

Original Article

A clinical study on the role of psychosomatic therapy in evaluation and treatment of patients with chronic obstructive pulmonary disease complicated with anxiety-depression disorder

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Abstract: This study aimed to evaluate the effect of psychotic therapy on patients with chronic obstructive pulmonary disease (COPD) complicated with anxiety-depression disorder by Hamilton Depression Scale (HAMD), Hamilton Anxiety Scale (HAMA), COPD Assessment Test (CAT) and modified British Medical research Council (mMRC). Thirty-five patients with COPD were evaluated by pulmonary physicians with CAT and mMRC. They were further evaluated with HAMD and HAMA by psychologists and diagnosed and grouped into group B and D according to the Global initiative for chronic Obstructive Lung Disease (GOLD) version 2014. Patients were given psychotic therapy and followed up for at least 1 month. Comparison and analysis were performed with clinical data before and after treatment. Fourteen patients were subscribed into B group, while 21 patients were subscribed into D group, accounting for 40% and 60% respectively. After psychotic therapy, the HAMA and MAMD score of patients in both groups improved significantly ($P < 0.05$). The CAT and Mmrc score of 8 patients in B group improved as A, while 10 patients in D group improved as B. The longest follow-up was 12 months. Symptoms were significantly alleviated after combined respiratory and psychotic therapy. COPD complicated with anxiety-depression is of high prevalence. The psychosomatic problems usually aggravate respiratory symptoms. Make better use of the evaluation methods such as HAMA, HAMA, CAT, mMRC may facilitate the treatment for patients.

Keywords: Chronic obstructive pulmonary disease, anxiety-depression disorder, subgrouping, evaluation

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic respiratory disease, which is frequently complicated with anxiety and depression [1, 2], as well as short of breath, dyspnea and heart tired. The evaluation of COPD is comprehensively based on the symptoms, risk of acute exacerbation, severity of pulmonary malfunction and complications, so as to guide the therapy. The most widely used evaluation on symptoms of COPD is the modified British Medical Research Council (mMRC) or COPD Assessment Test (CAT). However, both of them are somehow subjective, which may mislead the subgrouping and treatment of patients. Recently, researchers and the Global initiative for chronic Obstructive Lung Disease (GOLD) have paid great attention to anxiety and

depression that complicated with COPD [3, 4]. However, most of them are based on the respiratory perspective. Till now, it's still not clear about the role of treatment on anxiety on alleviation of COPD. In this study, we clinically observed and analyzed the diagnosis and treatment of COPD patients complicated with anxiety from psychotic point of view. The purpose of this study was to explore the effect of psychotic treatment on COPD patients complicated with anxiety, in order to contribute to the knowledge of COPD and guide the therapy.

Patients and methods

Patients

The study was approved by the ethics committee of Sichuan Academy of Medical Sciences &

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Table 1. General and anxiety-depression symptoms

		Short of breath (rest state)	Limb numbness	Feelings of mpending death	Sleeping disorder	Distress
Group B (n=14)	Before treatment	9/14 (64.29%)	11/14 (78.57%)	2/14 (14.29%)	12/14 (85.71%)	9/14 (64.29%)
	After treatment	1/14 (0.71%)	1/14 (0.71%)	0/14	5/14 (35.71%)	3/14 (21.43%)
Group D (n=21)	Before treatment	14/21 (66.67%)	9/21 (42.86%)	3/21 (14.29%)	21/21 (100%)	8/21 (38.10%)
	After treatment	4/21 (19.05%)	3/21 (14.29%)	1/21 (0.48%)	7/21 (46.67%)	9/21 (42.86%)

The anxiety-depression disorder manifested mainly with short of breath, and frequently with limb numbness. Decreased tolerance to labor due to impaired pulmonary function was correlated to anxiety-depression.

