

Original Article

The protective effect of Qingfei Huatan decoction on pulmonary function and its influence on the immunological function in children with severe pneumonia

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Abstract: Objective: This research explores and analyzes the protective effect of the mixed Chinese herbs Qingfei Huatan decoction on the pulmonary and immunological functions in children with severe pneumonia. Methods: 120 children with severe pneumonia hospitalized from May 2018 to May 2020 were enrolled in the study and randomly placed into an observation group or a control group (n=60 in each group). The control group was administered conventional treatment, and the observation group was administered the mixed Chinese herbs Qingfei Huatan decoction in addition to the treatment administered to the control group. The therapeutic efficacy, the changes in pulmonary function, the serum inflammatory levels, and the peripheral blood T lymphocyte subsets were compared between the two groups. Results: The total effective treatment rate in the observation group was critically superior to the total effective treatment rate in the control group ($P<0.05$). The FVC, FEV1, and FEV1/FVC levels in the two groups after the treatment were remarkably higher than they were before the treatment ($P<0.05$), and the observation group had superior post-treatment pulmonary function than the control group ($P<0.05$). The TNF- α , IL-6, and CRP levels in the two groups in after the treatment were lower than they were before the treatment ($P<0.05$), and the observation group had lower post-treatment inflammatory cytokine levels than the control group ($P<0.05$). The two groups' CD4⁺ and CD4⁺/CD8⁺ levels increased substantially after the treatment compared to before the treatment ($P<0.05$), and the posttreatment levels in the observation group were notably higher than they were in the control group ($P<0.05$). Conclusion: The mixed Chinese herbs Qingfei Huatan decoction and the routine treatment combination has a good clinical effectiveness in children with severe pneumonia. It can effectively promote the pulmonary function of children. Its effect may be correlated with the suppression of inflammation in the body and the improvement of the immunological function in children.

Keywords: Qingfei Huatan decoction, severe pneumonia, protection of pulmonary function, immunological function

Introduction

Severe pneumonia refers to severe poisoning symptoms or complications of pneumonia, and is the most common critical pediatric illness. People with severe pneumonia are prone to various clinical manifestations of infection, respiratory failure, toxic shock, upper gastrointestinal hemorrhage, and hypoxemia. The disease may even cause diffuse intravascular coagulation, multiple organ dysfunction induced by lung damage or immune impairment, which severely threatens the lives of children [1-3]. Severe pneumonia in children has a rapid onset and progression, is a dangerous condition, and has a high mortality rate. In western

medicine, symptomatic treatment is primarily carried out using antivirals, antibiotics, cough suppressants, and expectorants. Although these medicines have achieved certain therapeutic effects, the antibacterial drugs can impose a big impact on children's immune systems [4, 5]. Chinese medicine has achieved progress in the auxiliary treatment of severe pneumonia in children in recent years. This study, aiming to further improve the clinical therapeutic effect, explored and analyzed the protective effect of Qingfei Huatan decoction on the pulmonary function and its influence on the immunological function in children with severe pneumonia. The details are as follows.

Materials and methods

Research cohort

120 children with severe pneumonia hospitalized from May 2018 to May 2020 were recruited for the study and randomly placed in the observation group or the control group (n=60 in each group). Our hospital's ethics committee approved this study.

Inclusion and exclusion criteria

Inclusion criteria: (1) The children who met the diagnostic criteria for severe pneumonia [6]. Children with an increased respiratory rate >30 times/min, whose breathing is shallow, and whose oxygen partial pressure has progressively decreased to <60 mmHg and whose X-ray suggested pulmonary lesions and a consolidation of the lung lobes, etc. (2) The syndrome differentiation of traditional Chinese medicine was consistent with phlegm-heat obstruction of lungs. Children with a phlegm-heat cough, yellowish sputum, excessively red face and lips, high fever, thirst, irritability, less yellow urine, a red tongue, a yellow or greasy coating and rolling and a rapid pulse. (3) Children 3-14 years old, and (4) The children's families voluntarily signed the informed consent forms.

