

Influence of Montelukast Combined With Methylprednisolone on Liver Function, Platelet Count, Eosinophil Count, and Myocardial Enzymes in Bronchopneumonia Children With Wheezing

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Abstract

Aims/Background Bronchopneumonia is a common infectious disease in pediatrics, which can lead to myocardial and hepatic impairments. Children with bronchopneumonia accompanied by wheezing are vulnerable to hypoxia, which may damage other systems. Therefore, this study explored the influence of montelukast combined with methylprednisolone on liver function, platelet count, eosinophil count, and myocardial enzymes in children with bronchopneumonia accompanied by wheezing.

Methods The clinical data of this retrospective study included 82 pediatric cases diagnosed with bronchopneumonia and wheezing between April 2022 and April 2024. Based on treatment methods, patients were divided into the methylprednisolone group (40 cases) as well as the montelukast and methylprednisolone group (42 cases). Therapeutic efficacy, resolution time of clinical symptoms, and adverse effects were recorded. Furthermore, liver function indicators, platelet count, eosinophil count, and myocardial enzyme levels were comparatively assessed using biochemical analyzer, hematology analyzer and biological kits in both groups.

Results The total efficacy rate of the montelukast and methylprednisolone group was 95.2% (40/42), higher than the 77.5% of the methylprednisolone group ($p = 0.018$). Patients in the montelukast and methylprednisolone group had shorter hospitalization and clinical symptom disappearance times than the methylprednisolone group (both $p < 0.05$). In addition, there was no significant difference in total incidence of adverse reactions ($p = 0.700$). Methylprednisolone monotherapy or in combination with montelukast, substantially reduced liver function indicators, platelet count, eosinophil count, and myocardial enzyme levels ($p < 0.05$). Moreover, the platelet count, eosinophil count, and myocardial enzymes [aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatine kinase (CK), and creatine kinase isoenzyme (CK-MB)] were reduced in the montelukast and methylprednisolone group compared to the methylprednisolone group after treatment ($p < 0.05$). Compared to the methylprednisolone group, alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin (TBIL), direct bilirubin (DBIL) levels were significantly diminished in the montelukast and methylprednisolone group following treatment ($p < 0.05$).

Conclusion Montelukast and methylprednisolone combination therapy reduces platelet and eosinophil counts, alleviates myocardial and liver function damage, and demonstrates good therapeutic efficacy in children with bronchopneumonia accompanied by wheezing.

Key words: montelukast; methylprednisolone; bronchopneumonia; children; myocardium; liver function

Submitted: 6 November 2024 Revised: 9 February 2025 Accepted: 26 February 2025

How to cite this article:

Yuan W, Du C, Jiang K. Influence of Montelukast Combined With Methylprednisolone on Liver Function, Platelet Count, Eosinophil Count, and Myocardial Enzymes in Bronchopneumonia Children With Wheezing. *Br J Hosp Med*. 2025. <https://doi.org/10.12968/hmed.2024.0871>

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Introduction

Bronchopneumonia is a common infectious disease in pediatrics and has a high morbidity rate, mainly characterized by fever, cough, and dyspnea (Ling et al, 2023; Zhao et al, 2021). Epidemiological evidence shows that pneumonia accounts for 7% of deaths among children aged 5–9 years, with over 90% of pneumonia-associated childhood deaths occurring in those under 5 years of age (Kevat et al, 2022). A large-scale epidemiological survey conducted in Northeast China and Inner Mongolia reported that bronchopneumonia accounted for approximately 50–66% of *Mycoplasma pneumoniae* infections among children (Wang et al, 2024).

Bronchopneumonia has a rapid onset and progression, which highlights the need for prompt and effective treatment. Additionally, external stimulation can induce edema and congestion, leading to airway constriction; coupled with thick airway mucus, these factors result in wheezing symptoms, such as dyspnea, wheezing, and cough, usually accompanied by pulmonary rales (Douros and Everard, 2020; Wang et al, 2020). Patients with wheezing-related bronchopneumonia are vulnerable to hypoxia, which may damage other organ systems (Douros and Everard, 2020). Clinically, children with bronchopneumonia are often treated symptomatically, with fever reduction, oxygen supply, and infection control (Ling and Wan, 2023). While these measures offer some symptom relief, they often fail to achieve significant improvement in dyspnea or ensure a good prognosis.

Bronchopneumonia not only impairs lung health but also affects extrapulmonary organs in children. A study has revealed that children with bronchopneumonia show significantly increased levels of cardiac enzymes and alanine aminotransferase (ALT) compared to healthy children, suggesting potential myocardial injury (Ling et al, 2023). Additionally, severe pneumonia in children with community-acquired pneumonia has been associated with a higher risk of liver damage, which prolongs hospitalization time and increases the 30-day mortality rate (Zhang and Zhao, 2022). Another study found that 12.8% of children with community-acquired pneumonia experienced liver dysfunction, with pneumonia observed as an independent risk factor for hepatic dysfunction (Tong et al, 2024). Similarly, increased liver enzyme levels have been found in children with mycoplasma pneumonia infection (Jujaray et al, 2018). Therefore, managing cardiac and liver function is crucial during the treatment of bronchopneumonia in the pediatric population.

