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Retrospective Study

Clinical evaluation of prone position ventilation in the treatment of acute respiratory distress syndrome induced by sepsis

Wen-Han Xia, Chun-Li Yang, Zhi Chen, Cheng-Hong Ouyang, Guo-Quan Ouyang, Qiu-Gen Li

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Abstract

BACKGROUND

Acute respiratory distress syndrome (ARDS) is an acute, diffuse, inflammatory lung injury. Previous studies have shown prone position ventilation (PPV) to be associated with improvement in oxygenation. However, its role in patients with ARDS caused by sepsis remains unknown.

AIM

To analyze the clinical effects of PPV in patients with ARDS caused by sepsis.

METHODS

One hundred and two patients with ARDS were identified and divided into a control group ($n = 55$) and a PPV treatment group ($n = 47$). Outcomes included oxygenation index, lung compliance (Cst) and platform pressure (Pplat), which were compared between the two groups after ventilation. Other outcomes included heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), left ventricular ejection fraction (LVEF), the length of mechanical ventilation time and intensive care unit (ICU) stay, and levels of C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6) after ventilation. Finally, mortality rate was also compared between the two groups.

RESULTS

On the first day after ventilation, the oxygenation index and Cst were higher and

Pplat level was lower in the PPV group than in the conventional treatment group ($P < 0.05$). There were no significant differences in oxygenation index, Cst, and Pplat levels between the two groups on the 2nd, 4th, and 7th day after ventilation ($P > 0.05$). There were no significant differences in HR, MAP, CVP, LVEF, duration of mechanical ventilation and ICU stay, and the levels of CRP, PCT, and IL-6 between the two groups on the first day after ventilation (all $P > 0.05$). The mortality rates on days 28 and 90 in the PPV and control groups were 12.77% and 29.09%, and 25.53% and 45.45%, respectively ($P < 0.05$).

CONCLUSION

PPV may improve respiratory mechanics indices and may also have mortality benefit in patients with ARDS caused by sepsis. Finally, PPV was not shown to cause any adverse effects on hemodynamics and inflammation indices.

Key Words: Acute respiratory distress syndrome; Sepsis; Prone position; Supine position; Mechanical ventilation; Hemodynamics

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Core Tip: Acute respiratory distress syndrome (ARDS) is an acute, short-onset, diffuse, inflammatory lung injury disease. Previous studies have reported on the benefits of the prone position over the supine position in terms of mechanical ventilation and oxygenation; however, this has not been addressed in patients with ARDS caused by sepsis. Herein, we retrospectively reviewed the data of 106 patients who underwent mechanical ventilation for ARDS caused by sepsis. We found that mechanical ventilation in the prone position was associated with reduced mortality with no adverse effects on inflammatory and hemodynamic indices.

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) is an acute and diffuse inflammatory lung injury disease. It is usually caused by a variety of internal and external pathogenic factors, such as severe infection, trauma, and shock. Clinical manifestation may include respiratory failure, refractory hypoxemia, and respiratory distress, which can cause severe damage to the respiratory system[1,2]. Mechanical ventilation is an important clinical intervention for ARDS that improves bodily oxygenation, thus improving survival rate. A lung-protective ventilation strategy has been proposed based on the clinical pathophysiology of ARDS. This strategy mainly involves limiting tidal volume and airway pressure during mechanical ventilation to avoid lung over-inflation while allowing for the partial pressure of carbon dioxide to rise within a certain range. In addition, a higher level of positive end-expiratory pressure is used to improve lung compliance, suggesting that the lung recruitment strategy should be included in the lung-protective ventilation strategy. However, during the clinical application of mechanical ventilation, it was observed that different positioning influenced the effect of the intervention. Prone position ventilation improves oxygenation by changing the patient's position and is an important auxiliary method of mechanical ventilation[3-5]. However, few studies have evaluated the effect of prone position mechanical ventilation in patients with ARDS caused by sepsis, which limits its use in clinical practice. To this end, this study retrospectively analyzed the clinical data of patients with ARDS caused by sepsis treated with mechanical ventilation in the prone position and explored the effect of the intervention in this position.

