doi.org/10.36721/PJPS.2025.38.4.REG.13415.1

To observe the effect of acetylcysteine combined with diphylline on pulmonary function and inflammatory response in children with bronchopneumonia

Lian Zhang
Department of pediatrics, Lixin People's Hospital, Bozhou, Anhui, China.

Abstract: Bronchopneumonia is an extremely common respiratory disease in children, which may cause bronchiectasis, respiratory failure, and other complications. In this study, we observed the effect of acetylcysteine combined with diphylline in the treatment of bronchopneumonia. This includes the session time of the child's cough and wheezing symptoms, lung function, and the inflammatory response before and after treatment. In addition, we also counted the adverse reactions during the treatment of the children. The results of the study showed that children in the research group treated with acetylcysteine combined with diphylline had a shorter time to symptomatic relief compared to the control group using bronchopneumonia ($P<0.05$). Also, the lung function after treatment was better in the research group than in the control group, and the levels of inflammatory factors were lower in the research group than in the control group ($P<0.05$). There was no difference in the incidence of adverse reactions between the two groups ($P>0.05$). These results suggest that acetylcysteine combined with diphylline has excellent potential for the treatment of bronchopneumonia.

Keywords: Bronchopneumonia, acetylcysteine, diphylline, lung function, inflammatory response

Submitted on 13-09-2024 – Revised on 13-03-2025 – Accepted on 24-04-2025

INTRODUCTION

Bronchopneumonia, one of the most common respiratory diseases (Singh *et al.*, 2024). Bronchopneumonia has no specific epidemic tendency, with an average incidence of up to 5% (Taylor *et al.*, 2022). Due to the incomplete development of the respiratory and immune systems in children, the likelihood of contracting and having a relapse of bronchopneumonia is significantly increased compared to adults (Patel *et al.*, 2021). Statistics show that approximately 6% of children suffer from bronchopneumonia 6-8 times within a year (Hoerr, 2021). The occurrence of bronchopneumonia may not only lead to complications such as bronchiectasis and respiratory failure but also leave irreversible respiratory tract damage after the illness, ultimately resulting in the occurrence of asthma and other conditions (Ghazaly *et al.*, 2021). Thus, the treatment of children with bronchopneumonia holds extremely important clinical significance.

Most children with bronchopneumonia have bronchial mucosal inflammation. Therefore, anti-infective drugs are not routinely used in treatment but rather the focus is on relieving the tension of airway smooth muscles (Fu *et al.*, 2021). Among them, diphylline is a commonly used theophylline drug in clinical practice, which has been proven to have many advantages such as improving the relaxation of respiratory smooth muscles, promoting the discharge of respiratory secretions, and improving ventilation function (Morina *et al.*, 2018). diphylline is commonly employed in the treatment of asthma, emphysema, etc. (Adikusuma *et al.*, 2022). However, for bronchopneumonia, the use of diphylline alone has been shown to be less effective and cannot achieve rapid relief of clinical symptoms in children (Simpson *et al.*, 2009). Acetylcysteine is an excellent mucolytic agent, which also has anti-inflammatory and respiratory mucosa protection effects, and is suitable for respiratory diseases with excessive thick mucus secretions (Calverley *et al.*, 2021). In bronchopneumonia, the adjuvant therapeutic effect of Acetylcysteine has been preliminarily validated (Ershad *et al.*, 2024). However, there is no research to confirm the application effect of Acetylcysteine combined with diphylline.

In this regard, this study will confirm the application value of Acetylcysteine combined with diphylline in the treatment of bronchopneumonia by observing the symptom improvement of children with bronchopneumonia treated with this treatment regimen, so as to provide a new option for the future treatment of bronchopneumonia and further improve the prognostic health of children.

MATERIALS AND METHODS

Research subjects

Children with bronchopneumonia admitted to Lixin People's Hospital from March, 2022 to January, 2024 were randomly selected as the research subjects. The sample size required for the study was calculated using the Power and Sample Size (PASS) software. After the screening by inclusion and exclusion criteria presented below, 45 cases of bronchopneumonia children treated with Acetylcysteine combined with diphylline were included as the research

*Corresponding author: e-mail: 15088692424@163.com

group. Subsequently, 45 children with bronchopneumonia treated with diphylline were included as the control group in a 1:1 ratio. This study has been approved by the Ethics Committee of Lixin People's Hospital (KL2022041) and strictly followed the Helsinki Declaration. fig. 1 shows the flow of this research.

