



Effect of Xuebijing, thymopentin combined with symptomatic treatment on inflammatory response process in elderly patients with severe pneumonia

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ARTICLE INFO

Article history:

Received 28 Aug 2017

Received in revised form 3 Sep 2017

Accepted 9 Sep 2017

Available online 14 Sep 2017

Keywords:

Elderly severe pneumonia

Xuebijing

Thymopentin

Inflammatory response

ABSTRACT

Objective: To study the effect of Xuebijing, thymopentin combined with symptomatic treatment on inflammatory response process in elderly patients with severe pneumonia.

Methods: A total of 60 elderly patients with severe pneumonia who were treated in the hospital between August 2014 and July 2016 were collected and divided into control group and observation group according to the random number table, 30 cases in each group. Control group received clinical symptomatic treatment, and observation group received Xuebijing, thymopentin combined with symptomatic treatment. The differences in serum pro-inflammatory factors, anti-inflammatory factors as well as liver and kidney function indexes were compared between the two groups before and after treatment. **Results:** Before treatment, differences in serum levels of pro-inflammatory factors, anti-inflammatory factors as well as liver and kidney function indexes were not statistically significant between the two groups. After treatment, serum IL-1 β , IL-6, IL-8, IL-4, IL-13, TB, ALT, AKP, Scr and CysC levels of both groups of patients were lower than those before treatment, and serum IL-1 β , IL-6, IL-8, IL-4, IL-13, TB, ALT, AKP, Scr and CysC levels of observation group were lower than those of control group. **Conclusion:** Xuebijing, thymopentin combined with symptomatic treatment can effectively inhibit the degree of systemic inflammatory response and reduce the liver and kidney function injury in elderly patients with severe pneumonia.

1. Introduction

Severe pneumonia is that the acute pneumonia continuously aggravates and causes important viscera injury, which belongs to clinical critical condition and requires early active and effective treatment[1,2]. Although the symptomatic treatments such as reposing, oxygen uptake and anti-infection can partially alleviate

the condition of severe pneumonia, they cannot inhibit disease progression and are limited in optimizing the overall treatment outcome. Adding drugs with other mechanisms of action in the symptomatic treatment to expand the curative effect is the ideal therapy for severe pneumonia recommended by many scholars at present, the Xuebijing and thymopentin are the relatively popular drugs for auxiliary treatment of infectious diseases, Xuebijing antagonizes endotoxin, thymopentin improves the immunity, and the combination of the two helps to reverse the process of infection[3]. In the study, adjuvant Xuebijing and thymopentin therapy was added on the basis of symptomatic treatment of elderly patients with severe pneumonia, and the clinical application value was explored.

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Fund Project: Hebei Provincial Achievements of Science and Technology No: 201311133.

2. Information and methods

2.1 Case information

A total of 60 elderly patients with severe pneumonia who were treated in the hospital between August 2014 and July 2016 were selected as the study subjects, and the families of the patients signed the informed consent form. According to the random number table, the enrolled patients were divided into control group and observation group, 30 cases in each group. Control group included 17 men and 13 women that were 63-79 years old; observation group included 16 men and 14 women that were 62-78 years old. The differences in gender and age distribution were not statistically significant between the two groups of patients ($P>0.05$), and the hospital ethics committee approved the study.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) in accordance with the diagnostic criteria for clinical severe pneumonia; (2) 60 years old; (3) with no history of severe pneumonia; (4) completing the whole treatment and with complete clinical data. Exclusion criteria: (1) allergic to Xuebijing and thymopentin; (2) combined with severe heart, liver and kidney insufficiency; (3) combined with serious autoimmune diseases; (4) combined with chronic obstructive pulmonary disease, chronic bronchitis, asthma and other pulmonary diseases.

2.3 Therapy

The control group received routine therapy for severe pneumonia, including reposing, oxygen uptake, sensitive antibiotic application, electrolyte and acid-base balance regulation, and so on. Observation group, on the basis of regular treatment, received Xuebijing combined with thymopentin therapy, specifically as follows: Xuebijing (Tianjin Chase Sun Pharmaceutical Co., Ltd., approved by Z20040033) 50 mL was dissolved in 100 mL saline, by intravenous infusion, 2 times/d for 7 d in a row. Thymopentin (Beijing Scieure Pharmaceutical Co., Ltd., approved by H20061225) 1 mg was dissolved in 250 mL saline, by intravenous infusion, 1 time/d for 7 d in a row.