Table 2. General condition and COPD score before treatment

	Age (years)	Gender		CAT score	mMRC score
		Male	Female		
Group B (n=14)	67.7±19.35	10	4	17.14±6.11	2.25±0.97
Group D (n=21)	65.86±5.09	18	3	27.46±10.0	3.05±0.81

Sichuan Provincial People's Hospital. Thirty-five COPD patients who meet GOLD (version 2014) [5] during January to December 2014 in Sichuan provincial hospital were included into this study. The inclusion criteria were: 1), patients with diagnosis of COPD, mMRC≥2, CAT≥10, with pulmonary function in group B or D; 2), able to care himself/herself, remission stage or acute exacerbation stage; 3), diagnosis of anxiety-depression according to Hamilton Depression Scale (HAMD) and Hamilton anxiety scale (HAMA). The exclusion criteria were: 1), patients with Alzheimer disease; 2), disability in communication; 3), patients refused to participate; 4), patients with respiratory failure who refused mechanical ventilation; 5), cancer patients. Totally 35 patients were included in this study and finished the follow up.

Treatment and follow-up

Patients included this study were assigned into B or D groups according to GOLD grade as well as mMRC and CAT score. Group B is defined with low risk, pulmonary function GOLD 1 or GOLD 2, with 0~1 acute exacerbation per year, mMRC≥2 or CAT≥10. D group is defined as high risk, with pulmonary function GOLD 3 or GOLD 4, and more than 2 times of acute exacerbations per year, mMRC≥2 or CAT≥10. Then, patients were evaluated by two experienced psychologists independently, according to HAMA and HAMD. HAMA score over 7 or HAMD score over 8 was diagnosed with anxiety-depression disorder. The total score of HAMD

was 76. It was graded as follow: <8 normal; 8~20 possibly anxiety-depression; 20~35 anxiety-depression; >35 severe anxiety-depression. And the total score of HAMA was 56. It was graded as follows: <7 normal; 7~13 possibly anxiety-depression; 14~21 anxiety-depression; 21~29 strong anxiety-depression; >29 severe anxiety-depression. Addition to routine therapy on COPD, patients were given anti-psychotic treatment. Patients were followed up for HAMA, HAMA, CAT, mMRC, pulmonary function, and blood gas tests at 2 weeks and 1 month after treatment.

Statistical analysis

All the statistical analysis was performed with Statistical Package for the Social Science (SPSS version 16.0) software. Student t test was applied to compare the data between groups. A *p* value <0.05 was considered to be statistically significant.

Results

General data

Totally 35 patients enrolled this study. There were 28 male and 7 female, with age 54~82 years old, averaging 66.6±7.04. Among the male patients, 26/28 (92.86%) smokes. One patient had history of hyperthyroidism, who had been cured during admission. And 10 patients had history of hypertension, the blood pressure of whom had been well controlled. There are 21 patients seek medical care in the past year due to short of breath, distress etc, averaging 1~6 times per year. Sixteen patients got admission, and 6 patients had admission over 3 times per year (Table 1).

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Table 3. Anxiety-depression score of patients in group B

HAMD (n=8)	8~20	20~35	>35	Average
	1	6	2	30.22±15.27
HAMA (n=14)	7~14	14~29	>29	Average
	3	6	5	25.71±13.27

Table 4. Anxiety-depression score of patients in group D

HAMD (n=13)	8~20	20~35	>35	Average
	2	2	9	40.92±17.58
HAMA (n=21)	7~14	14~29	>29	Average
	5	6	10	28.14±14.47

General condition and COPD score of patients before treatment

There were 14 and 21 patients were assigned into B and D groups respectively. The general condition and COPD score of patients before treatment were shown in **Table 2**.

Anxiety-depression score

All the 35 patients have a HAMA score over 7. Among them, 15 patients have severe anxiety-depression (n=10 in group D and n=5 in group B). And 20 patients have slight to medium anxiety-depression (n=11 in group D and n=9 in group B). Besides, there were 21 patients have a HAMD score over 8. Among them, 11 patients have severe anxiety-depression (n=9 in group D and n=2 in group B). And 11 patients have slight to medium anxiety-depression (n=4 in group D and n=7 in group B, **Tables 3** and **4**).

Improvement of anxiety-depression and COPD after treatment

Referred to physicians' prescription from respiratory department, for patients in group B, 5 patients were treated with Zyprexa and 9 patients with mirtazapine. Meanwhile for patients in group D, 8 patients were treated with Zyprexa, 11 patients with mirtazapine and 2 patients with Alprazolam. Both HAMD and HAMA scores decreased after treatment, especially for patients in group D, which decreased significantly (**Table 5**).

The results of mMRC and CAT score also improved significantly. Eight patients in group D

improved to grade C, and one patient in group D had improved to grade A. Meanwhile 6 patients in group B improved to grade A. The treatment regime had also been revised accordingly (**Table 6**).

