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Effect of anxiety and depression on pulmonary function as well as airway inflammation and remodeling in patients with bronchial asthma

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ABSTRACT

Objective: To study the effect of anxiety and depression on pulmonary function as well as airway inflammation and remodeling in patients with bronchial asthma. **Methods:** A total of 118 adult patients with bronchial asthma who were treated in our hospital between September 2015 and January 2017 were divided into pure depression group (n=30), pure anxiety group (n=47), depression + anxiety group (n=19) and mental health group (n=22) according to the Self-Rating Depression Scale (SDS) and Self-rating Anxiety Scale (SAS) score. The differences in the levels of pulmonary function parameters as well as the contents of serum inflammatory factors and airway remodeling indexes were compared among the four groups. **Results:** FEV1, PEF and FVC levels as well as serum TIMP-1 contents of pure depression group, pure anxiety group and depression + anxiety group were lower than those of mental health group while serum IL-2, IL-4, IL-8, IL-33, VEGF, OPN, TGF-β 1 and MMP-9 contents were higher than those of mental health group, and FEV1, PEF and FVC levels as well as serum TIMP-1 content of depression + anxiety group were lower than those of pure depression group and pure anxiety group while serum IL-2, IL-4, IL-8, IL-33, VEGF, OPN, TGF-β 1 and MMP-9 contents were higher than those of pure depression group and pure anxiety group. **Conclusion:** Anxiety and depression can aggravate the pulmonary function injury, increase airway inflammation and promote airway remodeling process in patients with bronchial asthma.

1. Introduction

Adult bronchial asthma is common in clinical practice, those with poorly controlled illness can develop repeated airway infection and end up with irreversible organic airway changes, and they have increased probability of long-term chronic bronchitis, chronic obstructive pulmonary disease and other complex respiratory system diseases[1,2]. As the incidence of bronchial asthma increases, the role of psychological factors in the development and outcome of diseases is gradually concerned. Previous studies have pointed out that most patients with bronchial asthma have negative emotions such as anxiety and depression, and the negative emotions increase as the course of the disease is prolonged[3–5]. At present, there is no conclusion about the clear relationship between the negative emotions and bronchial asthma condition, the anxiety and depression scores were used in this study to group the patients with bronchial asthma, and the differences in lung function, airway inflammation, airway remodeling and other illness-related indexes were compared between them in order to clarify the influence of different psychological states on bronchial asthma condition, now reported as follows.

2. Information and methods

2.1 Case information

A total of 118 adult patients with bronchial asthma who were treated in our hospital between September 2015 and January 2017

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were selected, and the patients or the family members signed the informed consent. Inclusion criteria: (1) 18 years old; (2) with normal cognitive function and could conduct anxiety and depression scale evaluation; (3) completing the whole inspection and with complete data. Exclusion criteria: (1) combined with chronic bronchitis, chronic bronchitis and other airway inflammatory diseases; (2) the combination of severe cardiac renal insufficiency; (3) serious autoimmune disease is combined.

The self-rating scale (SDS) and the anxiety self-assessment scale (SAS) were evaluated for the enrolled patients, SDS 53 points was judged as depression and SAS 50 points was judged as anxiety. According to SDS and SAS scores, 118 patients were divided into pure depression group (n=30), pure anxiety group (n=47), depression + anxiety group (n=19) and mental health group (n=22). Pure depression group included 16 men and 14 women that were 24-61 years old; pure anxiety group included 24 men and 23 women that were 27-63 years old; depression + anxiety group included 9 men and 10 women that were 25-67 years old; mental health group included 12 men and 10 women that were 22-70 years old. The gender and age distribution of the four groups were not statistically different (P>0.05), and the hospital ethics committee approved the study.

2.2 Observation indexes

Immediately after admission, pulmonary function test was conducted, all the participants completed three times of pulmonary ventilation function tests, the best one was taken as the detection value, and the forced expiratory volume in one second (FEV1), peak expiratory flow (PEF) and forced vital capacity (FVC) were recorded. 3.0 mL of fasting cubital venous blood was extracted from four groups, anticoagulated with low molecular heparin sodium and centrifuged at low speed to get upper serum, and enzyme-linked immunosorbent assay (ELISA) was used to detect serum levels of inflammatory cytokines interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-8 (IL-8) and interleukin-33 (IL-33). ELISA was used to determine the serum levels of airway remodeling-associated factors vascular endothelial growth factor (VEGF), osteopontin (OPN), transforming growth factor β 1 (TGF-β 1), matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1).

