ASSESSMENT OF BRAIN ENERGY METABOLISM AND NUTRITIONAL STATUS OF COPD PATIENTS

Weidong Tang*, Qi Chen, Linlin Chen, Suping Chen, Xuebo Shao, Xia Wang, Lijun Zhu
Intensive Care Unit, The First people's Hospital of Fuyang, Hangzhou 311400, China

ABSTRACT

Purpose: *The aim of this study was to investigate the effects of recombinant human growth hormone on nutritional status and immune function in patients with chronic obstructive pulmonary disease.*

Methods: *The patients with moderate and severe chronic obstructive pulmonary disease were randomly divided into two groups, each of which was given routine treatment of anti-infection, expectorant and bronchiectasis. Group A was the control group, and standard nutrition support was added on the basis of routine treatment. Group B was a growth hormone treatment group. On the basis of group A's treatment, recombinant human growth hormone was added. All patients were measured 2 days before and after the treatment.*

Results: *Compared with group A, nutritional indicators including serum albumin, transferrin and prealbumin increased; creatinine and urea were reduced; the proportion of T lymphocyte subsets increased.*

Conclusion: *The above indicators are related to chronic obstructive pulmonary disease.*

Keywords: *COPD, Function Level of Brain Energy Metabolism, Nutritional Status.*

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease. The main characteristic is the progressive development of the incomplete and reversible airflow limitation. Smoking is the important cause of the disease. It is characterized by chronic inflammation of the airway, lung parenchyma and blood vessels. In the pathogenesis of COPD, there exist the imbalance of protease and protease, the decrease of antioxidative activity in the lungs, the imbalance of immune system, repeated bacterial infection and the joint action of cell adhesion molecules and cytokine. The current research shows that COPD is not only a lung disease with characteristics including decline in lung function, dyspnea and even respiratory failure, but also a systemic disease. Its pathophysiological changes are mainly due to systemic inflammation caused by lung inflammation, which then leads to a series of complications including poor nutrition, the decline of immune function, and the damage of multiple organs in the whole body. With the disease get worse, the patients gradually lose their ability to work, thus severely reducing the quality of personal life, which brings heavy burden to the family and society. Many complications are caused by COPD, including malnutrition, muscle atrophy, the decline of immune function, abnormal energy metabolism of the brain, osteoporosis and so on, all of which have become an important reason for the recurrence of the disease, the gradual loss of the labor force and the decline of the life quality.

Malnutrition: malnutrition is a common complication of COPD patients. Researchers have found that about 20% of COPD patients have malnutrition. As one of the important complications of COPD, it is an independent risk factor for poor prognosis in COPD patients. Malnutrition reduces the strength of respiratory muscle and the endurance of the patients. Immune function has also been seriously damaged, which increases the incidence of pulmonary infection[1].

Immunosuppression

COPD patients have immunosuppression, mainly manifested in the decrease of immunoglobulin (IgM, IgG, IgA), the apoptosis of CD3+, CD4+ and other lymphocytes, and the reduction of presentation ability of macrophage antigen. Immunoglobulin closely related to antibacterial immunity is mainly IgM, IgG and IgA. IgA is an important defense barrier for respiratory tract mucosa. IgA is in the form of dimer[2]. Its content decreases with the decrease of serum IgA. The study shows that the proportion of Fas positive CD8+T cells in peripheral blood of COPD patients with smoking increases. The results suggest that the apoptosis behavior of lymphocytes may be regulated by the apoptosis of Fas.FasL[3].

Decrease of energy metabolism in brain

COPD as a systemic disease may lead to a lot of complications, including damages to brain. As an organ highly depending on oxygen, the brain can be severely damaged by hypoxia. The study found that the volume of the hippocampus of oxygen dependent COPD patients decreases by 11% compared to that of the control group, which may be one of the causes of memory, cognition and emotional changes in COPD patients. The decrease of long-term blood oxygen saturation leads to the brain damage of COPD patients in normal activities[4]. With 1H-MRS, researchers found that the concentration of energy metabolites in the white matter in the brain of COPD patients with clinical symptoms was lower than that of the normal control group[5]. Although the literature has confirmed that the brain energy metabolism of COPD patients is lower than that of the normal people, the specific mechanism of brain energy metabolism changes is still lacking further clinical study.

Methods

General information

60 patients with moderate or severe AECOPD in Department of respiration, Fuzhou General Hospital of Nanjing military region (33 males and 27 females with an age span of 50~75, and the average age is 63.4±6.4 years old) were selected. They were randomly divided into routine treatment group A (28 patients) and Group B (32 patients) with routine treatment and recombinant human growth hormone. There was no significant difference in age, sex, height, body weight and CAT score between the two groups. The patients above were selected as the observation group, and another 12 patients without COPD were selected as healthy control group including 8 males and 4 females, of which the age range was 50-75 years old with an average age of 65.3±4.6 years old). There was no statistical difference in the age of the two groups.

