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ARTICLE

Clinical Efficacy of Pidotimod-Assisted Erythromycin in Treating Lobar Pneumonia in Children Over 3 Years Old

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Abstract

Aims/Background Lobar pneumonia is an acute inflammation with increasing incidence globally. Delayed treatment can lead to severe complications, posing life-threatening risks. Thus, it is crucial to determine effective treatment methods to improve the prognosis of children with lobar pneumonia. Therefore, this study aimed to assess the clinical efficacy of pidotimod-assisted erythromycin in treating lobar pneumonia in children over 3 years old.

Methods This study included 108 children with lobar pneumonia admitted to the Huoqiu First People's Hospital, China, between March 2021 and March 2024. However, 6 children (4 cases with missing clinical data, 1 with autoimmune disease, and 1 with asthma) who did not meet the predetermined inclusion criteria were excluded. Based on the treatment methods, the children were divided into a control group (n = 52, children receiving erythromycin treatment) and an observation group (n = 50, children receiving pidotimod-assisted erythromycin treatment). Furthermore, the clinical efficacy, clinical signs, resolution time of symptoms, cellular immune function, and incidence of adverse reactions were retrospectively evaluated.

Results The control group exhibited significantly lower treatment efficiency than the observation group (80.77% vs 94.00%; $p < 0.05$). Furthermore, the observation group showed better alleviating fever, cough, tachypnea, and pulmonary moist rales ($p < 0.001$). The $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ levels were comparable in both groups before treatment ($p > 0.05$). However, 7 days after treatment, the $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ levels increased significantly in the observation group compared to the control group ($p < 0.001$). Additionally, there was no significant difference in the incidence of adverse reactions in both groups ($p > 0.05$).

Conclusion Pidotimod-assisted erythromycin treatment can significantly improve the treatment efficiency in children with lobar pneumonia, improving clinical signs and symptoms and enhancing the cellular immune function without increasing the risk of adverse drug reactions.

Key words: pidotimod; erythromycin; lobar pneumonia; children

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Introduction

Pneumonia is one of the most common infectious diseases affecting children around the world. According to the World Health Organization (WHO) statistics, approximately 3 million children die from pneumonia every year, making it a severe threat to their physical and mental health (Wang et al, 2021b). Lobar pneumonia, a specific type primarily caused by *Streptococcus pneumoniae*, is characterized by

acute inflammation involving lung tissues at and above the lung segment. In recent years, lobar pneumonia has increased, often accompanied by extensive alveolar infiltration. Severe clinical manifestations include hyperpyrexia, coughing, and dyspnea, leading to additional pulmonary multi-system complications (Yin et al, 2017). Lobar pneumonia is community-acquired pneumonia (CAP) with acute onset, and can lead to severe complications, such as hydrothorax, pyothorax, necrotic pneumonia and pulmonary abscesses (Chang et al, 2019), and even can cause life-threatening risk to children if left untreated. Hence, seeking effective treatment methods is crucial to improving outcomes, reducing the incidence of complications, and enhancing the prognosis for children with lobar pneumonia.

In recent years, with the significant advancement in medical research, drug therapy has become increasingly important in treating lobar pneumonia. Erythromycin, a macrolide antibiotic, is known for its potential to penetrate cells (Kong et al, 2020) and its 14-membered structure which inhibits protein synthesis (Han et al, 2021). This mechanism effectively alleviates clinical symptoms in children (Han et al, 2020), making erythromycin a widely used treatment for lobar pneumonia in children. However, research has indicated that the global emergence of drug-resistant strains has led to a continuous rise in antibiotic resistance rates (Zhang et al, 2022). Furthermore, erythromycin is limited in its anti-infective role and does not affect the immune function of children. Moreover, studies have revealed that erythromycin alone offers limited efficacy, and the resolution of clinical symptoms, such as cough, fever, and improvements in lung function, may take longer.

Therefore, exploring improved treatment regimens is essential to shorten the recovery time in children (Wang et al, 2021a). Immunopotentiators have been identified to enhance the body's immune response (Zhao et al, 2023). Pidotimod, an immunomodulator and synthetic dipeptide molecule, stimulates the immune system and improves immune function, serving as an auxiliary drug to anti-infective treatments to enhance therapeutic outcomes (Xu et al, 2021). Extensive research over the past 30 years supports the role of pidotimod in preventing recurrent respiratory infections in susceptible children and alleviating respiratory exacerbations in patients with chronic bronchitis. The immunomodulatory effects of pidotimod indicate that it may be beneficial in managing respiratory infections and other immune-mediated disorders, including allergy, chronic obstructive pulmonary disease (COPD), and asthma (Marseglia et al, 2024).