2.3 Statistical methods

Pulmonary function parameters, inflammatory factors and airway remodeling indexes belonged to measurement data and were in terms of mean ± standard deviation, comparison among four groups was by variance analysis and pair-wise comparison between groups was by LSD methods. Statistic P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Pulmonary function

Comparison of pulmonary function parameters FEV1 (L), PEF (L/s) and FVC (L) levels among four groups of patients was as follows: FEV1, PEF and FVC levels of pure depression group, pure anxiety group and depression + anxiety group were lower than those of mental health group, FEV1, PEF and FVC levels of depression + anxiety group were lower than those of pure depression group and pure anxiety group, and differences in pair-wise comparison of FEV1, PEF and FVC levels were statistically significant among four groups of patients (P<0.05), shown in Table 1.

Table 1.

Comparison of pulmonary function parameter levels among four groups of patients.

Groups	n	FEV1	PEF	FVC
Mental health group	22	1.58±0.19	5.83±0.69	2.94±0.35
Pure depression group	30	1.31±0.16[a]	5.16±0.59[a]	2.54±0.26[a]
Pure anxiety group	47	1.30±0.15[a]	5.21±0.58[a]	2.52±0.27[a]
Depression + anxiety group	19	1.14±0.13[abc]	4.27±0.57[abc]	2.13±0.25[abc]
F		8.198	7.251	6.408
P		<0.05	<0.05	<0.05

Note: compared with mental health group, [a]P<0.05; compared with pure depression group, [b]P<0.05; compared with pure anxiety group, [c]P<0.05.

3.2 Inflammatory factors

Comparison of serum inflammatory factors IL-2, IL-4, IL-8 and IL-33 contents among four groups of patients was as follows: serum IL-2, IL-4, IL-8 and IL-33 contents of pure depression group, pure anxiety group and depression + anxiety group were significantly higher than those of mental health group, serum IL-2, IL-4, IL-8 and IL-33 contents of depression + anxiety group were higher than those of pure depression group and pure anxiety group, and differences in pair-wise comparison of serum IL-2, IL-4, IL-8 and IL-33 contents were statistically significant among four groups of patients (P<0.05), shown in Table 2.

Table 2.

Comparison of serum inflammatory factor contents among four groups of patients (pg/mL).

Groups	n	IL-2	IL-4	IL-8	IL-33
Mental health group	22	49.83±6.24	15.48±1.77	32.71±4.52	114.82±14.76
Pure depression group	30	59.74±6.35[a]	19.22±2.64[a]	40.83±4.61[a]	136.27±15.79[a]
Pure anxiety group	47	59.83±6.29[a]	19.35±2.59[a]	40.79±4.58[a]	135.36±14.83[a]
Depression + anxiety group	19	71.25±8.36[abc]	26.37±3.51[abc]	49.26±5.41[abc]	175.93±21.46[abc]
F		14.928	15.637	13.587	16.387
P		<0.05	<0.05	<0.05	<0.05

Note: compared with mental health group, [a]P<0.05; compared with pure depression group, [b]P<0.05; compared with pure anxiety group, [c]P<0.05.

Table 3.

Comparison of serum airway remodeling index contents among four groups of patients.

Groups	*n*	VEGF	OPN	TGF- β 1	MMP-9	TIMP-1
Mental health group	22	81.63±9.54	24.17±3.09	37.28±4.51	14.38±1.76	49.73±5.51
Pure depression group	30	89.72±9.61[a]	33.85±4.11[a]	45.19±5.36[a]	19.64±2.53[a]	32.74±4.18[a]
Pure anxiety group	47	89.68±9.45[a]	32.63±4.09[a]	45.23±5.28[a]	19.58±2.47[a]	31.69±4.32[a]
Depression + anxiety group	19	97.48±10.57[abc]	46.35±5.88[abc]	54.19±6.24[abc]	30.17±4.25[abc]	22.53±3.81[abc]
F		14.287	9.287	11.261	15.093	10.726
P		<0.05	<0.05	<0.05	<0.05	<0.05

Note: compared with mental health group, [a]$P<0.05$; compared with pure depression group, [b]$P<0.05$; compared with pure anxiety group, [c]$P<0.05$.

3.3 Airway remodeling indexes

Comparison of serum airway remodeling indexes VEGF (pg/mL), OPN (ng/mL), TGF- β 1 (pg/mL), MMP-9 (μg/mL) and TIMP-1 (ng/mL) contents among four groups of patients was as follows: serum VEGF, OPN, TGF- β 1 and MMP-9 contents of pure depression group, pure anxiety group and depression + anxiety group were significantly higher than those of mental health group while TIMP-1 contents were lower than those of mental health group, serum VEGF, OPN, TGF- β 1 and MMP-9 contents of depression + anxiety group were higher than those of pure depression group and pure anxiety group while TIMP-1 content was lower than that of pure depression group and pure anxiety group, and differences in pair-wise comparison of serum VEGF, OPN, TGF- β 1, MMP-9 and TIMP-1 contents were statistically significant among four groups of patients ($P<0.05$), shown in Table 3.