Exclusion criteria: (1) Children with serious complications. (2) Children with pulmonary tuberculosis, bronchiectasis and/or other respiratory diseases. (3) Children with malignant tumor. (4) Children with a history of immune diseases, or (5) Children with an allergic constitution.

Methods

The control group was administered the conventional treatment of antibiotics and antivirals. They were treated with low flow oxygen and chloral hydrate for reducing fever, and their electrolyte disturbances and acid-base imbalances were actively corrected. For the severe cases, hormone therapy was given according to each patient's actual situation.

The patients in the observation group took Qingfei Huatan decoction prepared in our hospital in addition to the treatment administered to the control group. The formulation of the medication was 15 g raw gypsum, 12 g

Rhizoma anemarrhenae, 9 g *Magnolia officinalis*, 9 g *Radix trichosanthis*, 9 g Honeysuckle, 9 g *Aster tataricus*, 6 g *Scutellaria baicalensis*, 5 g fried Ephedra, 5 g almond, and 6 g *Radix Glycyrrhizae* Prepare. The medicine was decocted water, with each dose of medicine decocted into 2 packets and each packet was 100 ml. The children 3-6 years old were given 75 ml each time, and the 7-14 year-old children took 100 ml each time, twice a day. The course of treatment was set at 10 d.

Evaluation criteria of the clinical efficacy

The clinical efficacy referred to the standards in *Guiding Principles for Clinical Research of New Chinese Medicines* [10]. Markedly effective meant that the children's post-treatment clinical symptoms and signs were critically reduced, and their body temperatures and white blood cell counts (WBC) were decreased to their normal levels. Effective meant that the children's post-treatment clinical symptoms and signs were improved, and their body temperatures and WBC were decreased compared to their pre-treatment levels. Ineffective meant that the children's post-treatment clinical symptoms, signs, and WBC levels had not improved or even worsened after the treatment. Total effective rate = (Markedly effective + effective)/total cases ×100%.

Observation of indexes

(1) The pulmonary function changes pre- and post-therapy were compared between the two groups. The forced vital capacities (FVC), the forced expiratory volumes in the first second (FEV1), and the FEV1/FVC ratios were measured using a Japanese Minato pulmonary function meter.

(2) The pre- and post-treatment changes in the serum inflammatory cytokines levels were compared. We extracted early-morning fasting venous blood from the two groups, and it was separated after centrifugation. The children's tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and C-reactive protein (CRP) levels were measured using ELISA, and the procedures were strictly carried out in accordance with the kits' instructions. These kits were used: Human TNF- α ELISA KIT (Solebo Biotechnology Co., Ltd. SEKH-0047), a Human IL-6 ELISA KIT (Solebo Biotechnology Co., Ltd. SEKH-0013),

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Table 1. Comparison of clinical data between the two groups

Group	Number of cases	Gender		Age (yd, $\bar{X} \pm s$)	Courses of disease (d, $\bar{X} \pm s$)
		Male	Female		
Observation group	60	35	25	6.18±2.29	6.75±2.10
Control group	60	33	27	6.33±2.46	6.89±2.78
t/ χ^2	-	0.136		0.346	0.311
P	-	0.713		0.730	0.756

Table 2. Comparison of the clinical efficacy between the two groups [n (%)]

Group	Number of cases	Markedly effective	Effective	Invalid	Total effective rate (%)
Observation group	60	32 (53.33)	27 (45.00)	1 (1.67)	98.33
Control group	60	27 (45.00)	25 (41.67)	8 (13.33)	86.67
χ^2	-	-	-	-	4.324
P	-	-	-	-	0.038

and Human CRP ELISA KIT (Abcam, USA, ab260058).

(3) The changes in the T lymphocyte subset levels pre- and post-treatment were compared. The children's early morning fasting venous blood was extracted and separated after centrifugation. The changes in the T lymphocyte subsets in children's blood, including their CD4⁺ and CD8⁺ levels and their CD4⁺/CD8⁺ ratios were measured using Beckman Kurt flow cytometry. The measurements were strictly performed according to the kit's instructions.

Statistical analysis

We used SPSS 23.0 for the data processing. The comparisons of the measurement data and the enumeration data were done using t-tests, and chi square tests. $P < 0.05$ was considered a statistically significant difference. We used GraphPad Prism 8.0 to plot the figures.

Results

Clinical materials

The differences in terms of gender, age, and course of the disease between the two groups was statistically insignificant ($P > 0.05$) (Table 1).

Clinical efficacy

The total effective rate in the observation group was 98.33%, and the total effective rate in

the control group was 86.67%. The clinical efficacy in the observation group was superior to the clinical efficacy in the control group (Table 2).

Changes in pulmonary function before and after the treatment

The FVC, FEV1, and FEV1/FVC levels in the two groups increased significantly after the treatment compared to before the treatment ($P < 0.05$), and the observation group had superior post-treatment pulmonary

function than the control group ($P < 0.05$) (Table 3).

Changes in the inflammatory cytokine levels before and after the treatment

The TNF- α , IL-6, and CRP levels in the two groups after the treatment dropped significantly compared to their pre-treatment levels ($P < 0.05$), and the observation group had lower post-treatment inflammatory cytokine levels than the control group ($P < 0.05$) (Table 4).

The changes in immunological function before and after the treatment

The two groups' CD4⁺ and CD4⁺/CD8⁺ levels increased substantially in after the treatment compared to their pre-treatment levels ($P < 0.05$), and the post-treatment indexes in the observation group were significantly higher than the post-treatment indexes in the control group ($P < 0.05$) (Table 5 and Figures 1-3).

Discussion

Severe pneumonia is a prevailing respiratory illness in clinical pediatrics. Its pathogenesis is primarily correlated with the invasion of viruses and toxins, and the immunity of the children [11, 12]. Children with severe pneumonia often also suffer from respiratory failure, as well as nervous system symptoms such as listlessness, irritability, or lethargy. Those with severe illnesses may even have edema, convulsions, coma, or disturbances of consciousness, and

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Table 3. The pulmonary function changes before and after the treatment in the two groups ($\bar{x} \pm s$)

Group	Time	FVC (L)	FEV1 (L)	FEV1/FVC (%)
Observation group (n=60)	Before treatment	1.63±0.33	1.54±0.31	44.58±5.86
	After treatment	2.89±0.60*	2.79±0.45*	58.39±6.44*
	t	14.253	17.719	12.286
	P	<0.05	<0.05	<0.05
Control group (n=60)	Before treatment	1.65±0.41	1.58±0.36	44.73±6.42
	After treatment	2.31±0.57	2.16±0.47	52.31±5.97
	t	7.281	7.589	6.697
	P	<0.05	<0.05	<0.05

Note: Compared with the control group, *P<0.05.

Table 4. Changes in the inflammatory cytokine levels before and after the treatment in the two groups

Group	Time	TNF-α (pg/ml)	IL-6 (pg/ml)	CRP (mg/L)
Observation group (n=60)	Before treatment	278.59±64.92	159.69±31.52	89.60±25.63
	After treatment	176.49±49.50*	65.49±17.69*	31.27±9.70*
	t	9.687	20.187	16.487
	P	<0.05	<0.05	<0.05
Control group (n=60)	Before treatment	283.94±70.38	164.29±33.75	87.62±24.37
	After treatment	216.42±54.20	83.27±21.59	42.65±13.26
	t	5.888	15.664	12.555
	P	<0.05	<0.05	<0.05

Note: Compared with the control group, *P<0.05.

