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The study on the mechanism of Tanreqing and ambroxol combined with Azithromycin for the treatment of mycoplasma pneumonia in children

Li Yu, Yan He✉

Pediatrics, People's Hospital of Yongchuan District, Chongqing, Chongqing 402160, China

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ABSTRACT

Objective: To observe the mechanism of Tanreqing and ambroxol combined with Azithromy for the treatment of mycoplasma pneumonia in children and offer help to mycoplasma pneumonia treatment. **Methods:** 86 cases of mycoplasma pneumonia patients in our hospital were selected and randomly divided into observation group and control group, each group were 43 cases. Control group was treated with conventional therapy, and observation group was treated with Tanreqing and ambroxol combined with Azithromy based on conventional therapy, the changes of lung function [V-T (Tidal volume)/kg, t-PTEF/t-E (time ratio of peak to peak), TEF25/PTEF (Instantaneous velocity of exhaling tidal volume 75% and Peak tidal expiratory flow ratio) and MTIF/MTEF (medium-term inspiratory flow rate and medium-term expiratory flow rate ratio)], cytokines (IL-2, IL-10, IL-6 and TNF-α) and the myocardial enzymes [LDH (lactate dehydrogenase), CK-MB (creatine kinase isoenzyme), CK (creatine kinase) and AST (glutamic-oxaloacetic transaminase)] were detected before and after treatment. **Results:** The comparison of lung function, cytokines and themyocardial enzymes in the two groups before treatment was not statistically significant (P>0.05). MTIF/MTEF, themyocardial enzymes (LDH, CK-MB, CK and AST) and cytokines (IL-10, IL-6 and TNF-α) in both groups after treatment significantly decreased compared with that before treatment (P<0.05); lung function (V-T/kg, t-PTEF/t-E, TEF25/PTEF), and IL-2 in both groups after treatment significantly increased compared with that before treatment (P<0.05). Lung function (V-T/kg, t-PTEF/t-E, TEF25/PTEF), and IL-2 in observation group after treatment increased more significantly than that in control group (P<0.05), and MTIF/MTEF, themyocardial enzymes (LDH, CK-MB, CK and AST) and cytokines (IL-10, IL-6 and TNF-α) decreased more significantly than that in control group (P<0.05). **Conclusions:** Tanreqing and ambroxol combined with Azithromy could improve lung function, cytokines and the myocardial enzymes in children with mycoplasma pneumonia, which has a very important clinical significance of the treatment to mycoplasma pneumonia.

1. Introduction

Mycoplasma pneumonia, a disease of acute infections of respiratory tract, is a common and frequently-occurring disease of children's lung tissues, which is caused by mycoplasma[1,2]. The main clinical manifestations of children with mycoplasma pneumonia are fever and expectoration. Meanwhile, the pathological changes, such as interstitial pneumonia and capillary bronchial pneumonia will occur, which will endanger the physical and mental health and life security of patients[3,4]. So, it is extremely important to treat the children with mycoplasma pneumonia timely and effectively. In this study, through studying the mechanism of Tanreqing and ambroxol combined with Azithromy for treatment of mycoplasma pneumonia in children, we aimed to provide help for the clinical treatment of mycoplasma pneumonia

2. Materials and methods

✉Corresponding author: Yan He, Pediatrics, People's Hospital of Yongchuan District, Chongqing, Chongqing 402160, China.

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2.1. General information

86 cases of mycoplasma pneumonia from May 2013 to January 2016 in our hospital were selected. All the children had a definitive diagnosis of pneumonia, which was diagnosed by X-rays and CT scan. The mycoplasma of the children was positive, which was tested by PCR. All patients were consistent with the diagnosis standard of the Textbook of Pediatrics. According to the random number table method, 86 cases patients were divided into two groups, the observation group and the control group (n = 43). In the observation group, there were 43 children (22 males and 21 females), aged from 2 to 6 years old. There were unilateral lesions in 27 cases, bilateral lesions in 16 cases. In the control group, there were 43 children (23 males and 20 females), aged from 2 to 6 years old. There were unilateral lesions in 28 cases, bilateral lesions in 15 cases. There had no differences in the age, sex and physical condition, and there was no statistical significance (P>0.05).