Therefore, this study retrospectively aimed to explore the clinical efficacy and safety of combining pidotimod with erythromycin in treating lobar pneumonia in children, providing a reference for clinical practice.

Methods

Study Population

This study retrospectively analyzed the clinical data from 102 children with lobar pneumonia admitted to the Huoqiu First People's Hospital, China, between March 2021 and March 2024. Based on the treatment methods, patients were divided into the control group (n = 52) and the observation group (n = 50). Both

groups received erythromycin treatment, while the observation group also underwent additional pidotimod-adjuvant therapy. The flow chart of the study design is shown in Fig. 1.

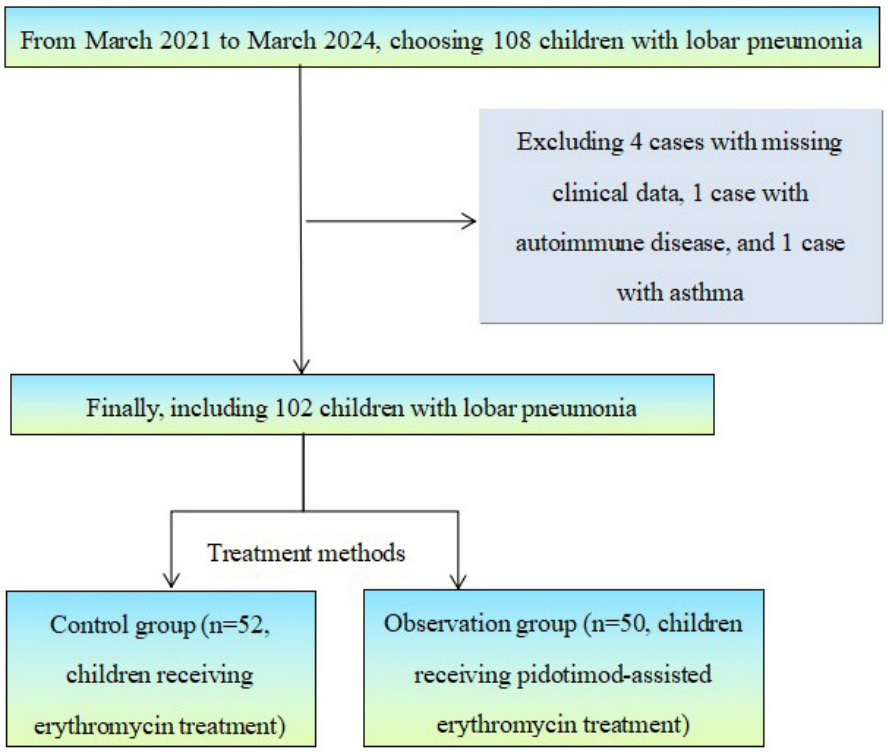

Fig. 1. A flow chart of the study design.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) children diagnosed with lobar pneumonia; (2) children with a history of fever and cough before admission, with chest plain film showing dense shadows in the lung lobes; (3) children with complete clinical data; and (4) aged between 3 to 14 years.

Exclusion criteria included: (1) children with autoimmune disease and immunodeficiency diseases; (2) children who received hormonal therapy within the 3 months before admission; (3) children affected with other respiratory diseases, such as tuberculosis and asthma; (4) children with pulmonary congenital disease or respiratory tract malformations; (5) children with heart, liver, and kidney dysfunctions; and (6) children with other infections or febrile illnesses.

Written informed consent was obtained from the guardians of the children. This study design followed the guidelines of the Declaration of Helsinki (World Medical Association, 2013). Ethical approval was obtained from the Ethics Committee of the Huoqiu First People's Hospital, China (Approval No. 20230020).

Treatment Protocol

The control group underwent erythromycin treatment. Erythromycin lactobionate (specification: 0.25 g equivalent to 25 million units; National Medical Prod-

ucts Administration (NMPA) approval number: H43020028; manufacturer: Hunan Kelun Pharmaceutical Co., Ltd., Yueyang, China) was injected at a dosage of 10–15 mg/kg. It was diluted in 100 mL of 5% glucose (specification: 100 mL, 5 g; NMPA approval number: H20023006; manufacturer: Furen Pharmaceutical Co., Ltd., Zhoukou, China) and administered through intravenous infusion. This treatment was given twice a day for 7 consecutive days.