Adverse events during treatment

Twelve patients became sleepy during the treatment. Nine patients felt tired, while 3 complained of thirst. Most of symptoms diminished spontaneously. The symptoms of nine patients alleviated after the dose was adjusted. One patient experienced transient decline of white cells. The regime of treatment was maintained. Renal malfunction was not observed in any patient during the whole study period. Most patients could tolerate the whole therapy. Two patients in D group experienced continuous hypercapnia. One patient recovered after withdrawn and received respiratory stimulants. His/her regime was adjusted as mirtazapine from Alprazolam. The patient was further followed up for two months and respiratory failure had not been observed again. The other patient experienced disturbance of consciousness. He/she was withdrawn and given mechanical ventilation for 72 hours. The dose of regime was reduced and the patient was long-term followed up and respiratory failure had not been observed again.

Follow-up

Most of patients could comply to the psychotic treatment. The longest follow-up was 12 months. Some patients had repetitive short of breath and distress, which was alleviated immediately after the psychotic regime was adjusted. Nine patients was admitted 1~2 times during the period of follow-up. Three of them were confirmed not acute exacerbation according to clinical evidence. After adjustment of psychotic regime the symptoms were alleviated and patients were discharged. None of the participants died during the study period.

Discussion

COPD is a chronic, progressive respiratory disease which is characterized as continuous airway obstruction. It threatens people's health and results in high morbidity and mortality [5]. Patients with COPD are of high frequency to complicate anxiety-depression disorder.

Table 5. Improvement of anxiety-depression after treatment

		Before treatment	After treatment	F value	t value
HAMA	B (n=14)	25.71±13.27*	15.50±7.71*	4.215	2.49
	D (n=21)	28.14±14.47**	14.95±9.11**	4.403	3.536
HAMD	B (n=14)	30.22±15.27**	17.44±7.11**	0.083	2.276
	D (n=21)	40.92±17.58**	25.15±15.95**	0.043	2.396

*: statistically significant; **: strongly significant.

Table 6. Improvement of COPD after treatment

		Before treatment	After treatment	F value	t value
CAT	B (n=14)	17.14±6.11**	9.29±3.85**	3.46	4.069
	D (n=21)	27.46±10.06**	12.25±8.50**	0.583	4.290
mMRC	B (n=14)	2.25±0.97*	2.00±0.53*	6.97	0.686
	D (n=21)	3.05±0.81**	1.81±0.81**	0.19	0.185

*: statistically significant; **: strongly significant.

Previous study showed that anxiety-depression disorder is correlated with dyspnea, daily self-care and quality of life while not correlated with forced expiratory volume in one second (FEV1) [6]. Although the association between COPD and psychosomatic disorder has been confirmed by clinical study, it has not been understood systematically. And anxiety-depression disorder has not been listed as routine screen for COPD patients. Therefore, up to now the anxiety-depression disorder of COPD patients has not been properly diagnosed and cured [7, 8]. Besides, due to the COPD patients tends to cover their psychotic problems [9, 10], while respiratory physicians are not good at diagnosing them, the real number of anxiety-depression disorder may be significantly higher than the report [11, 12].

Recently it has been reported that COPD is a kind of somatopsychic illness. The inflammatory factors secreted from airway enter blood circulation and systemic disorder, such as cardiovascular disease, osteoporosis, anxiety-depression and Metabolic Syndrome [13]. The high prevalence of anxiety-depression has drawn physicians' attention. The complications of psychosomatic disease not only impair patients' quality of life and lead to heavy economic burden, but also increased the rate of suicide, and make the routine respiratory therapy less effective. In order to control the symptoms, the respiratory physicians have to give strong regimes to patients, which increased the rate of adverse events as well as medical costs.

Therefore, the research from psychosomatic aspect to alleviate anxiety-depression is essential for the treatment of COPD patients [14].