MATERIALS AND METHODS

Baseline data

A retrospective analysis was performed using a sample of 102 patients who were treated with mechanical ventilation for ARDS caused by sepsis in the Intensive Care Unit (ICU) of our hospital from

January 2016 to January 2020. All enrolled patients received a lung-protective ventilation treatment strategy. The patients were divided into a control group ($n = 55$) (undergoing routine treatment) and prone position ventilation treatment group ($n = 47$) based on their positions during mechanical ventilation. The inclusion criteria were as follows: (1) all patients were diagnosed with ARDS after clinical examination; this diagnosis met the 2012 Berlin Criteria[6] and was caused by sepsis; and (2) the ICU admission time ≥ 24 h. The exclusion criteria were as follows: incidence of (1) pregnancy or lactation; (2) multiple rib fractures; (3) clavicle, spine, and facial fractures; (4) intracranial hypertension; (5) severe cerebral edema; and (6) hemodynamic instability.

Research methods

Patients in the control group were treated with mechanical ventilation in the supine position combined with the lung-protective ventilation strategy while patients in the prone position ventilation treatment group were treated with prone position ventilation combined with the lung-protective ventilation strategy. The mechanical ventilation methods also included sedative and analgesic treatment with fentanyl and midazolam in both groups; patients in the prone position ventilation treatment group received this treatment only after the airway secretions were completely cleared according to the prone position protocol. The Ramsay score was calculated if the patient was beyond 4 or 5 points on the scale. A healthcare provider with extensive clinical experience stood by the patient's head to prevent movement in the central venous line and artificial airway. Two healthcare providers stood on both sides of the patient. When the tubes were properly placed, the patient was required to lean to one side in the lateral decubitus position, and the posture was changed to a prone position. Soft pillows were placed at the chest, ilium, and knees to help minimize the abdominal pressure. Subsequently, for patients with tracheal intubation, the head was tilted to one side, and for those who underwent tracheotomy, the head was placed in the middle with the arms of the patient naturally extended and placed on either side. The ventilation mode remained unchanged in the prone position, with the patient required to remain in the prone position for more than 16 h every day. It was necessary to turn the patient back to a supine position urgently if a large amount of sputum in the airway could not be cleared or in cases of hemodynamic instability. Heart rate (HR), mean arterial pressure (MAP), and central venous pressure (CVP) measurements were required for hemodynamic monitoring of arterial and central venous catheterization. A Philips IntelliVue MP40 multifunctional monitor (Royal Philips, Netherlands) was selected to monitor various indicators, and color Doppler echocardiography was performed to assess the left ventricular ejection fraction (LVEF).

Observation items

Baseline characteristics, including age, sex, acute physiological and chronic health score (score), sequential organ failure score, and number of comorbid illnesses of the patients in the two groups were compared. Next, we compared respiratory mechanical indices, such as aerobic fitness index, lung compliance (Cst), and platform pressure (Pplat) between the two groups on days 1, 2, 4, and 7 after ventilation. We also compared hemodynamic indices between the groups, including HR, MAP, CVP, and LVEF, one day after ventilation. Clinical outcomes were also assessed between the two groups, including duration of mechanical ventilation and ICU stay of the patients. We also compared laboratory assessments between the two groups including levels of C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6) on the first day after ventilation. Finally, the mortality rate was compared between the two groups on days 28 and 90.

Statistical analysis

All statistical analyses were performed using SPSS 22.0 software. Continuous variables were summarized as means and standard deviations and compared between groups using a *t*-test. Categorical variables were reported as percentages, and compared between the two groups using the χ^2 test. Statistical significance was set at $P > 0.05$.

RESULTS

Comparison of baseline characteristics of patients between the two groups

We did not observe any significant differences in baseline characteristics between the two groups ($P > 0.05$) (Table 1).

Comparison of respiratory mechanical indices of patients between the two groups on days 1, 2, 4 and 7 after ventilation

On the first day after ventilation, the oxygenation index and Cst in the routine treatment group were lower and the Pplat level was higher than that of the prone position ventilation group ($P < 0.05$). There were no significant differences in oxygenation index, Cst, and Pplat levels between the two groups on the 2nd, 4th and 7th day after ventilation ($P > 0.05$) (Table 2).