Table 1.

Changes in serum IL-1 β , IL-6 and IL-8 before and after treatment (pg/mL).

Groups	n	IL-1 β		IL-6		IL-8	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	30	15.38 \pm 2.19	10.74 \pm 1.92 [*]	25.38 \pm 3.47	16.29 \pm 2.11 [*]	13.26 \pm 1.79	8.53 \pm 0.94 [*]
Observation group	30	15.27 \pm 2.06	6.15 \pm 0.74 [*]	25.29 \pm 3.52	7.35 \pm 0.86 [*]	13.42 \pm 1.68	3.17 \pm 0.46 [*]
t		0.183	11.271	0.254	18.372	0.168	9.287
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: serum index comparison between before and after treatment within group, ^{*} $P<0.05$.

2.4 Observation indexes

Before treatment and 7 d after treatment, 3-5 mL of fasting cubital venous blood was extracted from the two groups of patients, anti-coagulated, let stand at room temperature for stratification and centrifuged at low speed to get the upper serum, which was stored in a deep cryogenic environment. Enzyme-linked immunosorbent assay was used to detect levels of pro-inflammatory factors, anti-inflammatory factors as well as liver and renal function indexes in serum, including pro-inflammatory factors interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and interleukin-8 (IL-8); anti-inflammatory factors interleukin-4 (IL-4) and interleukin-13 (IL-13); liver function indexes total bilirubin (TB), alanine aminotransferase (ALT) and alkaline phosphatase (AKP); renal function indexes serum creatinine (Scr) and serum cystatin C (CysC).

2.5 Statistical processing

Statistical software was SPSS 24.0. Pro-inflammatory factors, anti-inflammatory factors, liver function indexes, renal function indexes and so on were measurement data, in terms of mean \pm standard deviation and compared by t test. Statistics $P<0.05$ was the standard of statistical significance in differences.

3. Results

3.1 Serum IL-1 β , IL-6 and IL-8 levels

Before treatment and 7 d after treatment, analysis of serum pro-inflammatory factors IL-1 β , IL-6 and IL-8 levels between two groups of patients was as follows: serum IL-1 β , IL-6 and IL-8 levels were not significantly different between the two groups before treatment ($P>0.05$). 7 d after treatment, serum IL-1 β , IL-6 and IL-8 levels of both groups of patients were significantly lower than those before treatment ($P<0.05$), and serum IL-1 β , IL-6 and IL-8 levels of observation group were lower than those of control group ($P<0.05$).

3.2 Serum IL-4 and IL-13 levels

Before treatment and 7 d after treatment, analysis of serum anti-inflammatory factors IL-4 and IL-13 levels between two groups of patients was as follows: serum IL-4 and IL-13 levels were not significantly different between the two groups before treatment ($P>0.05$). 7 d after treatment, serum IL-4 and IL-13 levels of both groups of patients were significantly lower than those before treatment ($P<0.05$), and serum IL-4 and IL-13 levels of observation group were lower than those of control group ($P<0.05$).

Table 2.

Changes in serum IL-4 and IL-13 before and after treatment.

Groups	n	IL-4		IL-13	
		Before treatment	After treatment	Before treatment	After treatment
Control group	30	11.93±1.76	7.34±0.86*	19.82±2.45	11.57±1.68*
Observation group	30	11.87±1.85	3.26±0.45*	19.76±2.37	6.09±0.75*
t		0.183	9.182	0.264	8.948
P		>0.05	<0.05	>0.05	<0.05

Note: serum index comparison between before and after treatment within group, * $P<0.05$.

3.3 Serum TB, ALT and AKP levels

Before treatment and 7 d after treatment, analysis of serum liver function indexes TB (umol/L), ALT (IU/L) and AKP (U/L) levels between two groups of patients was as follows: serum TB, ALT and AKP levels were not significantly different between the two groups before treatment ($P>0.05$). 7 d after treatment, serum TB, ALT and AKP levels of both groups of patients were significantly lower than those before treatment ($P<0.05$), and serum TB, ALT and AKP levels of observation group were lower than those of control group ($P<0.05$).

3.4 Serum Scr and CysC levels

Before treatment and 7 d after treatment, analysis of serum renal function indexes Scr (umol/L) and CysC (mg/L) levels between two groups of patients was as follows: serum Scr and CysC levels

were not significantly different between the two groups before treatment ($P>0.05$). 7 d after treatment, serum Scr and CysC levels of both groups of patients were significantly lower than those before treatment ($P<0.05$), and serum Scr and CysC levels of observation group were lower than those of control group ($P<0.05$).

