



# Effect of aerosol inhalation of ipratropium bromide combined with budesonide and terbutaline on cytokines in children with bronchopneumonia

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## ARTICLE INFO

### Article history:

Received  
Received in revised form  
Accepted  
Available online

### Keywords:

Budesonide  
Terbutaline  
Ipratropium bromide  
Aerosol inhalation  
Children with bronchopneumonia  
Cytokine

## ABSTRACT

**Objective:** To explore the clinical efficacy of aerosol inhalation of ipratropium bromide combined with budesonide and terbutaline in the treatment of bronchopneumonia in children and the effect on cytokines. **Methods:** A total of 70 children with bronchopneumonia who were admitted in our hospital from March, 2015 to March, 2016 were included in the study and randomized into the study group and the control group. The patients in the control group were given anti-infection, oxygen inhalation, cough and asthma relieving, acidosis correcting, mask+oxygen driven aerosol inhalation of budesonide (0.5 mg/time) and terbutaline (1.0 mg/time), with an oxygen flow rate of 5-7 L/min, 5-10 min every time, twice a day. On the above basis, the patients in the study group were given additional ipratropium bromide (1.0 mg/time). After 7-day treatment, the efficacy was evaluated. The levels of IL-6, TNF- $\alpha$ , CRP, and WBC before and after treatment were detected. PEF, FVC, and FEV1 before and after treatment were detected. The improvement of clinical symptoms and signs, and the occurrence of adverse reactions were observed. **Results:** The levels of IL-6, TNF- $\alpha$ , CRP, and WBC counting after treatment in the two groups were significantly reduced when compared with before treatment ( $P<0.05$ ), and the reduced degree in the study group was significantly superior to that in the control group ( $P<0.05$ ). PEF, FVC, and FEV1 after treatment in the two groups were significantly improved when compared with before treatment ( $P<0.05$ ), and the improved degree in the study group was significantly superior to that in the control group ( $P<0.05$ ). After treatment, the cough and asthma relieving, and rale and DR shadow disappearing time in the study was significantly shorter than that in the control group ( $P<0.05$ ). No severe adverse reactions occurred in the two groups, and the comparison between the two groups was not statistically significant ( $P>0.05$ ). **Conclusions:** Ipratropium bromide combined with budesonide and terbutaline in the treatment of bronchopneumonia in children can rapidly relieve the symptoms, and improve the cytokine level, without obvious adverse reactions; therefore, it deserves to be widely recommended in the clinic.

## 1. Introduction

Bronchopneumonia is a common pediatric disease. Due to low immunological function, incomplete maturity of pulmonary and bronchial function, and bronchial stenosis, the sputum is difficult to be expectorated, and the severe pulmonary inflammation occurs,

resulting in delayed healing, which can affect the patients' living qualities[1]. Routine anti-infection, maintaining the respiratory tract unobstructed, and improving the pulmonary ventilation and gas exchanging function are mainly involved in the clinical treatment. Improper treatment can induce a series of extrapulmonary complications[2]. With the clinical study on bronchopneumonia in children, in recent years, the combined aerosol inhalation is adopted, with a satisfactory effect, in that it can effectively improve the clinical symptoms, and reduce the occurrence of complications[3]. The study is aimed to explore the clinical efficacy of aerosol

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Foundation project: The study was supported by the Medical Science Achievement Project of Hebei Province with the number of 144110-5-3.

inhalation of ipratropium bromide combined with budesonide and terbutaline in the treatment of bronchopneumonia in children.

## 2. Materials and methods

### 2.1. General materials

A total of 80 children with bronchopneumonia who were admitted in our hospital from April, 2015 to April, 2016 were included in the study, among which 38 were male, and 32 were female; aged from 2 to 13 years old, with an average age of (5.8±2.3) years old; course from 2 to 8 d, with an average course of (3.7±2.6) d; weight from 15 to 34 kg, with an average weight of (19.5±5.2) kg. The patients were randomized into the study group and the control group with 40 cases in each group. The difference of general data between the two groups was not statistically significant ( $P>0.05$ ).

### 2.2. Inclusion and exclusion criteria

The patients were in accordance with the diagnostic criteria of bronchopneumonia[4]. The informed consents were obtained from the patients' relatives. Those who had severe respiratory and circulatory diseases, unknown pneumonia and bronchial asthma, and those who were merged with severe pulmonary infection and allergic to related drugs were excluded from the study.

