Effect of enteral nutrition support combined with prone mechanical ventilation on CRP and PCT levels in patients with severe pneumonia

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Abstract:	Objective: This study is intended to investigate the efficacy of enteral nutrition support combined with prone mechanical ventilation in patients with severe pneumonia. Methods: Fifty-five patients with severe pneumonia were enrolled and allocated into a control group (n = 35), receiving conventional mechanical ventilation combined with early enteral nutrition support, and an observation group (n = 20), receiving prone mechanical ventilation combined with early enteral nutrition support. The intervention lasted one week. Changes in blood gas indicators were compared before and after the intervention. Improvement in nutritional status and inflammatory indicators, including serum prealbumin (PAB), albumin (ALB), haemoglobin (HGB) and C-reactive protein (CRP), and procalcitonin (PCT), before and after the intervention were compared. The incidence of adverse events during the intervention was compared between the two groups. Results: After the intervention, both groups showed improved PaO_2, SpO_2, and PaO_2/FiO_2 levels and decreased $PaCO_2$ levels, with greater improvement observed in the observation group. Nutritional indicators (PAB, ALB, and HGB) improved noticeably in the observation group. CRP and PCT levels were reduced in both groups, with the observation group demonstrating lower levels. The incidence of adverse events was greatly lower in the observation group (15.00%) compared to the control group (42.86%). Conclusion: Enteral nutrition support combined with prone mechanical ventilation reduces adverse events, enhances respiratory function, improves nutritional status, and effectively controls the inflammatory response, contributing to patient recovery.

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Running title: Enteral nutrition & prone mechanical ventilation

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Abstract

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Methods: Fifty-five patients with severe pneumonia were enrolled and allocated into a control group (n = 35), receiving conventional mechanical ventilation combined with early enteral nutrition support, and an observation group (n = 20), receiving prone mechanical ventilation combined with early enteral nutrition support. The intervention lasted one week. Changes in blood gas indicators were compared before and after the intervention. Improvement in nutritional status and inflammatory indicators, including serum prealbumin (PAB), albumin (ALB), haemoglobin (HGB) and C-reactive protein (CRP), and procalcitonin (PCT), before and after the intervention were compared. The incidence of adverse events during the intervention was compared between the two groups.

Results: After the intervention, both groups showed improved PaO_2, SpO_2, and PaO_2/FiO_2 levels and decreased $PaCO_2$ levels, with greater improvement observed in the observation group. Nutritional indicators (PAB, ALB, and HGB) improved noticeably in the observation group. CRP and PCT levels were reduced in both groups, with the observation group demonstrating lower levels. The incidence of adverse events was greatly lower in the observation group (15.00%) compared to the control group (42.86%).

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Keywords: Severe pneumonia; Enteral nutrition support; Prone mechanical ventilation; Nutritional status; Inflammation; Adverse events

Introduction

Severe pneumonia remains a critical condition with high morbidity and mortality rates worldwide, posing a great challenge to healthcare systems [1]. Characterized by acute respiratory distress, systemic inflammatory responses, and organ dysfunction, severe pneumonia requires timely and effective intervention to prevent disease progression and improve patient outcomes [2]. Mechanical ventilation is a cornerstone in managing respiratory failure in such cases, ensuring adequate oxygenation and ventilation [3]. Mechanical ventilation entails utilizing a machine to facilitate a patient's breathing process, which involves delivering oxygen into the lungs and eliminating carbon dioxide from them [4]. However, conventional supine mechanical ventilation has limitations, including uneven alveolar ventilation, secretion retention, and increased ventilation-perfusion mismatch. These factors may compromise the efficacy of treatment and contribute to prolonged recovery times.

