

Original Research Article

Effect of tiotropium bromide, N-acetylcysteine and respiratory training on pulmonary function, activity tolerance and quality of life of patients with chronic obstructive pulmonary disease

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Abstract

Purpose: To investigate the effect of application of tiotropium bromide and N-acetylcysteine in combination with respiratory training on the treatment of patients with chronic obstructive pulmonary disease (COPD), and the effect of the combined treatment on pulmonary function, tolerance of physical activity, and quality of life.

Methods: One hundred COPD patients admitted to The First People's Hospital of Guiyang (February 2019 - March 2021) were randomly and equally assigned to groups X and Y. Patients in Y were given tiotropium bromide in combination with N-acetylcysteine, while group X was treated with respiratory training, in addition to the treatment regimen in Y. Treatment efficacy, incidence of adverse reactions, pulmonary function indices, activity tolerance, quality of life (QLI) score, activities of daily living (ADL) score, and incidence of COPD at 2 weeks, 1 month and 2 months after treatment were determined, and compared between the two groups.

Results: Relative to group Y, group X had significantly higher treatment efficacy, QLI score and ADL score ($p < 0.05$). Furthermore, group X also had better pulmonary function indices and activity tolerance, lower incidence of adverse reactions, and lower COPD incidence at 2 weeks, 1 month and 2 months after treatment ($p < 0.05$).

Conclusion: Tiotropium bromide and N-acetylcysteine in combination with respiratory training enhanced therapeutic effect, pulmonary function, activity tolerance and quality of life of COPD patients.

Keywords: Tiotropium bromide, N-Acetylcysteine, Breathing training, COPD, Pulmonary function, Activity tolerance, Quality of life

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation, the etiology of which includes but is not limited to smoking,

air pollution, occupational exposure to dust, and various chemical substances. Nicotine, tar and dust in cigarette smoke damage airway epithelial cells and hinder the movement of cilia in the respiratory tract, leading to reduction of the

filtration effect of respiratory tract on harmful substances, destruction of pulmonary elastic fibers, and emphysema or chronic bronchitis [1-3]. The mortality and morbidity of COPD patients are also increasing year by year, and they are correlated with air pollution and other factors [4-6]. Drugs for improving lung function, reducing phlegm and relieving cough are currently selected in clinics for the treatment of COPD patients. In addition, tiotropium bromide improves lung function and relieves asthma in COPD patients, while N-acetylcysteine is a popular expectorant. Both drugs protect the bronchial wall of patients and reduce the damage caused by some harmful substances to the bronchus [7, 8]. In addition, respiratory training improves the respiratory modes and respiratory function of COPD patients, and also alleviates clinical symptoms of the disease. The aim of the present investigation was to compare the effects of different treatment methods on COPD subjects with respect to treatment outcomes.

METHODS

Patient information

One hundred COPD subjects who were on admission at *The First People's Hospital of Guiyang* (February 2019 - March 2021) were randomly and equally assigned to groups Y and X. They were aged 42 - 76 years in group Y, and 40 - 75 years in group X. No obvious differences in gender, age, course of disease and other general data were observed between the two groups ($p > 0.05$), as shown in Table 1. The study followed the guidelines of Declaration of Helsinki [9], and was approved by the institutional ethics committee.

Inclusion conditions

Subjects with clinical evidence of COPD, subjects aged ≥ 18 years, patients with no other organic diseases, and patients with no record of adverse effect from drugs, substance abuse or

history of smoking and alcoholism, were included. This research received approval from the ethical committee of our institution. All subjects expressed willingness to take part in the investigation, and each of them did so in a signed permission statement.

Conditions for exclusion

Subjects with lung cancer, asthma and bronchiectasis; patients who had mental disorders, and patients with a family history of hereditary diseases, were excluded.

Treatments

Group Y was treated with tiotropium bromide in combination with N-acetylcysteine. The patients received inhalation therapy with tiotropium bromide powder (NMPA approval No.: H20140933; specification: 18 μg) before sleep, 18 μg at a time, once a day. The patients also received N-acetylcysteine (Hainan Zambon Pharmaceutical Co. Ltd; NMPA approval No.: H20080325; specification: 600 mg), 600 mg at a time, 2 times/day. The curative effect was evaluated after continuous treatments for one month [10-12]. Group X was treated with tiotropium bromide in combination with N-acetylcysteine, in addition to respiratory training. With respect to the latter, the patients used abdominal breathing instead of chest breathing by closing their mouths and inhaling through the nasal cavity for as long as possible while relaxing the body, sinking the shoulders and the extending spine naturally upward. They placed their hands on the upper abdomen to feel the changes in the abdomen when breathing. When exhaling, the patients opened their mouths naturally and exhaled slowly. With longer expiratory time than inspiratory time, the patients breathed naturally and avoided holding their breath. Respiratory training was performed twice a day, each time for 15 min, and the effect was evaluated after continuous training for one month.