Glucocorticoids effectively control the aggregation and activation of inflammatory cells, reduce vascular permeability, and alleviate airway hyperresponsiveness and inflammation (Reichardt et al, 2021). Methylprednisolone, a synthetic glucocorticoid, has effectively inhibited bronchial constriction and improved ventilatory function in patients (Meduri et al, 2022; Ye et al, 2021). Montelukast, a potent cysteinyl leukotrienes receptor 1 antagonist, exhibits a bronchial smooth muscle diastolic effect by antagonizing leukotriene activity, thereby relieving asthma and cough (Marques et al, 2022). Research has proven that combining montelukast and methylprednisolone can alleviate the inflammatory response in children with mycoplasma pneumonia (Wu et al, 2019). However, studies investigating the effect of this combination therapy on myocardial and liver function in children with

bronchopneumonia are limited. Hence, this study aimed to explore the effects of montelukast combined with methylprednisolone on liver function, platelet count, eosinophil count, and myocardial enzymes in bronchopneumonia children with wheezing. The innovation of this study was to explore the effect of combined therapy on myocardial and liver function in children with bronchopneumonia. We retrospectively analyzed the clinical information obtained from 82 cases of children with bronchopneumonia and wheezing who were admitted to the pediatrics department between April 2022 and April 2024. The findings of this study would contribute to optimizing rational and effective treatment approaches for managing bronchopneumonia in children with wheezing.

Methods

Recruitment of the Study Participants

This retrospective study included 82 pediatric cases diagnosed with bronchopneumonia and wheezing between April 2022 and April 2024. Based on treatment methods, patients were classified into the methylprednisolone group (40 cases) and the montelukast plus methylprednisolone group (42 cases).

The inclusion criteria were as follows: (1) Diagnosis of bronchopneumonia based on clinical diagnostic criteria for infant bronchopneumonia (Bradley et al, 2011), confirmed through chest X-ray and blood routine examination. (2) Patients with wheezing, dyspnea, cough, and pulmonary rales. (3) Those with complete clinical data. Patients were excluded if they met any of the following criteria: (1) Severe conditions affecting the heart, liver, lung, kidney, circulatory, and brain. (2) Children with other pulmonary or respiratory diseases, such as tuberculosis and asthma. (3) Patients diagnosed with immune and hematologic conditions. (4) Use of bronchodilator, antibiotic or hormonal medications within one month before treatment. (5) Allergy to montelukast or methylprednisolone, treatment with other medications.

Treatment Procedures

All patients received routine symptomatic treatment and nursing interventions, including oxygen therapy, fluid replacement, anti-infection assessments, fever reduction, a balanced diet, and adequate rest.

The patients in the methylprednisolone group received methylprednisolone sodium succinate (2 mg/kg/day, H20183039, Fuan Pharmaceutical Hubei People's Pharmaceutical Co., Ltd., Wuhan, China) diluted in 100 mL of glucose through intravenous infusion for 5 days. Patients in the montelukast and methylprednisolone group received oral montelukast (J20130054, Hangzhou Merck & Co., Ltd., Hangzhou, China) in addition to methylprednisolone therapy. The children aged 2–5 years were administered 4 mg montelukast once daily, and those aged 6–12 years received 5 mg once daily, for 7 days.

Efficacy Assessment

The effectiveness of the treatment was evaluated using the following criteria (Wang et al, 2020):

- Highly effective: Complete resolution of clinical symptoms with a normal chest X-ray.
- Effective: Substantial improvement in clinical symptoms and pronounced reduction in lesions on chest X-rays.
- Ineffective: No improvement in clinical symptoms or worsening of the condition.

Total efficiency rate (%) was assessed as: (Remarkably effective + Effective)/Total cases \times 100%.

The radiological interpretations of X-rays were performed by a pediatric pulmonologist and a pediatric radiologist. The disappearance (resolution) time of clinical symptoms was recorded for all patients, including hospitalization time, wheeze resolution time, cough disappearance time, fever disappearance time, and pulmonary rales resolution time. Additionally, any adverse reactions occurring during the treatment, such as nausea, diarrhea, vomiting, abdominal pain, and rash, were recorded.

Observation Indicators

Patients were clinically assessed using the following observation indicators:

- Liver function parameters: Fasting venous blood samples were collected before and after treatment. Liver function indicators were examined using an automatic biochemistry analyzer (CS-1200, DIRUI, Changchun, China), including alanine aminotransferase (ALT), γ -glutamyl transferase (GGT), alkaline phosphatase (ALP), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL).
- Platelet and eosinophil counts: Blood samples were collected in tubes containing ethylene diamine tetraacetic acid (EDTA). Eosinophil and platelet counts were analyzed using an automated hematology analyzer (Coulter STKS, Beckman, Fullerton, CA, USA) before and after treatment.
- Myocardial enzyme detection: Myocardial enzyme levels were evaluated in the patient serum before and after treatment. These enzymes included lactate dehydrogenase (LDH; SNM183, Beijing Baiaolaibo Technology Co., Ltd., Beijing, China), aspartate aminotransferase (AST; SP11063, Saipai Biotechnology, Wuhan, China), creatine kinase (CK; SNM166, Beijing Baiaolaibo Technology Co., Ltd., Beijing, China), and creatine kinase isoenzyme (CK-MB; SNM278; Beijing Baiaolaibo Technology Co., Ltd., Beijing, China).

