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Original Research Article

Effectiveness of triple inhalation therapy and non-invasive ventilation in the treatment of acute exacerbated chronic obstructive pulmonary disease

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Abstract

Purpose: *To determine the clinical effectiveness of combining triple inhalation therapy with non-invasive ventilation in treating acute exacerbated chronic obstructive pulmonary disease (AECOPD).*
Methods: *A total of 128 AECOPD patients admitted in the Department of Respiratory Medicine of our Hospital were involved in the study. Two groups of patients were used (64 patients per group). The study group was given triple inhalation therapy and non-invasive ventilation, while only non-invasive ventilation was given to the control group. The curative effects of the two treatments and their effects on arterial Pa_{CO2} (partial pressure of carbon dioxide), pH and Pa_{O2} (partial pressure of oxygen) were determined.*
Results: *The study group showed significantly higher treatment effectiveness than the control group ($p < 0.05$). Post-treatment Pa_{CO2}, pH, Pa_{O2}, respiratory rate and heart rate differed significantly between the two groups ($p < 0.05$). Improvements in the five indices were more in the study group than in the control group ($p < 0.05$).*
Conclusion: *Combining triple inhalation therapy with non-invasive ventilation in the treatment of AECOPD enhances therapeutic effect, improves pulmonary ventilation, and reduces side effects.*

Keywords: *Chronic obstructive pulmonary disease, Acute exacerbation, Triple inhalation, Non-invasive ventilation*

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD**)** is an emphysema and/or chronic bronchitis with airflow obstruction, which can develop into pulmonary heart disease and respiratory failure. The global incidence of COPD in people over 40 years old is 9 to 10 % [1]. Epidemiological studies have revealed that COPD ranks third amongst fatal diseases in China, inferior only to malignant tumors and cerebrovascular diseases [2,3]. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) results in high rate of hospitalization and morbidity, and the disease progresses so quickly during this period that it leads to high mortality rate if not timely treated [4]. The present study investigated the effectiveness of combining triple inhalation

therapy with non-invasive ventilation in the treatment of 128 AECOPD cases.

METHODS

Patient information

A total of 128 AECOPD patients seen in Xuanwu Hospital Capital Medical University from April 2016 to December 2016 were assigned (without bias) to control and observation groups (64 per group). In the study group, there were 33 men and 31 women aged 50 to 81 years (mean = 65 ± 10.5 years), with disease course ranging from 6 to 20 years (mean = 9.9 ±1.5 years). In the control group, there were 35 males and 29 females, aged from 51 to 79 years (mean age = 65 ± 10.6 years), with a disease course of 5 to 21 years (mean = 10.5 ± 2.1 years). There were no significant differences in sex, age, and duration of AECOPD between both groups ($p > 0.05$). All patients signed informed consent.

This research received approval from the Ethical section of Department of Respiratory Medicine, Xuanwu Hospital, Capital Medical University (approval no. 201810306), and was carried out according to the guidelines of Declaration of Helsinki promulgated in 1964 as amended in 1996 [5].

Treatments

The control group underwent non-invasive ventilation. Expiratory pressure was adjusted based on the disease status of each patient, and oxygen flow was set to 3.5 L/min in case of excessive or insufficient oxygen flow. The relevant parameters were gradually and slowly regulated downward after the patients were stable with blood oxygen saturation over 95 %.
Apart from non-invasive ventilation, the observation group was given triple inhalation therapy. The drugs and their applications were: 1 mg budesonide aerosol (AstraZeneca, specifications: 100 whiffs/5 ml, batch no. 227664) *bid* plus 2.5 mg salbutamol aerosol (GlaxoSmithKline, specifications: 100 mg/press, 200 presses, batch no. 970801), *bid*, plus 500 µg Ipratropium bromide aerosol (Boehringer Ingelheim Pharma GmbH & Co. /KG, specifications: 2 ml/ bottle, batch number: R281134), 500 µg, *bid*. The treatment duration for both groups was seven days.

Study indices and criteria for assessment of effectiveness

Arterial blood gas indices of the patients, viz, Pa_{CO2}, pH, and Pa_{O2} were determined before and after treatment, as well as respiratory rate and heart rate. The criteria for assessment of effectiveness were: 1 = marked effect: symptoms and signs like respiratory rate and heart rate subsided and all indices were normal; 2 = effective: symptoms, signs, and indices were improved without adverse reaction; 3 = ineffective: there was no improvement, or there was exacerbation.

Statistical analysis

The software, Epidata 3.03, was used for data entry and logical error correction, while the data were analyzed by SPSS 20.0 software, and are expressed as mean ± standard deviation (SD). Differences were compared using *t*-test. Ranked data were compared with rank sum test. Values of $p < 0.05$ were assumed as indicative of statistical significance of differences.

RESULTS

Clinical effectiveness

Treatment effectiveness was significantly higher in the study group than in the control group ($p < 0.05$, Table 1).