Prone mechanical ventilation has emerged as an alternative approach, offering distinct advantages in managing acute respiratory distress syndrome and severe pneumonia. By redistributing lung stress and strain, prone positioning facilitates alveolar recruitment, improves gas exchange, and enhances oxygenation [5]. This technique also reduces dorsal lung collapse and overinflation in ventral regions, promoting a more homogenous ventilation pattern [6]. Consequently, prone mechanical ventilation has gained recognition as a vital strategy for improving respiratory function in critically ill patients. In addition to respiratory management, nutritional support is increasingly emphasized in the treatment of severe pneumonia [7]. Malnutrition and metabolic disturbances are common in critically ill patients and can exacerbate the inflammatory response, impair immune function, and hinder recovery. Early enteral nutrition support has proven effective in decreasing complications, shortening hospital length of stay, and improving prognosis at the time of discharge [8]. Compared to parenteral nutrition, enteral feeding maintains gut mucosal function and supports the systemic immune response, making it the preferred method for nutritional support in critically ill patients [9].

Despite the benefits of prone ventilation and enteral nutrition support individually [10, 11], their combined effects on severe pneumonia have not been extensively studied. The integration of these two interventions could potentially address the dual challenges of respiratory compromise and systemic inflammation more effectively. This study aims to evaluate the synergistic effects of prone mechanical ventilation and enteral nutrition support in patients with severe pneumonia. By analyzing changes in respiratory parameters, nutritional indices, inflammatory markers, and adverse reaction rates, this research seeks to provide robust evidence for the clinical utility of this combined therapeutic strategy.

Materials and methods

Ethics statement

The study was approved by the Institutional Review Board of First People's Hospital of Linping District and written informed consent was obtained from all patients.

Study population

Fifty-five patients with severe pneumonia admitted to First People's Hospital of Linping District from August 2019 to December 2023 were included. Patients were assigned to a control group (n = 35) receiving conventional mechanical ventilation combined with early enteral nutrition support, or an observation group (n = 20) receiving prone mechanical ventilation combined with early enteral nutrition support.

Inclusion criteria

Patients were included in the study if they (1) were diagnosed with severe pneumonia based on laboratory test results, imaging studies such as X-rays and CT scans, and clinical examinations; (2) were assessed as having high nutritional risk upon admission using a nutritional risk screening; and (3) had stable vital signs and no barriers to communication.

Exclusion criteria

Patients were excluded from the study if they (1) had comorbid pulmonary organic diseases such as tuberculosis or malignancies; (2) had impaired gastrointestinal function; (3) had severe cardiac, hepatic, or renal diseases or dysfunctions; (4) were unable to adopt the prone position due to conditions such as cerebral hemorrhage or pneumothorax; or (5) were intolerant to enteral nutrition.

Treatment methods

All patients received routine examination and internal medicine care, the patient's condition changes and basic vital signs, whether there was any damage to the digestive, nervous, circulatory and other systems were closely observed, and the physician was immediately reported if the patient was found to have a grey face, dyspnea, breathlessness and other conditions. The patient should be helped to clean up respiratory secretions, and give nebulised sputum suction if necessary to keep the respiratory tract open. At the same time, the patient's family members were given health education, explaining the mechanism of severe pneumonia, common complications and related nursing measures.

The control group was given conventional mechanical ventilation combined with early enteral nutrition support. Patients were mechanically ventilated in the supine position, with ventilation parameters of 40%-50% H_2O, respiratory pressure of 15-30 cmH_2O, and end-expiratory positive pressure ventilation of 5-15 cmH_2O. Enteral nutritional support was initiated 24 hours after the patients were mechanically ventilated: nutritional risk screening was used to assess the nutritional status of the patients, and individualized nutritional programmes were formulated. Whole-protein enteral nutrition solution (Newdia Pharmaceutical Co., Ltd., National Drug Code H20130888) was used with a calorie supply of 20-25 kCal/(kg-d). The enteral nutrition suspension was heated and kept at a constant temperature (about 37℃), and the enteral nutrition suspension was infused through the nasogastric tube, 250 mL each time, with a daily dose of 1000-1250 mL.The starting rate of infusion was 10-20 mL/h, and the drip rate should be slow at the beginning, and the volume of infusion was gradually increased according to the tolerance of enteral nutrition, so as to satisfy the body's demand for nutrients. Intervention was given for 1 week.