Inclusion and exclusion criteria

Inclusion criteria: (1) Aged 1 to 12 years; (2) Exhibiting significant bronchopneumonia symptoms (cough, wheezing, etc.), meeting the bronchopneumonia diagnostic criteria (Manti *et al.*, 2023) and being diagnosed in our hospital; (3) Illness duration less than 72 hours; (4) Complete clinical data; (5) Signed informed consent provided by guardians. Exclusion criteria: (1) Previous history of respiratory tract surgery; (2) Complicated with other respiratory diseases (such as asthma, tuberculosis, etc.); (3) Complicated with functional impairments of other organs such as the heart, liver, and kidneys; (4) Drug allergies; (5) Congenital pulmonary hypoplasia or immunodeficiency.

Treatment methods

Upon the children's admission to the hospital, they were given corresponding targeted nursing management and budesonide nebulization (125 μg per time, twice a day for 14 consecutive days) for inhalation treatment. (1) Nurses closely monitored the children's consciousness, complexion, vital signs, and changes in peripheral circulation, and contacted the doctor in time once the condition changed. In the event of nausea and vomiting, the nebulization inhalation would be stopped, and then resumed after a short break. For those with hypoxia, oxygen was appropriately administered, the oxygen flow rate was controlled, and the patency of the oxygen supply conduit was checked. In case of mild hypoxia, oxygen was supplied through a nasal catheter with the oxygen flow rate controlled at 1-2 L/min. (2) During nebulization inhalation, appropriate nebulization equipment was selected based on the child's age. For younger children, mask inhalation nebulization was chosen as much as possible, while for older children, mouthpiece nebulization was adopted. The children and their families were guided to master the correct usage method of nebulization equipment to avoid improper operation that could stimulate the respiratory tract. After atomizing inhalation, the family members were told to use gauze to dry the mist near the mouth and nose of the child. In addition, the nursing staff paid attention to the relief of the symptoms of wheezing and the presence of hoarseness and candida infection in the mouth. (3) During treatment and nursing, medical staff diverted the child's attention through various means such as touching, telling stories, and watching cartoons to relieve the discomfort caused by the disease or treatment. (4) Adequate monitoring of the child's vital signs was carried out. If the child's body temperature rose, targeted cooling measures were implemented, adhering to the principle of physical cooling first and then drug cooling. (5) The child's parents were advised to give the child a liquid or semi-liquid diet rich in calories and vitamins and easy to digest, following the principle of eating small and frequent meals to avoid being overly full and affecting breathing. (6) Relevant knowledge about bronchopneumonia was popularized to children and their family members through various methods such as collective lectures, watching videos, and individualized guidance. Questions from children and their family members were answered in a timely manner, and interactions were enhanced through question-and-answer and other forms to mobilize their enthusiasm. In addition, the two groups of children received the following treatment: Control group: 0.10-0.15g of diphylline (Shaanxi Lizhong Pharmaceutical Co., Ltd., H20046691) was dissolved in 100mL of sodium chloride solution for intravenous drip, once a day for 7 consecutive days, Research group: On the basis of the control group, Acetylcysteine (Hunan Warrant Chiral Pharmaceutical Co., Ltd., H20183186, 0.3g/time, twice a day for 7 days in a row) nebulization therapy was additionally provided.

Follow-up for prognosis

All children were followed up for prognostic recurrence for six months in the form of regular reexaminations. The reexamination interval was no more than one month, and the prognostic recurrence status was recorded.

Endpoints

(1) Clinical efficacy (Baillie *et al.*, 2022). Cured: After treatment, all clinical symptoms disappear completely and the X-ray examination results are normal. Effective: The symptoms are alleviated, and punctate shadows can still be seen in the lungs on X-ray examination. Ineffective: Not meeting the above criteria. Total effective rate = (cured +effective) cases/total population × 100%. (2) Lung function. Before and after treatment, a pulmonary function instrument was used to detect forced vital capacity (FVC), forced expiratory volume in one second (FEV1), maximum mid-expiratory flow (MMEF), and fractional exhaled nitric oxide (FeNO). Arterial blood was collected, and arterial partial pressure of oxygen (PaO_2) and arterial partial pressure of carbon dioxide ($PaCO_2$) were detected using a blood gas analyzer. (3) Inflammatory reaction. The sputum of the child was collected into a sterile container. 3mL of thick sputum plugs was selected cracked, and centrifuged to discard the supernatant, followed by precipitation, smearing, and staining. The proportion of eosinophilic cells (EOS) in induced sputum was detected and recorded using an optical microscope. In addition, C-reactive protein (CRP) was measured with a biochemical analyzer, and endothelin-1 (ET-1) and interleukin-8 (IL-8) were detected by enzyme-linked immunosorbent assay before and after treatment. (4) Adverse reactions. The adverse reactions during treatment, such as nausea, vomiting, diarrhea, and rash, were counted. (5) compliance. Complete compliance: The child can complete the relevant treatment and follow-