Table 1: Profile of patients in the 2 groups

Parameter	Group X	Group Y	t/ χ^2	P-value
Gender (male/female)	28/22	30/20	0.16	0.69
Age (years)	58.83 \pm 5.22	58.95 \pm 5.38	0.11	0.91
Height (cm)	168.22 \pm 6.40	168.30 \pm 6.99	0.06	0.95
Weight (kg)	63.81 \pm 7.30	63.11 \pm 6.99	0.49	0.63
Medical history (years)	2.00 \pm 0.36	2.08 \pm 0.43	1.01	0.32
Smoking (years)	11.69 \pm 2.57	11.20 \pm 2.66	0.94	0.35
Drinking (years)	15.94 \pm 3.03	15.85 \pm 3.79	0.13	0.90
Hypertension (n)	9	11	0.25	0.62
Diabetes (n)	10	13	0.51	0.48
Hyperlipemia (n)	8	6	0.33	0.56

Data are presented as mean \pm SD

Assessment treatment indices

Treatment efficiency, incidence of adverse reactions, pulmonary function indices, activity tolerance, quality of life (QLI) score, activities of daily living (ADL) score, and incidence of COPD in patients at 2 weeks, 1 month and 2 months after treatment were determined and compared. If the clinical manifestations of the patients completely disappeared, and no symptoms occurred after treatment, with normal pulmonary function indices, the treatment was *markedly effective*. If the disease-free interval after treatment was significantly prolonged, and the clinical manifestations were obviously alleviated, with pulmonary function indices gradually normalized, therapeutic outcome was *effective*. However, if the clinical manifestations were not significantly relieved, with frequent occurrence of COPD and no significant improvement in lung function, the treatment was *ineffective*.

The pulmonary function indices comprised forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC and oxygen saturation (SpO₂) [13-15].

Assessment of activity tolerance included duration of each activity, the number of activities per day, and percentage of maximum heart rate during activity.

Quality of life (QLI) scoring criteria covered daily activities, work and life, and interpersonal relationship, with every index scoring 10 marks. An enhanced score indicated improved QLI.

Activities of daily living (ADL) scores covered eating, dressing and walking. Lower scores indicated worse ADL.

Statistical analysis

The results were subjected to analysis using SPSS version 20.0, while graphics were done with GraphPad Prism 7. The results included enumeration data and measurement data. Enumeration data are presented as numbers and percentages [n (%)], and they were statistically analyzed with χ^2 test. Measurement results are expressed as mean \pm SD, and were analyzed using *t*-test. Values of *p* < 0.05 indicated significance of differences.

RESULTS

Treatment efficacy

Table 2 depicts that treatment efficacy was significantly better in group X than in group Y.

Incidence of adverse reactions

As shown in Table 3, the incidence of adverse reactions in group X was significantly low, when compared with group Y (*p* < 0.05).

Pulmonary function indices

Values of pulmonary function indices in group X were better than those in group Y (*p* < 0.05), as shown in Table 4.

Table 2: Comparison of treatment efficacy

Group	Markedly effective	Effective	Ineffective	Total treatment effectiveness
X	29 (58)	18 (36)	3 (6)	47 (94)
Y	21 (42)	14 (28)	15 (30)	35 (70)
χ^2				9.76
<i>P</i> -value				0.002

Table 3: Incidence of adverse reactions in the two groups

Group	Insomnia	Headache	Fatigue	Total incidence (%)
X	2	1	1	8
Y	5	3	4	24
χ^2				4.76
<i>P</i> -value				0.03

Table 4: Comparison of pulmonary function indices (mean \pm SD)

Group	FEV1(L)	FVC(L)	FEV1/FVC (%)	SpO ₂ (%)
X	2.69 \pm 0.37	2.94 \pm 0.42	78.51 \pm 5.04	96.60 \pm 3.31
Y	2.22 \pm 0.25	2.41 \pm 0.29	72.60 \pm 4.87	88.12 \pm 3.34
<i>t</i>	7.44	7.34	5.96	12.75
<i>P</i> -value	< 0.001	< 0.001	< 0.001	< 0.001

Table 5: Comparison of activity tolerance

Group	Duration of each activity (min)	Number of activities per day (times)	Maximum heart rate during activity (%)
X	26.49 ± 5.18	3.32 ± 0.47	61.33 ± 5.80
Y	21.38 ± 5.02	2.39 ± 0.33	52.17 ± 5.07
<i>t</i>	5.01	11.45	8.41
<i>P</i> -value	< 0.001	< 0.001	< 0.001