Table 1: Clinical effectiveness data (N = 64)

Group	Markedly effective	Effective	Ineffective	Total effectiveness (%)
Control group	19	28	17	73.44
Study group	23	35	7	90.63[a]

[a]*P < 0.05, compared with control*

Clinical indices

Pre-treatment Pa_{CO2}, pH, Pa_{O2}, respiratory rate, and heart rate in the two groups were comparable ($p > 0.05$). However, post-treatment Pa_{CO2}, pH, Pa_{O2}, respiratory rate, and heart rate differed significantly between the two groups ($p < 0.05$). The study group had higher degrees of improvements in these indices than the control group, as shown in Table 2.

DISCUSSION

Obstructive pulmonary disease (OPD) is characterized by progressive exacerbation of airflow limitation. Exacerbation of airflow limitation may worsen the structural damage to respiratory tract wall and give rise to irreversible airflow limitation and dysfunction in pulmonary

ventilation [6,7]. Clinically, COPD is classified into stable COPD and acute exacerbation of COPD (AECOPD). The clinical features of AECOPD are aggravated expectoration and cough, aggravated polypnea and wheezing, very sticky sputum, and increased sputum volume, all of which worsen the airflow limitation and induce life-threatening dyspnea [9,10]. Medications, controlled oxygen therapy, and ventilation support are used for the treatment of AECOPD.

Table 2: Arterial blood gas, heart rate, and respiratory rate before and after treatment (mean ± SD)

Index	Study group		Control group	
	Pre-treatment	***Post-treatment***	***Pre-treatment***	***Post-treatment***
Pa_{O2}	45.2 ± 5.8*	73.1 ± 8.3$^{*\Delta}$	43.5 ± 6.3	57.7 ± 7.9$^{\Delta}$
Pa_{C02}	68.3 ± 8.7*	43.5 ± 7.1$^{*\Delta}$	65.7 ± 9.7	53.6 ± 6.8$^{\Delta}$
pH	7.15 ± 0.13*	7.41 ± 0.15$^{*\Delta}$	7.16 ± 0.17	7.31 ± 0.21$^{\Delta}$
Heart rate	117.5 ± 15.7*	91.3 ± 10.8$^{*\Delta}$	114.7 ± 12.4	97.7 ± 8.7$^{\Delta}$
Respiratory rate	51.4 ± 6.5*	19.3 ± 5.7$^{*\Delta}$	52.1 ± 7.8	35.5 ± 6.7$^{\Delta}$

$^{*}P > 0.05$, compared with the control group pre-treatment; $^{*}p < 0.05$, compared with control group post-treatment; $^{\Delta}p < 0.05$, compared with itself pre- and post-treatment

Non-invasive ventilation (NIV) method uses a respirator to conduct positive pressure ventilation through mouth or nose mask to connect the patient. The operation is simple in clinical settings: there are no artificial airways, making it readily acceptable to patients, and it has lower risk of airway infection. However, it requires that the patient should be conscious and it is not very conducive for the drainage of airway secretions.

Currently, non-invasive positive pressure ventilation is generally used for mild or moderate respiratory failure. The best situation for applying non-invasive ventilation is where the patient has respiratory mechanical abnormalities and respiratory muscle fatigue but sputum drainage is relatively less important [11,12]. Aerosol inhalation therapy can direct drugs to bronchia and lung, and it has such advantages as faster onset of effect, lower dose and less adverse reaction when compared with oral intravenous systemic medication [13]. Thus, it has been the first choice for the treatment of AECOPD.

Budesonide is currently the only second-generation inhaled adrenal hormone that efficiently binds airway cortisol receptors to exert an explicit anti-infective effect [14]. Some researchers have reported that the combination of glucocorticoid and β_2-agonists has a significant synergistic effect, and that salbutamol can reduce the drug dose by sensitization of hormonal receptor, while budesonide enhances activation of airway β_2 receptor [7]. In addition, ipratropium bromide combined with salbutamol acts on β_2 and M_3 receptors of the respiratory system together and then enlarges the bronchia [15].

The findings of this study show that the effectiveness of the observation group was much higher than that of the control group. This suggests that combining triple inhalation therapy with assisted non-invasive ventilation is able to improve the clinical symptoms and signs in AECOPD such as expectoration, cough, and dyspnea, with a significant advantage of controlling respiratory tract infection. Post-treatment Pa_{CO2}, pH, and Pa_{O2}, respiratory rate and heart rate differed significantly between the two groups, with greater improvements in the observation group. This implies that the combination therapy was effective in reducing airway resistance, thereby improving pulmonary ventilation.

Limitations of the study

The sample population used in this study was small. Moreover, the study was based on patients from the same hospital. In future studies, a multi-center study involving a higher population of patients is desirable. Moreover, adverse reactions were not evaluated in the present study. This should be included in subsequent investigations.

CONCLUSION

The combination of triple inhalation therapy with assisted non-invasive ventilation facilitates treatment of AECOPD by relieving clinical symptoms and signs and improving pulmonary ventilation, without increasing the risk of adverse reactions.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the author(s) named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. All authors

read and approved the manuscript for publication. Nie Xiuhong conceived and designed the study. Zhang Lin, Nie Xiuhong, Luo Zhiming, Wei Bing, Teng Guojie collected and analyzed the data, while Zhang Lin wrote the manuscript.

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