Table 5. Changes in the T lymphocyte levels before and after the treatment in the two groups ($\bar{x} \pm s$)

Group	Time	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Observation group (n=60)	Before treatment	31.89±3.27	25.74±3.11	1.25±0.39
	After treatment	47.69±5.49*	24.69±3.52	1.89±0.47*
	t	19.153	1.732	8.117
	P	<0.05	0.086	<0.05
Control group (n=60)	Before treatment	32.18±4.10	25.85±2.98	1.27±0.32
	After treatment	41.26±5.93	24.75±3.73	1.65±0.40
	t	9.756	1.785	5.746
	P	<0.05	0.077	<0.05

Note: Compared with the control group, *P<0.05.

these may further develop into brain herniation and lead to death due to central respiratory failure [13]. The conventional clinical treatment measures for children with severe pneumonia include antivirals, antibiotics, relieving the phlegm and cough, etc. However, the antibiotics have a negative impact on the immune systems of children, and their long-term application is prone to bring on drug resistance [15, 16].

In traditional Chinese medicine, severe pneumonia is classified into the categories of “lung

fever”, “syndrome of asthma”, or “fever disease”, among which the most common syndrome is phlegm-heat obstruction of the lungs [17]. In recent years, traditional Chinese medicine has made remarkable progress in treating severe pneumonia in children. In this study, the protective effect of Qingfei Huatan decoction made by our hospital on the pulmonary and immunological function in children with severe pneumonia were researched and analyzed. In this prescription, raw gypsum is pungent and cold in nature, the pungency goes outside and can relieve muscle fevers, and the quality of the

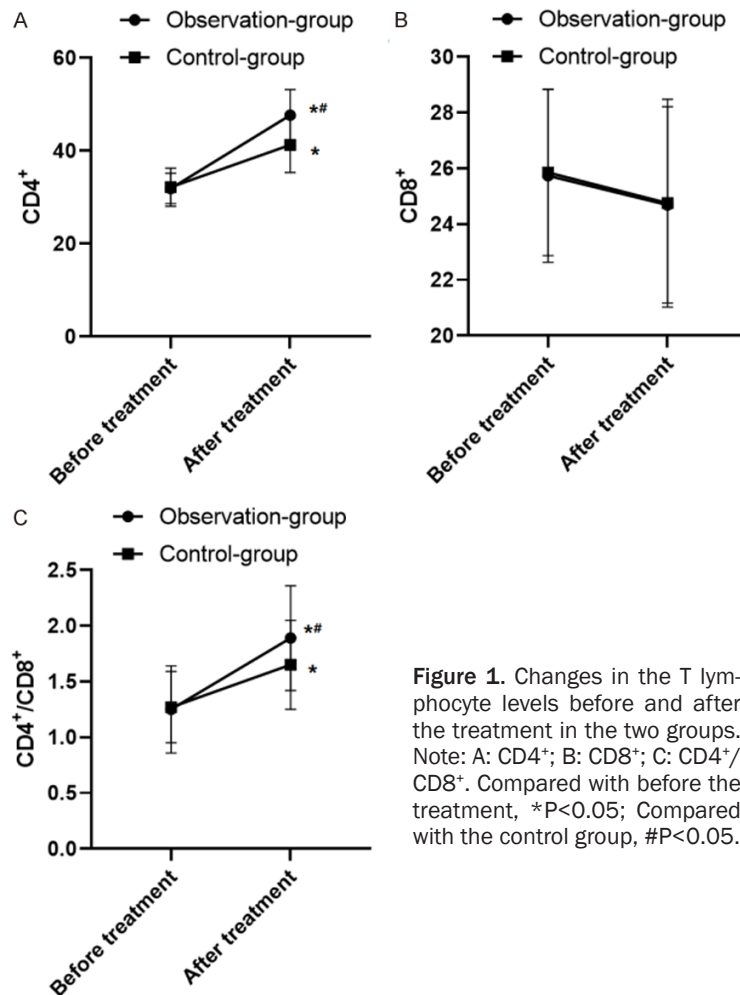


Figure 1. Changes in the T lymphocyte levels before and after the treatment in the two groups. Note: A: CD4⁺; B: CD8⁺; C: CD4⁺/CD8⁺. Compared with before the treatment, *P<0.05; Compared with the control group, #P<0.05.

pneumonia and bronchial asthma. *Magnolia officinalis* can lower Qi in the lungs, relieve asthma and eliminate phlegm. Honeysuckle clears away heat and detoxifies. *Scutellaria baicalensis* has the functions of clearing heat, dampness, and detoxification, and also the effects of broad-spectrum anti-pathogenic microorganisms, effectively inhibiting the activity of inflammatory cytokines [18-20]. The combined use of the above drugs can jointly exert the function of clearing the lungs, resolving phlegm, and relieving cough and asthma.

