group</td>
<td>45</td>
<td>Pre-intervention</td>
<td>17.65 ± 1.94</td>
<td>85.59 ± 11.13</td>
<td>123.04 ± 14.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post Intervention</td>
<td>11.63 ± 1.04</td>
<td>52.90 ± 8.82</td>
<td>118.15 ± 11.89</td>
</tr>
<tr>
<td>Study group</td>
<td>45</td>
<td>Pre-intervention</td>
<td>18.39 ± 2.02</td>
<td>88.90 ± 14.04</td>
<td>123.54 ± 13.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Post Intervention</td>
<td>9.97 ± 0.34</td>
<td>41.96 ± 8.72</td>
<td>84.18 ± 15.29</td>
</tr>
<tr>
<td>( t ) value</td>
<td></td>
<td>10.212</td>
<td>5.919</td>
<td>11.760</td>
<td></td>
</tr>
<tr>
<td>( p ) value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Note: Statistics in the table indicate comparison between the study group and the conventional treatment group after intervention. WBC: white blood cell; CRP: C-reactive protein; IL-6: levels of interleukin-6.

### TABLE 5. The incidence of complications.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Pneumothorax</th>
<th>VAP</th>
<th>Oropharyngeal gastrointestinal discomfort</th>
<th>Total complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional treatment group</td>
<td>45</td>
<td>5 (11.11)</td>
<td>4 (8.89)</td>
<td>6 (13.33)</td>
<td>33.33%</td>
</tr>
<tr>
<td>Study group</td>
<td>45</td>
<td>1 (2.22)</td>
<td>0</td>
<td>3 (6.67)</td>
<td>8.89%</td>
</tr>
<tr>
<td>( \chi^2 ) value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8.073</td>
</tr>
<tr>
<td>( p ) value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.004</td>
</tr>
</tbody>
</table>

VAP: ventilator-associated pneumonia.
that while reducing airway resistance, pulmonary surfactant consumption can also be reduced; in turn, this reduces ventilator oxygen consumption and shortens the overall duration of ventilation [26]. In addition, as shown in the comparison of outcomes before and after intervention, the program in the study group had a better impact on the improvement of arterial blood gas analysis indicators in patients, thus demonstrating that this program could effectively improve the alveolar oxygenation and reduce carbon dioxide retention in patients.

WBC, CRP and IL-6 are critical indicators of inflammatory response; these parameters not only directly reflect the inflammatory stress status of patients, but also represent important detection factors for treatment efficacy and prognosis [27, 28]. In comparison with the serum inflammatory factors, we found that the serum WBC, CRP and IL-6 levels in the study group were significantly reduced, thus indicating that the inflammatory stress status in these patients was lower than that in the conventional care group; this may have resulted from the significant trauma caused by long-term invasive mechanical ventilation therapy on the respiratory mucosa of the patients. This trauma can also activate the release of oxygen free radicals by leukocytes. However, non-invasive sequential ventilation therapy can significantly improve such drawbacks; therefore, this technique was more beneficial in reducing the inflammatory stress response and improving disease recovery [29, 30]. Furthermore, to verify the safety of this strategy, we finally compared the incidence of complications incidence between groups of subjects. The outcomes certified that the treatment regimen for this study effectively reduced the occurrence of complications, such as pneumothorax, VAP and oropharyngeal complications, such as pneumothorax, VAP and oropharyngeal discomfort, thus demonstrating the high safety profile of this regimen. The causes underlying this disease are complex, and the underlying mechanisms have yet to be fully elucidated. In this study, due to limitations imposed by time and samples, we only investigated four specific aspects. However, other effects, such as vascular endothelial function and oxidative stress status have yet to be investigated. Therefore, to further investigate the complete effect and principle of this program, there is a clear need to perform additional research with a larger sample size.

5. Conclusions

Non-invasive sequential ventilation based on the use of an invasive ventilator had a high safety profile and exerted a substantial therapeutic effect on patients with severe pneumonia and respiratory failure and effectively shortened the average treatment time, improved blood gas analysis indicators and reduced the inflammatory stress state and the incidence of complications.

AVAILABILITY OF DATA AND MATERIALS

All data generated or analyzed during this study are included in this published article.

AUTHOR CONTRIBUTIONS

JFG—designed the research study. XY—performed the research. JFX and HLZ—analyzed the data. WLW—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of the the Sixth Affiliated Hospital of Guangzhou Medical University, Qingyuan People’s Hospital (Reference number: QPH-IRB-A137). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES


