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Original Article

Effect of humidified high-flow nasal cannula oxygen therapy on respiratory function recovery in stable COPD patients

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Abstract: Objective: To investigate the effect of humidified high-flow nasal cannula oxygen therapy (HFNC) on the application effect and respiratory functional recovery of stable COPD patients. Methods: The data of 116 patients with stable COPD treated in our hospital from March 2019 to January 2021 were analyzed retrospectively. Among them, 54 patients treated with conventional oxygen therapy (COT) were enrolled into the control group (CG), and the remaining 62 treated with HFNC were divided to the experimental group (EG). The clinical efficacy and adverse reactions of both groups were assessed, and the blood gas analysis indexes pH, PaO_2, $PaCO_2$, respiratory function indexes FEV1, FEV1%, FEV1/FVC, quality of life and motor recovery were compared. Results: After treatment, compared with the CG, the FEV1, FEV1% and FEV1/FVC in the EG were obviously higher ($P<0.05$). Besides, the pH and PaO_2 in the EG were markedly higher ($P<0.05$), while $PaCO_2$ was lower ($P<0.05$). The total effective rate, SGRQ scores and 6MWT in the EG were markedly higher than those in the CG ($P<0.05$), while the incidence of adverse reactions in the EG was lower ($P<0.05$). Conclusion: HFNC can improve respiratory function and quality of life of stable COPD patients, with higher safety.

Keywords: HFNC, stable COPD, respiratory function recovery, 6MWT

Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease worldwide, and its morbidity is increasing annually with the aggravation of environmental pollution [1, 2]. COPD has gradually become the third leading cause of disease death, with extremely high mortality and disability rates [3, 4]. The World Health Organization estimates that the number of deaths caused by COPD and its related diseases will exceed 5.4 million per year by 2060 [5].

Airway obstruction caused by inflammation is the main feature of COPD, and it not only involves the lungs, but also further cause inflammation and diseases in other parts of the body, leading to respiratory diseases, pulmonary hypertension, heart failure, neurocognitive and neuromuscular disorders with a long course of disease. Hence, it is a complex and multicomponent disease [6-8]. The incidence of COPD is progressive, which can be divided into acute and stable stages [9]. There are persistent inflammatory reactions in the airway, pulmonary parenchyma and pulmonary vessels, resulting in persistent injury and repeated repair in the airway, and airway remodeling will lead to incomplete airflow limitation. Therefore, stable COPD patients are often accompanied by chronic cough, dyspnea, shortness of breath, etc., which seriously affect their quality of life. Without effective treatment, it may further bring about respiratory failure, endangering patient's lives due to systemic hypoxia [10, 11].

Mechanical ventilation can rescue patients with respiratory failure, but they also have the risk of invasive injury and common complications [12]. Non-invasive positive pressure ventilation (NPPV) can correct hypoxia in COPD patients, relieve dyspnea, increase pulmonary ventilation and ventilation function, and thus correct hypoxemia [13]. Although conventional NPPV is non-invasive; thus it will not bring invasive damage, but it will cause abdominal distension, dry mouth and nose and other complications [14]. High flow nasal catheterization (HFNC) is a new method of respiratory support technology, which can provide sufficient oxygen support for acute respiratory failure caused by various diseases. In the past 10 years, it has been well used in interstitial lung disease, pneumonia, septicemia, and multiple traumas, etc. [15]. HFNC as a new non-invasive respiratory support mode, has better tolerance in patients [16]. HFNC provides high-flow inhaled gases with adjustable and relatively constant oxygen concentration, temperature, and humidity to reduce nasal dryness and improve oxygenation in patients. Therefore, compared with traditional oxygen therapy, patients will tolerate it better [17]. At the same time, research has shown that HFNC patients have a lower probability of acute exacerbation of COPD than conventional oxygen therapy [18]. However, it is vague to what extent HFNC can improve respiratory function in patients with stable COPD.

Thus, this research will compare the efficacy of HFNC and traditional oxygen therapy (COT) in stable COPD patients, and observe the recovery of respiratory function, in order to provide clinical basis and direction.

Methods and materials

Patient data

The data of 116 patients with stable COPD treated in our hospital from March 2019 to January 2021 were analyzed retrospectively. Among them, 54 patients treated with COT were the control group (CG), including 30 males and 24 females, with an average age of (50.2±8.4) years. The other 62 patients treated with HFNC were the experimental group (EG), including 37 males and 25 females, with an average age of (51.0±9.1) years. All patients and their families were informed of the experiment and signed an informed consent form. The research was carried out after being approved by the Medical Ethics Committee of CR & WISCO General Hospital, Wuhan University of Science and Technology (Approval number: IRB2019031512).

Inclusion and exclusion criteria

Inclusion criteria: 1. All patients were diagnosed with COPD according to the COPD diagnostic criteria set out in the guidelines of Global Initiative for Chronic Obstructive Lung Disease (GOLD), and the condition was stable at least 4 weeks after the last exacerbation of the disease [19]; 2. The clinical data were complete.

Exclusion criteria: 1. Those who received drug treatment for bronchiectasis within a month of being enrolled; 2. Those who needed to have an artificial airway or mechanical ventilator; 3. Patients were unable to perform 6MWT; 4. Those who were unable to complete vital capacity measurement; 5. Patients with cognitive impairment; 6. Patients accompanied by severe heart, liver, brain, kidney and other organ dysfunction.

Mode of treatment

Patients in the CG inhaled oxygen through a nasal catheter. The oxygen inhalation device is supplied with oxygen by the wall center, and the oxygen is supplied uniformly by the hospital center. The oxygen flow rate was 1-2 L/min-1, and the arterial oxygen saturation was maintained at 92%-96%. The EG was treated with HFNC and the airway was humidified by MR850 high-flow heating humidification system and matching nasal catheters (provided by Fisher & Paykel). Patients were given a suitable type of nasal catheter to wear to keep the nasal catheter unclogged and unobstructed. The oxygen flow parameters were set to 2-10 L/min. Depending on patients' response after treatment, the oxygen flow rate was adjusted once every 5 min, with a maximum of 2 L/min each time, until the oxygen flow rate is 10 L/min or oxygen saturation >92%. The oxygen concentration parameters were set to 30%-40%, the temperature was set to 31°C, and the finger pulse oxygen saturation was maintained at >92%. The duration was 3 months.

Adverse reactions

The adverse reactions of both groups were collected, and patients with cough and asthma

were treated with compound ipratropium bromide and ambroxol hydrochloride. Nausea patients were treated by protecting the intestines and stomach and promoting digestion according to the situation. All patients with headache had symptom appearance at the beginning of treatment and they disappeared after a period of observation.

Related scores

APACHE II score: Based on the worst value of clinical indicators collected within 24 h of admission, a total of 14 items, including 3 dimensions of acute physiological parameters, chronic health status, and age, were calculated. The total score was 71, the higher the score, the worse the status. COPD assessment test (CAT) score: Cough, expectoration, chest tightness, sleep, mood, energy, exercise and endurance were evaluated in 8 aspects. The total score was 0.40, the higher the score, the greater the impact on life.

Outcome measures

The efficacy of both groups of patients was observed, and the evaluation criteria were as follows: Markedly effective: After treatment, the blood gas analysis parameters returned to normal, and the clinical symptoms such as dyspnea and lung wet rale disappeared; Effective: After treatment, the symptoms of hypoxia were relieved, the clinical symptoms were improved, and the lung wet rale was relieved; Ineffective: If the blood gas examination parameters and clinical symptoms were not improved, or the disease was aggravated. Total effective rate = Markedly effective cases + effective cases [20].

Altogether 3 mL arterial blood was collected from patients before and 3 months after treatment, and pH, $PaCO_2$ and PaO_2 were measured by Germany Roche Cobas b 123 automatic blood gas analyzer.

Patients' FEV1 and FEV1% were measured using a XEEK (Xiamen) Medical Portable Pulmonary function Tester before and after 3 months of treatment, and FEV1/FVC was calculated.

The quality of life of patients was evaluated via SGRQ respiratory questionnaire, including respiratory symptoms, motor ability and disease impact. The total score is 100; the lower the score, the higher the quality of life is. The rehabilitation of patients was detected by 6MWT, and the walking distance of 6 min on the flat ground was measured. The longer the distance, the better the exercise endurance is [21].

Statistical methods

Data were statistically analyzed via SPSS 22.0 software, and statistical charts were drawn via GraphPad Prism 8.2 software. The measurement data were in line with normal distribution. Those in accordance with the normal distribution were expressed as the mean ± standard deviation (Meas ± SD). Independent sample t-test was employed for inter-group comparison, and paired sample t-test was conducted for intra-group comparison. The counting data were expressed by%, using X^2 test. $P<0.05$ was statistically remarkable.

Results

Patient baseline data

Through statistics and comparison of the baseline data of both groups, it was found that there was no marked difference in age, gender, BMI, smoking history, course of disease, type of complications (pulmonary hypertension, asthma, bronchiectasis, hypertension), mechanical ventilation history, APACHE II and CAT ($P>0.05$, **Table 1**).

Comparison of efficacy between both groups

It was found that there was no remarkable difference in the effective rate between both groups ($P>0.05$). The significant rate and the total effective rate in the EG were obviously higher than those in the CG ($P<0.05$) (**Table 2**).

Occurrence of adverse reactions

Cough, nausea, dry nose and mouth, headache and asthma occurred in both groups. There were also 2 cases of diarrhea in the CG, and the total incidence of adverse reactions in the EG was obviously lower than that in the CG ($P<0.05$) (**Table 3**).

Improvement of pulmonary function before and after treatment

By observing the pulmonary function FEV1, FEV1% and FEV1/FVC of both groups, we discovered that the FEV1, FEV1% and FEV1/FVC

Table 1. Patient baseline data

	Control group (n=54)	Experiment group (n=62)	X^2/t	P
Age	50.2±8.4	51.0±9.1	0.489	0.626
Gender				
Male	30 (55.56)	37 (59.68)		
Female	24 (44.44)	25 (40.32)	0.201	0.654
BMI (kg/m^2)	20.71±4.10	20.52±4.05	0.251	0.803
Smoking history	26 (50.00)	37 (59.68)	1.071	0.301
Course of disease (year)	5.08±2.24	4.81±2.10	0.670	0.504
Types of complications				
Pulmonary hypertension	18 (33.33)	16 (25.81)	0.789	0.374
Asthma	12 (22.22)	10 (16.13)	0.697	0.404
Bronchiectasis	8 (14.81)	11 (17.74)	0.181	0.671
Hypertension	8 (14.81)	12 (19.35)	0.417	0.519
History of mechanical ventilation	24 (44.44)	25 (40.32)	0.201	0.654
APACHE II	16.7±3.4	15.8±3.5	1.400	0.164
CAT	30.2±3.0	29.4±3.1	1.407	0.162

Npte: BMI: Body Mass Index; APACHE II: Acute Physiology and Chronic Health Evaluation II; CAT: COPD assessment test.

Table 2. Therapeutic efficacy table

	Control group (n=54)	Experiment group (n=62)	X^2	P
Markedly effective	11 (20.37)	24 (38.71)	4.607	0.032
Effective	31 (57.41)	33 (53.23)	0.204	0.652
Ineffective [13, 14]	12 (22.22)	5 (8.06)	4.625	0.032
Total effective rate	42 (77.78)	57 (91.94)	4.625	0.032

Table 3. List of adverse reactions

	Control group (n=54)	Experiment group (n=62)	X^2	P
Cough	3 (5.56)	1 (1.61)		
Nausea	4 (7.40)	2 (3.23)		
Headache	2 (3.70)	1 (1.61)		
Asthma	3 (5.56)	1 (1.61)		
Diarrhea	2 (3.70)	0 (0.00)		
Dry nose and mouth	5 (9.26)	2 (3.23)		
Total rate of adverse reactions	19 (35.19)	7 (11.29)	9.478	0.002

after treatment were dramatically higher than those before treatment (P<0.05), and the FEV1, FEV1% and FEV1/FVC of the EG after treatment were higher than those of the CG (P<0.05, **Figure 1**).