This research conclusion indicates that the clinical efficacy in the observation group was critically superior to the clinical efficacy in the control group. It is similar to the results of other scholars, namely that the treatment of children with severe pneumonia using the combined integration of traditional Chinese and western medicine can obtain a remarkable clinical efficacy. The FVC, FEV1,

and FEV1/FVC levels in the observation group after the treatment were significantly higher than they were in the control group, and the serum TNF- α , IL-6, and CRP levels in the observation group were notably lower than they were in the control group. The related studies have shown that the human body can release a large number of inflammatory factors after the onset of severe pneumonia, and it can create a cascade of inflammatory reactions, inducing dysfunction in other tissues and aggravating the severity of the disease [21, 22]. This study found that the joint application of Qingfei Huatan decoction and conventional treatment measures can efficaciously promote the recovery of lung function in children with severe pneumonia, and at the same time reduce the inflammation level, thus helping to control the disease progression and promote the improvement of the disease condition. In addition, the CD4⁺ and CD4⁺/CD8⁺ levels in the observation

cold is kept inside the body and can overcome the stomach fire, which is the main ingredient in the prescription. *Anemarrhena* is bitter and cold in nature. It has the effects of clearing the internal heat, moistening the dryness, and it needs to be simultaneously adopted with gypsum. *Radix trichosanthis* is sweet in taste and slightly cold in nature. It has the functions of clearing and purging the internal heat, generating fluid, quenching thirst, and reducing swelling and fester. *Aster tataricus* is sharp, bitter, and warm in nature, and it can moisturize the lungs, relieve phlegm, regulate the Qi in the body and relieve cough. Ephedra, almonds, gypsum, and *Radix Glycyrrhizae* Prepare are the raw materials of the decoction of Ephedra, apricot kernel, gypsum, and licorice in the *Treatise on Febrile Diseases*. It has the functions of pungent and cool catharsis, the clearing of the lungs and relieving asthma, and it has crucial curative effects in the treatment of

