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# Fibrobronchoscope-Assisted Lavage Combined with Azithromycin in Regulating the Lung Function and Th17/Treg of Peripheral Blood in Children with *Mycoplasma pneumoniae* Pneumonia

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## ABSTRACT

The objective of this study was to investigate the role of bronchofiberoscope-assisted lavage combined with azithromycin in regulating the pulmonary function and Th17/Treg of peripheral blood in children with *Mycoplasma pneumoniae* pneumonia (MPP). From January 2018 to January 2020, 114 children with MPP in our hospital were selected and randomly divided into control group and experimental group, each containing 57 cases. The control group was given azithromycin. The experimental group was given fibrobronchoscope-assisted lavage on the basis of the control group. The curative effect, the time of remission of clinical symptoms (pulmonary rales, body temperature, cough), hospital stay, and adverse reactions, lung function [the forced expiratory volume in the first second as a percentage of the predicted value ($FEV_1$%), tidal volume (V-T), forced expiratory volume in the first second ($FEV_1$), forced vital capacity (FVC)], peripheral blood Th17, Treg, Th17/Treg cells, soluble B7 homolog 3 (sB7-H3), galectin 3 (Gal-3), and lung surfactant protein A (SP-A) before and after treatment were evaluated between the two groups. The total effective rate of treatment in the experimental group was higher than that in the control group ($P$<0.05); the cough relief time and hospitalization time of the experimental group were shorter than those of the control group ($P$<0.05); after treatment, $FEV_1$%, V-T, $FEV_1$, and FVC in the experimental group were higher than those in the control group ($P$<0.05); after treatment, the levels of Th17 and Th17/Treg cells in the peripheral blood of the experimental group were lower than those of the control group, and the levels of Treg cells were higher than that of the control group ($P$<0.05); after treatment, the peripheral blood sB7-H3, Gal-3, SP-A levels of the experimental group were lower than those of the control group ($P$<0.05); there was no significant difference in adverse reactions between the two groups ($P$>0.05). To conclude, Fibrobronchoscope-assisted lavage combined with azithromycin in the treatment of children with MPP can regulate the expression of Th17/Treg and sB7-H3, Gal-3, SP-A in peripheral blood, promote the improvement of clinical symptoms, improve lung function.

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**Authors' Contribution**
**HX, RL and YD collected the samples. MC, JZ and XS analysed the data. HX and RL conducted the experiments and analysed the results. All authors discussed the results and wrote the manuscript.**

**Key words**
**Fibrobronchoscope lavage, Azithromycin, *Mycoplasma pneumoniae* pneumonia, Lung function, Th17/Treg, Soluble B7 homolog 3, Galectin 3, Lung surfactant protein A.**

## INTRODUCTION

*Mycoplasma pneumoniae* pneumonia (MPP) is a common respiratory infectious disease in children, and data show that MPP accounts for 10 - 20% of community-acquired pneumonia in children (Zhang *et al*., 2016b; Yang *et al*., 2017). Currently, there is no specific method for the clinical treatment of MPP in children. It is mainly treated with macrolides, combined with phlegm reduction and symptomatic treatment. However, due to the damage of immune function and respiratory tract self-cleaning function, local blood drug concentration is difficult to reach the ideal standard. In addition, increased drug resistance of macrolides often leads to unsatisfactory efficacy (Wang *et al*., 2017a). Fibrobronchoscopy has become an important diagnostic and therapeutic method for MPP by penetrating into the bronchi to clear secretions and mucus plugs, reduce obstruction, reduce inflammation, and improve pulmonary ventilation (Zhang and Sheng, 2019). Studies have confirmed that imbalance of (Chang

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*et al*., 2018) Th17/Treg in peripheral blood, expression of soluble B7 homologue 3 (SB7-H3), galactin-3 (Gal-3), and surfactant protein A (SP-A) are involved in MPP occurrence and development (Xia *et al*., 2018; Ding *et al*., 2017). At present, there have been studies on the treatment of MPP in children by fibrobronchoscope-assisted lavage combined with azithromycin, but most of them focus on lung function, symptom improvement and curative effect. Few reports have reported its effects on peripheral blood Th17/Treg cell level, SB7-H3, Gal-3, SP-a.

## MATERIALS AND METHODS

*General information*

In this study, 114 children who had been treated for MPP in our hospital from January 2018 to January 2020 were selected as research objects. They were randomly divided into control group and experimental group, each containing 57 cases. There was no significant difference in gender, age, body weight, course of disease, degree of disease, body temperature and clinical pulmonary infection score (CPIS) between the two groups before treatment ($P > 0.05$), as shown in Table I. This study was approved by the medical ethics committee of our hospital.

*Inclusion and exclusion criteria*

Inclusion criteria were (i) meeting the relevant diagnostic criteria in the expert Consensus on diagnosis and treatment of MMP in children (2015 edition) (Chen *et al*., 2015); (ii) in the acute stage of attack; (iii) no bronchial dysplasia, bronchial asthma, congenital malformation of respiratory tract, *etc*; (iv) no use of immunomodulator in recent 2 months; and (v) family members were informed and signed an informed consent.

Exclusion criteria were (i) chronic cardiopulmonary diseases; (ii) azithromycin allergy; (iii) precardiac heart disease; (iv) co-infection with chlamydia pneumoniae, respiratory syncytial virus, adenovirus and other pathogens; (v) complicated with autoimmune diseases.

*Experimental plan*

Both the control and experimental groups were given comprehensive treatment such as spasmolysis, phlegm reduction, asthma relief, and adjustment of water and electrolyte disturbance, etc., and were given continuous low-flow oxygen inhalation for 1-2 L/min if necessary.

The control group was treated with azithromycin injection (Jiangsu Wuzhong Pharmaceutical Group Corporation, SFDA approval number H20010606) at dosage of 10 mg/ (kg•d) by intravenous drip for 5 consecutive days, and then was given oral azithromycin (Pfizer Pharmaceutical Co., Ltd, SFDA approval number H10960112) at dosage of10 mg/kg for 3 days.

The experimental group received fibrobronchoscope-assisted lavage on the basis of the control group. Olympus BF-3C30 or BF-XP260F bronchoscope was used. Preoperative diet and drinking were forbidden for 6 h. Intramuscular injection of atropium (0.01-0.03 mg/kg) and rumina (5 mg/kg, ≤100 mg) were performed 0.5 h before surgery. Intramuscular injection of midazolam (0.3 mg/kg, ≤10 mg) was administered 10 to 15 min before surgery to sedate and reduce respiratory secretions. For nasal cavity and throat, oxygen driven spray anesthesia (2% lidocaine) was used, and 10-15 min later oxygen inhalation was given. Airway mucosal surface anesthesia (2% lidocaine) was performed during the operation, and the lesions of trachea, main bronchus and lobes, segments and sub-segments were observed step by step through the nasal cavity. According to the imaging results, the corresponding bronchopulmonary segments were selected for lavage. The distal end of bronchoscope was fixed and warm saline was injected. For patients with body weight <20 k, the amount of lavage per time was 1 mL/kg; for patients with body weight ≥20 kg, the amount of lavage per time was 20 mL. The recovery of lavage fluid was repeated for 2 to 4 times. Blood oxygen saturation, respiration, heart rate, circulation, complexion and other conditions were continuously monitored during the operation. 1 - 3 times of lavage was carried out according to the actual condition during hospitalization.



**Table I.- General information of two groups used in this study.**

| Data | Control (n=57) | Experimental (n=57) | $t/\chi^2$ | P |
|---|---|---|---|---|
| Gender (male/female) | 32/25 | 34/23 | 0.144 | 0.704 |
| Age (years) | 4-12 (7.39±1.35) | 4-12 (7.51±1.49) | 0.451 | 0.653 |
| Body weight (kg) | 16-46 (26.08±4.82) | 16-46 (26.26±5.28) | 0.190 | 0.850 |
| Course of disease (d) | 3-7 (4.89±0.68) | 3-7 (5.01±0.72) | 0.915 | 0.362 |
| Condition | | | | |
| Mild | 36 (63.16) | 38 (66.67) | 0.154 | 0.695 |
| Severe | 21 (36.84) | 19 (33.33) | | |
| Body temp. (°C) | 38.2-39.8 (39.08±0.25) | 38.1-39.9 (39.11±0.27) | 0.616 | 0.540 |
| CPIS score (points) | 3-8 (5.36±0.69) | 3-8 (5.42±0.73) | 0.451 | 0.653 |