Statistical Analysis

Data were statistically analyzed using SPSS 20.0 (IBM Corp., Chicago, IL, USA). Shapiro-Wilk test was adopted to assess data normality. Normally distributed data were expressed as mean \pm standard deviation (SD), and comparisons between two groups were performed using the *t*-test. Non-normally distributed data were presented as median and quartile and analyzed using the Mann-Whitney U test. The categorical variable data were presented as n (%) and analyzed using the chi-square test for group comparison. A *p*-value of <0.05 determined statistical significance.

Table 1. Comparison of baseline characteristics between the two groups.

	Methylprednisolone group (n = 40)	Montelukast and methylprednisolone group (n = 42)	<i>t/Z/χ²</i>	<i>p</i> -value
Gender, n (%)			0.935	0.334
Male	27 (67.5%)	24 (57.1%)		
Female	13 (32.5%)	18 (42.9%)		
Age (year)	5.30 ± 2.08	6.05 ± 2.34	1.531	0.130
Weight (kg)	18.8 (15.9, 25.0)	22.6 (17.6, 26.6)	1.239	0.216
Clinical severity, n (%)			0.424	0.515
Mild	30 (75.0%)	34 (81.0%)		
Severe	10 (25.0%)	8 (19.0%)		
Pleural effusion, n (%)			0.152	0.697
Yes	14 (35.0%)	13 (31.0%)		
No	26 (65.0%)	29 (69.0%)		
Smoker(s) in the family, n (%)			0.105	0.746
Yes	12 (30.0%)	14 (33.3%)		
No	28 (70.0%)	28 (66.7%)		
Family history of chronic bronchitis, n (%)			0.746	0.388
Yes	9 (22.5%)	13 (31.0%)		
No	31 (77.5%)	29 (69.0%)		

Results

Comparison of General Information Between the Two Groups

The methylprednisolone group (n = 40) included 27 males and 13 females, with an average age of 5.3 years. The montelukast and methylprednisolone group (n = 42) consisted of 24 males and 18 females, with a mean age of 6.05 years. Clinical severity was assessed following the World Health Organization (WHO) criteria (2013). There were no significant differences in baseline information between the two groups ($p > 0.05$, Table 1).

Comparison of Therapeutic Efficacy Between the Two Groups

The treatment efficacy and clinical symptom disappearance time for the two groups are shown in Tables 2,3. The total efficacy rate in the montelukast and methylprednisolone group was 95.2%, which was significantly higher than the 77.5% found in the methylprednisolone group ($p = 0.018$, Table 2). Furthermore, patients in the montelukast and methylprednisolone group had a shorter hospitalization time and clinical symptoms disappearance time, such as wheeze disappearance time, cough disappearance time, fever reduction time, pulmonary rales resolution time, compared to those in the methylprednisolone group ($p < 0.05$, Table 3).

Table 2. Comparison of therapeutic efficacy between two groups.

Group	n	Remarkably effective	Effective	Ineffective	Total efficacy rate
Methylprednisolone group	40	20 (50.0%)	11 (27.5%)	9 (22.5%)	31 (77.5%)
Montelukast and methylprednisolone group	42	27 (64.3%)	13 (30.9%)	2 (4.8%)	40 (95.2%)
χ^2					5.550
<i>p</i> -value					0.018

Table 3. Comparison of hospitalization time and symptom resolution time between the two groups.

Group	n	Hospitalization time (days)	Wheeze disappearance time (days)	Fever disappearance time (days)	Cough disappearance time (days)	Pulmonary rales disappearance time (days)
Methylprednisolone group	40	11.78 ± 2.55	7.00 ± 1.59	4.30 ± 1.45	7.60 ± 1.97	8.93 ± 2.35
Montelukast and methylprednisolone group	42	8.71 ± 2.28	5.33 ± 2.24	3.31 ± 1.33	5.10 ± 2.06	7.12 ± 1.94
<i>t</i>		5.743	3.874	3.217	5.623	3.805
<i>p</i> -value		<0.001	<0.001	0.002	<0.001	<0.001

Comparison of Liver Function Indicators Between the Two Groups

Before treatment, there was no significant difference in liver function indicators between the two groups ($p > 0.05$). Both therapeutic methods significantly reduced liver function indicators ($p < 0.05$). However, compared to the methylprednisolone group, ALT, ALP, TBIL, and DBIL levels were substantially alleviated in the montelukast and methylprednisolone post-treatment ($p < 0.05$, Table 4).

Comparison of Platelet and Eosinophil Counts Between the Two Groups

Before treatment, both groups had no significant differences in platelet and eosinophil counts ($p > 0.05$). After treatment, both groups showed a significant reduction in platelet and eosinophil counts compared to their pre-treatment levels ($p < 0.05$, Table 5). Moreover, the montelukast and methylprednisolone group had lower platelet and eosinophil counts post-treatment than the methylprednisolone group ($p < 0.05$, Table 5).

Comparison of Myocardial Enzyme Levels Between the Two Groups

Before treatment, serum myocardial enzyme levels, such as AST, LDH, CK, and CK-MB, were comparable between the two groups ($p > 0.05$). After treatment, AST, LDH, CK, and CK-MB levels were substantially decreased compared to before-treatment levels ($p < 0.05$). Furthermore, post-treatment myocardial enzyme levels were lower in the montelukast and methylprednisolone group than in the methylprednisolone group ($p < 0.05$, Table 6).