### 2.3. Methods

The patients in the control group were given anti-infection, oxygen inhalation, cough and asthma relieving, acidosis correcting, mask+oxygen driven aerosol inhalation of budesonide (0.5 mg/time) and terbutaline (1.0 mg/time), with an oxygen flow rate of 5-7 L/min, 5-10 min every time, twice a day. On the above basis, the patients in the study group were given additional ipratropium bromide (1.0 mg/time). After 7-day treatment, the efficacy was evaluated.

### 2.4. Observation indicators

A volume of 3 mL elbow venous blood was extracted and

centrifuged for serum. ELISA was used to detect IL-6 and TNF- $\alpha$  levels. The immuno-scatter turbidimetry was used to detect CRP. The full automatic blood cell analyzer was used to detect WBC. PEF, FVC, and FEV1 before and after treatment were detected. The improvement of clinical symptoms and signs, including the cough and asthma relieving, and rale and DR shadow disappearing time, and the occurrence of adverse reactions were observed.

### 2.5. Statistical analysis

SPSS 18.0 software was used for the statistical analysis. The measurement data were expressed as mean±SD, and  $t$  test was used.  $\chi^2$ -square test was used for the enumeration data.  $P<0.05$  was regarded as statistically significant difference.

## 3. Results

### 3.1. Cytokine level and WBC counting before and after treatment

The levels of IL-6, TNF- $\alpha$ , CRP, and WBC counting after treatment in the two groups were significantly reduced when compared with before treatment ( $P<0.05$ ), and the reduced degree in the study group was significantly superior to that in the control group ( $P<0.05$ ) (Table 1).

### 3.2. PEF, FVC, and FEV1 before and after treatment

PEF, FVC, and FEV1 after treatment in the two groups were significantly improved when compared with before treatment ( $P<0.05$ ), and the improved degree in the study group was significantly superior to that in the control group ( $P<0.05$ ) (Table 2).

### 3.3. Improvement of clinical symptoms and signs after treatment

After treatment, the asthma relieving, cough relieving, rale disappearing, and DR shadow disappearing time in the study group were (3.47±0.51) d, (5.18±1.43) d, (4.65±0.82) d, and (5.25±0.53)

**Table 1**

Cytokine level and WBC counting before and after treatment (mean±SD).

Groups	<i>n</i>	Time	IL-6 (pg/mL)	TNF- $\alpha$ (pg/mL)	CRP (mg/L)	WBC ( $\times 10^9/L$ )
Study group	40	Before treatment	98.72±8.54	31.54±3.34	13.38±1.15	16.02±5.32
		After treatment	22.35±4.37 <sup>#</sup>	8.27±2.15 <sup>#</sup>	5.78±0.52 <sup>#</sup>	10.17±3.14 <sup>#</sup>
Control group	40	Before treatment	97.86±8.83	30.75±2.18	13.27±1.25	16.03±5.41
		After treatment	58.44±6.17 <sup>*</sup>	16.18±2.41 <sup>*</sup>	10.44±0.46 <sup>*</sup>	12.47±4.65 <sup>*</sup>

<sup>#</sup> $P<0.05$ , when compared with before treatment; <sup>\*</sup> $P<0.05$ , when compared with the control group.

**Table 2**

PEF, FVC, and FEV1 before and after treatment (mean±SD).

Groups	n	Time	PEF (L/s)	FVC (L)	FEV1 (L)
Study group	40	Before treatment	2.38±0.41	1.20±0.15	1.10±0.17
		After treatment	2.97±0.54 <sup>#</sup>	1.32±0.23 <sup>#</sup>	1.24±0.18 <sup>#</sup>
Control group	40	Before treatment	2.37±0.51	1.21±0.13	1.10±0.18
		After treatment	2.65±0.32 <sup>*</sup>	1.26±0.31 <sup>*</sup>	1.16±0.17 <sup>*</sup>

<sup>\*</sup> $P < 0.05$ , when compared with before treatment; <sup>#</sup> $P < 0.05$ , when compared with the control group.

d, respectively; while in the control group were (5.72±0.32) d, (6.46±2.41) d, (6.57±0.71) d, (6.68±0.72) d, respectively. After treatment, the cough and asthma relieving, and rale and DR shadow disappearing time in the study was significantly shorter than that in the control group ( $P < 0.05$ ).