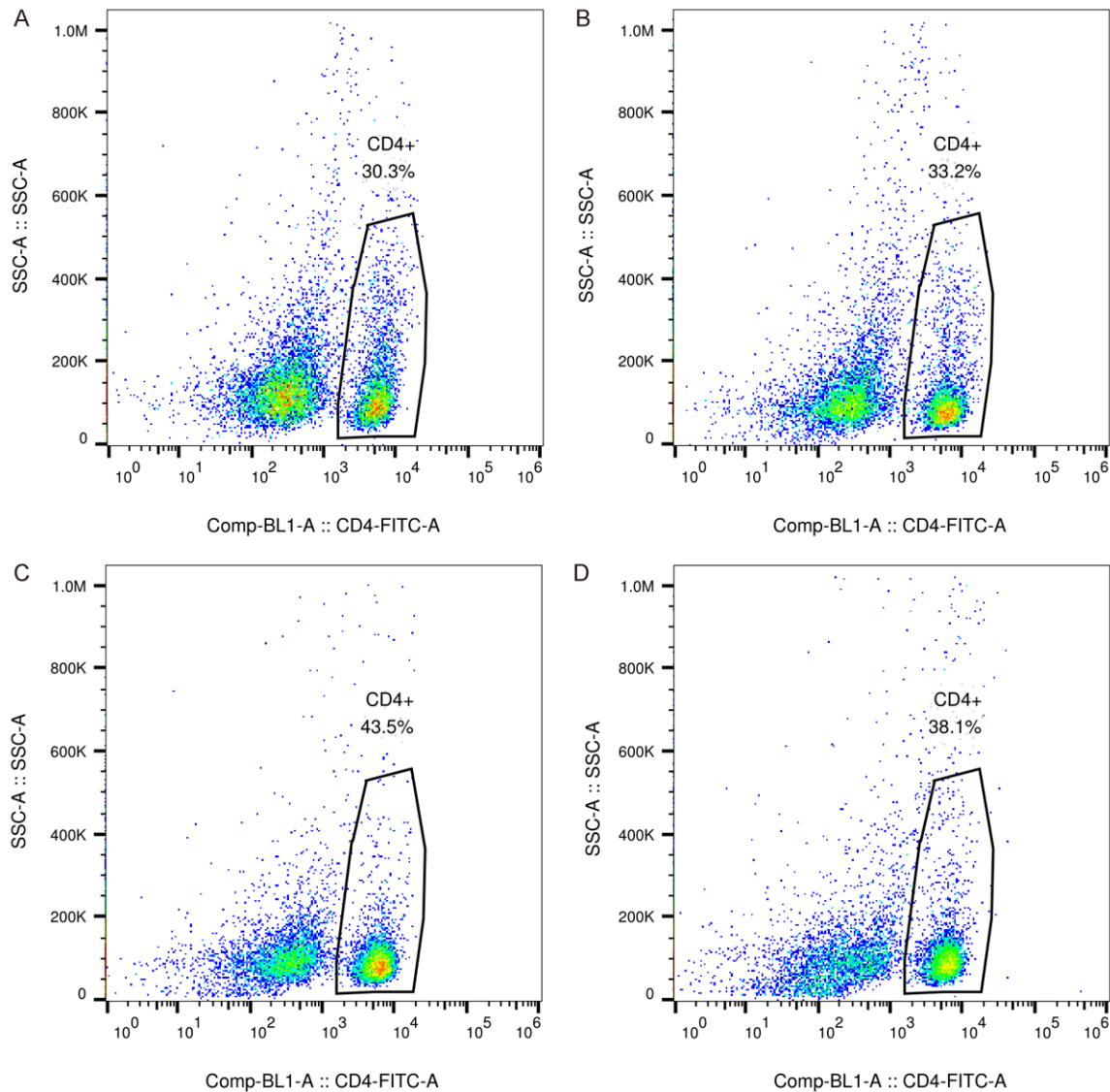


Figure 2. Changes in the CD4⁺ cell levels in the two groups. A: Observation group before the treatment; B: Observation group after the treatment; C: Control group before the treatment; D: Control group after the treatment.

group were apparently higher than they were in the control group after the treatment. The immune systems in children are not fully established, and one of the important mechanisms of severe pneumonia is low immune function, so this leads to a difficult recovery from the disease [23]. This study's results confirmed that the combined treatment of Chinese and Western medicine can effectively improve the immunological function of the children and improve their adaptability to both the internal and external environments.

These study results are consistent with those of related studies [24, 25], indicating that the

clinical symptoms of children with severe pneumonia can be effectively improved by the integrated treatment of traditional Chinese and Western medicines. The mechanism is related to the regulation of immune function and the inhibition of the inflammatory response through multi-channel and multi-functional targets.

However, the scope of the cohort included in this research was limited, and an in-depth analysis of the mechanism of the home-made Qingfei Huatan decoction was not analyzed. This suggests that the sample size needs to be further expanded in the follow-up research, and