Table 4.

Changes in serum Scr and CysC before and after treatment.

Groups	n	Scr		CysC	
		Before treatment	After treatment	Before treatment	After treatment
Control group	30	98.37±10.29	71.48±8.62*	1.84±0.25	1.27±0.15*
Observation group	30	98.28±10.53	40.71±5.36*	1.86±0.23	0.65±0.08*
t		0.173	14.382	0.164	7.827
P		>0.05	<0.05	>0.05	<0.05

Note: serum index comparison between before and after treatment within group, * $P<0.05$.

4. Discussion

Severe pneumonia is because that acute pneumonia is improperly controlled and causes important viscera function damage, independent sputum excretion function is weakened and the immunity declines in the elderly, so the probability of severe pneumonia is higher and the prognosis is relatively not ideal[4,5]. Early positive symptomatic treatment can avoid further disease progress, but it is less effective in controlling infection and reducing the tissue organ damage, and some patients are still progressing after symptomatic treatment. How to further improve the treatment effect of elderly severe pneumonia is the key of the current clinical research, the Xuebijing and thymopentin are the more respected adjuvant drugs for serious infectious diseases, Xuebijing has the effect of antagonizing endotoxin in vitro, and can alleviate the toxemia and sepsis caused by pathogenic bacteria infection[6]; thymopentin is the compound agent synthesized by five amino acids and used to improve the immunity, and it has been successfully applied to patients with malignant tumor radiotherapy[7]. In this study, Xuebijing and thymopentin were used together in the treatment of elderly patients with severe pneumonia, and their value was defined in inflammatory processes such as inflammatory response as well as liver and kidney injury.

After pathogen infection leads to acute pneumonia, the inflammatory cytokines are massively released, and the pro-

Table 3.

Changes in serum TB, ALT and AKP before and after treatment.

Groups	n	TB		ALT		AKP	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	30	43.28±5.19	30.17±4.23*	102.63±13.42	71.09±8.54*	119.73±14.52	85.42±9.38*
Observation group	30	42.76±5.32	18.64±2.18*	102.78±14.51	40.62±5.28*	118.96±13.57	37.17±4.52*
t		0.172	15.482	0.264	17.291	0.194	20.463
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: serum index comparison between before and after treatment within group, * $P<0.05$.

inflammatory factors IL-1 β , IL-6 and IL-8 can further induce neutrophil accumulation, release inflammatory mediators and cause inflammation expansion[8,9]; anti-inflammatory factors IL-4 and IL-13 neutralize pro-inflammatory factors and inhibit the inflammatory response expansion, their secretion increases early after infection, but in the acute phase of inflammation, their secretion cannot balance the increase of pro-inflammatory factor contents, but their overall content change trend is the same as the change trend of inflammatory response[10,11]. In the study, serum levels of pro-inflammatory factors and anti-inflammatory factors were compared between the two groups of patients before and after treatment, and it was found that compared with those before treatment, serum levels of pro-inflammatory factors IL-1 β , IL-6 and IL-8 as well as anti-inflammatory factors IL-4 and IL-13 of both groups of patients decreased after treatment, indicating that both kinds of treatments can relieve systemic inflammatory reaction degree; further compared with those of control group, serum levels of pro-inflammatory factors IL-1 β , IL-6 and IL-8 as well as anti-inflammatory factors IL-4 and IL-13 of observation group were lower after treatment, confirming that adjuvant Xuebijing and thymopentin therapy based on symptomatic treatment can effectively inhibit the systemic inflammatory response progression.

Systemic inflammatory response is constantly expanding, and inflammatory factors flow into the blood circulation and flow into the liver, kidneys and other important tissue organs, which can cause inflammation in the organs and result in dysfunction[12,13]. Patients with severe pneumonia have higher risk of liver and kidney dysfunction, and liver and kidney failure is an important cause of death of these patients[14,15]. In this study, the levels of liver function indexes TB, ALT and AKP as well as renal function indexes Scr and CysC were compared between the two groups of patients, and it was found that compared with those before treatment, serum levels of liver function indexes TB, ALT and AKP as well as renal function indexes Scr and CysC of both groups decreased after treatment, indicating that both kinds of therapies can protect the liver and kidney function to different extent; further compared with those of control group, serum levels of liver function indexes TB, ALT and AKP as well as renal function indexes Scr and CysC of observation group were lower after treatment, confirming that the adjuvant Xuebijing and thymopentin therapy can more effectively relieve viscera injury, which is mainly because that Xuebijing antagonizes tissue damage effect of endotoxin, thymopentin enhances the body's immunity, etc.