Table 4. Comparison of liver function indicators between the two groups.

Liver function indicators	Detection time	Methylprednisolone group (n = 40)	Montelukast and methylprednisolone group (n = 42)	<i>t</i>	<i>p</i> -value
ALT (U/L)	Pre-treatment	35.34 ± 10.91	34.18 ± 9.46	0.512	0.610
	Post-treatment	18.92 ± 8.22*	14.13 ± 7.73*	2.717	0.008
GGT (U/L)	Pre-treatment	13.34 ± 3.59	13.28 ± 5.17	0.056	0.955
	Post-treatment	9.72 ± 3.90*	8.99 ± 3.66*	0.880	0.382
ALP (U/L)	Pre-treatment	167.93 ± 38.15	170.21 ± 41.58	0.258	0.797
	Post-treatment	120.50 ± 33.53*	100.16 ± 38.92*	2.530	0.013
TBIL (μmol/L)	Pre-treatment	38.75 ± 6.01	37.22 ± 5.43	1.211	0.229
	Post-treatment	17.44 ± 4.02*	15.23 ± 3.54*	2.643	0.010
DBIL (μmol/L)	Pre-treatment	13.23 ± 3.04	12.65 ± 2.98	0.864	0.390
	Post-treatment	3.88 ± 1.61*	2.84 ± 1.48*	3.046	0.003
IBIL (μmol/L)	Pre-treatment	25.53 ± 6.29	24.57 ± 7.13	0.643	0.522
	Post-treatment	13.56 ± 4.20*	12.39 ± 3.62*	1.350	0.181

**p* < 0.05 vs. pre-treatment. ALT, alanine aminotransferase; GGT, γ-glutamyl transferase; ALP, alkaline phosphatase; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, indirect bilirubin.

Table 5. Comparison of platelet and eosinophil counts between the two groups.

Group	Platelet count (10 ⁹ /L)		Eosinophil count (10 ⁹ /L)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Methylprednisolone group (n = 40)	343.95 ± 53.80	225.13 ± 57.28*	0.50 ± 0.21	0.29 ± 0.11*
Montelukast and methylprednisolone group (n = 42)	357.69 ± 47.65	193.10 ± 58.74*	0.52 ± 0.16	0.20 ± 0.09*
<i>t</i>	1.226	2.498	0.487	4.064
<i>p</i> -value	0.224	0.015	0.628	<0.001

**p* < 0.05 vs. pre-treatment.

Comparison of Adverse Reactions Between the Two Groups

A comparison of adverse reactions between the two groups is summarized in Table 7. Vomiting was the most frequent adverse reaction found in both groups. Furthermore, the total incidence of adverse reactions in the montelukast and methylprednisolone group was 19.0%, which was less than the 22.5% observed in the methylprednisolone group (22.5%), though the difference was statistically insignificant (*p* = 0.700).

Discussion

Bronchopneumonia is primarily caused by bacterial infections, such as pneumococcus, staphylococcus aureus, and streptococcus (Zade et al, 2023). Due to narrow airways and small lung volumes, children are vulnerable to airway congestion, swelling, and increased mucus secretion, further exacerbating airway obstruction in bronchopneumonia (Ling et al, 2023; Wang et al, 2020). Current treatment for

Table 6. Comparison of myocardial enzyme levels between the two groups.

Myocardial enzymes	Detection time	Methylprednisolone group (n = 40)	Montelukast and methylprednisolone group (n = 42)	<i>t</i>	<i>p</i> -value
AST (U/L)	Pre-treatment	61.25 ± 8.19	59.30 ± 7.75	1.107	0.271
	Post-treatment	30.04 ± 7.43*	26.71 ± 6.54*	2.159	0.034
LDH (U/L)	Pre-treatment	299.59 ± 37.14	294.55 ± 27.90	0.559	0.578
	Post-treatment	214.77 ± 33.41*	167.84 ± 30.99*	6.599	<0.001
CK (U/L)	Pre-treatment	208.86 ± 25.54	200.22 ± 28.05	1.456	0.149
	Post-treatment	175.25 ± 19.64*	124.44 ± 21.62*	11.121	<0.001
CK-MB (U/L)	Pre-treatment	38.56 ± 9.99	36.21 ± 9.95	1.067	0.289
	Post-treatment	25.10 ± 7.77*	17.51 ± 5.17*	5.231	<0.001

**p* < 0.05 vs. pre-treatment. AST, aspartate aminotransferase; LDH, lactate dehydrogenase; CK, creatine kinase; CK-MB, creatine kinase isoenzyme.

Table 7. Comparison of adverse reactions between the two groups.