2.2. Exclusion and inclusion criteria

Every child had no medical history of respiratory system, other infections, endocrine disease and liver and renal dysfunction. Every child could cooperate with relevant treatment actively. Also, all children were not allergic to related drugs. These patients did not receive related treatment before and had detailed information before the treatment. This study was approved by the ethics committee of our hospital, and the children′s parents all signed the informed consent.

2.3. Treatment method

The control group was given Azithromycin to anti-mycoplasma, oxygen inhalation, correcting acidosis, relieving cough and reducing, defervescence, and other routine treatment. The observation group were given Tanreqing (Shanghai Kaibao Pharmaceutical Co. Ltd., Chinese medicine standard word: Z20030054), 0.4 mL/kg per day in 200 mL glucose injection, 1 time a day; and ambroxol (Bright Future Pharmaceuticals Factory, Chinese medicine standard word: HC20120013), oral of 2.5 mL/time, 3 times/d; Azithromycin (Jiangxi Huireng Pharmaceutical Co. Ltd., Chinese medicine standard word: H20023871); the usage of children, 10 mg/kg per day for 3 d; The treatment period of the two groups was 1 week.

2.4. Blood sample collection

3 mL of fasting peripheral venous blood of mycoplasma pneumonia children in two groups were collected before treatment and 1 week after treatment. And then the related indexes were detected by clinical laboratory.

2.5. Detection of cytokines and oxidative stress parameters

LDH (lactate dehydrogenase), CK-MB (creatine kinase isoenzyme), CK (creatine kinase), AST (glutamic-oxaloacetic transaminase), IL-2 (Interleukin-2), IL-6 (Interleukin-6), IL-10 (Interleukin-10) and TNF-α (tumor necrosis factor) were detected by ELISA kits. The kits were purchased from Shanghai Enzyme Research Biological Technology Co., Ltd., Nanjing Kaiji Biological Technology Development Co., Ltd., Nanjing Jinsirui Biological Technology Co, Ltd., Hangzhou Dianbang Biological Technology Co, Ltd., Shanghai Jianglai Biological Technology Co, Ltd., and Shanghai Chaoyan Biologic Technology. Enzyme standard instrument of Infinite 200 (company: TECAN, Switzerland) is used to detected the absorbance OD value at 450 nm. And then, the corresponding concentration value was calculated by the standard curve. The operation process was performed according to the instruction strictly

2.6. Detection of the lung function

The main parameters include V-T (Tidal volume), TEF25/PTEF (Instantaneous velocity of exhaling tidal volume 75% and Peak tidal expiratory flow ratio), t-PTEF/t-E (time ratio of peak to peak) and MTIF/MTEF (medium-term inspiratory flow rate and medium-term expiratory flow rate ratio) were detected by MIR Spirolab for children of JAEGER in two groups. The experimental operation was performed according to the instruction strictly.

2.7. Statistical analysis

SPSS 17.0 statistical package was conducted for statistical analysis. Lung function, cytokines and themyocardial enzymes were described as mean ± standard deviation ($\bar{x}\pm s$) with variance analysis, intergroup comparison was conducted by t test, and values of P<0.05 were considered to be statistically significant.

3. Results

3.1. Comparison lung function of the mycoplasma pneumonia children in the two groups before and after treatment

V-T/kg, t-PTEF/t-E, TEF25/PTEF, MTIF/MTEF and related factors of lung function of the mycoplasma pneumonia children were detected and analyzed before and after treatment. The comparison of lung function in the two groups before treatment was not statistically significant (P>0.05). V-T/kg, t-PTEF/t-E andTEF25/PTEF in observation group after treatment significantly increased, while MTIF/MTEF significantly decreased compared with that before treatment. The difference was considered to be statistically significant (P<0.05). V-T/kg, t-PTEF/t-E and TEF25/PTEF in control group after treatment significantly increased, while MTIF/MTEF significantly decreased compared with that before treatment. V-T/kg, t-PTEF/t-E and TEF25/PTEF in observation group after treatment increased more significantly than that in control group (P<0.05), while MTIF/MTEF in observation group after treatment decreased more significantly than that in control group (P<0.05) (Table 1).

