doi.org/10.36721/PJPS.2025.38.3.REG.13122.1

Drug efficacy and safety of azithromycin combined with pulmonary physical therapy for bacterial pneumonia in children

Lingxiao Shi[1], Yangjin Chen[1], Huidan Yang[1] and Shuai Wei[2]*
[1]Department of pediatrics, Panan County People's Hospital, Jinhua, Zhejiang, China
[2]Department of neurologyt, Panan County People's Hospital, Jinhua, Zhejiang, China

Abstract: The drug effect and safety of azithromycin combined with lung physical therapy in the treatment of bacterial pneumonia in children were studied. A total of 112 cases were selected and divided into a study group and a control group with 56 cases in each group. The control group used azithromycin and the study group received assisted lung physical therapy. The drug effects, symptom disappearance time, inflammatory factors, lung function indicators and adverse reaction incidence of the two groups were compared. The results showed that the drug effect of the study group was higher than that of the control group, the level of inflammatory factors was lower than that of the control group, the symptom disappearance time was shorter and the lung function indicators were better. The incidence of adverse drug reactions in the two groups was comparable. Using the same drug azithromycin, under the action of pulmonary physical therapy, azithromycin can better exert its efficacy without affecting the safety of the drug.

Keywords: Azithromycin, pulmonary physiotherapy, bacterial pneumonia, safety

Submitted on 22-07-2024 – Revised on 18-02-2025 – Accepted on 25-02-2025

INTRODUCTION

Bacterial pneumonia in children is a respiratory disease caused by bacterial infection, which is manifested by an inflammatory response after the alveoli and bronchi are invaded by bacteria (Lyon E, Olarte L, 2024). In developing countries, the incidence of bacterial pneumonia in children aged 3-12 years is between 5% and 10%. In developed countries, due to better vaccination and medical conditions, the incidence of bacterial pneumonia in children is around 1%.The main pathogenic bacteria of bacterial pneumonia in children include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, etc. The most common pathogen is *Streptococcus pneumoniae* (Cotter Jillian M *et al*., 2022). Patients often experience symptoms such as high temperature, cough, wheezing and chest pain. In severe cases, it can easily lead to serious complications such as dyspnea, poor oxygenation and even respiratory failure. At present, antibiotics are mainly used to treat bacterial pneumonia in children. Antibiotics are divided into penicillin antibiotics, macrolide antibiotics, third-generation cephalosporins, doxycycline antibiotics, etc. Clinical protocols for bacterial pneumonia in children, the main penicillin antibiotics are amoxicillin, the main macrolide antibiotics are azithromycin, the third-generation cephalosporins are mainly ceftriaxone and cefazolin and the main doxycycline antibiotics are Choose doxycycline. Among these drugs, azithromycin is currently used relatively frequently. Azithromycin can prevent bacterial growth and reproduction by inhibiting bacterial protein synthesis. This drug has a good bactericidal effect on a variety of common bacteria in the respiratory tract (*Mycoplasma pneumoniae*, *Streptococcus pneumoniae*, etc.). Both groups of patients in this study received azithromycin, but the patients in the study group also received pulmonary physical therapy. Some scholars have pointed out that pulmonary physical therapy has a good effect on the recovery of children with pneumonia (Lewińska A and Shahnazaryan K, 2020). By combining this therapy, observing whether the drug can work better under the action of pulmonary physical therapy has strong guiding significance for clinical medication plans.

**Corresponding author:* e-mail: shilxpanan@163.com

MATERIALS AND METHODS

Data sources

The research data were selected from children with bacterial pneumonia who were treated at the People's Hospital of Pan'an County, Zhejiang Province from January 2021 to June 2023. According to the research plan, 112 eligible cases were screened out. According to the number of consultation, they were divided into the study group (n=56) and the control group (n=56) according to the odd and even numbers. The medication regimen of the study group was injection of azithromycin combined with lung physical therapy, while the control group was injected with azithromycin alone. According to the collected data: there were 29 males and 27 females in the study group, with an age of (6.18±2.87) years and a disease duration of (4.62±0.46) days; There were 28 males and 28 females in the control group, with an age of (6.21±2.82) years and a disease course of (4.59±0.47) days. The data of the two groups were almost the same.

Inclusion criteria

Aged 3-12 years old; symptoms of respiratory tract infection, such as cough, dyspnea, chest tightness, etc.;

bacterial pneumonia confirmed by routine blood test, CT and sputum culture examination. Exclusion criteria: Pneumonia pathogens are non-bacterial pneumonias such as viruses and fungi; combined with pneumonia caused by other causes, such as tuberculosis; combined with other serious complications or complications, such as lung abscess, etc. Ethical issues. This study was reviewed by the Ethics Committee of Pan'an County People's Hospital of Zhejiang Province, with the ethics approval number: LL20201218.

Medication method

All patients underwent conventional measures such as atomization, phlegm reduction and cough relieving and some patients with high fever also received medications and physical cooling.

Control group

Intravenous injection of azithromycin injection. Drug information: Manufacturer: CSPC Ouyi Pharmaceutical Co., Ltd., national drug approval number H20050099, specifications: 0.5g / tube. Medication plan: Once a day, the dosage standard is 8-12 mg per kilogram based on the patient's weight. It is administered intravenously. After 5 days of injection, the drug is stopped for 3 days to observe the patient's symptoms.

The research group was supplemented with lung physical Clinical plan for the control group. Lung physical therapy is completed by nursing staff and mainly includes three major items: chest percussion, postural drainage and mechanical suction. Chest percussion: Have the patient sit on the edge of the bed or on a chair and gently tap on the patient's back and chest with the palm of your hand or hands, starting from the lower end of the lungs to the upper end. Pay attention to the moderate intensity and frequency of percussion to help the patient expel sputum. Postural drainage: Change the patient's position to promote sputum discharge, including head-down, prone and side-lying positions. Mechanical suction: Using a suction device to suck sputum out of the patient's body.

Observation indicators and judgment criteria

Evaluation of drug efficacy

After the medication is completed, the patient's clinical symptoms are observed. Markedly effective: clinical symptoms of pneumonia completely disappear, chest X-ray results show that lesions disappear and blood test results show that pneumonia symptoms disappear; Effective: clinical symptoms of pneumonia almost disappear, chest X-ray and blood test results show that there are still abnormalities; Ineffective: clinical symptoms, laboratory symptoms No improvement or worse. Total effective rate of drugs = marked effective rate + effective rate.

Inflammatory factors

Inflammatory factor indicators of bacterial pneumonia mainly include white blood cell (WBC),C-reactive protein (CRP) and procalcitonin (PCT) (Dawid Ciepłucha H *et al*., 2023). WBC is an important indicator reflecting the body's inflammatory response. When bacterial pneumonia occurs, the body will release white blood cells to respond to the infection, so WBC will increase. As an acute phase protein, CRP can increase rapidly during infection or inflammation and is mainly used to reflect the degree of inflammation. PCT is a hormone synthesized by the liver and its concentration also increases during infection and inflammation. In bacterial pneumonia, the endotoxin released by bacteria can easily stimulate the body to produce PCT, so PCT levels will also increase. Therefore, the higher the values of the three indicators, the higher the degree of inflammation.

Lung function

The forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and peak expiratory flow (PEF) were measured by a portable pulmonary function tester. The greater the FEV1, FEV1/FVC and PEF, the higher the lung function level.FEV1 reflects the airway flow rate at the beginning of exhalation and its decrease indicates airway obstruction. FVC represents the amount of air exhaled after the maximum deep inspiration and its decrease may be due to restrictive ventilation disorder caused by lung parenchymal inflammation or pleural effusion. The combination of the two can distinguish between obstructive (decreased FEV1/FVC) and restrictive (normal or increased FEV1/FVC) case patterns. Bacterial pneumonia often leads to mixed ventilation abnormalities due to alveolar infiltration, consolidation and airway mucus plug formation, which requires a comprehensive judgment based on these two indicators. FEV1/FVC is a key parameter for distinguishing chronic obstructive pulmonary disease from restrictive lung disease. Although pneumonia in children is mostly an acute course, severe or repeated infections may induce small airway remodeling, leading to persistent obstruction. Dynamic monitoring of this ratio helps to identify complications early, such as obliterative bronchiolitis. PEF reflects the patency of large airways in the early stage of exhalation and its decrease indicates increased proximal airway resistance. Children with pneumonia usually have a decrease in PEF due to airway hyper responsiveness or increased secretions. PEF measurement is simple and suitable for children and can quickly assess acute disease conditions and treatment responses.

STATISTICAL ANALYSIS

SPSS22.0 software was used to process the data in this study and $P<0.05$ was regarded as statistically significant.

RESULTS

Drug efficacy

The results showed that the total effective rate of the drug in the study group was 92.86%, which was much higher than the 82.14% in the control group ($P<0.05$). See table 1.

Table 1: Comparison of drug effects between the two groups (n, %)

Group	n	marked effective	effective	ineffective	total effective rate
research group	56	16	36	4	52 (92.86)
control group	56	11	35	10	46 (82.14)
χ^2					8.752
P					0.001

Table 2: Comparison of symptom disappearance time between two groups of patients（$\bar{x}\pm s$）

Group	n	Time for body temperature to return to normal	cough disappearance time	Pulmonary rales disappear time	Asthma disappearance time	length of stay
research group	56	2.58±1.17	4.42±1.23	5.12±1.36	4.86±1.43	7.14±1.05
control group	56	2.69±1.24	7.58±1.52	8.45±1.89	7.98±1.85	9.68±1.36
t		0.092	1.964	2.236	2.127	1.437
P		0.286	0.000	0.000	0.000	0.001

Table 3: Comparison of inflammatory factor levels before and after medication（$\bar{x}\pm s$）

Group	n	WBC（$\times10^9$/L）		CRP（mg/L）		PCT(ng/L)	
		before medication	after medication	before medication	after medication	before medication	after medication
research group	56	24.92±2.42	10.86±2.56	62.17±12.46	9.16±3.16	3.51±1.03	0.65±0.08
control group	56	25.08±2.44	13.22±2.61	61.89±12.38	12.32±3.38	3.50±1.02	0.96±0.09
t		0.042	1.508	0.039	1.526	0.032	1.635
P		0.782	0.001	0.816	0.001	0.896	0.001

Table 4: Comparison of pulmonary function indicators between the two groups of patients before and after medication ($\bar{x}\pm s$)

Group	n	FEV1（L）		FEV1/FVC (%)		PEF (L/s)	
		before medication	after medication	before medication	after medication	before medication	after medication
research group	56	1.31±0.21	1.73±0.25	49.52±4.37	61.28±5.31	1.62±0.74	2.71±0.28
control group	56	1.31±0.22	1.59±0.23	49.18±4.26	56.32±4.76	1.61±0.72	2.42±0.26
t		0.018	0.828	0.021	0.819	0.022	0.965
P		0.962	0.001	0.925	0.001	0.908	0.001

Table 5 Comparison of adverse drug reactions between the two groups of patients ($\bar{x}\pm s$, cases)

Group	n	Gastrointestinal discomfort	Skin allergies	abnormal liver function	muscle damage	Arrhythmia
research group	56	3	1	0	0	0
control group	56	3	0	0	0	0
χ^2						
P						

Time for symptoms to disappear

After treatment, the study found no significant difference in the time it took for the body temperature to return to normal between the two groups (P>0.05), but the study showed that the time to disappear for cough, lung rales, asthma and the length of hospitalization were significantly shortened in the study group (P<0.05).See table 2.

Levels of inflammatory factors

The indicators of inflammatory factors of the patients before and after treatment are shown in table 3.

Lung function indicators

The comparison of pulmonary function indicators between the two groups of patients is shown in table 4.

Drug safety

The main adverse reaction of azithromycin is gastrointestinal discomfort, including diarrhea, nausea, vomiting, abdominal pain, etc. (Aït Moussa L *et al*.,2023) Other adverse reactions include skin allergies (such as rash, urticaria, itching, etc.), abnormal liver function (such as jaundice, elevated liver enzymes, etc.), muscle damage (muscle pain, weakness, etc.), arrhythmia (abnormal electrocardiogram, tachycardia, etc.). (Speed, etc.) (Ahmad A and Rehman M, 2023). The adverse drug reactions of the two groups of patients are shown in table 5.

DISCUSSION

Azithromycin is a broad-spectrum antibiotic classified as a macrolide antibiotic with antibacterial effects. Its main drug mechanism relies on inhibiting bacterial protein synthesis, thereby blocking bacterial growth and reproduction and achieving the effect of killing bacteria. Azithromycin can reduce the release of inflammatory mediators by inhibiting the chemotaxis, adhesion and migration of inflammatory cells, thereby alleviating inflammation and minimizing lung tissue damage. Azithromycin can also regulate the function of the immune system, enhance the body's immunity and improve the body's ability to fight bacteria. It can promote the activation of macrophages and the ability to phagocytose bacteria, increase the chemotaxis and bactericidal effect of neutrophils and thus improve the body's immune defense capabilities. The effect of azithromycin in treating bacterial pneumonia in children has also been widely recognized by researchers. The effectiveness of azithromycin in treating bacterial pneumonia in children has also been widely recognized by researchers. Some studies believe that azithromycin, as a broad-spectrum antibiotic, is effective in treating bacterial pneumonia in children. It can quickly kill pathogenic bacteria, reduce inflammation and help children recover (Hafner M *et al*., 2021). Research data shows that during the treatment of bacterial pneumonia in children with azithromycin, patients are generally able to quickly relieve symptoms and perform well in the process of bacterial clearance and recovery of pneumonia lesions (Wenting L *et al*., 2023). The results of this study also illustrate these results shown by our research.