The annual morbidity of generalized anxiety disorder (GAD) in community is 1%~3%. And the lifetime incidence of GAD is 6%. GAD is also high in comorbidity rate. It has been reported that 68% of GAD patients comorbid with at least one other psychological disorder [15]. And 31.4% of GAD patients comorbid with depression. GAD is considered as a kind of cerebral dysfunction characterized with continuous an-

xious, fear, nervous and autonomic disorder, which is usually accompanied with somatic uncomfortable. The precipitating factor of GAD is mainly correlated with personality and the environment. The rational symptoms of GAD are usually strong. Anxiety-depression is the most prevalent negative emotions of COPD [16]. Due to the long course of COPD, the income as well as social activity usually weakened, which may induce psychosomatic disorder, thus aggravate COPD [17]. In this study we found that in patients of D group, 42.9% was complicated with severe anxiety, and 42.9% complicated with severe depression. In comparison, in patients of B group, the number was 14.3% and 19% respectively. The result showed that higher grade COPD complicated with more severe anxiety-depression, which is echoed by other's research [18]. For COPD patients that can't care themselves, or with complications such as diabetes mellitus, have greater chance to comorbid anxiety-depression [19]. It has been reported that 2%~74% COPD patients comorbid with anxiety, while 6%~80% COPD patients has potential or clinical depression symptoms [20, 21]. In china, the incidence of anxiety and depression comorbid with COPD was 19.8%~71% and 35.2%~69% respectively [22, 23].

After examination of pulmonary function combined with mMRC and CAT evaluation, 35 patients were assigned into B (n=14) and D (n=21) group. Standard respiratory therapy was given. Patients in group D were given inhaled

glucocorticoids and long active β_2 agonists (ICS/LABA) as well as inhaled long active anticholinergics (LAMA). Patients in group B were given inhaled LAMA. However, most patients complained that the symptoms such as distress and short of breath were not alleviated. And all the patients complained they could not sleep well due to symptoms of COPD. The regime was intensified for 80% of patients. Aminophylline and corticosteroid were applied. However, due to the side effects, patients suffered from palpitation, sleeping disorder, as well as obesity and weakened tolerance to labor. Additionally, worsen of COPD induced negative emotion. There were 62.9% (20/35) patients felt helpless. Ten patients had the thought of suicide. And one patient took action. There was evidence that the anxiety-depression of COPD was associated with application of corticosteroid, aminophylline and antibiotics such as quinolone [24]. Therefore, inappropriately strengthen the regime may not alleviate COPD. Furthermore, the side effects may induce and worsen the psychosomatic disorder of COPD patients, thus aggravate the disease.

After psychosomatic therapy, most patients have lower CAT and mMRC scores. And the psychosomatic therapy did not impair cardiovascular function. Besides, 90% patients had better sleep. As the "golden standard" for diagnosis of COPD, pulmonary function may be interfered by negative emotions, thus misguide the treatment for COPD. Eleven of the 35 patients took the pulmonary function test after psychosomatic therapy. One of them improved from COPD grade 4 to grade 1. The finding may indicate that psychosomatic therapy may have positive effect on the compliance of patients for pulmonary function test. However, due to only a few patients took the pulmonary function test, the analysis was somehow limited to get a strong statistical power.

Most COPD patients meet doctors at outpatient clinics. In China, due to limited time, it's quite difficult for the respiratory physicians to diagnosis anxiety-depression disorder that complicated with COPD patients. Additionally, the CAT is kind of subjective for patients [25]. Dyspnea is a parameter of mMRC, which is also included in HAMA and HAMD. Therefore, it should draw physicians' attention that it could be induced by psychosomatic problems. Most

of patients could tolerate the psychosomatic therapy. Two patients experienced continuous hypercapnia. After withdrawn and given respiratory stimulants, both of them recovered. There was not severe adverse events occurred during the whole study period. However, some patients didn't comply with psychosomatic therapy and lost in follow-up. One of the limitations is the small number and loss of patients in follow-up, which limited the statistical power of the analysis. Larger number of patients will be recruited for future study.

Currently a number of studies have focused on the intervention of anxiety-depression disorder to treat COPD [26]. Therapy on anxiety-depression could effectively alleviate COPD [27]. However, the overlap of symptoms of COPD and anxiety-depression may misguide the diagnosis and treatment, thus aggravate the disease progression. Early diagnosis and treatment of anxiety-depression disorder is essential and would make positive effect immediately. HAMD and HAMA is accurate and user-friendly for evaluation of depressive symptoms such as depression, mania and neurosis [28]. Therefore, special attention should be paid to anxiety-depression disorder complicated to COPD patients. And multidisciplinary treatment should be applied.

Disclosure of conflict of interest

None.

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