However, in addition to the control group's treatment, the observation group received dispersible tablets (specification: 0.4 g, NMPA approval number, H20060718; manufacturer: Beijing Jincheng Taier Pharmaceutical Co., Ltd., Beijing, China). Pidotimod was administered 0.4 g per dose, twice daily for 1 week.

Data Collection

Baseline Characteristics

We collected details on baseline characteristics, such as sex, age, disease status before admission, body mass index (BMI), body temperature at admission, lesion location, clinical pulmonary infection score (CPIS), education level of primary caregivers, and family monthly income from the medical record system of the Huoqiu First People's Hospital, China.

Outcome Measurement

The treatment outcomes measures were assessed as follows:

Clinical efficacy: A treatment was considered cured if patients had no symptoms and signs such as expectoration and cough, normal body temperature, and exhibited no abnormalities on chest plain film after treatment. The treatment was considered effective, if patients had normal body temperature, improved clinical symptoms, and significant absorption or disappearance of lung shadows on chest plain film. If patients exhibited normal temperature but no improvement in clinical symptoms or signs, and no improvement was found on chest plain film, the treatment was considered ineffective. The treatment efficiency between the two groups was statistically compared, with the total effective rate calculated as below: Total effective rate = cure rate + obvious effective rate.

Resolution time of clinical signs and symptoms: The time it took for fever, cough, tachypnea, and pulmonary moist rales to resolve after 7 days of treatment was documented and compared between the two groups.

Cellular immune function: The levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ were determined in the two groups before and after 7 days of treatment. Peripheral venous blood (3 mL) was extracted and centrifuged at 3500 r/min for 5 minutes, and the separated serum was stored at a low temperature for subsequent analysis. The stored serum samples were thawed at 37 °C, diluted, and 100 μL of buffer solution was added. After thorough mixing, samples were maintained at room temperature for 30 minutes. After this, $CD3^+$, $CD4^+$ and $CD8^+$ (Reagent kit: HBP31226R: Haihuabang Pharmaceutical Technology Co., Ltd., Shanghai, China) were assessed using flow cytometry (FACSCalibur, BD company, Franklin Lake, NJ, USA). The $CD4^+/CD8^+$ ratio was further evaluated using the Bioconductor library and R statistical software package.

Adverse reactions: The number of cases with adverse reactions, like diarrhoea, abdominal pain, rash, drowsiness, nausea and vomiting, were documented in the two groups, and the incidence of adverse reactions was statistically compared (the number of cases with adverse reactions in each group/total number in each group $\times$ 100%).

Statistical Analysis

The clinical data was statistically analyzed using SPSS 26.0 (IBM, Armonk, NY, USA). Categorical variables were expressed as [n (%)] and analyzed using the chi-square test. Continuous variables were evaluated using the Shapiro-Wilk test to observe if they followed a normal distribution. Data following a normal distribution were expressed as mean $\pm$ SD and analyzed using the *t*-test. However, data not following a normal distribution were expressed as M (P_{25}, P_{75}) and tested using the Mann-Whitney U test. A two-sided *p*-value of <0.05 was considered statistically significant. Fig. 1 was created using WPS Office Excel (version: 2021; Kingsoft Software Co., Ltd., Beijing, China).

Results

Comparison of Baseline Characteristics between the Two Groups

The baseline characteristics of the study participants, including sex, age, duration of disease before admission, BMI, body temperature at admission, lesion location, CPIS, education level of primary caregivers, and family monthly income, are detailed in Table 1. We observed that the baseline characteristics were comparable between the two groups, with no significant differences ($p > 0.05$).

Comparison of Clinical Efficacy between the Two Groups

As shown in Table 2, treatment efficiency was significantly higher in the observation group compared to the control group (80.77% vs 94.00%; $p < 0.05$).

Comparison of Disappearance Time of Clinical Signs and Symptoms

The observation group exhibited significantly shorter disappearance time of fever, cough, tachypnea, and pulmonary moist rales than the control group ($p < 0.001$, Table 3).

Comparison of Cellular Immune Function between the Two Groups

As detailed in Table 4, the $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ levels in both groups were comparable before treatment ($p > 0.05$). However, after 7 days of treatment, the observation group exhibited a substantial improvement in $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ levels compared to the control group ($p < 0.001$).

Comparison of Adverse Reactions between the Two Groups

Table 5 shows the incidence of adverse reactions in both groups. We observed 1 case of diarrhoea and abdominal pain, 1 case of diarrhoea, 1 case of abdominal pain, 1 case of rash and drowsiness, and 2 cases of nausea and vomiting in the control group. In the observation group, there were 5 adverse reactions, including

Table 1. Comparison of baseline characteristics between the two groups [M (P_{25}, P_{75})/n (%)].