### 3.4. Occurrence of adverse reactions

In the study group, 1 had skin rash, 2 had vomiting, 1 had diarrhea, and the occurrence rate was 11.4%; while in the control group, 1 had skin rash, 1 had vomiting, 1 had diarrhea, and the occurrence rate was 8.6%. No severe adverse reactions occurred in the two groups, and the comparison between the two groups was not statistically significant ( $P > 0.05$ ).

## 4. Discussion

The lesions of bronchopneumonia are mainly distributed in the pulmonary alveoli adjacent to the bronchus. Due to bronchial mucosal edema, alveoli wall congestion, sputum filling the cavity, poor ciliary movement of the bronchial mucosa, and weak pulmonary retractive force, the sputum can not be preferably eliminated, and the respiratory tract can be obstructed, which can affect the lung ventilation and gas exchanging function, and severely endanger the patients' lives; therefore, effective elimination of respiratory secretions, and maintaining the respiratory tract unobstructed are key in the treatment of bronchopneumonia in children[5,6]. On the basis of oxygen inhalation, anti-infection, and cough and asthma relieving, the respiratory secretions should be timely eliminated to maintain the respiratory tract unobstructed, and the respiratory smooth muscle spasm should be removed to improve the clinical symptoms[7]. It is reported that the routine treatment combined with aerosol inhalation in the treatment of bronchopneumonia in children can not only humidify the respiratory tract, but also can preferably dilute the sputum and promote the discharge of sputum, and make the drugs actively act on local lesions, which can better improve the clinical symptoms and effectively shorten the course[8].

Budesonide is a kind of glucocorticoid with highly effective local anti-inflammatory effect, can inhibit the immune response, reduce the

antibody synthesis, strengthen the cell membrane stability, lessen the release of histamine and other allergic active transmitters, and lower its biological activity to reach the goal of anti-inflammation and anti-allergy[9]. Budesonide, with a preferable local anti-inflammatory effect, can rapidly disperse to all the lung after medication to combine with the glucocorticoid receptors on the surface of bronchus, effectively inhibit the release of allergic mediators and the exudation of inflammatory cells, reduce the biological effects of various inflammatory cells to play an anti-inflammatory effect, and lessen the bronchial mucosal edema and mucus secretion in order to alleviate the bronchial spasm[10]. Terbutaline,  $\beta_2$  receptor agonist with a short-term effect, can reduce the release of mastocyte and basophil, dilate the tracheal smooth muscle, greatly reduce the microvascular permeability, enhance the scavenging ability of tracheal mucosal cilia, promote CI to transfer to the airway direction, reduce the tracheal vascular permeability, effectively dilute the mucus produced in the airway, and accelerate the eliminating speed of mucus[11,12]. Ipratropium bromide, an anticholinergic drug with strong efficacy and high selectivity, effectively expand the bronchus, alleviate the respiratory muscle spasm, reduce the mucus secretion, improve the ciliary movement, maintain the respiratory tract unobstructed, and improve the ventilation function[13]. It is reported that on one hand, budesonide can effectively promote terbutaline to expand the bronchus; on the other hand, terbutaline can increase the amount of budesonide entering the bronchus, and enhance the anti-inflammatory effect produced in the local tissues; therefore, the combination in the treatment of bronchopneumonia in children can receive a satisfactory effect in the clinic[14,15].

IL-6, a cytokine with a wide biological activity, plays an important role in the inflammatory reaction and autoimmunity, is an important cytokine to mediate the inflammatory reaction at an acute phase, and is involved in the inflammatory pathological process. TNF- $\alpha$  is an inflammatory mediator with important biological activity, can mediate the inflammatory pathological process, and induce the local inflammatory reaction. CRP is a non-specific acute phase reactive protein, and is involved in the inflammatory reaction and tissue injury repairing process. WBC can activate the inflammatory cytokine, resist the invasion of pathogens, devour the foreign bodies, and strengthen the immunoresistance ability[16,17].

The results in the study showed that the levels of IL-6, TNF-

$\alpha$ , CRP, and WBC counting after treatment in the two groups were significantly reduced when compared with before treatment ( $P<0.05$ ), and the reduced degree in the study group was significantly superior to that in the control group ( $P<0.05$ ); PEF, FVC, and FEV1 after treatment in the two groups were significantly improved when compared with before treatment ( $P<0.05$ ), and the improved degree in the study group was significantly superior to that in the control group ( $P<0.05$ ); after treatment, the cough and asthma relieving, and rale and DR shadow disappearing time in the study was significantly shorter than that in the control group ( $P<0.05$ ); no severe adverse reactions occurred in the two groups, and the comparison between the two groups was not statistically significant ( $P>0.05$ ), indicating that ipratropium bromide combined with budesonide and terbutaline can effectively treat bronchopneumonia in children.

