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Effect of Shenqi Fuzheng Injection and naloxone and BiPAP ventilator on serum inflammatory factors, immune function and blood gas analysis indexes in patients with AECOPD with type Ⅱ respiratory failure

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ABSTRACT

Objective: To investigate the effect of Shenqi Fuzheng Injection combined with naloxone and BiPAP ventilator on serum inflammatory factors, immune function and blood gas analysis indexes in treatment of AECOPD with type II respiratory failure. **Methods:** A total of 82 patients with AECOPD and type II respiratory failure were divided into control group (n=40) and observation group (n=42) according to random data table, patients in the control group received naloxone and BiPAP ventilator therapy, and observation group patients were treated with Shenqi Fuzheng Injection on the basis of control group. The levels of serum inflammatory factors, immune function and blood gas analysis indexes were compared between the two groups before and after treatment. **Results:** There were no significant difference in levels of CRP, TNF-α, IL-6, $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, PaO_2, $PaCO_2$, SaO_2 and pH before and after treatment in the two groups. After treatment, the levels of CRP, TNF-α, IL-6, $CD8^+$and $PaCO_2$ in two groups were significantly lower than those in same group before treatment, moreover observation group was significantly lower than control group; and levels of CRP, TNF-α, IL-6, $CD8^+$ and $PaCO_2$ in the observation group was significantly lower than those of the control group, the difference was statistically significant; When compared with the group before treatment, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$, PaO_2, SaO_2 and pH levels of both groups after treatment were significantly increased, and the level of each index of observation group after treatment were significantly higher than the control group, the difference was statistically significant. **Conclusion:** The clinical effect of Shenqi Fuzheng Injection Combined with naloxone and BiPAP ventilator in treatment of AECOPD with type II respiratory failure is significant, can effectively reduce the body's inflammatory reaction, improve immune function, regulate blood gas analysis index, with a certain clinical value.

1. Introduction

Chronic obstructive pulmonary disease (COPD) was common and multiple in respiration system disease, its fatality rate was fourth in global death reasons[1]. Acute exacerbation COPD (AECOPD) always caused respiration tract infection and respiratory muscle fatigued, it was easy to develop as type II respiratory failure which was main death reason of COPD patients[2,3]. Clinical treatment almost was respiratory stimulant, invasive and non-invasive positive ventilation treatment. Pure ventilator treatment easily resulted in pulmonary damage, naloxone was good pulmonary encephalopathy drug, combined these two treatments could effectively enhance efficacy[4,5]. In recent combined treatment of traditional Chinese medicine and western medicine for severe disease was research hot. This research was aimed to explore effect of Shenqi fuzheng injection adjvant therapy on biochemical indexes in patients with AECOPD accompanying type II respiratory failure.

2. Subjects and material

2.1. General data

A total of 82 cases of patients with AECOPD accompanying type II respiratory failure who were admitted in our hospital from April 2016 to June 2017 were selected as research subjects. All of

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patients were conformed to related diagnostic criteria etsblished by this research and divided to control group (n=40) and obsevation group (n=42) according to the random data table. In control group 27 males, 13 females, aged from 55-78 years old; average course of COPD was (8.24±1.07) years; In observation group, 28 males, 14 females, aged from 54-77 years old; average course of COPD was (8.06±1.19) year. There was no difference in gender, age and average course of COPD (P>0.05), it was comparable. Research was conformed to standard of ethic committee and was approved.

2.2. Selection criteria

Incorporation criteria: (1) all patients were conformed to related diagnosis and grading criteria of 'Diagnosis and treatment guidance of chronic obstructive pulmonary disease'[6]; (2) accompanying with obvious chest distress, cough, breath hard and color change of sputum; (3) conformed to type II respiratory failure blood oxygen partial pressure (PaO_2)<60 mmHg, and carbon dioxide partial pressure ($PaCO_2$)>50 mmHg; (4) All subjects was with complete clinical data when was admitted; (5) All patients and their family were informed and signed informed consent and willing to accept treatment.

