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Short Communication

Effect of Pulmonary Rehabilitation Combined with Tiotropium Bromide on BODE Index in Clinical Stable Patients with Chronic Obstructive Pulmonary Disease

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TL designed the study. JL and NJ analysed the data and performed the experiments. TL, JL and NJ wrote the article.

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Pulmonary rehabilitation, Tiotropium bromide, Combination therapy, Chronic obstructive pulmonary disease, Stable BODE index

ABSTRACT

This paper observes the effect of pulmonary rehabilitation combined with tiotropium bromide on BODE index in clinical stable patients with chronic obstructive pulmonary (COPD) disease. For this purpose, a retrospective cohort was designed**.** In this work, 200 patients with COPD at stable stage were enrolled as research subjects. They were divided into the control group (n=100) given conventional treatment (bronchodilator, antioxidant, expectorant antitussive) and the research group (n=100) given pulmonary rehabilitation combined with tiotropium bromide treatment. The BODE indexes of two groups were compared and observed at 4 and 8 months of follow-up. After four months the research group showed significant improvement in dyspnea, 6MWD, FEVl% pred, BMI and BODE index, $p<0.05$. At eight months of treatment, the improvement was sustained for all outcomes at the research group, at $p<0.05$. Pulmonary rehabilitation combined with tiotropium bromide therapy for clinical stable patients with COPD can produce significant improvement in patients' BODE index.

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistent airflow limitations. It is associated with increased chronic inflammatory responses to toxic particles or gases in the airways and lungs. The exact etiology of COPD remains unclear. It is generally believed that the factors associated with COPD and obstructive emphysema may be involved in the pathogenesis of COPD. Existing risk factors can be roughly divided into two categories: external factors (i.e. environmental factors) and internal factors (i.e. individual susceptibility factors). External causes include smoking, dust and chemical inhalation, air pollution, respiratory tract infection, and low socioeconomic status (Liu *et al*., 2016; Chen, 2018; Yang *et al*., 2018). Internal causes include genetic factors, increased airway reactivity, lung development or poor growth.

For clinical stable patients with COPD, there is currently no drug that can alter the progressive decline in lung function. With the continuous advancement of medical research, many scholars have put forward a comprehensive intervention treatment plan for patients with chronic respiratory diseases, which can improve their self-perceived symptoms, increase their exercise tolerance and improve their life quality. BODE index is a comprehensive multi-factorial classification system, which comprises of body- mass indexes (B), degree of airflow obstruction (O), dyspnea (D), exercise capacity (E) (Gawlitza *et al*., 2018; Jian *et al*., 2018; Gabrielda *et al*., 2018). This study observes the effect of pulmonary rehabilitation combined with tiotropium bromide on BODE index in clinical stable patients with COPD.

Data and methods

In this study, 200 clinical stable patients who were treated for COPD in our hospital from January 2016 to May 2019 were selected as research subjects in this retrospective cohort study. Patients who met the diagnostic criteria of COPD formulated by the respiratory branch of the Chinese Medical Association, and who could cooperate with medical staff in treatment and rehabilitation training were included in this study. Patients with cardiovascular and cerebrovascular diseases (myocardial infarction, cerebral infarction, congestive heart failure, etc.), liver

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and kidney diseases, or tumors were excluded. All patients had the right to know and signed the informed consent form. This study was approved by the ethics association of hospital.

The patients were divided into two groups, including control group (n=100) and research group (n=100). There were 60 male patients and 40 female patients in the research group, with an average age of (65.2±2.1) years old. There were 55 male patients and 45 female patients in the control group, with an average age of (64.7±3.6) years old.

All patients in the control group were given tiotropium bromide dry powder (Zhengda Tianqing Pharmaceutical Co., Ltd., 18 μg/particle) on the basis of conventional drug therapy such as bronchodilator, antioxidant, expectorant antitussive. In contrast, all patients in the research group inhaled 1 tiotropium bromide dry powder capsule every day on the basis of conventional drugs and comprehensive pulmonary rehabilitation. Thiamethoxam bromide chemical name is 6 beta epoxy - 3 alpha [alpha hydroxy - 2, 2-2 (alpha) thiophene acetoxyl group] - 8, 8- dimethyl -12 H, 5 alpha H-tropic alkyl bromide. Tiotropium bromide is a specific and selective anticholinergic agent with similar affinity of muscarinic receptor subtype mi-m5, which produces bronchiectasis by inhibiting smooth muscle M3 receptor. The preclinical in vitro and in vivo studies show that the effect of tiotropium bromide on acetylcholine-induced bronchoconstriction resistance sites is dose-dependent and can be maintained for more than 24 h.