The observation group was given prone position mechanical ventilation combined with early enteral nutrition support. Firstly, the patient's mouth, nose and airway secretions were suctioned, and then 4 healthcare workers divided the work into co-operation, 1 healthcare worker was at the head of the bed to fix the head and the tubes, 2 healthcare workers were located beside the patient, and 1 healthcare worker was in charge of helping the other staffs to complete the various operations. One healthcare worker initiated the command to lift the patient up and move him/her to the side of the bed, and at this time the patient was changed from the prone position to the lateral position, and then the patient was turned over and placed on a special sponge mattress made by the hospital. The patient was turned over and placed on a special sponge cushion for the prone position, a concave pillow was placed under the patient's head, and all parts of the patient’s body were placed in the comfortable position or the functional position. Patients were instructed to hold their hands vertically on both sides of the body, check the smoothness of the tubes, dislodgement, and tidy up the tubes. For patients with irritability, sedation and analgesia should be provided as appropriate to avoid extubation. During mechanical ventilation in the prone position, patients were routinely given vibration sputum expectoration or knocking back to expel sputum, and intermittently massaging the skin of the vulnerable position. The patient's heart rate, blood pressure and transcutaneous oxygen saturation were continuously monitored. If no abnormality occurs, the electrocardiogram electrodes and wires can be placed on the patient's back. The specific methods of early enteral nutritional support remained the same as the control group. Intervention was given for 1 week.

Observation indicators

Changes in blood gas indicators before and after intervention were compared, including arterial partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), blood oxygen saturation (SpO_2) and other indicators, and calculate the oxygenation index (PaO_2/FiO_2)

Improvement of nutritional status and inflammatory indices before and after the intervention was compared. Fasting venous blood (5 mL) was collected from patients, centrifuged at 3500 r/min, and the supernatant was taken after 10 minutes for biochemical tests. The main indicators of nutritional status included serum prealbumin (PAB), albumin (ALB) and haemoglobin (HGB), which were measured by fully automatic biochemical analyzer. The main indicators of inflammation included C-reactive protein (CRP) and procalcitonin (PCT), which were measured by enzyme-linked immunosorbent assay (ELISA) and immunochemiluminescent assay (ICA), respectively. The reagent kits were purchased from mlbio (Shanghai, China), and the experimental operation was implemented in strict accordance with the reagent instructions.

The incidence of adverse events during the intervention was compared between the two groups, including agitation, tracheospasm, and ventilator-associated lung injury, as well as symptoms of intolerance to enteral nutrition, vomiting, bloating, diarrhoea, and gastric retention.

Statistics

GraphPad Prism 8.0 software (Graph Pad Inc., La Jolla, CA, USA) was applied for data processing, and the statistical description of the measurement data was performed using the median (Q1,Q3), and the Mann-Whitney U test was used for comparison between groups. Categorical data were expressed as (%) and the χ^2 test was used. The test level was $\alpha = 0.05$, and $P < 0.05$ was considered a statistically meaningful difference.

Results

General information

No significant differences were observed between groups in terms of gender, age, weight, pathogen type, or disease duration ($P > 0.05$) (Table 1).

Changes in blood gas indicators before and after intervention

Compared with pre-intervention, PaO_2, SpO_2 and PaO_2/FiO_2 increased and $PaCO_2$ decreased in both groups, and PaO_2, SpO_2 and PaO_2/FiO_2 were higher and $PaCO_2$ was lower in the observation group than in the control group after intervention ($P < 0.05$). It is suggested that enteral nutrition support combined with prone mechanical ventilation has an important role in promoting respiratory function in patients with severe pneumonia (Table 2).

Nutritional statu before and after intervention

After intervention, PAB, ALB and HGB were higher than before intervention in both groups, and the observation group exhibtied higher levels compared to the control group ($P < 0.05$). It is suggested that enteral nutrition support combined with prone position mechanical ventilation is beneficial to improve the nutritional status of patients with severe pneumonia (Table 3).

Improvement of inflammatory indicators before and after intervention

CRP and PCT were reduced in both groups after intervention, and the levels of CRP and PCT in the observation group were lower than those in the control group after intervention ($P < 0.05$). It is suggested that enteral nutrition support combined with prone position mechanical ventilation is more favorable to control the inflammatory response of patients with severe pneumonia (Table 4).

