CLINICAL APPLICATION OF TANREQING INJECTION COMBINED WITH NUTRITIONAL SUPPORT IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Introduction: *The purpose of this study was to investigate the clinical application value of Tanreqing injection combined with nutritional support (enteral nutrition emulsion TPF-T) in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) patients.*

Materials and method*: A total of 126 AECOPD patients admitted to our hospital from January 2017 to February 2021 were randomly divided into study group (n=63) and control group (n=63) according to a random number table. Tanreqing injection was used in control group. In the study group, nutritional support (enteral nutrition emulsion TPF-T) was added on the basis of the control group. Nutrition indexes serum Hb (Hb) , total lymphocyte count (TLC) ,pre-albumin (PA), albumin (ALB), serum TF (TF) ; serum immunoglobulins IgA, IgG and IgM and serum inflammatory markers CRP, IL-1β, COX-2 and PGE2 levels were compared.*

Results*: After treatment, the levels of serum Hb, TLC, PA, ALB and TF in study group were significantly higher than those in control group (all p< 0.001); serum immunoglobulin indexes IgA, IgG and IgM in study group were higher than those in control group (p = 0.003, 0.008 and 0.025, respectively);levels of serum inflammatory markers CRP, IL-1β, COX-2, and PGE2 in the study group were lower than those in control group (p<0.001, p=0.001, p=0.032 and p=0.014, respectively).*

Conclusion*: Tanreqing injection combined with nutritional support (enteral nutrition emulsion TPF-T) can improve nutrition and immune indexes and reduce the level of inflammation in AECOPD patients, so it has certain clinical application value.*

Keywords: *Tanreqing injection, nutritional support, acute exacerbation of chronic obstructive pulmonary disease (AECOPD), Inflammatory markers.*

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Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic and progressive respiratory disease defined as the presence of incomplete reversible airflow obstruction. The acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is contributive to the death of patients, who develop clinical symptoms of cough, shortness of breath or increased wheezing, increased sputum in purulent or mucopurulent form, accompanied by fever in a short period[(1)].

Currently, the exact pathogenesis of AECOPD is not fully understood, but it has been proposed that the condition of AECOPD patients is associated with decreased pulmonary function and inflammatory response. Malnutrition, which is commonly seen in COPD patients, leads to decreased immune defense function and affects pulmonary ventilation function, further resulting in recurrent acute exacerbation, which is detrimental to the prognosis of patients[(2)] At present, conventional western clinical therapies for AECOPD patients include anti-infective, antispasmodic, and antiasthmatic treatment.

Although they can improve the clinical symptoms of patients, the effect is not good enough[3]

Viral infection plays a vital role in the pathogenesis of AECOPD[4] However, there has been a lack of effective antiviral drugs. Tanreqing injection is composed of Scutellaria baicalensis, cornu gorais, bear gall powder, lonicera japonica, and forsythia. This formula has five flavors that are compatible with each other, exerting effects of clearing heat, detoxifying, and reducing phlegm[5] It has been shown that the combination of Tanreqing injection with conventional western therapies can effectively improve the clinical efficacy in treating COPD patients[6] But no final conclusion has yet been reached on the efficacy of Tanreqing injection in the treatment of AECOPD due to small sample size and inconsistent assessment criteria of existing studies, which has limited the clinical promotion of Tanreqing injection.

The effects of malnutrition on COPD patients are manifold, such as worsening the patients' condition, increasing mortality and treatment costs[7] Nutritional support for COPD patients significantly improves body and muscle masses, respiratory muscle strength, and quality of life[8] However, the exact dose and duration of nutritional support remain unclear. It has been suggested that oral nutritional supplements effectively improve nutritional intake and status in elderly patients[9] Enteral nutritional emulsion TPF-T (trade name Ruining) is a high energy (5.46 kJ/ml), high protein (18%) nutritional supplement for tube feeding or oral use.10 Currently, application of Tanreqing injection combined with nutritional support (enteral nutritional emulsion TPF-T) in the clinical treatment for COPD patients has been rarely reported.

The purpose of this study was to investigate the clinical application value of Tanreqing injection combined with nutritional support (enteral nutrition emulsion TPF-T) in AECOPD patients.

Materials and methods

Clinical materials

With the approval of the Research Ethical Committee of the Xianning Central Hospital, The First Affiliated Hospital of Hubei University of Science And Technology, China. A total of 126 AECOPD patients admitted to our hospital from January 2017 to February 2021 were selected as research subjects. Inclusion criteria were that patients who met relevant diagnostic criteria in the Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease revised by the Chinese Medical Association in 2013; lung function graded II-III; duration of acute exacerbation ≤7 d; classified as phlegm-heat obstructing lung according to TCM, as evidenced by fever, cough and sputum, increased sputum, chest tightness and shortness of breath, abdominal distension and constipation, red tongue, white greasy coating, and taut slippery pulse; score of the Nutrition Risk Screening 2002 (NRS-2002) for the inpatients ≥3; signed informed consent.