Group	n	Nausea	Diarrhea	Vomiting	Abdominal pain	Rash	Total
Methylprednisolone group	40	2 (5.0%)	2 (5.0%)	4 (10.0%)	1 (2.5%)	0 (0)	9 (22.5%)
Montelukast and methylprednisolone group	42	2 (4.7%)	1 (2.4%)	3 (7.1%)	1 (2.4%)	1 (2.4%)	8 (19.0%)
χ^2							0.149
<i>p</i> -value							0.700

children with bronchopneumonia accompanied by wheezing, mainly targets infection control and inflammation reduction through medication and oxygen therapy (Liapikou and Torres, 2016; Ye et al, 2021). Medication usually includes glucocorticoids, antibiotics, and bronchodilators (Ye et al, 2021). However, monotherapy strategies often require longer treatment duration, which may elevate the risk of secondary complications (Mani, 2017). Therefore, shortening the treatment course and improving therapeutic efficacy are crucial in managing the disease. Methylprednisolone, a glucocorticoid drug, exerts a strong anti-inflammatory effect by effectively inhibiting inflammatory mediator release and alleviating inflammatory reactions (Mehta et al, 2022). Furthermore, montelukast helps to expand the bronchi and suppress airway inflammation (Aliyali et al, 2024).

In the present study, combining montelukast and methylprednisolone effectively improved the clinical symptoms of children with bronchopneumonia accompanied by wheezing and reduced hospitalization time. The total efficacy of combination therapy was 95.2% (40/42), and both hospitalization time and symptom disappearance time (including fever, cough, wheezing, and pulmonary rales) were significantly reduced compared to the methylprednisolone group. These results suggest that combination therapy accelerates recovery in children with bronchopneumonia and wheezing. Previous research has proven the application of montelukast combined with methylprednisolone in children with mycoplasma pneumonia (Wu

et al, 2019). To our knowledge, no studies have reported the efficacy of montelukast combined with methylprednisolone in children with bronchopneumonia accompanied by wheezing. Our study showed that combination therapy alleviated bronchopneumonia, improved clinical symptoms, and enhanced clinical efficacy. Meanwhile, an innovative aspect of this study was to investigate the ameliorative effect of combination therapy on hepatic and myocardial function impairment due to bronchopneumonia. Furthermore, a total of 8 cases displayed adverse reactions in montelukast and methylprednisolone group, slightly lower than that in the methylprednisolone group, but the difference was not statistically significant. The observed adverse reactions include nausea, diarrhea, vomiting, abdominal pain, and rash. The most frequent adverse reaction was vomiting, followed by nausea and diarrhea. Rash was observed in only one child. Overall, the symptoms of these adverse reactions were mild, and did not develop serious symptoms. We did not use medication to ameliorate these symptoms. These symptoms gradually resolved after discontinuing the medication.

Myocardial enzymes are common indicators of myocardial damage. Under normal physiological conditions, serum myocardial enzyme levels remain extremely low; however, when the myocardium is damaged, the levels significantly increase in the bloodstream (Tilea et al, 2021). In children with bronchopneumonia accompanied by wheezing, airway obstruction can lead to myocardial cell damage due to lack of oxygen. Furthermore, high levels of myocardial enzymes, including AST, LDH, CK, and CK-MB, have been reported in children with pneumonia, suggesting a certain degree of myocardial injury (Ling et al, 2023). In this study, we also observed high levels of AST, LDH, CK, and CK-MB in patients with bronchopneumonia accompanied by wheezing, which aligns with previous findings. The combination therapy of montelukast and methylprednisolone significantly reduced these myocardial enzyme levels, suggesting an improvement in myocardial injury.

Furthermore, the combination therapy showed higher efficacy than methylprednisolone alone. The cardioprotective effect of methylprednisolone has been previously reported, with its mechanism involving oxidative stress regulation, inflammation suppression, and matrix metalloproteinase activation (Bahr et al, 2021; Krasic et al, 2023). Similarly, animal studies reported that montelukast can regulate oxidative stress, reduce inflammation, improve myocardial fibrosis, and reduce doxorubicin-induced cardiotoxicity (Hafez and Hassanein, 2022; Wu et al, 2022). These observations indicate that the combination treatment of montelukast and methylprednisolone exerts synergistic cardioprotective effects.

Hepatocyte damage can lead to the release of intracellular specific factors and metabolic enzymes into the bloodstream, along with a reduced ability of fatty acid metabolism, and albumin production (Kalas et al, 2021; Kim et al, 2021). Among liver function indicators, elevated ALT and AST levels indicate hepatocyte injury, high ALP and GGT levels suggest cholestasis, and TBIL, DBIL, and IBIL are associated with bile metabolism (Church et al, 2019; Kalas et al, 2021). Notably, AST serves as both a myocardial enzyme and a liver function indicator due to its widespread distribution in the myocardium and hepatocyte (Kobayashi et al, 2020). Previous study has reported that elevated liver enzymes are the most common ex-

trapulmonary manifestations in children with *Mycoplasma pneumoniae* pneumonia (Choi et al, 2022). Similarly, another study observed elevated liver enzymes in *Mycoplasma pneumoniae* infection, with seasonal variations, though the liver involvement was usually benign and asymptomatic (Jujaray et al, 2018). In our study, increased liver enzyme levels (ALT, ALP, and AST) were observed in patients with bronchopneumonia accompanied by wheezing, aligning with previous research (Choi et al, 2022; Jujaray et al, 2018). Additionally, the combination therapy of montelukast and methylprednisolone significantly reduced the levels of liver enzymes and bilirubin, ALT, AST, ALP, TBIL, and DBIL levels compared to methylprednisolone alone. These results suggested that montelukast and methylprednisolone can help reduce liver function impairment in bronchopneumonia. The hepatoprotective efficacy of montelukast has been reported; a randomized controlled study showed that montelukast significantly reduced liver stiffness and liver aminotransferase levels in patients with non-alcoholic steatohepatitis (Abdallah et al, 2021). However, the effects of methylprednisolone on liver function vary in different studies. One study observed methylprednisolone as an independent risk factor for drug-induced liver injury in hospitalized coronavirus disease 2019 (COVID-19) patients (Chen et al, 2023), whereas another study reported that methylprednisolone reduced chronic drug-induced liver injury, restoring liver enzyme levels to normal (Huang et al, 2024). These variations in outcomes may be attributed to differences in dosage, treatment duration, and patient populations. In our study, combination therapy demonstrated stronger hepatoprotective effects than methylprednisolone alone. However, since we did not perform long-term follow-up, we could not infer potential differences in the long-term effects of these two treatment methods on liver and cardiac health in children with bronchopneumonia and wheezing, which warrants further studies.