Variables		Control group (n = 52)	Observation group (n = 50)	χ^2/Z	*p*-value
Sex	Male	30 (57.69)	29 (58.00)	0.001	0.975
	Female	22 (42.31)	21 (42.00)		
Age (years)		9.00 (7.00, 12.00)	10.00 (7.00, 12.00)	–0.303	0.762
Course of disease before admission (d)		6.00 (6.00, 7.00)	7.00 (6.00, 7.00)	–0.581	0.561
BMI (kg/m^2)		19.12 (18.88, 19.51)	18.98 (18.83, 19.40)	–0.750	0.453
Body temperature at admission (°C)		38.80 (38.40, 39.40)	38.75 (38.40, 39.30)	–0.470	0.638
Lesion location	Left lobe	17 (32.69)	21 (42.00)	0.945	0.331
	Right lobe	35 (67.31)	29 (58.00)		
Involvement of the two lobes and above	Yes	7 (13.46)	6 (12.00)	0.049	0.825
	No	45 (86.54)	44 (88.00)		
CPIS (points)		9.00 (8.00, 10.00)	8.00 (7.00, 9.00)	–1.709	0.087
Education level of primary caregivers	Senior high school and below	14 (26.92)	18 (36.00)	0.975	0.323
	College and above	38 (73.08)	32 (64.00)		
Family monthly income	≤8000 CNY	20 (38.46)	17 (34.00)	0.219	0.639
	>8000 CNY	32 (61.54)	33 (66.00)		

Note: BMI, body mass index; CPIS, clinical pulmonary infection score; 1 USD = 7.14 CNY.

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

Experimental groups	Cases	Cured	Obviously effective	Invalid	Total effective rate
Control group	52	22 (42.31)	20 (38.46)	10 (19.23)	42 (80.77)
Observation group	50	32 (64.00)	15 (30.00)	3 (6.00)	47 (94.00)
χ^2	-	4.815	0.810	4.012	4.012
p-value	-	0.028	0.368	0.045	0.045

1 case of diarrhoea and abdominal pain, 1 case of diarrhoea, 1 case of rash, and 2 cases of nausea and vomiting. The incidence of adverse reactions was comparable in the two groups ($p > 0.05$).

Discussion

Lobar pneumonia typically has a sudden onset leading to a long disease duration. Children are particularly susceptible to lobar pneumonia due to their incompletely developed immune systems, low antibody levels, and unique physiological structures (Yang et al, 2024). Delayed or inadequate treatment can cause rapid disease progression, posing a severe risk to the life and safety of affected children (Zinserling et al, 2022).

Erythromycin, a macrolide antibiotic derived from streptomyces erythreus, is widely used in treating pediatric pneumonia (Shahabadi and Razlansari, 2022). Its primary active ingredient, erythromycin A, inhibits protein synthesis by binding to the 50S ribosomal subunit in sensitive organisms (Mahfouz et al, 2023). However, long-term antibiotic use can result in elevated drug resistance in children, potentially prolonging recovery time or leading to frequent recurrences after initial recovery. At this stage, incorporating drugs that enhance the immune function of children can improve treatment efficacy. Pidotimod, an immunopotentiator, promotes both specific and non-specific immune responses, impacting different stages of immune activation and activating the immune system to eliminate pathogenic microorganisms (Kim et al, 2018). Thus, we explored the effect of pidotimod combined with erythromycin in treating lobar pneumonia. The results indicated higher treatment efficiency in the observation group compared to the control group. Particularly, the time to resolve fever, cough, tachypnea, and pulmonary moist rales was substantially shorter in the observation group, which aligns with the findings of Li et al (2021).

Furthermore, this study observed significant improvements in cellular immune function in the observation group. After treatment, the levels of $CD3^+$, $CD4^+$, and $CD4^+/CD8^+$ ratio exhibited significant improvement in the observation group than the control group, consistent with the results of Dong et al (2018). These observations indicate that pidotimod-assisted erythromycin in treating lobar pneumonia can effectively alleviate clinical symptoms and significantly enhance cellular immune function in children with lobar pneumonia.

Table 3. Comparison of disappearance time of clinical signs and symptoms [M (P_{25}, P_{75}), d].