Exclusion criteria were that patients with severe heart, liver, kidney, brain and other important organ insufficiency; patients with serious complications such as septic shock, unconsciousness or in need of mechanical ventilation; patients with tuberculosis or fungal infection, malignant tumor, diabetes mellitus or immunodeficiency; patients with diffuse bronchitis, bronchiectasis, occlusive bronchitis and other diseases of airflow obstruction; patients who received relevant drug treatment within the last month; patients who were allergic or hypersensitive to Tanreqing injection; patients with contraindications to enteral nutrition therapy.

Methods

The 126 AECOPD patients were randomly divided into a study group (n=63) and a control group (n=63) according to a random number table. Conventional therapy, namely symptomatic treatment such as routine oxygen inhalation, anti-infection, eliminating phlegm and bronchodilator with full diet was given in both groups. In the control group, 20 mL Tanreqing injection was added once a day by intravenous drip for 10 days of continuous treatment. In the study group, nutritional support was added, namely part of the energy was provided by the enteral nutrition emulsion TPF-T (trade name Ruineng) instead, which was given 200 ml/d orally, 3 times/d, providing 546 kJ/100 ml of calories, for 10 days of continuous treatment.

Observed indexes

Before and after treatment, 5 mL fasting peripheral venous blood was taken in the morning, and the nutrition indexes serum Hb (Hb) and total lymphocyte count (TLC) were measured on a hematocrit analyzer; the nutrition indexes serum pre-albumin (PA), albumin (ALB), serum TF (TF) and serum immunoglobulins IgA, IgG and IgM on a fully automated biochemical analyzer; the serum inflammatory marker CRP level by scatter immune

turbidity method, and the serum inflammatory markers IL-1β, COX-2 and PGE2 levels by enzyme-linked immunosorbent assay.

Statistic analysis

SPSS 25 software was used to analyze data. Measurement data were expressed by mean±standard deviation, and tested by independent sample t test. Counting data were expressed by n (%), and tested by Chi-square test. P<0.05 indicates that difference is significant.

Results

Comparison of demographic data

There was no statistically significant difference in sex (male), age, duration of COPD, duration of acute exacerbation, and pulmonary function grading between the two groups (p=0.688, 0.171, 0.362, 0.441 and 0.581, respectively, Table 1).

Parameter	Study group (n=63)	Control group (n=63)	X^2/t	P-value
Male[n(%)]	47(74.60)	45(71.43)	0.161	0.688
Age(year)	63.92±7.70	62.19±6.36	1.375	0.171
Duration of COPD (year)	11.28±3.57	10.75±2.95	0.915	0.362
Duration of acute exacerbation (year)	4.35±1.21	4.18±1.34	0.773	0.441
Pulmonary function grading II [n(%)]	38(60.32)	41(65.08)	0.305	0.581
Pulmonary function grading III [n(%)]	25(39.68)	22(34.92)		

Table 1: Comparison of demographic data.

Comparison of serum nutrition indexes

Before treatment, there were no differences in the levels of serum nutrition indexes Hb, TLC, PA, ALB and TF between the two groups (p=0.199, 0.470, 0.129, 0.351 and 0.198, respectively). After treatment, the levels of serum Hb, TLC, PA, ALB and TF in the study group were significantly higher than those in the control group (all p< 0.001), as shown in Table 2.

Parameter	Time	Study group (n=63)	Control group (n=63)	*t*	*P-value*
Serum Hb(g/L)	Before treatment	115.55±7.29	117.04±5.54	-1.290	0.199
	After treatment	129.62±5.12	125.75±4.79	4.382	<0.001
Serum TLC(**×10⁹**/L)	Before treatment	1.28±0.39	1.33±0.46	-0.725	0.470
	After treatment	1.87±0.46	1.62±0.28	3.619	<0.001
Serum PA(mg/L)	Before treatment	171.60±23.32	177.22±17.55	-1.527	0.129
	After treatment	251.94±37.09	231.10 ± 27.43	3.586	<0.001
Serum ALB(g/L)	Before treatment	28.43±3.46	28.99±3.17	-0.936	0.351
	After treatment	33.25±3.28	31.34±2.53	3.669	<0.001
Serum TF (mg /L)	Before treatment	1.24±0.15	1.26±0.09	-1.295	0.198
	After treatment	1.67±0.09	1.48±0.17	8.186	<0.001

Table 2: Comparison of serum nutrition indexes.

Comparison of serum immunoglobulin indexes

Before treatment, there were no significant differences in the levels of serum immunoglobulin indexes IgA, IgG and IgM between the two groups (p = 0.876, 0.084 and 0.424, respectively). After treatment, the serum immunoglobulin indexes IgA, IgG and IgM in the study group were higher than those in the control group (p = 0.003, 0.008 and 0.025, respectively), as shown in Table 3.

Parameter	Time	Study group (n=63)	Control group (n=63)	*t*	*P*-value
Serum IgA (g /L)	Before treatment	2.48±0.45	2.49±0.42	-0.156	0.876
	After treatment	2.64±0.27	2.51±0.19	3.080	0.003
Serum IgG (g /L)	Before treatment	11.89±1.74	11.43±1.23	1.741	0.084
	After treatment	12.78±1.46	12.12±1.26	2.700	0.008
Serum IgM (g /L)	Before treatment	0.96±0.23	1.00±0.22	-0.802	0.424
	After treatment	1.10±0.24	1.03±0.05	2.262	0.025

Table 3: Comparison of serum immunoglobulin indexes .