Improvement of blood gas analysis before and after treatment

Comparing the blood gas analysis indexes of both groups before and after treatment, we found that the pH and PaO_2 were higher than those before treatment (P<0.05), and the $PaCO_2$ was lower than that before treatment (P<0.05). In comparison to CG, PH and PaO_2 in the EG after treatment were higher, and $PaCO_2$ was lower (P< 0.05). Besides, compared with the CG, the pH and PaO_2 of the EG were higher, while the $PaCO_2$ was lower (P<0.05) (**Figure 2**).

Improvement of quality of life and motor ability before and after treatment

The SGRQ scores of quality of life in both groups were compared before and after treatment, and those decreased obviously after treatment (P< 0.05). This indicated that the quality of life of patients was improved (P< 0.05), and the SGRQ scores of the EG was lower than that of the CG after treatment (P<0.05). Meanwhile, the 6MWT of both groups increased after treatment, and the EG after treatment was higher than that of the CG (P<0.05) (**Table 4**).

Discussion

COPD is related to personal habits, the surrounding environment and genetic factors, including chronic airway inflammation and progressive airflow limitation caused by pulmonary parenchyma [22]. Patients may not only have respiratory symptoms, but also cardiovascular disease, osteoporosis, myasthenia, etc. [23]. Long-term study of COPD found that the pathogenesis of COPD is usually mediated by neutrophils and Th1 cells, which leads to various degrees of inflammation in different parts of patients [24]. As an effective auxiliary means for the treat-

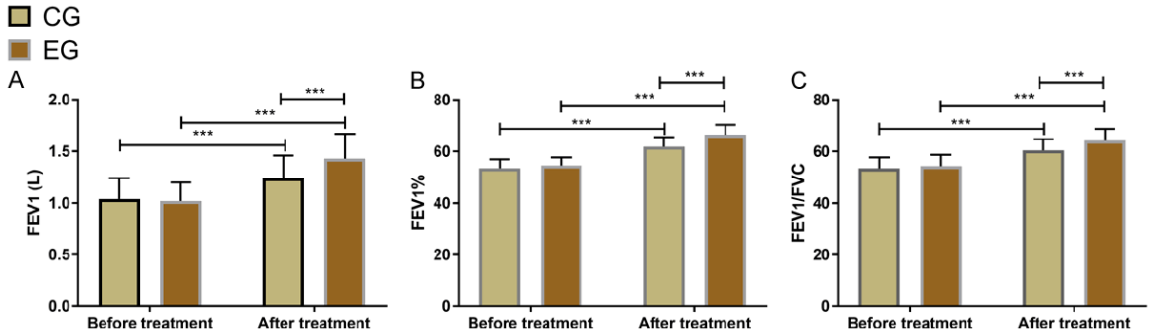

Figure 1. Improvement of pulmonary function before and after treatment. A. The FEV1 of both groups after treatment is higher than that before treatment, and the observation group is higher than the control group after treatment. B. The FEV1% of both groups after treatment is higher than that before treatment, and the observation group is higher than the control group after treatment. C. The FEV1/FVC of both groups after treatment is higher than that before treatment, and the observation group is higher than the control group after treatment.

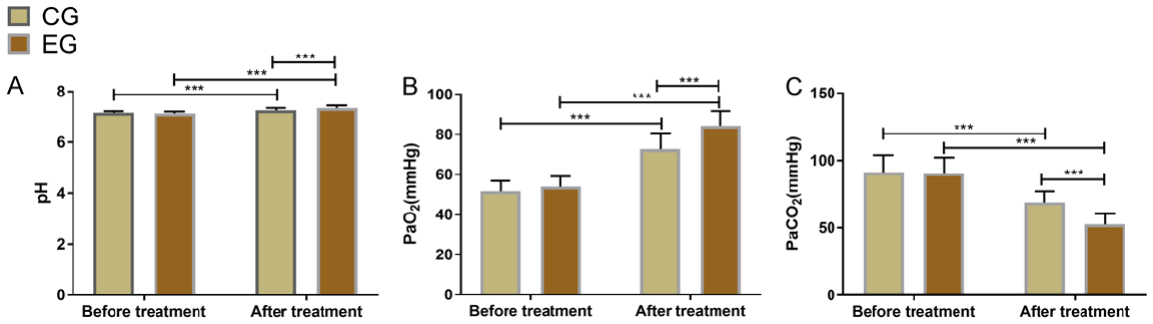

Figure 2. Improvement of blood gas analysis before and after treatment. A. The pH of both groups after treatment is higher than that before treatment, and the observation group is higher than the control group after treatment. B. The PaO_2 of both groups after treatment is higher than that before treatment, and the observation group is higher than the control group after treatment. C. The $PaCO_2$ of both groups after treatment is lower than that before treatment, and the observation group is lower than the control group after treatment.