Methods

According to the study, group A and B were given routine treatment of anti-infection, expectorant, and bronchiectasis. Standard nutritional support on the basis of routine treatment was given to group A which is the control group (28 cases). Group B was a growth hormone treatment group (32 cases). On the basis of group A's treatment, recombinant human growth hormone (r-hGH) was added[6]. Serum albumin (ALB), transferrin (TRF), prealbumin (PA), creatinine, urea, immunoglobulin (IgA, IgM, IgG) and T lymphocyte subsets (CD3+, CD4+, CD4+/CD8+) in peripheral blood were measured by flow cytometry in all patients two days before and after the treatment[7,8].

15 cases of AECOPD patients and 12 age-matched cases in control group were examined by 1H-MRS: Axial T1WI, T2WI and sagittal T1WI are carried out by GE 1.5 T or Siemens 3.0 T MRI scanners on all subjects. The axis plane T2WI was used to determine the region of interest and volume element is 2.0cm×2.0cm×2.0cm[9-13].

The chemical shift of N- acetyl aspartic acid (NAA) is 2.0ppm; the chemical shift of the creatine complex (Cr) is 3.0ppm; the chemical shift of the choline complex (Cho) is 3.3ppm.

Statistical method

Data were analyzed by SPSS19.0 statistical software, and $P < 0.05$, which was considered statistically significant.

Results and discussion

Nutrition index

Compare group B with group A: serum albumin (ALB), transferrin (TRF) and prealbumin (PA) were significantly increased ($P<0.05$), while creatinine and urea decreased significantly ($P<0.05$). The difference was statistically significant as shown in Table 1.

Groups	Prealbumin (g/L)	Transferrin (g/L)	albumin (g/L)	Creatinine (ummol/L)	Urea (mmmol/L)
Group A					
Before treatment	0.24±0.08	1.98±0.41	30.11±3.2	72.0±16.2	5.62±1.30
After treatment	0.25±0.07	2.04±0.40	31.14±2.9	72.5±15.1	5.65±1.25
Group B					
Before treatment	0.25±0.08	1.90±0.29	29.47±2.2	68.9±12.7	5.20±1.62
After treatment	0.35±0.11△#	2.11±0.31△#	32.8±2.8△#	62.8±11.0△#	4.55±1.46△#

Table. 1: Changes in nutritional status before and after treatment in both groups of patients.
Compared with group A after treatment, △P<0.05, compared with group B before treatment, #P<0.05.

Immunological index

Compare group B with group A: immunoglobulin (Ig A, Ig M, Ig G), T lymphocyte subgroup (CD3+, CD4+, CD4+/CD8+)increased significantly, the difference of which was statistically significant as shown in Table 2.

Groups	Ig A (g/L)	Ig G (g/L)	Ig M (g/L)	CD3+ (%)	CD4+ (%)	CD4+ /CD8+
Group A						
Before treatment	2.25±0.57	10.2±2.7	0.95±0.47	33.9±6.7	29.3±7.1	0.81±0.26
After treatment	2.27±0.56	10.3±2.5	0.99±0.46	34.2±7.5	29.8±7.5	0.84±0.22
Group B						
Before treatment	2.39±0.55	10.1±2.6	1.09±0.32	32.1±4.4	30.9±8.5	0.83±0.31
After treatment	2.75±0.58△#	12.4±3.3△#	1.25±0.34△#	37.2±4.6△#	34.9±7.8△#	1.27±0.34△#

Table. 2: Comparison of changes in immunological parameters before and after treatment in the two groups of patients.
Compared with group A after treatment, △P<0.05, compared with group B before treatment, #P<0.05.

Arterial blood gas analysis and Results (mm Hg) Analysis of FEV1%pred

Pa O2 of AECOPD group was lower than that of control group (P<0.05); Pa CO2 was higher than that of control group (P<0.05), and the basic FEV1%pred in AECOPD group was (46.4±9.3).

Determination of 2/3 metabolite concentration.

• The NAA integral value, Cho integral value, Cr integral value and NAA/Cr ratio of occipital part of the AECOPD group were lower than those of healthy control group (P<0.05).

• The NAA integral value, Cr integral value and NAA/Cr ratio of group AECOPD were lower than those of the top-temporal part of the healthy control group (P<0.05).

• There was no statistical significance in the difference in the Cho/Cr ratio in occipital part between AECOPD group and healthy control group.

• There was no statistical significance in the difference in the Cho value and Cho/Cr ratio of the top-temporal part of AECOPD group and the healthy control group (6.50 (1.70), 0.79 + 0.18).

• The occipital NAA integral value, Cho integral value and top-temporal NAA/Cr value of the AECOPD group have positive correlation with the FEV1%pred (P<0.05). Details are shown in Table 3, 4, 5, and 6.