Lung function indicators [the 1st second forced expiratory volume as a percentage of the expected value (FEV1%), tidal volume (V-T), the 1st second forced expiratory volume (FEV1), forced vital capacity (FVC)] were measured by S-980A II pulmonary function detector (Sichuan Skida Technology Co., Ltd.). 2 ml of peripheral venous blood was extracted under fasting state and centrifuged (radius 8cm, 3500r/min, 9min) to obtain serum. Soluble B7 homolog 3 (sB7-H3), galactin-3 (GAL-3) and surfactant protein A (SP-A) were determined by enzyme-linked immunosorbent assay (ELISA) with the kit provided by Guangzhou Huafen Biotechnology Co., Ltd. The proportions of Th17 and Treg cells were measured by flow cytometry (BD, USA).

*Observation indices*

The observation indices included (1) curative effect, (2) remission time of clinical symptoms (rales, body temperature, cough) and hospital stay, (3) lung function before and after treatment (FEV1%, V-T, FEV1, FVC), (4) peripheral blood Th17/Treg cell level before and after treatment, (5) levels of soluble B7 homologous 3 (SB7-H3), galactin-3 (GAL-3) and pulmonary surfactant protein A (SP-A) in peripheral blood before and after treatment, and (6) adverse reactions (transient decrease of blood oxygen saturation, increased heart rate, nausea and vomiting).

*Curative effect criterion*

The disease is thought to be cured when the cough stops, the body temperature returns to normal, and the X-ray shows that the inflammation of the lungs has completely disappeared. When the cough abates or stops, the body temperature returns to normal, and the X-ray shows an improvement in pulmonary inflammation, the disease is thought to be improved to a certain extent. Invalid treatment is defined when the cough does not stop, body temperature of the children does not return to normal, and the X-ray shows no improvement or even worsening of pulmonary inflammation. The cured cases and getting-better cases were all regarded as effective cases.

*Statistical method*

Software SPSS22.0 was used for statistical analysis of data. The statistical data were expressed in terms of rate, with chi-squared test conducted for inter-group difference comparison. Measurement data in line with normal distribution were represented by $\bar{x}\pm s$, with independent sample t-test conducted for inter-group comparison, and paired t-test was used for intra-group comparison. The difference was considered statistically significant when $P<0.05$.

## RESULTS

Table II shows that the total effective rate of the experimental group was higher than of the control group ($P < 0.05$), whereas the lung rales remission time, body temperature relief time, cough relief time and hospital stay in the experimental group were shorter than those in the control group ($P < 0.05$). Table III shows that before treatment, there was no significant difference in lung function indices between the two groups ($P > 0.05$). After treatment, $FEV_1$%, V-T, $FEV_1$, FVC of the experimental group were higher than those of the control group ($P < 0.05$). There was no significant difference in Th17/Treg cell level and the levels of sB7-H3, Gal-3, SP-A in peripheral blood between the two groups before treatment ($P > 0.05$). After treatment, Th17 and Th17/Treg cell levels and the the levels of sB7-H3, Gal-3, SP-A in peripheral blood of the experimental group were lower than those of the control group. Treg cell level in the experimental group was however higher than that of the control group ($P < 0.05$). There was no significant difference in adverse reactions between the two groups ($P > 0.05$), as shown in Table IV.