Incidence of adverse reactions

The incidence of adverse reactions in the observation group (15.00%) was significantly lower than that in the control group (42.86%) ($P < 0.05$). It suggests that the safety of the clinical application of enteral nutrition support combined with prone position mechanical ventilation therapy is better (Table 5).

Discussion

Despite all modern advancements, pneumonia continues to be a prevalent infection with significant morbidity and mortality [12]. Patients with severe pneumonia may develop severe hypoxaemia, acute respiratory distress syndrome (ARDS) or even death [13], which requires mechanical ventilation. Prone positioning is among the limited number of measures that have shown an effect on patient outcomes, resulting in a substantial decrease in the mortality rate of patients with ARDS who are on mechanical ventilation [14]. Some patients with severe pneumonia are malnourished, therefore, nutritional support is necessary for them. This study is conducted to investigate the combined efficacy of prone mechanical ventilation and enteral nutritional support in patients with severe pneumonia.

Improved respiratory outcomes were a notable finding, with the observation group showing significant increases in PaO_2, SpO_2, and PaO_2/FiO_2, alongside reductions in $PaCO_2$. These improvements underscore the effectiveness of prone positioning in enhancing alveolar recruitment and reducing ventilation-perfusion mismatch, which has been shown in a previous research [15]. Evidence has been shown in a previous study that prone position ventilation typically results in a noticeable enhancement of arterial blood gases, primarily attributed to improved overall ventilation/perfusion matching [16]. Nutritional improvements further supported the efficacy of the combined intervention. Post-intervention levels of PAB, ALB, and HGB were higher in the observation group, indicating the critical role of enteral nutrition support in meeting metabolic demands and preventing malnutrition. By providing essential proteins, calories, and micronutrients, enteral feeding supports cellular repair, enhances immune function, and mitigates catabolic stress. These effects are particularly important in severe pneumonia, where systemic inflammation and metabolic dysregulation often lead to rapid nutritional depletion [17].

The reduction in inflammatory markers observed in the observation group provides additional evidence of the combined strategy's benefits. CRP and PCT levels, both key indicators of systemic inflammation [18, 19], were markedly lower post-intervention in the observation group. This suggests that the integrated approach not only reduces lung inflammation but also mitigates the systemic inflammatory cascade. Actually, a retrospective study has indicated that prone position mechanical ventilation reduces systemic inflammation by finding that there is a steadily decreased plasma IL-6 concentrations (a marker of systemic inflammation) in the prone group, suggesting a close relationship between systemic inflammation and prone ventilation [10]. Enteral nutrition likely contributes to this effect by preserving gut integrity, preventing bacterial translocation, and modulating immune responses [20]. Combined with the improved oxygenation achieved through prone ventilation, this dual approach addresses both local and systemic contributors to disease progression.

The safety profile of the combined intervention was also favorable, with the observation group experiencing fewer adverse reactions compared to the control group. The lower incidence of complications such as restlessness, breathing convulsions, ventilator-associated lung injury and gastric retention reflects the feasibility and practicality of the integrated approach. The reason for less adverse reactions might be that prone positioning minimizes the disparity between dorsal and ventral transpulmonary pressures, resulting in more uniform ventilation and subsequently reducing ventral alveolar overinflation and dorsal alveolar collapse [21]. These findings are particularly relevant for clinical practice, where minimizing complications is essential for improving patient outcomes and reducing healthcare burdens.

In conclusion, this study demonstrate that the combination of prone mechanical ventilation and early enteral nutrition support greatly improves respiratory function, nutritional status, and inflammatory responses in patients with severe pneumonia. By simultaneously addressing respiratory and metabolic challenges, this integrated approach demonstrates significant advantages over standard care. These findings highlight the clinical potential of an integrated approach in managing critically ill patients with complex needs. Despite its promising results, this study has limitations that warrant consideration. The relatively small sample size and single-center design may limit the generalizability of the findings. Future research should focus on multi-center, randomized controlled trials with larger cohorts to validate these results.

