Research Paper

Efficacy of Naloxone in Conjunction with Non-Invasive Ventilation in Managing Acute Exacerbation of Chronic Obstructive Pulmonary Disease with Type II Respiratory Failure

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The focus of this research was to investigate the efficacy of using naloxone in conjunction with non-invasive ventilation for managing type II respiratory failure in acute exacerbations of chronic obstructive pulmonary disease. The scope of this retrospective study encompassed the admission of 50 individuals with acute exacerbation of chronic obstructive pulmonary disease and type II respiratory failure to our hospital between January 2019 and December 2022. 25 patients were assigned to both the control group and the observation group. The former was subjected to non-invasive ventilation, whereas the latter received a combination of naloxone and non-invasive ventilation. Comparison was made between the two groups in terms of clinical efficacy, alterations in clinical symptoms, blood gas analysis, and follow-up. The total effective rate for the observation group reached 96.00 %, markedly exceeding the 68.00 % achieved in the control group, with a remarkable variance between the two ($p<0.05$). Post-treatment, the observation group displayed notable enhancements in respiratory rate, dyspnea score, heart rate, and other parameters, with more evident improvements compared to the control group ($p<0.05$). Additionally, there were marked enhancements in blood gas analysis parameters (pH, partial pressure of carbon dioxide, partial pressure of oxygen, and oxygen saturation) observed in the observation group, surpassing the improvements in the control group ($p<0.05$). Both groups encountered adverse effects such as dry mouth, nausea, stomach bloating, and restlessness, yet there was no noteworthy distinction in the comprehensive occurrence of unfavorable reactions between the groups ($p>0.05$). The conjunction of naloxone and non-invasive ventilation significantly ameliorated the clinical effectiveness of patients dealing with acute chronic obstructive pulmonary disease exacerbations and type II respiratory failure, relieving symptoms and enhancing oxygenation status, resulting in improved long-term results. Although this treatment regimen indicates a level of safety and viability, further research and extensive randomized controlled trials are required to authenticate its long-term effectiveness and safety.

Key words: Naloxone, non-invasive ventilation, chronic obstructive pulmonary disease, respiratory failure, efficacy

With substantial health ramifications and a global burden, Chronic Obstructive Pulmonary Disease (COPD) is a highly prevalent respiratory condition[1,2]. As the ailment advances, it commonly culminates in type II respiratory failure and frequently precipitates Acute Exacerbations of COPD (AECOPD)[3,4].

Widely utilized in managing AECOPD with type II respiratory failure, non-invasive ventilation administers positive airway pressure to enhance overall ventilation[5,6]. Yet, non-invasive ventilation may not elicit a favorable response in certain instances, possibly as a consequence of respiratory depression triggered by factors like cough suppressants[7]. Utilized as an opioid receptor antagonist, naloxone has been utilized to alleviate respiratory depression elicited by opioids and

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sedatives[8,9]. According to recent studies, naloxone might also have a positive impact on the respiratory function of individuals with obstructive respiratory diseases[10].

Yet, additional research and exploration are required to study the efficacy of pairing naloxone with non-invasive ventilation in addressing acute exacerbation of COPD with type II respiratory failure. As such, this study seeks to evaluate the effectiveness of melding naloxone with non-invasive ventilation for treating AECOPD with type II respiratory failure, presenting practicality and effectiveness guidance for clinical application. This has the potential to enhance patient's oxygenation, alleviate symptoms, shorten hospital stays, decrease complications, and improve treatment success rates and quality of life.

MATERIALS AND METHODS

General information:

We conducted a retrospective investigation and selected 50 individuals with AECOPD complicated by type II respiratory failure, who received treatment at our hospital from September 2019 to September 2022. Twenty-five individuals were allocated to both the control and observation groups. The control group included 12 male and 13 female individuals, aged between 55 and 79, with an average age of (66.35±4.05) y. In contrast, the observation group comprised 13 male and 12 female participants, aged between 56 y and 77 y, with an average age of (66.45±4.00) y. Between the two groups, the comparison of general information revealed no statistically significant distinctions ($p>0.05$), indicating comparable characteristics.

Inclusion criteria: Compliance with the diagnostic guidelines prescribed in the "Guidelines for the Diagnosis and Treatment of COPD (revised in 2021)"[11]; Partial pressure of oxygen (PaO_2) <60 mmHg and Partial Pressure of Arterial Carbon Dioxide ($PaCO_2$) >50 mmHg and Voluntary agreement to participate in the study and signing an informed consent form were included.

Exclusion criteria: Severe renal dysfunction and respiratory suppression; occurrence of congestive heart failure, and related factors; exclusion of individuals with mental disorders and inability to tolerate face masks were excluded.

Methods:

Upon admission, patients receive treatment consisting of antispasmodic and anti-asthmatic therapy, antimicrobial treatment, and active sputum removal to ensure that their airways remain unobstructed. Furthermore, low-flow continuous oxygen therapy *via* nasal cannula, diuretic therapy, and measures to support cardiac function are administered. This aids in rectifying the body's acid-base equilibrium and electrolyte imbalances, and involves guiding patients in scientifically valid respiratory function exercises.