**Table II.- Effect of fibrobronchoscope-assisted lavage combined with azithromycine on curation (%),clinical symptom relief time (Mean±SEM, days) and hospital stay of children with *Mycoplasma pneumoniae* infection.**

| | Control (n=57) | Experimental (n=57) | $\chi^2$ | *t* | *P* |
|---|---|---|---|---|---|
| **Curative effects** | | | | | |
| Cure | 29 (50.88) | 32 (56.14) | | | |
| Getting better | 15 (26.32) | 21 (36.84) | | | |
| Invalid | 13 (22.81) | 4 (7.02) | | | |
| Total efficiency | 44(77.19) | 53 (92.98) | 5.600 | - | 0.018 |
| **Clinical symptom relief time** | | | | | |
| Lung rales remission time | 8.31±1.78 | 6.44±1.53 | | 6.015 | < 0.001 |
| Temperature relief time | 4.85±1.41 | 3.62±1.24 | | 4.946 | < 0.001 |
| Cough relief time | 6.44±1.49 | 5.31±1.52 | | 4.008 | < 0.001 |
| Hospital stay | 14.63±3.61 | 12.30±2.85 | | 3.825 | < 0.001 |

**Table III.- Effect of fibrobronchoscope-assisted lavage combined with azithromycine on lung function indices, Th17/Treg cell level, sB7-H3, Gal-3 and SP-A levels in peripheral blood of children with *Mycoplasma pneumoniae* infection.**

| | Before treatment | | *P* | After treatment | | *t* | *P* |
|---|---|---|---|---|---|---|---|
| | Control (n=57) | Exp. (n=57) | | Control (n=57) | Exp. (n=57) | | |
| **Lung function indices** | | | | | | | |
| $FEV_1$%(%) | 64.92±5.86 | 65.51±5.38 | 0.577 | 68.16±5.23[a] | 72.05±4.66[a] | 4.193 | < 0.001 |
| V-T(ml/kg) | 8.01±1.02 | 7.75±1.23 | 0.222 | 9.66±1.14[a] | 11.13±1.35[a] | 6.281 | < 0.001 |
| $FEV_1$(L) | 1.30±0.34 | 1.24±0.41 | 0.397 | 1.61±0.47[a] | 1.90±0.52[a] | 3.124 | 0.002 |
| FVC(L) | 1.60±0.38 | 1.56±0.41 | 0.590 | 2.33±0.42[a] | 2.65±0.56[a] | 3.451 | < 0.001 |
| **Th17/Treg cell level** | | | | | | | |
| Treg (%) | 3.74±0.41 | 3.65±0.44 | 0.261 | 5.14±0.59[a] | 6.55±0.78[a] | 10.885 | < 0.001 |
| Th17 (%) | 3.17±0.36 | 3.23±0.32 | 0.349 | 2.34±0.28[a] | 1.62±0.23[a] | 15.002 | < 0.001 |
| Th17/Treg | 0.85±0.30 | 0.88±0.26 | 0.570 | 0.46±0.21[a] | 0.25±0.16[a] | 6.005 | < 0.001 |
| **sB7-H3, Gal-3 and SP-A levels in peripheral blood** | | | | | | | |
| sB7-H3 (pg/ml) | 3488.78±1053.39 | 3505.21±1051.52 | 0.934 | 2017.79±781.61[a] | 1530.48±456.26[a] | 4.065 | < 0.001 |
| Gal-3 (ng/ml) | 39.89±5.23 | 40.11±4.78 | 0.815 | 29.93±4.67[a] | 20.26±4.45[a] | 11.318 | < 0.001 |
| SP-A (g/L) | 0.75±0.18 | 0.72±0.21 | 0.415 | 0.67±0.16[a] | 0.44±0.15[a] | 7.918 | < 0.001 |

Exp., experimental group.

**Table IV.- Comparison of adverse reactions between two groups n (%).**

| | Control (n=57) | Exp. (n=57) |
|---|---|---|
| Transient decrease in blood oxygen saturation | 0 (0.00) | 3 (5.26) |
| Increased heart rate | 1 (1.75) | 2 (3.51) |
| Nausea | 2 (3.51) | 1 (1.75) |
| Vomiting | 2 (3.51) | 1 (1.75) |
| Total incidence | 5 (8.77) | 7 (12.28) |

## DISCUSSION

Macrocyclic lipid antimicrobial agents are the first choice for MPP treatment in children. Azithromycin belongs to the second generation of cyclolactone antibacterial drugs. By binding the 50S subunit of the bacterial ribosome, it hinders the peptide transfer process in RNA translation, inhibits the protein synthesis of mycoplasma cells, and thus plays an antibacterial role (Zeng *et al*., 2018). In recent years, due to the increased resistance to macrolides and the increased difficulty in MPP treatment in children, the adoption of new treatment regimens has become a hot spot in clinical research (Li *et al*., 2018).