Exclusion criteria: (1) accompanying with severe blood circulation, respiratory organ dysfunction, cardiovascular and cerebrovascular diseases, mental disease and cancer; (2) patients with coma and weak autonomous respiration; (3) patients with severe upper gastrointestinal hemorrhage, viscous sputum, dysprea; (4) intolerance to ventilator treatment; (5) malformation, burn and wound caused faical and neck abnormality that seriously affected mask use; (6) condition aggravating that needed invasive ventilation through trachea cannula; (7) accepted aspirin and other immune regulator that affected research indexes; (8) patients with bad compliance, fall off in midway; (9) clinical data was incomplete after admission and did not accept treatment.

2.3. Treatment method

All subjects were given conventional treatment, including spasm and asthma, relieving cough and reducing sputum, anti-infection, rectifying electrolyte. On this basis, control group was given BiPAP V60 ventilator treatment (American Philips Respironics), chose autonomous respiration or timing mode (S/T), ventalitor parameter setting: respiratory rate (RR)10-16 times/min, inspiration time 0.8-1.2 s, oxygen concentration 30%-50%, initial inhale positive airway pressure (IPAP) 6-8 cmH2O, initial exhale positive airway pressure (EPAP) 2-4 cmH_2O, gradually increased by 2 cmH_2O/time, respectively incresed to 12-20 cmH_2O and 4-6 cmH_2O, regulated ventalitor parameter every 10 min until breathed stably, maintained aterial oxygen saturation (SpO_2) at 90%-95%. At the start, ventalition 2 times/d, over 10 h/d, rest every 20 min for feeding and suptum excretion. In the meanwhile, naloxone hydrochloride for injection was given (Na Leshu, Chongqing Meilai pharmaceutical Co. Ltd, approval number: H20073029, product standard 1 mg/bottle × 4 bottles), added this drug into 500 mL 0.9% normal saline, concentration was 0.004 mg/mL. On the base of BiPAP V60 ventalitor and naloxone hydrochloride for injection in control group, observation group was given Shenqi Fuzheng injection in the same time (Lizhu Group Limin pharmaceutical Co. Ltd, approval number: Z19990065, product standard: 250 mL/bottle), intravenous drip, 1 time/d, 1 bottle/time. Both groups were continuously treated for 7 d.

2.4. Observation indexes

Extracted fasting periphery venous blood of patients before treatment and after 7 d of treatment, Observation indexes including inflammatory factor, T lymphocyte and blood gas analysis. Centrifuge for serum, stocked at -70 ℃ freezer for using. Inflammatory factor including hypersensitive C-reaction protein (hs-CRP), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), ELISA was applied to detect these levels, its coresponding ELISA kits were provided by Shanghai Meilian biotechnoloy Co., Ltd. T lymphocyte: $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ level was detected by American Beckman Coulter flow cytometry, in the same time deteted blood oxygen partial pressure PaO_2, carbon dioxide partial pressure $PaCO_2$, SaO_2 and pH, operation was strict with kits instruction.

2.5. Statistcal analysis

Statistical Software SPSS 17.0 was used for all row data processing and analyzing, inflammatory factors, T lymphocyte and blood gas analysis was conformed to normal distribution and represented by Mean ± SD, t-test was applied to comparison of intra-group before and after treatment and inter-block, P<0.05 indicated the difference was statistical significant.

3. Results

3.1 Comparison of inflammatory factor of both groups

Before treatment, serum CRP, TNF-α and IL-6 level in observation group and control group were very close, the difference was not statistical significant (P>0.05). After treatment CRP, TNF-α and IL-6 level in control group were respectively (9.53±1.27) mg/L, (42.03±9.36) ng/L and (24.58±9.16) ng/L, which were lower than before treatment intragroup, the difference was significant statistical (P<0.05); After treatment CRP, TNF-α and IL-6 level in observation group were respectively (5.85±1.36) mg/L, (31.06±8.55) ng/L and (20.28±4.59) ng/L, which was significantly lower than befre treatment intragroup (P<0.05); moreover, obviously lower than control group after treatment (P<0.05). As shown in Table 1.

Table 1.
Comparison of inflammatory factor of both groups.