Experimental groups	Cases	Disappearance time of fever	Disappearance time of cough	Disappearance time of tachypnea	Disappearance time of pulmonary moist rales
Control group	52	4.00 (4.00, 5.00)	7.00 (7.00, 9.00)	7.00 (6.00, 8.00)	7.00 (5.50, 8.00)
Observation group	50	4.00 (3.00, 4.00)	5.00 (4.00, 6.00)	6.00 (5.00, 7.00)	5.00 (4.00, 6.00)
Z	-	–6.599	–7.200	–5.798	–6.178
p-value	-	<0.001	<0.001	<0.001	<0.001

Table 4. Comparison of cellular immune function between the two groups [M (P_{25}, P_{75})].

Experimental groups	Cases	$CD3^+$ (%)		$CD4^+$ (%)		$CD4^+/CD8^+$	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	52	53.00 (51.00, 55.00)	57.00 (56.00, 59.00)	23.00 (21.00, 25.00)	24.00 (23.00, 25.00)	0.94 (0.83, 1.01)	1.18 (1.14, 1.25)
Observation group	50	53.00 (51.00, 55.00)	62.50 (61.00, 64.00)	23.00 (21.00, 25.00)	29.00 (28.00, 31.00)	0.91 (0.80, 0.98)	1.59 (1.50, 1.70)
Z	-	–0.634	–8.537	–0.304	–8.780	–1.129	–8.706
p-value	-	0.526	<0.001	0.761	<0.001	0.259	<0.001

Table 5. Comparison of adverse reactions between the two groups [n (%)].

Experimental groups	Cases	Diarrhoea	Nausea and vomiting	Abdominal pain	Rash	Drowsiness	Incidence rate
Control group	52	2 (3.85)	2 (3.85)	2 (3.85)	1 (1.92)	1 (1.92)	6 (11.54)
Observation group	50	2 (4.00)	2 (4.00)	1 (2.00)	1 (2.00)	0 (0.00)	5 (10.00)
χ^2	-	-	-	-	-	-	0.063
p-value	-	-	-	-	-	-	0.802

Improving immune function is particularly crucial for children with lobar pneumonia, as their relatively weak immune systems make them prone to inflammation and immune responses induced by pathogens (Gwela et al, 2019). A well-functioning immune system is crucial for maintaining overall health (Morales et al, 2023), effectively improving children's resistance to pathogens, thus promoting recovery from pneumonia and reducing the risk of recurrence and complications through enhanced immune function (Govers et al, 2022). In terms of adverse reactions or safety, this study found no significant difference in the incidence of adverse reactions between the two groups. Most adverse reactions were mild and resolved after timely treatment, suggesting that pidotimod combined with erythromycin is a safe and reliable strategy for treating lobar pneumonia.

Although this study confirmed the effectiveness of pidotimod-assisted erythromycin in treating lobar pneumonia in children over 3 years old, several areas need further investigation. Firstly, the small sample size may not fully represent the broader population of children with lobar pneumonia. Future studies should expand the sample size to provide a more comprehensive evaluation of its effect on lobar pneumonia. Additionally, this study focused on the short-term efficacy and safety of pidotimod-assisted erythromycin, leaving the long-term efficacy unexplored. Therefore, future studies should extend the observation period to evaluate the long-term effectiveness and safety of this treatment strategy for lobar pneumonia.

Conclusion

The pidotimod-assisted erythromycin method reveals significant clinical efficacy in treating children with lobar pneumonia, alleviating clinical symptoms, improving cellular immune function, and maintaining an excellent safety profile. This treatment method provides new options and perspectives for the clinical management of lobar pneumonia.

Key Points

- Pidotimod-assisted erythromycin treatment method can improve therapeutic efficacy in children with lobar pneumonia.
- Pidotimod-assisted erythromycin can accelerate the resolution of clinical symptoms and signs in these children.
- This treatment approach can improve the cellular immune function of children with lobar pneumonia.
- Pidotimod-assisted erythromycin does not significantly increase the incidence of adverse drug reactions in children with lobar pneumonia.
- Treating children with lobar pneumonia, pidotimod combined with erythromycin offers several therapeutic advantages.

Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Author Contributions

JK designed the study. Both authors conducted the study. XQT collected and analyzed the data. JK and XQT participated in drafting the manuscript, and both authors contributed to the critical revision of the manuscript for important intellectual content. Both authors gave final approval of the version to be published. Both authors participated fully in the work, took public responsibility for appropriate portions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study has been approved by the Medical Ethics Committee of Huoqiu First People's Hospital (Approval No. 20230020). Written informed consent was obtained from the guardians of the children.

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Conflict of Interest

The authors declare no conflict of interest.

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