In conclusion, ipratropium bromide combined with budesonide and terbutaline in the treatment of bronchopneumonia in children can rapidly relieve the symptoms, and improve the cytokine level, with no obvious adverse reactions; therefore, it deserves to be widely recommended in the clinic.

## References

- [1] Wang XX, Liu SM, Yao WR, et al. Analysis of the common pathogenic bacteria and their drug resistance in children with bronchitis. *Chin J Gen Pract* 2014; **12**(7): 1090-1092.
- [2] Wang L, Wang LN, Zhang LM, et al. Analysis of the efficacy of aerosol inhalation of N-acetylcysteine in the treatment of bronchopneumonia in infants. *Chin J Gen Pract* 2015; **18**(8): 335-338.
- [3] Chen XP. Analysis of the efficacy of aerosol inhalation of budesonide suspension in combined with ipratropium bromide in the treatment of bronchopneumonia in children. *J Commun Med* 2015; **13**(12): 31-32.
- [4] Hu YM, Jiang ZF. *Practical peditonology of Zhufutang*. The 7th edition. Beijing: People's Medical Publishing House 2002; p. 1175.
- [5] DU HZ, Jin L, Chen HJ, et al. Clinical observation on modified Maxing Shigan decoction according to symptoms for 18 children with bronchial pneumonia. *J Tradit Chin Med* 2014; **55**(10): 842-845.
- [6] Bai CX, Kang P. Clinical diagnosis and treatment of bronchopneumonia in children. *Chin J Modern Drug Appl* 2014; **8**(2): 113-114.
- [7] Huang X, Zhang DF. Clinical analysis of the combination of traditional Chinese and western medicine in the treatment of 50 children with bronchopneumonia. *World Chin Med* 2014; **9**(8): 1005-1007.
- [8] Liu YC. Observation on the effect of aerosol inhalation of budesonide in combined with ambroxol hydrochloride in the treatment of bronchopneumonia in children. *China Modern Med* 2015; **22**(1): 89-91.
- [9] Li MH, Dong C, Dong WH, et al. Analysis of the efficacy of aerosol inhalation of budesonide in combined with ipratropium bromide in the treatment of bronchopneumonia in children. *China Pract Med* 2015; **10**(15): 1-3.
- [10] Wang YF. Analysis of the efficacy of aerosol inhalation of budesonide suspension in combined with ipratropium bromide in the treatment of bronchopneumonia in children. *Jilin Med J* 2015; **36**(4): 684-685.
- [11] Zhang Y. Observation on the efficacy of aerosol inhalation of budesonide in combined with terbutaline in the treatment of bronchopneumonia in children. *Healthy People* 2014; **8**(16): 133.
- [12] Chen QC, Meng YR, Chen YJ. Aerosol inhalation of terbutaline injection in combined with 3% NaCl in the treatment of pneumonia in children. *China Med Pharm* 2014; **4**(17): 51-53.
- [13] Wang XP, Chou YM, Wan ZH. Analysis of the efficacy of budesonide suspension in combined with ipratropium bromide in the treatment of bronchopneumonia in children. *Modern Diagn Treat* 2015; **26**(2): 337-338.
- [14] Zhang CY, Li YJ, Han HM, et al. Analysis of the clinical efficacy of aerosol inhalation of budesonide suspension and terbutaline in combined with ambroxol hydrochloride in the treatment of pneumonia in children. *Chin J Mod Drug Appl* 2015; **9**(8): 124-125.
- [15] Zhang GD. Observation on the efficacy of aerosol inhalation of budesonide, terbutaline in combined with ipratropium bromide in the treatment of bronchopneumonia in children. *China Prescrip Drug* 2016; **14**(1): 94-95.
- [16] Hu B. Clinical efficacy of ambroxol hydrochloride in combined with budesonide in the treatment of bronchopneumonia in children and the effect on CRP and WBC counting. *Pract J Card Cerebr Pneum Vas Dis* 2015; **23**(8): 68-70.
- [17] Li FQ. Clinical effect of aerosol inhalation of budesonide, ipratropium bromide, and salbutamol in the treatment of asthmatic pneumonia in children. *China Modern Med* 2015; **22**(34): 136-138.