Xuebijing combined with thymopentin therapy can effectively inhibit the systemic inflammatory response, and relieve the liver and kidney injury caused by inflammatory factors and endotoxin in elderly patients with severe pneumonia, it helps improve the overall curative effect and optimize the treatment prognosis, and it is worthy of popularization and application in clinical practice in the future.

References

- [1] Shibuya S, Nakamura T, Miyazaki E. Anatomical segmentectomy with a hybrid vats approach in a patient with intralobar pulmonary sequestration after severe pneumonia: a case report. *Eur J Pediatr Surg Rep* 2017; **5**(1): e21-e25.
- [2] Ohta R, Shimabukuro A. Rural physicians' scope of practice on remote islands: A case report of severe pneumonia that required overnight artificial airway management. *J Rural Med* 2017; **12**(1): 53-55.
- [3] Morton B, Pennington SH, Gordon SB. Immunomodulatory adjuvant therapy in severe community-acquired pneumonia. *Exp Rev Respir Med* 2014; **8**(5): 587-596.
- [4] Xiao B, Wang M, Hu X, Li J, Wang F, Sun J. Antibiotic de-escalation principle in elderly patients with chronic obstructive pulmonary disease complicated with severe pneumonia. *Exp Ther Med* 2017; **13**(4): 1485-1489.
- [5] Heikens GT, Manary MJ, Trehan I. African children with severe pneumonia remain at high risk for death even after discharge. *Paediatr Perinat Epidemiol* 2017; **31**(3): 243-244.
- [6] Wang P, Song Y, Liu Z, Wang H, Zheng W, Liu S, et al. Xuebijing injection in the treatment of severe pneumonia: study protocol for a randomized controlled trial. *Trials* 2016; **17**(1): 142.
- [7] Romani L, Oikonomou V, Moretti S, Iannitti RG, D'Adamo MC, Vilella VR, et al. Thymosin α 1 represents a potential potent single-molecule-based therapy for cystic fibrosis. *Nat Med* 2017; **23**(5): 590-600.
- [8] Tang L, Li Q, Bai J, Zhang H, Lu Y, Ma S. Severe pneumonia mortality in elderly patients is associated with downregulation of Toll-like receptors 2 and 4 on monocytes. *Am J Med Sci* 2014; **347**(1): 34-41.
- [9] Xu H, Mei B, Wang M, Xu S. Inhibitor κ B protein therapy alleviates severe pneumonia through inhibition of nuclear factor κ B. *Exp Ther Med* 2017; **13**(4): 1398-1402.
- [10] Chen C, Shi L, Li Y, Wang X, Yang S. Disease-specific dynamic biomarkers selected by integrating inflammatory mediators with clinical informatics in ARDS patients with severe pneumonia. *Cell Biol Toxicol* 2016; **32**(3): 169-184.
- [11] Tang L, Li Q, Bai J, Zhang H, Lu Y, Ma S. Severe pneumonia mortality in elderly patients is associated with downregulation of Toll-like receptors 2 and 4 on monocytes. *Am J Med Sci* 2014; **347**(1): 34-41.
- [12] Li C, Li C, Zhang AJ, To KK, Lee AC, Zhu H, et al. Avian influenza A H7N9 virus induces severe pneumonia in mice without prior adaptation and responds to a combination of zanamivir and COX-2 inhibitor. *PLoS One* 2014; **9**(9): e107966.
- [13] Qi GJ, Chao YL, Xi XY, Liu KX, Li WH. Effect analysis of early bedside hemo-filtration in treatment of severe pneumonia with acute renal failure of children. *Eur Rev Med Pharmacol Sci* 2015; **19**(24): 4795-4800.
- [14] Tu G, Ju M, Zheng Y, Xu M, Rong R, Zhu D, et al. Early- and late-onset severe pneumonia after renal transplantation. *Int J Clin Exp Med* 2015; **8**(1): 1324-1332.
- [15] Tu GW, Ju MJ, Zheng YJ, Zhu DM, Xu M, Rong RM, et al. An interdisciplinary approach for renal transplant recipients with severe pneumonia: a single ICU experience. *Intens Care Med* 2014; **40**(6): 914-915.