With the rapid progress of medical technology, the clinical application of fiberoptic bronchoscopy has become an interventional therapy. The fiberoptic bronchoscope has a fine diameter. By using fiberoptic bronchoscopy, the lesions were irrigated with normal saline to clear the remaining substances in the respiratory tract and alveoli, so as to reduce airway obstruction and improve respiratory function. Drugs could also be injected directly via fiberoptic bronchoscopy to play a therapeutic role (Tao and Xia, 2019). At the same time, the components of bronchoalveolar lavage fluid can also be analyzed to study the etiology, diagnosis and pathogenesis of the disease, and to evaluate the efficacy and prognosis (Shi *et al*., 2017). The study of Li *et al*. (2017) showed that, on the basis of azithromycin sequential treatment, symptomatic treatment and physical treatment, the bronchoscopy-assisted lavage can effectively promote the remission of clinical symptoms in children with MPP, reduce the level of inflammatory factors, and improve blood gas indicators. The results of this study showed that fibrobronchoscope-assisted lavage combined with azithromycin in the treatment of MPP children has a high safety and can improve clinical symptoms and lung function, with a total effective rate of 92.98%. Its treatment mechanism mainly includes the following two aspects: (1) Fibrobronchoscope lavage can effectively remove mucus plug or secretions, reduce the local content of mycoplasma pneumoniae (MP), toxins and inflammatory factors, reduce direct and indirect damage to bronchi, relieve clinical symptoms, and improve lung function (Huang *et al*., 2017); (2) The bronchial mucosa of MPP children are in different degrees of edema and congestion, which results in local blood supply disorder and the local concentration of antibiotics. Under such circumstance, saline irrigation makes the local hypertonic state, eliminates or reduces edema, improves local blood supply, alleviates symptoms of hypoxia, increases the local concentration of antibiotics, and enhances the anti-inflammatory effect (Wang and Wang, 2019).

sB7-H3 is a helper stimulant of T cells, which can regulate both co-stimulation and co-inhibition of T cells. Zhang *et al*. (2016) found that sB7-H3 participated in the occurrence and development of refractory MPP by regulating the secretion of IL-2, IL-1β, IL-36 and other inflammatory factors. Gal-3 is a member of the galactin family, which mediates the immune response state of various inflammatory diseases by interacting with cell surface molecules, intracellular glycoproteins, and extracellular matrix. Zhao *et al*. (2019) found that Gal-3 was closely related to neutrophil chemotaxis and luminal infiltration in children with refractory MPP, and was involved in airway inflammation. SP-A is mainly secreted by alveolar type II epithelial cells (AT II), which can alleviate respiratory inflammatory damage by interfering with the eosinophils-mediated biological clearance effect focusing MP. Huang *et al*. (2018) showed that SP-A levels in serum and bronchoalveolar lavage fluid of MPP children were higher than those of children without significant pulmonary infection. It shows that MP infection of the lungs can stimulate the AT II cells to secrete a large number of SP-A, thereby exerting a role of immune regulation. This study innovatively analyzes the effects of fibrobronchoscope-assisted lavage combined with azithromycinon sB7-H3, Gal-3, SP-A levels in peripheral blood of MPP children. The results showed that sB7-H3, Gal-3, SP-A expressions in peripheral blood could be reduced by such combined therapy. This may be because fibrobronchoscope-assisted lavage can effectively remove the mucus plugs, secretions and part of the MP attached to tracheal epithelial cells, block the inflammatory response and immune response, and thus leading to the decrease of sB7-H3, Gal-3, SP-A levels in peripheral blood.