Comparison of serum inflammatory markers

Before treatment, there were no statistically significant differences in the levels of serum inflammatory markers CRP, IL-1β, COX-2, and PGE2 between the two groups (p=0.858, 0.962, 0.909 and 0.163). After treatment, the levels of serum inflammatory markers CRP, IL-1β, COX-2, and PGE2 in the study group were lower than those in the control group (p<0.001, p=0.001, p=0.032 and p=0.014, respectively), as shown in Table 4.

Parameter	Time	Study group (n=63)	Control group (n=63)	*t*	*P*-value
Serum CRP (mg/L)	Before treatment	38.46±4.53	38.32±3.87	0.179	0.858
	After treatment	26.62±2.58	30.35±2.39	-8.399	<0.001
Serum IL-1β (pg/mL)	Before treatment	9.15±1.04	9.16±0.97	-0.048	0.962
	After treatment	6.24±1.00	6.83±0.91	-3.423	0.001
Serum COX-2 (pg/mL)	Before treatment	16.13±3.26	16.21±4.05	-0.114	0.909
	After treatment	9.87±1.18	10.38±1.41	-2.170	0.032
Serum PGE2 (pg/mL)	Before treatment	90.80±7.07	92.40±5.60	-1.405	0.163
	After treatment	40.55±3.88	42.02±2.64	-2.485	0.014

Table 4: Comparison of serum inflammatory markers.

Discussion

Malnutrition makes a negative impact on the outcome of COPD patients, especially in patients with acute exacerbation, where malnutrition is more likely seen. Presently, nutritional support therapy constitutes an essential part of respiratory

rehabilitation treatment. Enteral nutritional support has been shown to be more effective than parenteral nutritional support[11]. The treatment of AECOPD patients should, based on the TCM principle of removing the primary in chronic cases and relieving the secondary symptoms in acute cases, regulate the general condition and body functions, so as to restore the vital qi and dispel pathogens. Tanreqing injection is a pure TCM injection with functions of clearing heat, reducing phlegm and detoxifying[12]. The increase of ALB and TF is indicative of enhanced substance synthesis and hematopoiesis, as well as improved nutritional status of the body[13-14]. Immunoglobulins (Ig), a group of globulins with antibody activity that are synthesized and secreted by plasma cells, can reflect the humoral immune function of the body[15]. It was found in this study that after treatment, the levels of serum nutrition indexes Hb, TLC, serum PA, serum ALB and serum TF, and serum immunoglobulin indicators IgA, IgG and IgM in the study group were significantly higher than those in the control group, which suggested that the combination of Tanreqing injection with nutritional support (TPF-T) promotes the nutritional recovery and improves the immune function of the patients. The reason may be that Tanreqing injection can improve the body's responsiveness to anti-infective drugs and has a good effect on enhancing immune function; TPF-T can help maintain the structural and functional integrity of intestinal mucosal cells, promote the production of secretory IgA, reduce the probability of enterogenic endotoxemia, stimulate the proliferation of T lymphocytes, regulate the secretion of cytokines, and thus improve the immune function of the body;10 Tanreqing injection combined with TPF-T can exert a synergistic effect to enhance the immune function.

Although serum ALB, TF, PA and other indicators reflect nutrition status to a certain degree in nutriology, their levels are affected by various factors like inflammation and dilution effect of infusion which lead to their redistribution, as well as liver function. Therefore, as they alone cannot be the most sensitive indicators for monitoring the effect of nutritional support, they are in want of combination with inflammation indicators for comprehensive evaluation. It has been shown that CRP plays a key role in the inflammatory response of the airway and airflow obstruction in AECOPD patients[16-17]. Studies also show that airway inflammation can cause bronchial mucosal edema and aggravate the damage to lung tissue and airway structures by increasing COX -2 activity and stimulating IL-1β secretion.18 The inflammatory index PGE2 is involved in the development and progression of COPD[19]. In the present study, it was found that serum inflammatory markers CRP, IL-1β, COX-2, and PGE2 levels were lower in the study group than those in the control group after treatment. Consequently, the use of Tanreqing injection combined with TPF-T was effective in reducing the airway inflammatory response in patients. The reason may be that Tanreqing injection can reduce the inflammatory response caused by endotoxemia, down-regulate the expression of inflammatory factors, and significantly inhibit the elevation of central fever media; TPF-T helps patients correct malnutrition, enhance their anti-inflammatory ability, and attenuate their inflammatory response; the combination of the two can better inhibit the mucus hypersecretion state and airway inflammation, and therefore significantly improve the clinical symptoms of patients.

Conclusion

Tanreqing injection combined with nutritional support (enteral nutrition emulsion TPF-T) can improve nutrition and immune indexes and reduce the level of inflammation in AECOPD patients, so it has certain clinical application value.

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