Our research shows that after combined with pulmonary physical therapy, patients in the study group had better drug effects. Analysis of the reasons for this result may be: (1) Improved drug absorption. Pulmonary physical therapy can help patients breathe better, promote smooth and pulmonary blood circulation and thus help the absorption and distribution of drugs. This may increase the concentration of azithromycin in the lungs, enhancing the drug's efficacy. (2) Promote phlegm discharge. Lung physical therapy can help patients expel phlegm better and clear secretions from the respiratory tract. This result helps reduce bacterial reproduction and infection in the respiratory tract, thereby increasing the direct effect of azithromycin on pathogens. (3) Reduce drug concentration fluctuations. Pulmonary physical therapy can promote uneven distribution of drugs in the lungs and reduce fluctuations in drug concentration between different parts. This can increase the concentration of azithromycin in the infection focus and increase the bactericidal effect of the drug. Overall, pulmonary physical therapy interacts favorably with azithromycin, improving drug absorption and distribution, enhancing drug efficacy and promoting pathogen clearance. One study showed that for patients with bacterial pneumonia, combined treatment with pulmonary physical therapy and azithromycin had better therapeutic effects, especially in terms of inflammatory markers and lung function (Li P *et al*., 2024). There is also a clinical study that shows that the combined application of pulmonary physical therapy and azithromycin in the treatment of pneumonia can significantly shorten the patient's hospitalization time, greatly reduce the incidence of complications and greatly improve the success rate of treatment (Songlin W *et al*., 2022).

The results of the study showed that the study group showed a higher effect in treatment, which is consistent with the conclusions of other studies. In addition, some scholars pointed out that the use of lung physical therapy combined with azithromycin to treat bacterial pneumonia in children is helpful for improving treatment effects, rapid recovery and reducing the occurrence of complications (Zhen W, 2020). In terms of the time for symptoms to disappear, there was no significant difference in the time for the body temperature to return to normal between the two groups of patients. Analyzing the results, it may be that the effect of pulmonary physiotherapy on drugs is limited to improving pulmonary ventilation and its effect on promoting fever reduction in patients is extremely limited. Compared with other items, the time for cough disappearance, lung rales disappearance time and asthma disappearance time were all shorter in the study group. This result illustrates that the combined treatment of pulmonary physical therapy and azithromycin may exert pharmacological synergy through local concentration of the drug, promoting intracellular drug delivery, accelerating drug metabolism and excretion and improving immune response. One study pointed out that pulmonary physical therapy can effectively reduce the retention time of azithromycin in sputum by promoting the discharge and clearance of sputum, thereby improving the bioavailability and drug effect of the drug (Catherine E O *et al*., 2024). As mentioned earlier, the inflammatory factor indicators of bacterial pneumonia mainly include WBC, CRP and PCT. Therefore, the research on inflammatory factors in this study mainly focused on WBC, CRP and PCT. Azithromycin, as an antibiotic, can affect inflammatory indicators WBC, CRP and PCT. Therefore, regardless of the study group or the control group, the inflammatory indicators WBC, CRP and PCT were reduced. However, the study group had lower values. The reason may also be

the synergistic effect of lung physical therapy and the drug azithromycin. In this study, the pulmonary function indicators of patients in the study group were better. The reason is that lung physical therapy can promote the discharge of sputum, improve lung ventilation and promote the matching of alveolar ventilation and blood perfusion. Moreover, the synergistic effect of lung physical therapy and azithromycin can better exert the efficacy of azithromycin. It is not difficult to understand that the lung function of patients in the research group is better than that of the control group. There was no significant difference in adverse drug reactions between the two groups and no serious adverse drug reactions occurred. Gastrointestinal complaints were the most common in this study, a result consistent with other studies. Some studies have pointed out that the most common cause of azithromycin is damage to the digestive system, with its incidence accounting for 28%-43% of the total adverse reactions (Antonucci R *et al*., 2022).