Eosinophils are crucial inflammatory cells which play a key role in airway hyperresponsiveness and asthma by infiltrating the entire respiratory system (Dhanjal et al, 2022). Respiratory infections can lead to increased platelet levels, as external stimuli can trigger vascular endothelial damage, inflammatory mediator release, platelet activation, coagulation, and microthrombosis (Rommel et al, 2020). In recent years, platelets have received attention as crucial components of inflammation and immunity. They interact with eosinophils by binding through ligands, forming platelet-eosinophil aggregations, which in turn enhance the production of cysteine leukotrienes (Laidlaw et al, 2012). This study found that both methylprednisolone monotherapy and combination treatment with montelukast reduced platelet and eosinophil counts in children with bronchopneumonia accompanied by wheezing, with combination therapy exhibiting better efficacy. It has been previously reported that methylprednisolone induces eosinophil apoptosis and reduces the release of inflammatory mediators, highlighting its role in managing inflammation-related conditions (Pazdrak et al, 2016). Additionally, montelukast has been reported to inhibit platelet activation (Camera et al, 2022; Trinh et al, 2019), which aligns with our results. The combination therapy of montelukast and methylprednisolone can exert a synergistic effect, potentially reducing platelet and eosinophil levels in patients with bronchopneumonia.

However, there are some limitations to this study. The sample size was small, and future investigations with expanded samples are needed to validate the findings. Furthermore, the safety and side effects of combination treatment should be further explored through prospective cohorts with larger sample sizes. Lastly, this study lacked long-term follow-up, preventing investigation of long-term effects on heart and liver health. Therefore, future studies should address these gaps by performing long-term follow-up investigations.

Conclusion

In summary, the combination of montelukast and methylprednisolone reduces platelet and eosinophil counts, alleviates myocardial and liver function damage, and demonstrates good therapeutic efficacy in children with bronchopneumonia accompanied by wheezing.

Key Points

- The combination of montelukast and methylprednisolone effectively improves clinical symptoms and shortens hospitalization time in children with bronchopneumonia accompanied by wheezing. This combination therapy exhibits better efficacy than methylprednisolone alone.
- Montelukast combined with methylprednisolone reduces platelet and eosinophil counts in bronchopneumonia children with wheezing.
- Montelukast combined with methylprednisolone reduces myocardial enzymes and liver enzyme levels in children with bronchopneumonia and wheezing, alleviating myocardial and liver damage.
- This combination therapy does not increase adverse reactions in children with bronchopneumonia accompanied by wheezing.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

WY designed the research. CD performed the experiments. KJ contributed to data analysis. WY and CD wrote the first draft. All authors contributed to revising the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the Yingshang County People's Hospital ethics committee (Approval number: 20220402). Patients and guardians were informed

and consented to the study. Research procedures complied with the Declaration of Helsinki.