Table 1 Comparison of general data of patients between the two groups, *n* (%)

| Group | Sex | | Age (yr) | Acute physiological and chronic health score (score) | Sequential organ failure score (score) | Number of basic illnesses | | | | | |
|---|------------|------------|---------------|--|--|---------------------------|------------|------------|------------|----------|----------|
| | Female | Male | | | | 1 type | 2 type | 3 type | 4 type | 5 type | 6 type |
| Conventional treatment group (<i>n</i> = 55) | 15 (27.27) | 40 (72.73) | 53.82 ± 16.08 | 27.71 ± 4.55 | 11.76 ± 3.15 | 5 (9.09) | 11 (20.00) | 17 (30.91) | 14 (25.45) | 5 (9.09) | 3 (5.45) |
| Prone position ventilation treatment group (<i>n</i> = 47) | 14 (29.79) | 33 (70.21) | 53.15 ± 14.16 | 28.28 ± 4.49 | 10.57 ± 3.01 | 5 (10.64) | 14 (29.79) | 19 (40.43) | 4 (8.5) | 4 (8.51) | 1 (2.13) |
| χ^2 / <i>t</i> value | 0.079 | | 0.222 | 0.634 | 1.941 | 6.551 | | | | | |
| <i>P</i> value | 0.779 | | 0.825 | 0.527 | 0.055 | 0.256 | | | | | |

Comparison of hemodynamic indicators of patients between the two groups on the first day after ventilation

There were no significant differences in HR, MAP, CVP, and LVEF on the first day after ventilation between the two groups ($P > 0.05$) (Table 3).

Comparison of mechanical ventilation time and ICU stay of patients between the two groups

There were no significant differences in duration of mechanical ventilation or length of ICU stay between the two groups ($P > 0.05$) (Table 4).

Comparison of the levels of inflammatory factors in patients of each group on the first day after ventilation

There were no significant differences in the levels of CRP, PCT, and IL-6 between the two groups on the first day after ventilation ($P > 0.05$) (Table 5).

Comparison of day 28 and day 90 mortality in each group

The mortality on the 28th and 90th days was higher in the control group than in the prone position ventilation treatment group ($P < 0.05$) (Table 6).

DISCUSSION

ARDS is a hypoxic, progressive, and acute respiratory failure caused by indirect or direct factors. Patients may experience dyspnea and tachypnea. Arterial blood gas analysis in patients with this condition shows that all indicators fail to reach the normal level, and hypoxemia is often difficult to treat. Therefore, close attention should be paid to the correction of hypoxemia in the clinical intervention for ARDS. Symptomatic intervention using ventilation treatment with auxiliary ventilation instruments such as ventilators is common in clinical practice[7-9]. ARDS is also characterized by lung injury caused by the action of local alveolar inflammatory factors on the alveoli and capillaries, resulting in increased lung permeability, exudation of substances such as plasma protein into the alveolar cavity and mesenchyme and leading ultimately to dyspnea[10,11]. Therefore, correction of dyspnea is particularly important in ARDS treatment.

Mechanical ventilation treatment for patients can improve lung volume; however, if used improperly, it can lead to excessive expansion of lung tissue, repeated opening and closing of the alveoli, and subsequently, ventilator-associated lung injury[12,13]. Patients are usually in the supine position for ventilation using a ventilator. In the supine position, under the influence of gravity, the blood flow may remain distributed on the dorsal side, and the proportion of ventilated blood flow becomes imbalanced. Thus, the supine position may be ineffective for ventilation in patients with severe lung consolidation in gravity-dependent parts[14,15]. In a study by Walter *et al*[16], prone position ventilation for patients with ARDS resulted in significant improvement in lung compliance, shortening of mechanical ventilation time, and improvement in oxygenation. Therefore, Walter *et al*[16] believed that prone position ventilation could be effective for oxygenation capacity and hypoxia. In this study, on the first day after ventilation, the oxygenation index and Cst level in the prone position ventilation treatment group were higher than those in the control group. The prone position ventilation treatment group had a lower Pplat level compared to the control group ($P < 0.05$). From our results, it can be inferred that the prone position may have improved oxygenation by the following mechanisms: (1) the volume of the lung tissue is reduced as it is compressed by the heart; (2) the ventilation/blood flow ratio is further improved in the prone position as compared to that in the supine position, thus significantly reducing

Table 2 Differences in respiratory mechanics indices of patients in each group before and after ventilation