In general, this study focused on the drug synergy between azithromycin and pulmonary physical therapy, but ignored whether this therapy also has synergy with other drugs or the synergy between azithromycin and other drugs. This study also ignored the comparison of hospital stays between different groups, which can essentially show the efficacy of the two groups. At the same time, the comparison of hospitalization costs between different groups can also show the direct social effects of the two methods from the perspective of economic benefits. In future studies, the sample size should be increased to enhance the reliability and stability of the results and improve the test efficiency. The risks that arise during the research process should also be fully considered and there should be detailed plans for the corresponding measures for different risk results.

CONCLUSION

The results of this study show that azithromycin combined with pulmonary physical therapy can better exert the efficacy of the drug and have a good effect on the rehabilitation of children with bacterial pneumonia and is worthy of promotion.

ACKNOWLEDGEMENTS

We would like to thank all the colleagues in the Department of Pediatrics of Pan'an People's Hospital of Zhejiang Province for their strong support for this study.

Declaration of interests

This study does not involve any conflicts of interest.

REFERENCES

Ahmad A and Rehman M (2023).Comparative study evaluating the efficacy of topical azithromycin versus oral doxycycline in the treatment of meibomian gland dysfunction. *J Pak Med Assoc*., **5**(73):995-999.

Aït Moussa L, Tebaa A, Alj L, Sefiani H, Meski Fatima Z, Khattabi A and Soulaymani Bencheikh R (2023). Adverse drug reactions to chloroquine/ hydroxychloroquine in combination with azithromycin in COVID-19 in-patients: Data from intensive pharmacovigilance in Morocco, 2020.N-S. *Arch Pharmacol*., **12**(396): 3847-3856.

Antonucci R, Cuzzolin L, Locci C, Dessole F and Capobianco G (2022). Use of azithromycin in pregnancy: More doubts than certainties. *Clin Drug Investig*., **42**(11): 921-935.

Catherine EO, Mamadou O, Mamadou B, Valentin B, Thierry O, Guillaume C, Clarisse D, Alphonse Z, Boubacar C, Cheik B, Huiyu H, Kieran SO, Fanice N, Jeremy DK, Thuy D, Travis CP, Benjamin FA, Elodie L, Ali Sié and Thomas ML (2024). Mass azithromycin distribution to prevent child mortality in burkina faso: *The CHAT Randomized Clinical Trial. JAMA*., **6**(331): 482-490.

Cotter Jillian M, Hall M, Shah Samir S, Molloy Matthew J, Markham Jessica L, Aronson Paul L, Stephens John R, Steiner Michael J, McCoy E, Collins M and Tchou Michael J (2022).Variation in bacterial pneumonia diagnoses and outcomes among children hospitalized with lower respiratory tract infections. *J Hosp Med*., **11**(17): 872-879.

Dawid Ciepłucha H, Bożejko M, Paweł P, Serafińska S and Bartosz S (2023). Bacterial pneumonia and cryptogenic pleuritis after probable monkeypox virus infection: A case report. *Infect Dis Rep*., **6**(15): 795-805.

Hafner M, Paukner S, Wicha Wolfgang W, Hrvačić B, Cedilak M, Faraho I and Gelone Steven P (2021).Anti-inflammatory activity of lefamulin versus azithromycin and dexamethasone *in vivo* and *in vitro* in a lipopolysaccharide-induced lung neutrophilia mouse model. *PLOS ONE*., **9**(16): e0237659-e0237659.

Lewińska A and Shahnazaryan K (2020). The use of diaphragm ultrasonography in pulmonary physiotherapy of COPD patients: A literature review. *J Clin Med*., **11**(9): 3525-3525.

Li P, Wenxiu Q, Min Z and Kai C (2024). Analysis of the effects of azithromycin and erythromycin in the treatment of *Mycoplasma pneumonia* in children. *Chin. Community Doct*., **40** (06): 83-85.

Lyon E and Olarte L (2024).Community-acquired bacterial pneumonia in children: An update on antibiotic duration and immunization strategies. *Curr. Opin. Pediatr*., **2**(36): 144-149.

Songlin W, Lirong Y and Ying X (2022). The efficacy of ultrashort wave combined with azithromycin in the treatment of mycoplasma pneumonia in children and its impact on inflammatory factors and immune function. *J Nor Sichuan Med Coll*., **37**(04): 513-516.

Wenting L, Xiaohong W, Haifeng Y and Kaiming H (2023).

Efficacy of bailing capsule combined with azithromycin in the treatment of mycoplasma pneumonia in children and its effect on serum sPD-1 and CYTL1 levels. *Chin J Diff Compli Cases*., **22** (02): 124-131.

Zhen W (2020). Effect of pulmonary physical therapy on the rehabilitation effect of pediatric pneumonia. *Reflexol Rehab Med*., **13**(29): 4-6.