3.2. Comparison cytokines of the mycoplasma pneumonia children in the two groups before and after treatment

IL-2, IL-10, IL-6 and TNF-α of the mycoplasma pneumonia children in the two groups were detected by ELISA. The comparison of cytokines in the two groups before treatment was not statistically significant (P>0.05). IL-10, IL-6 and TNF-α in observation group after treatment significantly decreased and IL-2 significantly

increased compared with that before treatment ($P<0.05$). The comparison of cytokines in the two groups before treatment was not statistically significant ($P>0.05$). IL-10, IL-6 and TNF-α in control group after treatment significantly decreased and IL-2 significantly increased compared with that before treatment ($P<0.05$). IL-10, IL-6 and TNF-α in observation group after treatment decreased more significantly than that in control group ($P<0.05$). IL-2 in observation group after treatment increased more significantly than that in control group ($P<0.05$) (Table 2).

3.3. Comparison themyocardial enzymes of the mycoplasma pneumonia children in the two groups before and after treatment

LDH, CK-MB, CK and AST of the mycoplasma pneumonia children in the two groups were detected by ELISA. The comparison of themyocardial enzymes in the two groups before treatment was not statistically significant ($P>0.05$). LDH, CK-MB, CK and AST in observation group after treatment significantly decreased compared with that before treatment ($P<0.05$). LDH, CK-MB, CK and AST in control group after treatment significantly decreased compared with that before treatment ($P<0.05$). LDH, CK-MB, CK and AST in observation group after treatment decreased more significantly than that in control group ($P<0.05$) (Table 3).

4. Discussion

Mycoplasma pneumonia, a disease of acute infections of respiratory tract, is a common and frequently-occurring disease in children[5]. Children's lung function is not yet mature with their low immune function of the body, which makes the incidence rate of mycoplasma pneumonia in children higher. Also, this disease is mostly occurred in spring and autumn[6]. The main clinical manifestations of children with mycoplasma pneumonia are coughing with asthma, fever and expectoration. The course of this disease is longer and the illness relapsed easily. Meanwhile, the serious pathological changes, such as lobar pneumonia and capillary bronchial pneumonia, will occur, which will endanger the lung function of the children. Lung function impairment will cause myocardial hypoxia, thus, the themyocardial enzymes would be changed[7,8]. At the same time, various inflammatory reactions will be caused. If the children with mycoplasma pneumonia can't receive timely and effective treatment, they will be in a serious threat to life and health[9]. So, the treatment of mycoplasma pneumonia is a top priority for medical workers.

This study found that Tanreqing and ambroxol combined with Azithromycin can improve effectively lung function factors (V-T/Kg, t-PTEF/t-E, TEF25/PTEF and MTIF/MTEF), cytokines (IL-10, IL-6 and TNF-α) and themyocardial enzymes (LDH, CK-MB, CK and AST) on children with mycoplasma pneumonia. And the effect of observation group is superior to the effect of control group. *Mycoplasma pneumonia* enter the body, inducing adhesion molecule adhering to the mucosal epithelial cells of respiratory tract, releasing superoxide anion, hydrogen peroxide, neurotoxin, which results in the cytotoxic reaction. All these will lead to mucosal epithelial damage, mucus cilia clearance dysfunction, epithelial cell death and shedding, airway obstruction and airway hyper responsiveness, which influence the lung function in children[10]. Ambroxol can accelerate the exudation of airway fluid and pulmonary surfactant liquid, which makes the viscous polysaccharide fiber in phlegm breaking and Phlegm dissolving. At the same time, Ambroxol can enhance the movement of bronchial cilia, promoting the discharge of sputum[11]. Tanreqing has a good effect of clearing heat and resolving phlegm. The two in combination can improve the pulmonary physical and chemical environment, keep breathing unobstructed for the children, which will improve the lung function

Table 1

Comparison lung function of the mycoplasma pneumonia children in the two groups before and after treatment ($n = 43$, $\bar{x}\pm s$).

Groups	Time	V-T/kg (Ml/kg)	t-PTEF/t-E (%)	TEF25/PTEF (%)	MTIF/MTEF
Observation group	Before treatment	8.67±0.58	37.56±3.21	0.65±0.06	1.28±0.11
	After treatment	12.53±1.25*#	45.81±3.74*#	0.79±0.08*#	1.21±0.09*#
Control group	Before treatment	8.64±0.73	37.44±3.08	0.64±0.05	1.29±0.13
	After treatment	10.40±0.92*	40.22±3.53*	0.71±0.07*	1.25±0.10*

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

Table 2

Comparison cytokines of the mycoplasma pneumonia children in the two groups before and after treatment ($n = 43$, $\bar{x}\pm s$).