| Group | Oxygenation index | | | | Cst (mL/cmH ₂ O) | | | | Pplat (cmH ₂ O) | | | |
|---|-------------------|----------------|----------------|----------------|-----------------------------|--------------|--------------|--------------|----------------------------|--------------|--------------|--------------|
| | Day 1 | Day 2 | Day 4 | Day 7 | Day 1 | Day 2 | Day 4 | Day 7 | Day 1 | Day 2 | Day 4 | Day 7 |
| Routine treatment group (<i>n</i> = 55) | 85.31 ± 25.69 | 198.33 ± 42.81 | 254.86 ± 49.56 | 308.03 ± 57.47 | 24.09 ± 2.87 | 36.06 ± 3.62 | 36.38 ± 3.75 | 36.45 ± 3.82 | 25.32 ± 1.06 | 21.96 ± 0.79 | 21.80 ± 0.72 | 21.73 ± 0.65 |
| Prone position ventilation treatment group (<i>n</i> = 47) | 129.34 ± 40.02 | 205.23 ± 41.81 | 255.50 ± 54.54 | 320.81 ± 66.15 | 29.80 ± 3.52 | 36.24 ± 3.65 | 36.42 ± 3.72 | 36.55 ± 3.90 | 22.01 ± 0.82 | 21.90 ± 0.75 | 21.76 ± 0.68 | 21.70 ± 0.61 |
| <i>t</i> value | 6.704 | 0.820 | 0.062 | 1.044 | 9.024 | 0.249 | 0.054 | 0.131 | 17.410 | 0.391 | 0.287 | 0.239 |
| <i>P</i> value | 0.001 | 0.414 | 0.951 | 0.299 | 0.001 | 0.804 | 0.957 | 0.896 | 0.001 | 0.696 | 0.775 | 0.812 |

Cst: Lung compliance; Pplat: Platform pressure.

pulmonary shunting; and (3) when the gravitational intrapleural pressure gradient is changed, the gravity-dependence of pulmonary edema fluid is redistributed. Furthermore, during prone position ventilation treatment, the curvature of the dorsal diaphragm is significantly reduced compared with that of the ventral diaphragm, which is affected by tension. When the posture of the patient changes, the pressure-forming direction of the abdominal contents also change correspondingly. In the supine position, the pressure from the abdominal contents mainly acts on the dorsal diaphragm, thus counter-acting the pressure of the ipsilateral diaphragm and keeping the diaphragm position unchanged[17,18]. In the prone position, the pressure acting on the dorsal diaphragm is reduced. Subsequently, the diaphragm position changes, leading to an increase in the functional residual air volume, redistribution of the air in the lungs along with the blood flow, and improvement in the ventilatory blood perfusion ratio in line with bodily requirement; thus, it is effective for the oxygenation capacity and hypoxia[19]. Prone position ventilation may also impact hemodynamics[20]. However, the findings of the present study showed that there were no significant changes in the hemodynamic indicators and inflammatory factor levels on the first day after ventilation in either group. In this study, the 28- and 90-day mortality were lower in the prone position ventilation group than in the control group ($P < 0.05$). Analysis of the results of the study reveal that the development of prone position ventilation therapy can reduce patient mortality. When patients' oxygenation capacity is improved, conditions such as hypoxemia and respiratory failure are also significantly improved, leading to a reduced disease mortality rate.

Prone position ventilation can reduce the regional heterogeneity of lung ventilation and optimize the regional distribution of transpulmonary pressure in the lung, thus improving gas exchange and reducing the risk of mechanical lung injury[21]. The multicenter PROSEVA trial found that the prone position significantly improved survival and shortened mechanical ventilation time compared with the supine position[22]. Unlike many previous trials, the PROSEVA trial included only patients with moderate or severe ARDS ($\text{PaO}_2/\text{FiO}_2 < 150 \text{ mmHg}$), using prone position early in the treatment process, requiring patients to maintain a prone position for at least 16 h a day, customizing a rehabilitation plan for the patient, and using low tidal volume ventilation, which are potential necessary conditions for achieving the final therapeutic effect 3[23]. Therefore, most recommendations now require patients with severe ARDS to be treated in the prone position for a long time[24].

Table 3 Differences in hemodynamic indices of patients in each group on the first day after ventilation

| Group | HR (time/min) | MAP (mmHg) | CVP (cmH ₂ O) | LVEF (%) |
|---|---------------|--------------|--------------------------|--------------|
| Conventional treatment group (<i>n</i> = 55) | 95.60 ± 10.31 | 89.11 ± 5.67 | 8.87 ± 1.92 | 44.32 ± 1.35 |
| Prone position ventilation treatment group (<i>n</i> = 47) | 97.82 ± 12.51 | 90.50 ± 5.72 | 9.17 ± 2.32 | 44.30 ± 1.30 |
| <i>t</i> value | 0.983 | 1.229 | 0.715 | 0.076 |
| <i>P</i> value | 0.328 | 0.222 | 0.477 | 0.940 |

HR: Heart rate; MAP: mean arterial pressure; CVP: Central venous pressure; LVEF: Left ventricular ejection fraction.