Table 4. Improvement of quality of life and motor ability

		Control group (n=54)	Experiment group (n=62)	t	P
SGRQ scores	Before treatment	58.60±7.58	58.20±8.98	0.257	0.798
	After treatment	48.63±6.39	42.99±6.46	4.714	<0.001
6MWT (m)	Before treatment	368.85±40.56	372.50±36.43	0.511	0.611
	After treatment	403.29±39.10	444.04±42.82	5.322	<0.001

ment of acute respiratory failure, HFNC can not only improve the mucosal ciliary function, but also increase the comfort and tolerance of patients [25].

In our study, we first compared the efficacy of HFNC and COT, and found that the total effective rate of the former was better. During the treatment, both groups had adverse reactions including cough, nausea, headache and asthma. It was found that the adverse reactions of HFNC were lower than those of patients treated with COT. At the same time, we also tested the improvement of pulmonary function before and after treatment. Both COT and HFNC improved the pulmonary function of patients, and the efficacy of FEV1, FEV1% and FEV1/FVC was higher. Emphysema, as a typical phenotype of COPD, greatly limits the survival rate of patients. The decline rate of pulmonary function of this phenotype is high, and severe airflow limitation is a prominent feature of patients [26]. HFNC

can alleviate the symptoms of patients by improving the recovery of lung function. After treatment, pH and PaO_2 were increased, while $PaCO_2$ was decreased, and the efficacy of blood gas index by HFNC was more remarkable. HFNC promotes the exchange of qi and blood and the re-expansion of end-expiratory alveoli by maintaining a stable high concentration of oxygen inhalation, which is beneficial to flushing the ineffective cavity. Chronic respiratory failure is a very familiar complication of COPD, and about 7% of patients develop hypoxemia after a median follow-up of 5 years, which greatly affects the respiratory function and exercise endurance of patients and increases the mortality [27]. Thus, oxygen therapy can relieve dyspnea and improve hypoxia, while HFNC has a better effect.

Hence, effective treatment is needed to relieve patients' symptoms, so as to improve their activity level and prognosis [28]. We compared the SGRQ score of the quality of life of both groups, and found that after HFNC treatment, the score of patients was reduced and their quality of life was improved, which was higher than that of COT. When HFNC steadily delivers a large flow of gas, it can form a certain positive pressure, thus reducing the resistance of the upper respiratory tract and keeping the respiratory tract unobstructed. It can effectively clear the respiratory tract cilia, enhance lung compliance, improve oxygenation and correct hypoxia. Compared with HFNC, COT has lower oxygen utilization and comfort. The exercise endurance of COPD patients will be reduced because of impaired cardiopulmonary function. We evaluated the exercise endurance and recovery of patients after treatment by 6MWT, and found that 6MWT after HFNC treatment was higher than that of patients treated with COT. Zeng et al. [29] mentioned that the function and quality of life of 6MWT and COPD are correlated with various parameters indicating the severity of the disease. It also denotes that HFNC can improve the function and quality of life of COPD patients.

Nevertheless, there are also some shortcomings in this research. First of all, HFNC is more frequently-used in patients with acute respiratory failure, so more research on COPD treatment is needed to explore a better model. Secondly, many studies are exploring the treatment mode of different drugs combined with HFNC in COPD treatment, such as different doses of inhaled antibiotics or steroids [30], hoping to explore more appropriate treatment options in later studies. Finally, the main groups are mild and moderate COPD patients. Hence, the efficacy cannot be directly applied to severe COPD patients, and corresponding studies need to be added later to support our point of view.

To sum up, HFNC can improve the efficacy of stable COPD patients, and enhance their respiratory function and blood oxygen. It can be used as an effective treatment for stable COPD patients in the future.

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