Groups	Time	IL-2 (μg/mL)	IL-10 (pg/mL)	IL-6 (pg/mL)	TNF-α (μg/mL)
Observation group	Before treatment	3.33±0.27	37.82±4.66	18.55±1.92	2.20±0.18
	After treatment	8.45±0.76*#	24.12±3.03*#	8.24±1.16*#	0.67±0.09*#
Control group	Before treatment	3.31±0.25	37.79±4.50	18.58±2.04	2.23±0.24
	After treatment	6.18±0.52*	31.62±3.29*	12.57±1.63*	1.61±0.16*

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

Table 3

Comparison themyocardial enzymes of the mycoplasma pneumonia children in the two groups before and after treatment (U/L, $n = 43$, $\bar{x}\pm s$).

Groups	Time	LDH	CK-MB	CK	AST
Observation group	Before Treatment	275.69±11.32	34.89±4.01	183.81±8.41	54.65±5.16
	After Treatment	161.35±8.46*#	18.25±2.68*#	122.57±6.29*#	24.10±3.77*#
Control group	Before Treatment	274.98±10.81	35.21±4.38	184.62±8.83	54.33±4.87
	After Treatment	188.75±9.23*	26.09±3.43*	144.26±7.17*	34.26±4.18*

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

of the mycoplasma pneumonia children. *Mycoplasma pneumonia* in children is a specific antigen. It can stimulate the production of antibodies and related cytokines by allergic reaction, causing the occurrence of inflammatory reaction[12]. Pathological changes of lung tissue and capillary bronchus in mycoplasma pneumonia children will occur, further lead to the occurrence of inflammation and the changes of IL-2, IL-10 and IL-6[13,14]. Azithromycin, a macrolide antibiotic, can interfere with the synthesis of bacteria protein. The susceptibility of mycoplasma pneumonia to macrolide antibiotic is high. So, the macrolide antibiotic can inhibit the growth and reproduction of mycoplasma pneumonia, and suppress the occurrence of inflammatory reactions fundamentally[15]. Tanreqing and ambroxol can improve sputum excretion, prevent further damage to the lung cells and promote the recovery of damaged cells. Thus, Tanreqing and ambroxol can reduce the secretion of proinflammatory factors and increase the secretion of anti-inflammatory factors. Related studies show that mycoplasma pneumonia can invade the myocardial tissues directly and cause the inflammatory reaction at the same time, which cause the damages to the myocardial tissues[16]. *Mycoplasma pneumonia* will damage the lung tissues, increase the level of free radicals *in vivo* and lead to the damages of myocardial tissues[17–19]. The damages of myocardial tissues will further lead to the myocardial cells rupturing and releasing a large number of myocardial enzymes. The study found that after the children with mycoplasma pneumonia using Tanreqing and ambroxol combined with Azithromycin for the treatment, the level of the myocardial enzymes decreased, which indicated the myocardial injury alleviated. Maybe Tanreqing and ambroxol combined with Azithromycin can decrease the mycoplasma level, improve the cellular state and physical and chemical environment of lung tissues, decrease the production of radicals. So, the damages of myocardial tissues will be alleviated, which makes the release of myocardial enzyme decreased. The lung function of the patients improved after the combination therapy, which increases the blood oxygen content. It is beneficial to the myocardial oxygen supply and damaged myocardial cell repair. So, the myocardial enzymes were reduced in blood.

In conclusion, the influence of lung function related factors (V-T/Kg, t-PTEF/t-E, TEF25/PTEF and MTIF/MTEF), cytokines (IL-2, IL-10, IL-6 and TNF-α) and the myocardial enzymes (LDH, CK-MB, CK and AST) were detected in the research. Also the mechanism of Tanreqing and ambroxol combined with Azithromycin for the treatment of mycoplasma pneumonia in children was discussed. This study provides help for the clinical treatment of mycoplasma pneumonia.

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