Table 4 Differences in mechanical ventilation time and intensive care unit stay in patients in each group (d)

| Group | Mechanical ventilation time | ICU hospitalization |
|---|-----------------------------|---------------------|
| Conventional treatment group (<i>n</i> = 55) | 24.38 ± 7.95 | 30.02 ± 9.75 |
| Prone position ventilation treatment group (<i>n</i> = 47) | 23.88 ± 7.02 | 28.45 ± 8.23 |
| <i>t</i> value | 0.334 | 0.870 |
| <i>P</i> value | 0.739 | 0.386 |

ICU: Intensive care unit.

Table 5 Differences in inflammatory factors (ug/L) in patients of each group before and after ventilation

| Group | CRP (mg/L) | PCT (ug/L) | IL-6 (ug/L) |
|---|--------------|--------------|--------------|
| Conventional treatment group (<i>n</i> = 55) | 12.92 ± 1.06 | 20.85 ± 2.21 | 76.29 ± 3.75 |
| Prone position ventilation treatment group (<i>n</i> = 47) | 12.80 ± 1.01 | 20.80 ± 2.25 | 76.25 ± 2.26 |
| <i>t</i> value | 0.582 | 0.113 | 0.064 |
| <i>P</i> value | 0.562 | 0.910 | 0.949 |

CRP: C-reactive protein; PCT: Procalcitonin; IL-6: Interleukin-6.

Table 6 Difference in death rate on day 28 and day 90 for patients in each group, *n* (%)

| Group | Day 28 mortality | Day 90 mortality |
|---|------------------|------------------|
| Conventional treatment group (<i>n</i> = 55) | 16 (29.09) | 25 (45.45) |
| Prone position ventilation treatment group (<i>n</i> = 47) | 6 (12.77) | 12 (25.53) |
| χ^2 value | 3.993 | 4.352 |
| <i>P</i> value | 0.046 | 0.037 |

CONCLUSION

Prone position ventilation in patients with ARDS caused by sepsis can improve respiratory mechanics and reduce patient mortality on the first day after ventilation and does not cause significant fluctuations in patients' hemodynamic indicators and inflammatory factor levels, thus playing an important role in ARDS treatment.

ARTICLE HIGHLIGHTS

Research background

Previous studies have shown prone position ventilation (PPV) to be associated with improvement in oxygenation. However, its role in patients with acute respiratory distress syndrome (ARDS) caused by sepsis remains unknown.

Research motivation

This study analyzed the clinical effects of PPV in patients with ARDS caused by sepsis.

Research objectives

The study aimed to investigate whether PPV treatment can significantly improve patients' heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), left ventricular ejection fraction (LVEF), mechanical ventilation time and intensive care unit (ICU) stay. And reduced post-ventilation C-reactive protein (CRP), procalcitonin (PCT) and interleukin-6 (IL-6) Levels and mortality.

Research methods

All enrolled patients received a lung-protective ventilation treatment strategy. The patients were divided into a control group ($n = 55$) (undergoing routine treatment) and prone position ventilation treatment group ($n = 47$) based on their positions during mechanical ventilation. Patients in the control group were treated with mechanical ventilation in the supine position combined with the lung-protective ventilation strategy while patients in the prone position ventilation treatment group were treated with prone position ventilation combined with the lung-protective ventilation strategy. HR, MAP, and CVP measurements were required for hemodynamic monitoring of arterial and central venous catheterization. The length of mechanical ventilation time and ICU stay, and levels of CRP, PCT, and IL-6 after ventilation. Finally, mortality rate was also compared between the two groups.

Research results

On the first day after ventilation, the oxygenation index and Cst were higher and Pplat level was lower in the PPV group than in the conventional treatment group. There were no significant differences in oxygenation index, Cst, and Pplat levels between the two groups on the 2nd, 4th, and 7th day after ventilation. There were no significant differences in HR, MAP, CVP, LVEF, duration of mechanical ventilation and ICU stay, and the levels of CRP, PCT, and IL-6 between the two groups on the first day after ventilation. There were significant differences on days 28 and 90 mortality in the PPV and control groups.

Research conclusions

Finally, PPV was not shown to cause any adverse effects on hemodynamics and inflammation indices.

Research perspectives

We will continue to investigate the improvement effect of prone position ventilation on other pulmonary function diseases.

FOOTNOTES

Author contributions: Xia WH and Li QG designed this retrospective study, Xia WH and Yang CL wrote the manuscript; Xia WH, Yang CL, Chen Z, Ouyang CH and Ouyang GQ were responsible for sorting the data.

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