FEV1 % pred of the patients was determined by spirometer (Cosmed, Italy). Six-minute walk distance (6MWD) was recorded as follows. The indoor corridor with a length of about 30 meters was set up for measurement. The walking distance of the subject within 6 minutes was measured by an electronic timer. The body mass index (BMI) was calculated after the patient's height and body mass were measured. The modified medical research council's dyspnea score scale (mMRC) was used to evaluate patients, including grades 0-4. Using the abovementioned parameters, the BODE index score was calculated.

The patients were treated with drugs such as bronchodilators, glucocorticoids and expectorants. For long-term home oxygen therapy, if the oxygen partial pressure is less than 60 mmHg, at least 15 h of low-flow oxygen should be inhaled every day. Patients were given nutritional support and given oral nutrition supplements under the guidance of a dietitian. In addition, the exercise of respiratory muscle function exercise (involving labial breathing and abdominal breathing exercises) as well as whole body exercises such as slow walking, stair climbing, treadmill and bicycle are carried out for the research group.

Statistical analysis software SPSS21.0 was used to process data. The measurement data were expressed by mean ± average ($\bar{x}\pm s$), with t test conducted for intergroup comparison. Enumeration data were expressed by natural (n) and percentage (%), with X2 used for intergroup comparison. The intergroup difference was considered statistically significant when $P < 0.05$.

Results

Table I shows the changes of body mass index and FEV1% pred of patients after treatment. The results show that all indexes of the research group are significantly superior than those of the control group (p=0.02).

As shown in Table II, the degree of dyspnea and BODE index of patients after treatment in the research group are better than that of the control group, p<0.05.

The improvement in 6MWD is more significant in the research group than in the control group, p<0.05 (Table III).

Table I. Changes of body mass index and FEV1% pred after treatment in the two groups ($\bar{x}\pm s$).

Group	Time	Body mass index	FEV1% pred
Research group	Before treatment	18.4±0.4	53.2±3.1
	After 4 months of treatment	19.8±0.6	58.7±2.1
	After 8 months of treatment	23.7±1.0	70.8±4.2
Control group	Before treatment	18.5±0.6	53.6±3.0
	After 4 months of treatment	18.9±0.4	55.6±2.7
	After 8 months of treatment	19.1±0.8	57.8±2.0

Table II. Changes of dyspnea degree and BODE index after treatment in the two groups ($\bar{x}\pm s$).

Group	Time	mMR classification	BODE
Research group	Before treatment	2.4±0.4	4.5±1.2
	After 4 months of treatment	1.8±0.4	3.8±1.1
	After 8 months of treatment	1.2±1.1	3.4±1.2
Control group	Before treatment	2.3±0.5	4.6±1.0
	After 4 months of treatment	1.9±0.6	4.4±1.7
	After 8 months of treatment	1.7±0.8	4.2±1.3

Discussion

Many patients with moderate to severe COPD have limited mobility. The pulmonary rehabilitation program can improve the exercise function of COPD patients and weaken the symptoms of dyspnea. Currently, pulmonary rehabilitation is one of the key strategies recommended

by the global initiative for the prevention and treatment of COPD guidelines for non-drug treatment for clinical stable COPD patients (Jian *et al*., 2017; Hu and Yang, 2017).

Table III. Change of 6MWD after treatment in the two groups ($\bar{x}$±s).

Group	Time	6MWD(m)
Research group	Before treatment	166.8±25.9
	After 4 months of treatment	200.9±32.7
	After 8 months of treatment	262.2±40.3
Control group	Before treatment	165.3±22.8
	After 4 months of treatment	175.9±23.6
	After 8 months of treatment	180.7±30.5

The BODE index can comprehensively evaluate patients' general state, including nutritional status, clinical symptoms, exercise ability and lung function, indicating the quality of life of patients with COPD. The effect of pulmonary rehabilitation can be reflected by BODE score. The content of pulmonary rehabilitation comprehensive treatment includes oxygen therapy (low-flow oxygen absorption), standardized drug therapy, nutritional support therapy, strengthening rehabilitation exercise, and smoking cessation education, etc. Long-term home oxygen therapy can improve the patient's chronic hypoxia, reduce pulmonary artery contraction and spasm, delay the development of pulmonary hypertension, improve lung function, hinder the development of pulmonary heart disease. The implementation of nutritional support can improve the body's chronic malnutrition status and enhance immunity. Lip contraction breathing and respiratory muscle exercise can increase the positive pressure in the airway, avoid early closure of small airways, promote the effective distribution of air in the lungs, promote the exchange of air in the lungs, and increase the tidal volume. By practicing abdominal breathing, respiratory fluctuation is increased, respiratory muscle strength is improved, dynamic lung compliance is enhanced, lung ventilation is increased, and lung function is improved.