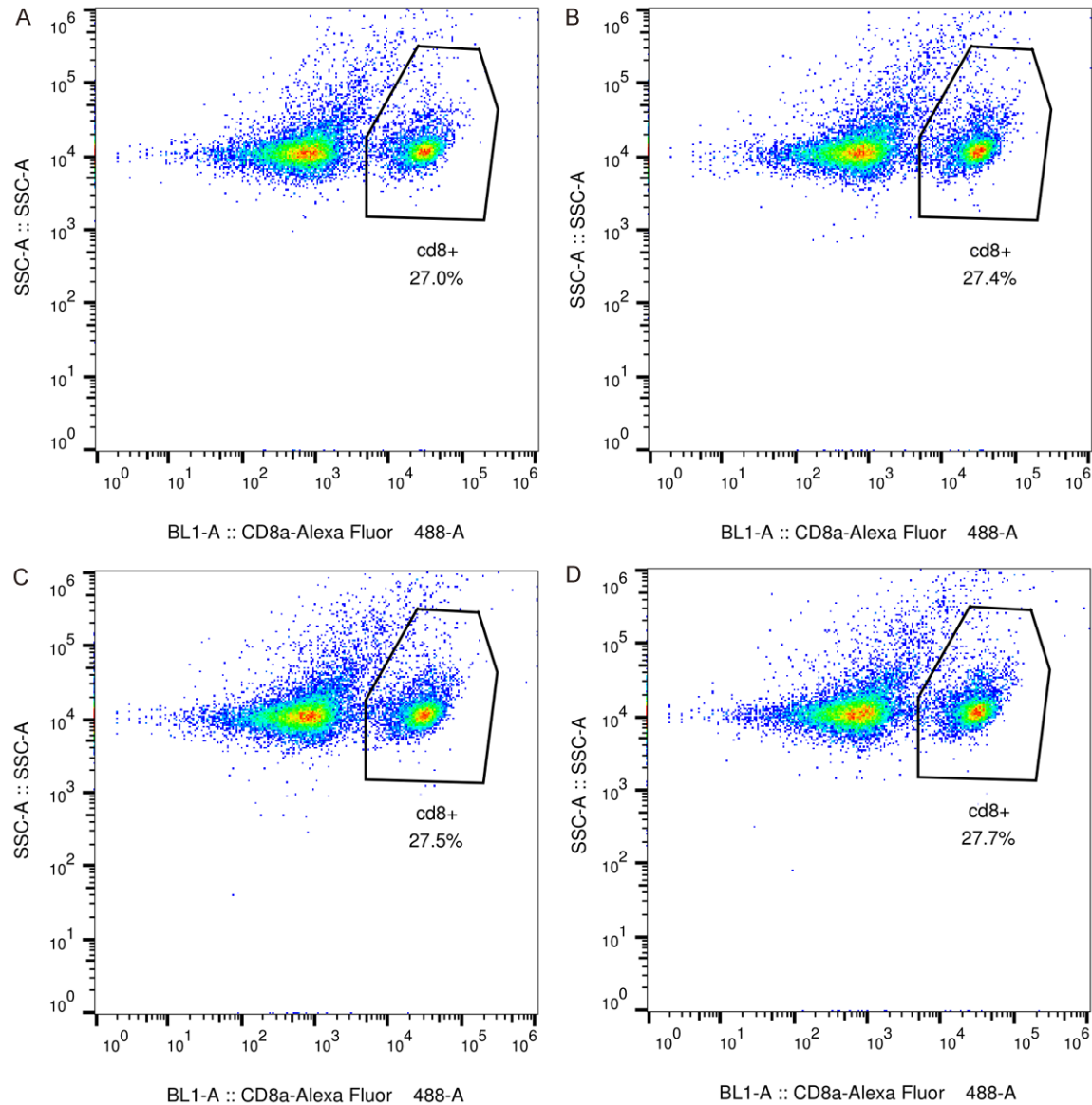


Figure 3. Changes in the CD8⁺ cell levels in the two groups. A: Observation group before treatment; B: Observation group after the treatment; C: Control group before the treatment; D: Control group after the treatment.

the possible mechanism of the combination of the traditional Chinese and western medicine needs to be analyzed to better guide the clinical treatment work and to understand the mechanism of the traditional Chinese medicine in children with severe pneumonia.

In summary, the combined therapy using the mixed Chinese herbs Qingfei Huatan decoction and routine treatment has a distinct clinical effect on children with severe pneumonia, as it can effectively promote the pulmonary function of children. Its effect may be correlated with

the suppression of inflammation in the body and the improvement of immunological function in children.

Disclosure of conflict of interest

None.

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