Acknowledgement

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

- Abdallah MS, Eldeen AH, Tantawy SS, Mostafa TM. The leukotriene receptor antagonist montelukast in the treatment of non-alcoholic steatohepatitis: A proof-of-concept, randomized, double-blind, placebo-controlled trial. *European Journal of Pharmacology*. 2021; 906: 174295. <https://doi.org/10.1016/j.ejphar.2021.174295>
- Aliyali M, Abedi S, Sharifpour A, Ghadirzadeh E, Fattahi M, Yazdani Charati J, et al. Effects of oral montelukast on pulmonary function and clinical symptoms in acute asthma exacerbations: a randomized, double-blind, placebo-controlled trial. *Annals of Medicine and Surgery*. 2024; 86: 5837–5843. <https://doi.org/10.1097/MS9.0000000000002507>
- Bahr AC, Luz JPD, Teixeira RB, Türk P, Zimmer A, Castro ALD, et al. The brief methylprednisolone administration is crucial to mitigate cardiac dysfunction after myocardial infarction. *Anais Da Academia Brasileira De Ciencias*. 2021; 93: e20210297. <https://doi.org/10.1590/0001-376520210210297>
- Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2011; 53: e25–76. <https://doi.org/10.1093/cid/cir531>
- Camera M, Canzano P, Brambilla M, Rovati GE. Montelukast Inhibits Platelet Activation Induced by Plasma From COVID-19 Patients. *Frontiers in Pharmacology*. 2022; 13: 784214. <https://doi.org/10.3389/fphar.2022.784214>
- Chen Y, Shi C, Zhan H, Yang B, Liu J, Rong P, et al. Drug-induced liver injury in COVID-19 patients during hospitalization. *Medicine*. 2023; 102: e33294. <https://doi.org/10.1097/MD.00000000000033294>
- Choi YJ, Chung EH, Lee E, Kim CH, Lee YJ, Kim HB, et al. Clinical Characteristics of Macrolide-Refractory Mycoplasma pneumoniae Pneumonia in Korean Children: A Multicenter Retrospective Study. *Journal of Clinical Medicine*. 2022; 11: 306. <https://doi.org/10.3390/jcm11020306>
- Church RJ, Kullak-Ublick GA, Aubrecht J, Bonkovsky HL, Chalasani N, Fontana RJ, et al. Candidate biomarkers for the diagnosis and prognosis of drug-induced liver injury: An international collaborative effort. *Hepatology*. 2019; 69: 760–773. <https://doi.org/10.1002/hep.29802>
- Dhanjal DS, Sharma P, Mehta M, Tambuwala MM, Prasher P, Paudel KR, et al. Concepts of advanced therapeutic delivery systems for the management of remodeling and inflammation in airway diseases. *Future Medicinal Chemistry*. 2022; 14: 271–288. <https://doi.org/10.4155/fmc-2021-0081>
- Douros K, Everard ML. Time to Say Goodbye to Bronchiolitis, Viral Wheeze, Reactive Airways Disease, Wheeze Bronchitis and All That. *Frontiers in Pediatrics*. 2020; 8: 218. <https://doi.org/10.3389/fped.2020.00218>
- Hafez HM, Hassanein H. Montelukast ameliorates doxorubicin-induced cardiotoxicity via modulation of p-glycoprotein and inhibition of ROS-mediated TNF- α /NF- κ B pathways. *Drug and Chemical Toxicology*. 2022; 45: 548–559. <https://doi.org/10.1080/01480545.2020.1730885>

- Huang A, Zhu Y, Liu S, Sun Y, Liu Z, Liang QS, et al. An optimized short-term steroid therapy for chronic drug-induced liver injury: A prospective randomized clinical trial. *Liver International*. 2024; 44: 1435–1447. <https://doi.org/10.1111/liv.15899>
- Juvaray D, Juan LZ, Shrestha S, Ballgobin A. Pattern and Significance of Asymptomatic Elevation of Liver Enzymes in Mycoplasma Pneumonia in Children. *Clinical Pediatrics*. 2018; 57: 57–61. <https://doi.org/10.1177/0009922816688737>
- Kalas MA, Chavez L, Leon M, Taweeseedt PT, Surani S. Abnormal liver enzymes: A review for clinicians. *World Journal of Hepatology*. 2021; 13: 1688–1698. <https://doi.org/10.4254/wjh.v13.i11.1688>
- Kevat PM, Morpeth M, Graham H, Gray AZ. A systematic review of the clinical features of pneumonia in children aged 5-9 years: Implications for guidelines and research. *Journal of Global Health*. 2022; 12: 10002. <https://doi.org/10.7189/jogh.12.10002>
- Kim TH, Hong DG, Yang YM. Hepatokines and Non-Alcoholic Fatty Liver Disease: Linking Liver Pathophysiology to Metabolism. *Biomedicines*. 2021; 9: 1903. <https://doi.org/10.3390/biomedicines9121903>
- Kobayashi A, Suzuki Y, Sugai S. Specificity of transaminase activities in the prediction of drug-induced hepatotoxicity. *The Journal of Toxicological Sciences*. 2020; 45: 515–537. <https://doi.org/10.2131/jts.45.515>
- Krasic S, Vukomanovic V, Ninic S, Pasic S, Samardzija G, Mitrovic N, et al. Mechanisms of redox balance and inflammatory response after the use of methylprednisolone in children with multisystem inflammatory syndrome associated with COVID-19. *Frontiers in Immunology*. 2023; 14: 1249582. <https://doi.org/10.3389/fimmu.2023.1249582>
- Laidlaw TM, Kidder MS, Bhattacharyya N, Xing W, Shen S, Milne GL, et al. Cysteinyl leukotriene overproduction in aspirin-exacerbated respiratory disease is driven by platelet-adherent leukocytes. *Blood*. 2012; 119: 3790–3798. <https://doi.org/10.1182/blood-2011-10-384826>
- Liapikou A, Torres A. The clinical management of lower respiratory tract infections. *Expert Review of Respiratory Medicine*. 2016; 10: 441–452. <https://doi.org/10.1586/17476348.2016.1156537>
- Ling BJ, Wan YM. The application of probiotic after antibiotics treatment promotes the recovery of pediatric bronchopneumonia infection. *European Review for Medical and Pharmacological Sciences*. 2023; 27: 4103–4107. https://doi.org/10.26355/eurrev_202305_32318
- Ling Y, Yang D, Yang S. Clinical characteristics, early blood biochemical indicators, and prognostic status of children with bronchopneumonia. *Medicine*. 2023; 102: e36162. <https://doi.org/10.1097/MD.00000000000036162>
- Mani CS. 34 - Acute Pneumonia and Its Complications. In Long SS, Prober CG, Fischer M (eds.) *Principles and Practice of Pediatric Infectious Diseases*. 5th edn. Elsevier: Philadelphia. 2017. <https://doi.org/10.1016/B978-0-323-40181-4.00034-7>
- Marques CF, Marques MM, Justino GC. Leukotrienes vs. Montelukast-Activity, Metabolism, and Toxicity Hints for Repurposing. *Pharmaceuticals*. 2022; 15: 1039. <https://doi.org/10.3390/ph15091039>
- Meduri GU, Shih MC, Bridges L, Martin TJ, El-Solh A, Seam N, et al. Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. *Intensive Care Medicine*. 2022; 48: 1009–1023. <https://doi.org/10.1007/s00134-022-06684-3>
- Mehta J, Rolta R, Mehta BB, Kaushik N, Choi EH, Kaushik NK. Role of Dexamethasone and Methylprednisolone Corticosteroids in Coronavirus Disease 2019 Hospitalized Patients: A Review. *Frontiers in Microbiology*. 2022; 13: 813358. <https://doi.org/10.3389/fmicb.2022.813358>
- Pazdrak K, Moon Y, Straub C, Stafford S, Kurosky A. Eosinophil resistance to glucocorticoid-induced apoptosis is mediated by the transcription factor NFIL3. *Apoptosis*. 2016; 21: 421–431. <https://doi.org/10.1007/s10495-016-1226-5>
- Reichardt SD, Amouret A, Muzzi C, Vettorazzi S, Tuckermann JP, Lühder F, et al. The Role of Glucocorticoids in Inflammatory Diseases. *Cells*. 2021; 10: 2921. <https://doi.org/10.3390/cells10112921>
- Rommel MGE, Milde C, Eberle R, Schulze H, Modlich U. Endothelial-platelet interactions in influenza-induced pneumonia: A potential therapeutic target. *Anatomia, Histologia, Embryologia*. 2020; 49: 606–619. <https://doi.org/10.1111/ahc.12521>
- Tilea I, Varga A, Serban RC. Past, Present, and Future of Blood Biomarkers for the Diagnosis of Acute Myocardial Infarction-Promises and Challenges. *Diagnostics*. 2021; 11: 881.