At present, it is generally believed that children with MPP have Th1/Th2 cell imbalance. The discovery of new immunological T cell subsets Th17 and Treg is an important supplement to the cellular immunity of the body. Th17 plays a biological role in promoting inflammation by secreting IL-17. Treg mainly plays a negative regulatory role on immune cells and inhibits T cell activation and proliferation by secreting IL-10 and transforming growth factor TGF-β1 (Li *et al*., 2016; Wang *et al*., 2017). Th17 and Treg are mutually correlated in differentiation and mutually inhibited in function to maintain dynamic balance and immune homeostasis. Tu and Tian (2019) found that the decrease of Treg cells and increase of Th17 cells in peripheral blood of children with MPP, and abnormal expression of Th17 /Treg and its secreted cytokines may play an important role in the occurrence and development of MPP. The results of this study showed that fibrobronchoscope-assisted lavage combined with azithromycin could regulate Th17/Treg imbalance in peripheral blood of children with MPP. MP metabolism produces hydrogen peroxide, oxygen free radicals and activates the oxidative stress response. At the same time, MP-related virulence factors produce community acquired respiratory distress syndrome (CARDS) toxin, which can promote the host cells to secret pro-inflammatory factors such as IL-6, tumor necrosis factor TNF-α and IL-17, aggravating immune injury (Ma *et al*., 2018). Therefore, fibrobronchoscope-assisted lavage combined with azithromycin can regulate Th17/Treg imbalance by promoting inflammatory factors and MP clearance at the lesion site. However, the sample size of this study is small, and further analysis and discussion is needed (Cooper *et al*., 2018).

## CONCLUSION

The treatment of fibrobronchoscope-assisted lavage combined with azithromycin can regulate the expression of Th17/Treg and sB7-H3, Gal-3, SP-A levels in peripheral blood, so as to improve clinical symptoms and pulmonary function. Such therapy has significant curative effect and high safety.

*Statement of conflict of interest*

The authors have declared no conflict of interests.

## REFERENCES

Chang, G.N., Zhang, H. and Shang, Y.X., 2018. Efficacy of fibrobronchoscope-assisted lavage of ambroxol hydrochloride in the treatment of children with refractory mycoplasma pneumonia. *Int. J. Pediatr.*, **45**: 652-654.

Chen, Z.M., Shang, Y.X., Zhao, S.Y., Xin, D.L., Xu, B.P., Zheng, Y.J., Lu M., Zhang, H.L. and Bao, JH., 2015. Expert consensus on diagnosis and treatment of MMP in children. *Chin. J. appl. clin. Pediat.,* **30**: 1304-1308.

Cooper, R., Newman, P. and Herachwati, N., 2018. RAPD molecular markers to analyze the DNA variation of the three bruguiera species on Kemujan island. *CCAMLR Sci.,* **25**: 209-214.

Ding, B., Li, X.B. and Li, L.L., 2017. The role of Th17/Treg cells in the pathogenesis of mycoplasma pneumonia in children. *Chin. J. Hlth. Lab. Technol*., **27**: 1758-1760.

Huang, S.L., Li, Z. and Zhang, C., 2018. Changes of surfactant protein A, surfactant protein D and toll-like receptor 2 in serum and bronchoalveolar lavage fluid of children with mycoplasma pneumonia and their clinical significance. *J. Xinxiang Med. Coll.,*

**35**: 605-611.

Huang, Y.H., Liu, J.H. and Zhang, Y.L., 2017. Clinical observation of 81 cases of severe *Mycoplasma pneumoniae* pneumonia in children treated by bronchoscopy lavage. *Chin. J. Med.,* **52**: 88-91.

Li, J.H., Zhu, L. and Guo, X.H., 2018. Effect of Jiapei mixture and azithromycin on lung function and chemokines of MMP children. *Chin. J. Inform. Trad. Chin. Med.,* **35**: 112-115.

Li, J.W., Ni, L.J. and Wu, Z.B., 2017. Effect of alveolar lavage on children with *Mycoplasma pneumoniae* combined with atelectasis under fiberoptic bronchoscopy. *Matern. Child Hlth. Care China*, **32**: 4263-4266.