Tiotropium bromide is a new generation of long-acting inhaled anticholine for COPD, which acts on M1 and M3 receptors, making the tracheobronchial dilation, improving dyspnea, reducing acute attack rate and shortening the process of pulmonary function decline. Relevant studies have indicated that tiotropium bromide can inhibit inflammatory response and play a role in airway remodeling. The effect of tiotropium bromide on airway once a day is 24 h. ATS, ERS, GOLD guidelines recommend that thiamethoxam bromide long-acting bronchodilator should be used as a main drug for treatment of clinical stable patients with grade II COPD. This study results show that, compared with therapy of only taking inhaled thiamethoxam bromide powder, combined therapy of pulmonary rehabilitation and thiamethoxam bromide can achieve more significant improvement in exercise tolerance and breathing difficulty, nutritional status, several indexes of lung function. In addition, the effect is even more significant on the basis of increasing pulmonary rehabilitation and the inhalation time of tiotropium bromide. This result shows that the long-term application of pulmonary rehabilitation combined with bronchodilator has a positive effect on lung function, which is consistent with the reported results of relevant studies (Aishwarya *et al*., 2019; Mao *et al*., 2019).

Conclusion

In conclusion, the combined therapy of comprehensive pulmonary rehabilitation and tiotropium bromide powder inhalant for clinical stable patients with COPD can exert a certain degree of influence on BODE related indicators and BODE index, effectively improve the patient's conscious symptoms and degree of dyspnea, improve social adaptability, prevent further disease deterioration and improve exercise tolerance. Therefore, such combined therapy can be popularized in the majority of basic hospitals.

Statement of conflict of interest

The authors have declared no conflict of interest.

References

Aishwarya, N., Gopala, K.A., Shyam, K., Santhosh, Anand, R., Vishak, A., Preetam, A. and Roberto, W.D., 2019. *Pulm. Med*., **35**: 45-350.

Chen, S.T., 2018. *China Mod. Med*., **25**: 44-46. https://doi.org/10.5553/JV/016758502018044006002

Gabrielda, C.M., Luana, B.V., Auriléia Aparecida, D.B., Cintia, E.A., Nicole Cristine, R.D.O., Alanado, S.D., Yves Silva, T.M., Manoel Carneiro, O.J., Luisvicente, F.O., Renata Kelly, D.P., Larissa, C.C., Adriana Lino, D.S.F., Anna Carolina, R.T.H., João Antonio, G.J., Flavio, A., Rodolfo, P.V. and Ana-Paula, L.D.O., 2018. *Oxid. Med. Cell. Longev.*, **12**: 230-236.

Gawlitza, J.S., Trinkmann, F.D., Scheffel, H., Fischer, A.D., John, W., Nance, Claudia, H., Joachim, S., Ibrahim, A., Martin, B.F., Stefan, O., Schoenberg. and Thomas, H.L., 2018. *Can. Respir. J*., **12**: 110-115. https://doi.org/10.1155/2018/9493504

Hu, L.B. and Yang, J.Q., 2017. *China Med. Herald*, **14**: 104-107. https://doi.org/10.1109/CC.2017.7868159

Jian, L.M., Jing, J.C., Xiao, F.Q., Rui, J.L. and Noriyoshi,

S., 2018. *BioMed. Res. Int*., **30**: 125-130.

Jiang, R.F., Xu, L. and Li, X.H., 2017. *J. clin. Med. Pract*., **21**: 28-30+34. https://doi.org/10.1111/dme.12_13303

Liu, H.K., Zhou, M. and Wu, Z.Q., 2016. *China Mod. Med*., **23**: 23-25+28.

Mao, J., Li, Y., Li, S.Y., Li, J.S., Tian, Y.G., Feng, S.X., Liu, X.F., Bian, Q.Q., Li, J.Z., Hu, Y.Y., Zhang, L.X., Ji, H.G. and Evan, P.C., 2019. *Evid. Based Complement. Altern. Med*., **59**: 456-460. https://doi.org/10.1155/2019/1216305

Yang, Y., Liu, X.R. and Xiao, X., 2018. *Sichuan J. Physiol. Sci*., **40**: 82-85.