Declaration

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Conflict of interest

The authors declare that they have no conflicts of interest.

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Table 1 Comparison of clinical indicators between the two groups of patients

Indicators	Control group (n = 35)	Observation group (n = 20)	*P*
Gender			0.775
Male	20 (57.14%)	13 (65.00%)	
Female	15 (42.86%)	7 (35.00%)	
Age (year)	51.0 (49.0,55.0)	50.0 (49.0,52.3)	0.390
Weight (kg)	70.8 (67.3,75.6)	71.6 (69.8,75.1)	0.643
Pathogen type			0.801
Gram-positive bacteria	15 (42.86%)	7 (35.00%)	
Gram-negative bacteria	16 (45.71%)	11 (55.00%)	
Fungus	4 (11.43%)	2 (10.00%)	
Duration of disease (day)	10.0 (8.5,12.0)	11.0 (10.0,12.0)	0.443

Table 2 Changes in blood gas indicators before and after intervention in two groups of patients

Groups	PaO_2 (mmHg)		$PaCO_2$ (mmHg)	
	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 35)	56.0 (54.0,60.0)	89.0 (85.5,93.0)*	55.0 (52.5,58.0)	46.0 (44.5,49.0)*
Observation group (n = 20)	56.5 (55.0,59.0)	95.0 (93.8,98.3)*	55.0 (54.0,58.0)	41.0 (40.0,43.0)*
P	0.893	< 0.001	0.705	< 0.001

Groups	SpO_2 (%)		PaO_2/FiO_2 (mmHg)	
	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 35)	88.0 (83.5,92.0)	92.0 (88.0,96.5)*	187.8 (179.6,198.9)	296.1 (284.9,311.2)*
Observation group (n = 20)	88.0 (86.0,91.3)	95.0 (93.8,99.0)*	188.6 (184.4,197.2)	324.7 (318.8,337.0)*
P	0.771	0.012	0.832	< 0.001

Note: *$P < 0.05$ vs the same group before intervention.

Table 3 Comparison of the nutritional status two groups of patients before and after intervention

Groups	PAB (g/L)		ALB (g/L)		HGB (g/L)	
	Before intervention	After intervention	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 35)	171.3 (164.3,180.8)	183.4 (176.2,193.2)*	32.6 (30.8,35.0)	35.8 (34.1,38.0)*	91.7 (88.4，96.3)	97.7 (93.8,102.9)*
Observation group (n = 20)	171.5 (168.0,178.9)	203.9 (198.3,215.4)*	31.5 (30.7,33.1)	39.0 (38.0,41.2)*	92.6 (90.9,95.9)	104.8 (102.9,108.7)*
P	0.969	< 0.001	0.242	< 0.001	0.570	< 0.001

Note: *$P < 0.05$ vs the same group before intervention.

Table 4 Improvement of inflammatory indicators before and after intervention in both groups of patients

Groups	CRP (mg/L)		PCT (ng/L)	
	Before intervention	After intervention	Before intervention	After intervention
Control group (n = 35)	101.0 (93.8,110.7)	85.3 (81.0，91.05)*	4.8 (4.3,5.6)	3.3 (3.0,3.9)*
Observation group (n = 20)	102.4 (98.8,109.8)	72.4 (70.7,76.1)*	4.7 (4.5,5.2)	2.5 (2.3,2.7)*
P	0.661	< 0.001	0.512	< 0.001

Note: *P < 0.05 vs the same group before intervention.

Table 5 Comparison of the incidence of adverse reactions between the two groups of patients

Groups	Restlessness	Breathing convulsions	Ventilator-associated lung injury	Vomiting	Bloating and diarrhoea	Gastric retention	Incidence
Control group (n = 35)	3 (8.57%)	2 (5.71%)	1 (2.86%)	4 (11.43%)	3 (8.57%)	2 (5.71%)	15 (42.86%)
Observation group (n = 20)	1 (5.00%)	0 (0.00%)	0 (0.00%)	1 (5.00%)	1 (5.00%)	0 (0.00%)	3 (15.00%)
P							0.041