Li, W., Liu, Y. J., Zhao, X.L., Shang, S.Q., Wu, L., Ye, Q. and Xu, H., 2016. Th1/Th2 cytokine profile and its diagnostic value in *Mycoplasma pneumoniae* pneumonia. *Iran. J. Pediatr.,* **26**: e3807. https://doi.org/10.5812/ijp.3807

Ma, X., Sun, J., Han, Y.L., Jiang, F.R., Zhao, X.X., Li, J.Z. and Ding, M.J., 2018. Clinical significance of toxin level determination in children with community-acquired respiratory distress syndrome caused by *Mycoplasma pneumoniae* pneumonia. *Chin. J. Appl. Clin. Ped.,* **33**: 1703-1706.

Shi, Y.Y., Hua, S., Wei, W. and Luo, M.X., 2017. Clinical observation of fibrobronchoscopy combined with methylprednisolone succinate in the treatment of refractory mycoplasma pneumonia. *Anhui Med. Pharm. J.,* **21**: 1699-1701.

Tao, P. and Xia, W.M., 2019. The clinical value of early interventional therapy with fiberoptic bronchoscopy in children with mycoplasma pneumonia complicated with airway mucus plug obstruction. *China Med. Her.,* **16**: 107-110.

Tu, C.M. and Tian, Y., 2019. Study on Th17, Treg cell subsets and cytokine expression in peripheral blood and CRP and PCT levels in children with mycoplasma pneumonia. *J. Mod. Lab. Med.,* **34**: 108-111.

Wang, M. and Wang, F.L., 2019. Effects of glucocorticoid combined with fibrobronchoscope lavage on inflammatory response in children with lobar pneumonia. *J. Pediat. Pharm.,* **25**: 8-12.

Wang, Y., Xu, G., Wang, J., Li, X.H., Sun, P., Zhang, W., Li, J.X. and Wu, C.Y., 2017. Relationship of Th17/Treg cells and radiation pneumonia in locally advanced esophageal carcinoma. *Anticancer Res.,* **37**: 4643-4647. https://doi.org/10.21873/anticanres.11866

Xia, L., Jia, Q.Y. and Zhu, S.Y., 2018. Expression of B7-H3 and G-CSF in serum of children with mycoplasma pneumonia and their clinical significance. *J. Clin. Pulm. Med.*, **23**: 511-514.

Yang, M., Meng, F., Wang, K., Gao, M., Lu, R., Li, M., Zhao, F., Huang, L., Zhang, Y. and Cheng, G., 2017. Interleukin 17A as a good predictor of the severity of *Mycoplasma pneumoniae* pneumonia in children. *Scient. Rep.,* **7**: 1-11. https://doi.org/10.1038/s41598-017-13292-5

Zeng, W.Y., Li, Y., Xu, Z.L., Xie, X.L., Xu, F.Q. and Rui, N., 2018. Severe mycoplasma pneumonia in child with bilateral parapneumonic effusion successfully treated with integrated Chinese and Western medicine: A case report. *Chinese J. Integrat. Med.,* **24**: 683-685. https://doi.org/10.1007/s11655-018-2978-2

Zhang, H. and Shang, Y.X., 2019. The diagnostic and therapeutic value of fiberoptic bronchoscopy in children with refractory mycoplasma pneumonia. *Chin. J. Pract. Pediat.*, **34**: 504-507.

Zhang, X.X., Chen, Z.R., Gu, W.J., Yan, Y.D., Wang, Y.Q., Zhu, C.H., Huang, L., Wang, M.J., Shao, X.J. and Ji, W., 2016a. The expression of SB7-H3 and cytokines in alveolar lavage fluid in children with refractory mycoplasma pneumonia. *J. clin. Pediat.,* **34**: 561-565.

Zhang, Y., Zhou, Y., Li, S., Yang, D., Wu, X. and Chen, Z., 2016b. The clinical characteristics and predictors of refractory *Mycoplasma pneumoniae* pneumonia in children. *PLoS One,* **11**: e0156465. https://doi.org/10.1371/journal.pone.0156465

Zhao, Q.Y., Shi, S.J., Sun, D.Q., Zhang, S.S. and Zhou, X.H., 2019. Correlation between galectin-3 level in bronchoalveolar lavage fluid and cellular immunity in children with refractory *Mycoplasma pneumoniae* pneumonia. *Chinese J. Contemp. Pediat.,* **21**: 150-154.