Group	n	Treatment time	CRP (mg/L)	TNF-α (ng/L)	IL-6 (ng/L)
Control group	40	Before treatment	11.86±2.04	77.31±10.47	45.47±10.69
		After treatment	9.53±1.27*	42.03±9.36*	24.58±9.16*
Observation group	42	Before treatment	11.96±1.98	76.86±10.84	45.64±10.36
		After treatment	5.85±1.36*#	31.06±8.55*#	20.28±4.59*#

Note: compared with before treatment intragroup, *P<0.05; Compared with control group after treatment, #P<0.05.

Table 2.
Comparison of immune function of both groups.

Group	n	Treatment time	$CD3^+$ (%)	CD4+ (%)	$CD8^+$ (%)	$CD4^+/CD8^+$
Control group	40	Before treatment	59.82±6.04	30.21±4.38	32.79±4.92	1.06±0.21
		After treatment	63.05±4.63*	34.07±4.79*	29.91±3.36*	1.24±0.32*
Observation group	42	Before treatment	59.57±5.94	30.35±3.92	33.05±4.47	1.06±0.27
		After treatment	68.58±4.89*#	38.94±3.82*#	25.04±3.19*#	1.54±0.39*#

Note: compared with before treatment intragroup, *P<0.05; Compared with control group after treatment, #P<0.05.

Table 3.
Comparison of blood gas analysis of both groups.

Group	n	Treatment time	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	SaO_2 (%)	pH
Control group	40	Before treatment	46.82±5.96	81.37±11.42	82.59±6.45	7.16±0.13
		After treatment	67.72±5.93*	62.22±7.26*	88.99±7.86*	7.32±0.08*
Observation group	42	Before treatment	47.02±5.61	81.56±10.34	83.12±5.82	7.16±0.09
		After treatment	78.43±5.48*#	51.68±5.85*#	97.61±5.38*#	7.39±0.10*#

Note: compared with before treatment intragroup, *P<0.05; Compared with control group after treatment, #P<0.05.

3.2 Comparison of immune function of both groups

T lymphocyte level in observation group and control group before and after treatment was shown in Table 2. Before treatment, $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ level in both groups were close, the difference was not statistical significant (P>0.05). After treatment, $CD8^+$ level in control group and observation group were (29.91±3.36)% and (25.04±3.19)%, compared with intragroup before treatment, its level was significantly decreased (P<0.05), moreover after treatment $CD8^+$ level in observation group was obviously lower than control group,there was significant statistical difference (P<0.05); after treatment $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ level in observation group were (68.58±4.89)%, (38.94±3.82)% and (1.54±0.39), which was dramatically higher than intra-group before treatment (P<0.05), moreover significantly higher than control group after treatment, the difference was significant (P<0.05).

3.3. Comparison of blood gas analysis of both groups

Blood gas analysis indexes results of observation group and control group before and after treatment was shown in Table 3. Before treatment, PaO_2, $PaCO_2$, SaO_2 and pH level in both groups were close, the difference was not statistical significant (P>0.05). Compared with intragroup before treatment, $PaCO_2$ level of both groups after treatment was significantly decreased (P<0.05), moreover observation group (51.68±5.85) mmHg was dramatically lower than control group (62.22±7.26), there was statistical significant difference (P<0.05), PaO_2, SaO_2 and pH level in observation group and control group were higher than before treatment intragroup (P<0.05), moreover these level in observation group were (78.43±5.48) mmHg, (97.61±5.38)%, (7.39±0.10) which was dramatically higher than control group (67.72±5.93) mmHg, (88.99±7.86)% and (7.32±0.08), there was statistical significant difference (P<0.05).