The Philips (Respironics) V60 ventilator is utilized in synchronized bi-level positive airway pressure mode within the control group (non-invasive ventilation). Initially, the inspiratory pressure is calibrated to 4-8 cm Water (H_2O), subsequently being finely adjusted according to the patient's capacity, degree of respiratory distress, and respiratory rate, to a target range of 3-6 cm H_2O, ensuring a controlled respiratory rate of 14-20 breaths/min. Continuous low-flow oxygen therapy is instituted for the patients, with oxygen administered every 6 h, three times a day.

The ventilator used in the observation group (non-invasive ventilation+naloxone) mirrors the one utilized in the control group. Moreover, patients are administered naloxone hydrochloride injection. The initial dose comprises the addition of 0.8-3.2 mg of naloxone hydrochloride injection into 20 ml of normal saline, and is delivered intravenously *via* an infusion pump for a period exceeding 24 h, depending on the patient's clinical condition. Each subsequent dose is 0.4 mg, given two times a day, for a period of 3-5 d, with a total of two courses administered.

Observational indicators:

Clinical efficacy, clinical symptoms, lung function, blood gas analysis, and follow-up outcomes are all subjects for comparison. In clinical efficacy; following 24 h under treatment, the patient experiences the disappearance of asthma, chest tightness, and cough symptoms, along with a significant reduction in pulmonary edema and rales, an improvement in blood gas parameters, and a lowered heart rate, signifying marked improvement. Meeting the effectiveness criteria after 72 h of treatment would indicate an improvement. However, after 72 h of treatment, there is no significant improvement in symptoms such as asthma, chest tightness, and cough, persisting rales in the lungs, no enhancement in blood gas parameters, and an elevated heart rate, suggesting ineffectiveness[12]. Clinical symptom indicators such

as respiratory rate, dyspnea score, heart rate; blood gas analysis indicators including pH, $PaCO_2$, PaO_2, and Oxygen Saturation (SpO_2); follow-up indicators such as subsequent treatment situations, including endotracheal intubation and acute exacerbation of COPD within 6 mo and adverse reactions.

Statistical analysis:

Utilizing the Statistical Package for the Social Sciences (SPSS) 25.0 statistical software, the analysis was performed. By utilizing an independent sample t-test, a comparison between the two groups was performed using the measurement data presented as mean±standard deviation. Utilizing the Chi-square (χ^2) test, the count data were analyzed. The criteria for establishing statistical significance were defined at a level of $p<0.05$.

RESULTS AND DISCUSSION

The overall effective rate in the observation group reached 96.00 %, contrasting with 68.00 % in the control group, and demonstrating a statistically notable disparity ($p<0.05$) as shown in Table 1.

Post-treatment, both groups demonstrated marked improvements in respiratory rate, dyspnea score, and heart rate, with the observation group displaying more pronounced enhancements ($p<0.05$) as shown in Table 2.

After the intervention, both groups experienced remarkable improvements in pH, $PaCO_2$, PaO_2, and SpO_2, with more marked enhancements observed in the observation group ($p<0.05$) as shown in Table 3.

The observation group showed noticeably reduced rates of endotracheal intubation and acute exacerbations of COPD within 6 mo in comparison to the control group ($p<0.05$) as shown in Table 4.

Both groups encountered adverse effects, including dry mouth, nausea, gastrointestinal distention, and restlessness, with no substantial difference in the overall occurrence of adverse reactions ($p>0.05$) as shown in Table 5.

TABLE 1: CURATIVE EFFECT

Group (n=25)	Marked improvement	Improvement	Ineffectiveness	Overall effective rate
Observation	7 (28.00)	17 (68.00)	1 (4.00)	24 (96.00)
Control	5 (20.00)	12 (48.00)	8 (32.00)	17 (68.00)
χ^2				6.640
p				0.010

TABLE 2: CLINICAL SYMPTOMS

Group (n=25)	RR (min^{-1})		Dyspnea score (points)		HR (min^{-1})	
	Before	After	Before	After	Before	After
Observation	26.08±1.75	18.48±1.39*	3.12±0.67	2.40±0.50*	124.08±11.49	83.52±7.62*
Control	26.28±1.67	19.72±1.40*	2.96±0.73	2.80±0.58*	123.80±12.03	98.68±10.48*
t	0.413	3.145	-0.807	2.619	-0.084	5.851
p	0.682	0.003	0.424	0.012	0.933	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 3: BLOOD GAS ANALYSIS

Group (n=25)	pH		$PaCO_2$ (mmHg)		PaO_2 (mmHg)		SpO_2 (%)	
	Before	After	Before	After	Before	After	Before	After
Observation	7.30±0.07	7.37±0.05*	56.19±4.38	47.97±4.54*	49.71±5.15	70.48±5.89*	80.74±4.03	95.24±3.99*
Control	7.30±0.06	7.31±0.07*	55.57±5.07	51.19±5.16*	48.70±4.45	63.21±6.15*	81.35±3.25	88.90±4.54*
t	-0.044	-3.766	-0.464	2.346	-0.744	-4.268	0.583	-5.238
p	0.965	0.000	0.645	0.023	0.461	0.000	0.562	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 4: FOLLOW-UP INDICATORS n (%)