Occipital metabolite concentration	AECOPD group	Control group	P value
NAA	8.86±3.30	13.74±4.70	0.004*
Cho	4.85±1.49	7.59±2.42	0.001*
Cr	5.83±1.99	8.44±3.03	0.013*
NAA/Cr	1.52±0.15	1.65±0.17	0.049*
Cho/Cr	0.85±0.10	0.85±0.10	0.15

Table. 3: Comparison of brain metabolite concentrations between AECOPD group and healthy control group.
**Difference between groups, P<0.05.*

Top-temporal metabolite concentration	AECOPD group	Control group	P value
NAA	8.78±3.36	13.44±3.06	0.001*
Cho	4.86(3.40)	6.50(1.70)	0.09
Cr	6.56±2.12	8.75±1.07	0.003*
NAA/Cr	1.32±0.18	1.53±0.20	0.013*
Cho/Cr	0.85±0.15	0.79±0.18	0.34

Table. 4: Comparison of brain metabolite concentrations between AECOPD group and healthy control group.
**Difference between groups, P<0.05.*

Occipital metabolite concentration	AECOPD Group metabolite concentration	Correlation coefficient rs	P value
NAA	8.86±3.30	0.54	0.038*
Cho	4.85±1.49	0.56	0.03*
Cr	5.83±1.99	8.44±3.03	0.013*
NAA/Cr	1.52±0.15	0.53	0.04*
Cho/Cr	0.85±0.10	0.34	0.21

Table. 5: Correlation between brain metabolite concentration and FEV1% pred in AECOPD group.
**AECOPD group occipital, NAA integral, Cho integral, NAA/Cr values positively correlated with FEV1%pred, P<0.05.*

Top-temporal metabolite concentration	AECOPD Group metabolite concentration	Correlation coefficient rs	P value
NAA	8.78±3.36	0.036	0.9
Cho	4.86(3.40)	-0.17	0.55
Cr	6.56±2.12	-0.19	0.49
NAA/Cr	1.32±0.18	0.63	0.013*
Cho/Cr	0.85±0.15	0.079	0.78

Table. 6: Correlation between brain metabolite concentration and FEV1% pred in AECOPD group.
**The AECOPD group had a positive correlation between NAA/Cr values (standard *) and FEV1% pred, P<0.05*

Conclusion and outlook

NAA, Cho and Cr are the metabolites that reflect the normal energy metabolism of the brain. NAA, a neurotransmitter, is a marker of the neuron and its axons. The loss of neuron and axon damage can reduce NAA. The study shows that the content of NAA in the brain decreases with the increase of age and many brain diseases, such as tumors, Infarct, stroke and hypoxia can cause the decrease of NAA concentration in the brain. Cho reflects the total choline content in the brain. The decrease of Cho reflects the weakening of cell membrane transport, cholinergic neurons (see Figure 1) and memory function of the brain are closely related with each other; Cr is the marker of the energy metabolism of brain cells, the wave peak of which is relatively stable. NAA, as a neurotransmitter, reflects the damage of neurons and axons, and hypoxia may decrease its concentration. However, some studies have found that long-term oxygen therapy may conducive to NAA recovery in the brain. In addition, Cr participates in the metabolism and storage of brain energy. According to the study, the decrease of Cr in the brain of AECOPD patients may be due to brain energy deficiency induced by hypoxia, and cognitive impairment of AECOPD patients may also be relative to the decrease of Cho in the brain.

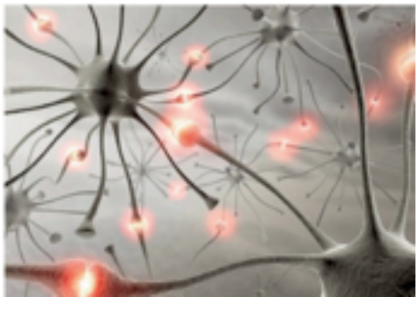

Figure 1: Neurons.

The study pointed out that the severe lack of protein and energy as well as malnutrition of COPD patients resulted in the weakening of immune function, the decrease in the number of T lymphocytes and the inhibitation of the synthesis of immunoglobulin, all of which result in recurrence and aggravation. This study showed the levels of peripheral blood immunoglobulin (Ig A, Ig M, Ig G), the proportions of CD3+ and CD4+ in T lymphocyte subsets and the increase of CD4+/CD8+ after treatment, indicating that the humoral immunity and cellular immune function of the patients were improved.

In the study of the mechanism and treatment of local pulmonary lesions, related researches on COPD extra-pulmonary complications should be enhanced so that to strengthen the systemic treatment of COPD, reduce the mortality of COPD, and improve the quality of life of the patients with COPD.

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Corresponding Author:
Weidong Tang
Intensive Care Unit, The First people's Hospital of Fuyang, Hangzhou311400, China
Email: tangweidongfuyang@163.com
(China)