<https://doi.org/10.3390/diagnostics11050881>

- Tong S, Gao S, Cui Y, Jin H, Liu L, Xie X, et al. Incidence, Associated Factors, and Prognosis of Liver Dysfunction in Children with Community-Acquired Pneumonia: A Multicenter Prospective Study. *Journal of Pediatric Infectious Diseases*. 2024; 19: 294–300. <https://doi.org/10.1055/s-0044-1789012>
- Trinh HKT, Nguyen TVT, Choi Y, Park HS, Shin YS. The synergistic effects of clopidogrel with montelukast may be beneficial for asthma treatment. *Journal of Cellular and Molecular Medicine*. 2019; 23: 3441–3450. <https://doi.org/10.1111/jcmm.14239>
- Wang C, Zhang X, Qian W, Liu X, Zhang W. Budesonide combined with ipratropium bromide in the treatment of bronchopneumonia and its efficacy on pulmonary function. *International Journal of Clinical and Experimental Medicine*. 2020; 13: 1092–1097. <https://e-century.us/files/ijcem/13/2/ijcem0104805.pdf>
- Wang F, Cheng Q, Duo H, Wang J, Yang J, Jing S, et al. Childhood Mycoplasma pneumoniae: epidemiology and manifestation in Northeast and Inner Mongolia, China. *Microbiology Spectrum*. 2024; 12: e00097-24. <https://doi.org/10.1128/spectrum.00097-24>
- World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses. 2nd edn. World Health Organization: Geneva. 2013. <https://www.ncbi.nlm.nih.gov/books/NBK154447/>
- Wu H, Ding X, Zhao D, Liang Y, Ji W. Effect of montelukast combined with methylprednisolone for the treatment of mycoplasma pneumonia. *The Journal of International Medical Research*. 2019; 47: 2555–2561. <https://doi.org/10.1177/0300060518820412>
- Wu Y, Cui C, Bi FF, Wu CY, Li JR, Hou YM, et al. Montelukast, cysteinyl leukotriene receptor 1 antagonist, inhibits cardiac fibrosis by activating APJ. *European Journal of Pharmacology*. 2022; 923: 174892. <https://doi.org/10.1016/j.ejphar.2022.174892>
- Ye J, Ye H, Wang M, Zhao Y. Total serum IL-6 and TNF- α levels in children with bronchopneumonia following treatment with methylprednisolone in combination with azithromycin. *American Journal of Translational Research*. 2021; 13: 9458–9464. <https://e-century.us/files/ajtr/13/8/ajtr0129239.pdf>
- Zade A, Akhuj A, Lalwani L, Jhunjunwala S, Daf RV. Physiotherapy Approach for Treating Bronchopneumonia: A Case Report. *Cureus*. 2023; 15: e51246. <https://doi.org/10.7759/cureus.51246>
- Zhang L, Zhao S. Severe liver injury affects the outcomes and length of hospital stay in children with community-acquired pneumonia. *African Health Sciences*. 2022; 22: 578–589. <https://doi.org/10.4314/ahs.v22i3.62>
- Zhao D, Chen M, Shi K, Ma M, Huang Y, Shen J. A long short-term memory-fully connected (LSTM-FC) neural network for predicting the incidence of bronchopneumonia in children. *Environmental Science and Pollution Research International*. 2021; 28: 56892–56905. <https://doi.org/10.1007/s11356-021-14632-9>