4. Discussion

COPD was a disease that companied with extrapulmonary effect, it truly was airway limitation that resulted fron inflammatory reaction, further developed to chronic respiratory failure, caused pulmonary heart disease severely, threated patients life, brought heavy economic burden to family and society[7]. AECOPD could aggravate inflammatory reaction, appeared edema, impeled phlegm, CO_2 retention, hyoxemia, which further sharpen respiratory muscle tired and made disease worsen[8,9]. Therefore clinical treatment for patients with AECOPD and type II respiratory failure was mainly as following: relieved respiratory muscle tired, rectified anoxia, improved CO_2 retention. At present, there was still no specific drug that cured patients with AECOPD and type II respiratory failure, efficacy of conventional drug usually slow and side-effect was great, in clinic, usually adopted non-invasive postive pressure ventilation and respiratory stimulant for treatment[10,11]. British Throacic Society thought that BiPAP non-invasive postive pressure ventilation was optimal choice of AECOPD treatment[12]. A lot of researches have demonstrated that non-invasive postive pressure ventilator treatment could effectively improve pulmonary ventilation and respiratory muscle tired[13,14]. Naloxone was a specific opioid antagonist which played protected effect of respiratory stimulant through competing opiate receptor, antagonism respiratory depression induced by β-endorphin, improving anoxia of brain tissue and CO_2 retention, eliminating free radical[15]. Related researches pointed out that on the base of conventional drug, naloxone combined with non-invasive postive pressure ventilator could further improve sign of patients and perfect result of blood gas analysis[16].

Chinese traditional medicine thought that AECOPD with type II respiratory failure was syndrome of lung distension and unconsciousness, respiration weaken, its treatment mainly was tonifying qi, supporting the healthy energy and invigorating splenic function[17]. Shenqi fuzheng injection was common traditional Chinese medicine in clinic, the whole prescription was radix codonopsis and astragali radix, radix codonopsis could tonify qi, promote secretion of saliva, nourish blood, mainly treat insufficiency of splenogastric qi, lung qi deficiency disease, astragali radix could tonify qi and strengthen exterior and enhance splenic function, mainly treat insufficiency of vital energy and blood, spleen-lung qi deficiency. Modern pharmacological study found that radix codonopsis could decrease blood viscosity, enhance oxygen resistance ability, improve microcirculation and immune function; astragali radix could enhance cellular immune function, eliminate free radical. This prescription principally inhibited excessive secretion of inflammatory factors and improved microcirculation[18,19]. This research was aimed to determine efficacy of Shenqi Fuzheng Injection combined with naloxone and BiPAP non-invasive ventilator therapy through analyzing serum inflammatory factor, immune function and blood gas analysis.

Developed mechanism of COPD was related to excessive inflammatory stress reaction[20]. AECOPD chiefly was related to infection, under the effect of bacteria and (or) its metabolite (endotoxin), body generated and released massive inflammatory factors which resulted in general inflammatory reaction activation thereby caused pulmonary damage. CRP, TNF-α and IL-6 as

clinical common inflammatory factors, increased significantly in patients with AECOPD with type II respiratory failure, this revealed there was strong inflammatory reaction in patients, its activity was positive relevant to illness severe degree[21,22]. This revealed both treatment methods could reduce inflammatory reaction, improve clinical sign of patients, moreover, combined with Shenqi Fuzheng Injection, the level decreased more obviously, this showed on the base of western medicine, combined with Chinese traditional medicine could further enhance efficacy and demonstrated that Shenqi fuzheng injection was able to effectively inhibit overexpression of inflammatory factors.

In recent, it has been demonstrated that there was always severe immune dysfunction in patients whatever in relieved stage or acute attack stage[23]. Improved immune function not only could enhance resistance to disease but be beneficial to recovery. Shenqi fuzheng injection was a better immunoregulator, which increased transfer ability of lymphoctye and immunoglobulin[24]. This result found that combined with Shenqi fuzheng injection on the base of naloxone and BiPAP non-invasive ventilator therapy could further improve $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ level and enhance cellular immune function, and then improve symptom and recovery. Except for inflammatory factors and immune fucntion, this research compared with blood gas analysis indexes of both groups, results revealed that BiPAP non-invasive ventilator therapy and naloxone could improve blood gas indexes level, improved efficacy of PaO_2, $PaCO_2$, SaO_2 and pH level was better through combination of Shenqi fuzheng injection, the difference was significant statistical. It showed that Chinese traditional medicine could enhance pulmonary ventilation function effectively, improve dyspnea, its reason might be Shenqi fuzheng injection increase blood supply of pulmonary tissue, ameliorate anoxia.

In conclusion, efficacy of Shenqi Fuzheng Injection combined with naloxone and BiPAP ventilator in the treatment of AECOPD with type II respiratory failure was significant, further decreased inflammatory reaction, enhanced immune function and improved blood gas analysis index, which was good to recovery of pulmonary damage, with critical clinical value.

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