Group (n=25)	Tracheal intubation	Acute exacerbation within 6 mo
Observation	2 (8.00)	5 (20.00)
Control	6 (24.00)	14 (56.00)
χ^2	4.153	5.556
p	0.042	0.018

TABLE 5: ADVERSE REACTIONS n (%)

Group (n=25)	Dry mouth	Nausea	Flatulence	Be on edge	Overall incidence
Observation	1 (4.00)	2 (8.00)	1 (4.00)	2 (8.00)	6 (24.00)
Control	1 (4.00)	1 (4.00)	2 (8.00)	1 (4.00)	5 (20.00)
χ^2					0.117
p					0.733

AECOPD treatment is extended, leading to a gradual decrease in the patient's immune system function and contributing to significant impairment in nutritional support. Consequently, patients frequently present with clinical symptoms such as malnutrition, respiratory discomfort, and fatigue, which contribute to a progressive decline in their ventilator capacity, inadequate oxygen intake, and substantial carbon dioxide retention, ultimately resulting in type II respiratory failure. The prevalent focus of respiratory machine therapy for this condition is currently the improvement of respiratory function, correction of hypoxemia and hypercapnia, alleviation of respiratory conditions, and relief of hypoxia[13,14]. Nevertheless, traditional invasive respiratory machine therapy can result in significant harm and heightened risk of complications, ultimately substantially increasing the risk of patient mortality.

Non-invasive ventilation has found extensive application in managing respiratory system illnesses, effectively minimizing harm to the patient's airways. Furthermore, patients can partake in eating and conversing to the extent compatible with their condition. Nevertheless, the prolonged application of non-invasive ventilation might lead to a decline in respiratory center function and the potential for inducing respiratory suppression, hence requiring intervention with naloxone. Naloxone, functioning as an opioid receptor antagonist, can stimulate the respiratory center, increase respiration, enhance blood flow, and boost tissue oxygenation, all of which significantly contribute to protecting cerebral and myocardial tissues[15].

This study aimed to evaluate how well naloxone, when combined with non-invasive ventilation, works in treating AECOPD complicated by type II respiratory failure. The study results revealed that the total effective rate in the observation group, which received a combination of naloxone and non-invasive ventilation, was 96.00 %, markedly surpassing the 68.00 % rate in the control group ($p<0.05$). Post-treatment, the observation group demonstrated significant enhancements in respiratory rate, dyspnea score, and heart rate, with more marked improvements compared to the control group ($p<0.05$), underscoring the effective alleviation of breathing difficulty in patients with naloxone combined with non-invasive ventilation treatment. Additionally, the observation group exhibited noteworthy enhancements in blood gas analysis parameters (pH, $PaCO_2$, PaO_2, and SpO_2) compared to the control group, with lesser advancements observed in the latter ($p<0.05$). This indicates that the combination of naloxone and non-invasive ventilation treatment can bolster patient oxygenation and acid-base equilibrium, consequently enhancing their physiological function. Crucially, the study also revealed that the observation group had notably reduced rates of endotracheal intubation and acute exacerbation of COPD within 6 mo compared to the control group, indicating that the combination of naloxone and non-invasive ventilation treatment could lead to improved long-term outcomes and prognosis.

Naloxone primarily functions by activating the respiratory centers and counteracting opioid receptors, thereby amplifying the patient's respiratory drive, potentially attenuating the progression of the patient's condition and reducing the necessity for endotracheal intubation. Furthermore, naloxone has the capacity to enhance the patient's ventilatory

function, leading to reduced airway resistance and consequent fewer occurrences of acute exacerbations. Besides, naloxone is non-tolerance forming and exerts minimal impact on the patient's mental and physiological state, indicating a high level of safety[16].

Regarding adverse reactions, both groups encountered side effects such as dry mouth, nausea, gastrointestinal distention, and restlessness, with no substantial disparity in the general occurrence of adverse reactions ($p>0.05$). These outcomes verify the relatively favorable safety profile and reduced incidence of adverse reactions with the combination of naloxone and non-invasive ventilation treatment.

Nonetheless, this study comes with certain limitations. Firstly, being a retrospective study, it carries the risk of recall bias and incomplete information. Secondly, the sample size is relatively small, which might impact the reliability and generalizability of the findings. Consequently, subsequent research should employ larger sample sizes and rigorous randomized controlled designs to validate these results.

To conclude, the combination of naloxone and non-invasive ventilation treatment brings about a substantial enhancement in the clinical efficacy and oxygenation status of individuals with AECOPD complicated by type II respiratory failure. This improvement is critical for boosting the treatment success rate, minimizing the duration of hospitalization and the incidence of complications, and augmenting the quality of life for patients.

Author's contributions:

Jiali Xing and Yan Zhang have contributed equally to this work.

Conflict of interests:

The authors declared no conflict of interests.

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