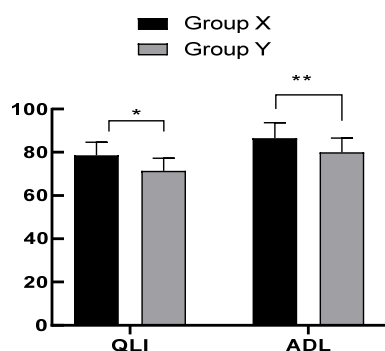
Values are presented as mean ± SD

Tolerance of activity

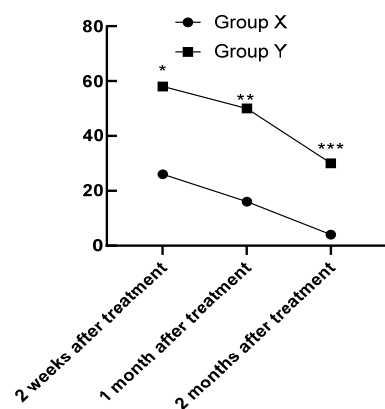
The activity tolerance in group X was better, when compared with group Y, with statistical significance ($p < 0.05$), as shown in Table 5.

QLI and ADL scores

Figure 1 shows that compared with group Y, group X achieved markedly higher QLI and ADL scores.

**Figure 1:** Comparison of QLI and ADL scores.

* $P < 0.05$, QLI scores of group X vs scores of group Y; ** $p < 0.05$, ADL scores of group X vs scores of group Y

**Figure 2:** Comparison of incidents of COPD at 2 weeks, 1 month and 2 months after treatment. * $P < 0.05$, COPD incidence at 2 weeks after treatment in group X vs COPD incidence at 2 weeks after treatment in group Y; * $p < 0.05$, COPD incidence at 1 month after treatment in group X vs COPD incidence at 1 month after treatment in group Y; ** $p < 0.05$, COPD incidence at 2 months after treatment in group X vs COPD incidence at 2 months after treatment in group Y

Incidence of COPD

Figure 2 depicts lower incidents of COPD at 2 weeks, 1 month and 2 months after treatment in group X than in group Y.

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is irreversible and destructive. Patients with COPD present with symptoms such as chronic cough, expectoration and suffocation, which are hard to cure as the disease worsens [16-18]. While COPD patients have no obvious manifestations in the early stage of the disease, they may experience tachypnea, shallow breathing, and occasional suffocation as the disease worsens, which seriously affects their survival in the absence of effective intervention. Respiratory training is a form of intervention aimed at improving the respiratory modes and breathing habits of the patients so as to help them develop good breathing patterns. Thus, they are able to find appropriate breathing intensity, thereby reducing the impact of COPD on breathing through long-term and continuous breathing training [19-21].

Tiotropium bromide and N-acetylcysteine are popular clinical drugs used for treating airway diseases such as asthma and COPD. This is due to the fact these drugs resolve phlegm, relieve cough, dilate the bronchus, stabilize smooth muscle, and mitigate dyspnea. This study investigated the effect of combination of tiotropium bromide, N-acetylcysteine and respiratory training on COPD patients. The results obtained showed that, compared with group Y treated only with tiotropium bromide in combination with N-acetylcysteine, the treatment efficiency, pulmonary function, quality of life, activity tolerance and incidence of adverse reactions in group X treated with tiotropium bromide and N-acetylcysteine in combination with respiratory training, were markedly improved. Thus, the treatment method which included respiratory training produced higher therapeutic value.

Activity tolerance is an indicator of changes in heart rate after an exercise, exercise time, and

exercise intensity of a subject. Following exercise, patients with COPD may have obvious manifestations such as suffocation and asthma, and even asphyxia in severe cases. Pulmonary function is a direct reflection of the severity of COPD: a more severe disease condition reveals a worse pulmonary function. Therefore, improvement in the pulmonary function of patients through treatment alleviates the clinical symptoms of COPD.

The results obtained in this study showed that patients given respiratory training had better outcomes than those who did not receive respiratory training, suggesting that breathing training plays a key role in the treatment of COPD. These results are consistent with those reported in a study in which therapeutic effect was significantly improved, with reduced adverse effects, in COPD patients who received tiotropium bromide and N-acetylcysteine in combination with respiratory training [22].

Limitations of the study

This study is a single-center investigation with a small sample size. Therefore, it is necessary to conduct more multi-center and in-depth studies with a larger sample size in future in order to validate the results obtained here.

CONCLUSION

The use of tiotropium bromide and N-acetylcysteine in combination with respiratory training improved the therapeutic effect, pulmonary function, activity tolerance and quality of life of COPD patients.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Ning Peng and Min Chen conceived and designed the study, and drafted the manuscript. Ning Peng, Min Chen and Zhinan Shou collected, analyzed and interpreted the experimental data. NP and MC revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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