4. Discussion

Bronchial asthma is a chronic airway inflammatory disease, the duration of the disease can be long, and mental state changes may occur in the patients and affect the disease outcome[6,7]. Epidemiological cross-sectional studies have shown that patients' anxiety and depression status are closely related to the control of asthma, but there is no clear research report on the specific aspects and extent of the effects. SDS and SAS are the conventional scales judging the existence and severity of depression and anxiety, they have been proven to have good reliability and validity in judging the negative emotions[8,9], and their scores were used as boundary in the study to group the enrolled patients in order to clarify the effect of emotional state on the concrete bronchial asthma condition and lay a foundation for subsequent clinical intervention.

With the evolution of bronchial asthma condition, the lung function may be obviously abnormal when there is irreversible airway function change, and therefore, the pulmonary function parameter levels can objectively and accurately reflect the bronchus asthma severity[10–12]. Abnormal lung function is mainly characterized by the decrease in FEV1, PEF and FVC levels, the differences in the levels of the above parameters were compared among the four groups of patients in this study, and it was found that compared with those of mental health group, FEV1, PEF and FVC levels of the other three groups decreased, indicating that the lung function abnormality is more obvious in bronchial asthma patients with negative emotions; FEV1, PEF and FVC levels of depression + anxiety group were lower than those of pure depression group and pure anxiety group, showing that the influence on lung function is more severe in bronchial asthma patients with multiple negative emotions, which may be closely related to their low medication compliance, abnormal hormone levels and so on.

Chronic airway inflammatory disease is a fundamental change in patients with bronchial asthma. The aggravation of asthma is also due to the aggravation of the airway inflammatory response. Allergens can cause allergic diseases after they stimulate the patient's airway, and a large number of inflammatory factors are secreted in the airway and released into circulating blood, causing local and systemic inflammation[13,14]. IL-2, IL-4 and IL-8 are typical inflammatory mediators, it has been confirmed in different studies that they are massively present in patients with acute stage of asthma, and their levels can determine the severity of asthma[15,16]. The activation of IL-33/ST2L signaling pathway may activate Th2 cells, encourage other pro-inflammatory factors to be released and amplify the inflammatory response. Therefore, the detection of IL-33 levels is conducive to the diagnosis and assessment of bronchial asthma[17,18]. In this study, the differences in serum contents of these inflammatory factors were compared among the four groups of patients, and it was found that compared with those of mental health group, serum IL-2, IL-4, IL-8 and IL-33 contents of the other three groups increased; serum IL-2, IL-4, IL-8 and IL-33 contents of depression + anxiety group were higher than those of pure depression group and pure anxiety group, indicating that the degree of airway inflammation increases in patients with bronchial asthma with the aggravation of negative emotions, confirming the negative effect of anxiety and depression on the bronchial asthma condition.

With the increased attack frequency of local airway inflammation and the aggravation of asthma, patients gradually develop airway remodeling, which specifically includes subepithelial collagen

deposition, subepithelial fibrosis proliferation, basement membrane hyalin denaturation, false basement membrane thickening, etc. A variety of factors in circulating blood are involved in the above changes in airway epithelial cells, and VEGF is mainly involved in the proliferation of epithelial cells; OPN affects collagen deposition; TGF-β1 is a key factor that stimulates the synthesis of extracellular matrix and it plays its role by promoting the synthesis and release of connective tissue growth factor; MMP-9 and TIMP-1 mainly promote airway smooth muscle hyperplasia, and the ratio of MMP-9/TIMP-1 of bronchial asthma patients is significantly lower than that of normal people. In the study, the differences in serum levels of these airway remodeling indexes were compared among the four groups of patients, and it was found that compared with those of mental health group, serum VEGF, OPN, TGF-β1 and MMP-9 contents of the other three groups increased while TIMP-1 contents decreased; serum VEGF, OPN, TGF-β1 and MMP-9 contents of depression + anxiety group were higher than those of pure depression group and pure anxiety group while TIMP-1 content was lower than that of pure depression group and pure anxiety group, confirming that the airway remodeling is more serious in bronchial asthma patients with severe negative emotions, and negative emotion is one of the causes of airway remodeling progress.

The lung function is poorer, and the airway inflammation and airway remodeling are more serious in patients with bronchial asthma if they have anxiety and depression. Negative emotion is one of the direct causes of exacerbation of bronchial asthma, which should be taken seriously and targeted in future clinical intervention.

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