up strictly in accordance with the doctor's advice. Partial compliance: The child can complete the relevant treatment following the doctor's advice most of the time. Non-compliance: The child has non-cooperative behavior. Total compliance rate = (complete compliance + partial compliance) cases/total number of people × 100%. (6) Family satisfaction. The evaluation was carried out at discharge by the Newcastle Satisfaction with Nursing Scale (NSNS) (Rodriguez-Herrera *et al.*, 2021). 85-100 points: very satisfied, 60-85 points: satisfied, 0-60 points: dissatisfied. (7) The prognostic recurrence rate of bronchopneumonia was recorded.

STATISTICAL ANALYSIS

SPSS 22.0 software was utilized for statistical analysis. All the counting data [n(%)] were compared by chi-square test. For continuous variables, the Shapiro-Wilk test was used to test for normality. For continuous variables conforming to a normal distribution ($\bar{\chi}$±s), independent sample t-test and paired t-test were used for comparison; for data not conforming to a normal distribution [median (interquartile range)], Mann-Whitney U test and Wilcoxon rank sum test were employed for comparison. The recurrence rate was calculated by the Kaplan-Meier method, and the comparison was made by the Log-rank test. A P value less than 0.05 was considered statistically significant.

RESULTS

Research on comparability between groups

To ensure the reliability of the research results, we first comparatively analyzed the clinical baseline data of the two groups. The two groups were confirmed to be comparable as there was no statistically significant difference in the comparison of data such as age, gender, disease duration, and family disease history (P>0.05, table 1).

Clinical efficacy

The clinical efficacy of the two groups of children was counted (table 2). The number of cured children was greater in the research group compared to the control group (P<0.05). In terms of symptom relief, the relief time of wheezing, coughing, and expectoration in the research group was (3.51±0.99)d, (5.62±0.94)d, and (4.13±0.97)d, respectively, all of which were shorter compared with the control group (P<0.05).

Lung function

As shown in fig. 2, there was no difference in the lung function test results between the two groups of children before treatment (P>0.05). After treatment, FVC, FEV1, MMEF, and PaO_2 in both groups increased, while FeNO and $PaCO_2$ decreased (P<0.05). Among them, the post-treatment FVC, FEV1, MMEF, and PaO_2 of the research group were (2.65±0.34)L, (16.69±4.39)L, (3.33±0.30)L/s, and (84.82±6.71)mmHg, respectively, all of which were higher than those in the control group (P<0.05); FeNO and $PaCO_2$ were $(16.69±4.39)×10^9$ mol/mL, (36.41±5.26) mmHg after treatment, respectively, lower compared to the control group (P<0.05).

Inflammatory reaction

As shown in fig. 3, the two groups were also not statistically different in the comparison of inflammatory factors before treatment (P>0.05). After treatment, the detection results of sputum EOS proportion, CRP, ET-1, and IL-8 in the control group were (3.29±0.94)%, (5.56±1.14)mg/L, (59.55±9.96)pg/mL, and (57.39±7.75) pg/mL, respectively, all of which were lower than those before treatment (P<0.05). While those in the research group were (2.20±0.59)%, (4.67±0.84)mg/L, (37.95±8.95) pg/mL, and (39.73±7.60)pg/mL, respectively, which were also reduced compared to the pre-treatment levels and slightly lower than those in the control group (P<0.05).

Adverse reactions

Statistics (table 3) showed that the children in the research group developed adverse reactions such as rash, vomiting, diarrhea, and insomnia, while adverse reactions such as rash, vomiting, diarrhea and headache occurred in the control group. No significant difference in the incidence of each adverse reaction was found between the two groups (P>0.05).

Treatment compliance rate and family satisfaction

According to the survey (table 4), the total compliance rate of the research group was 88.89%, which was not statistically different compared to the 88.89% of the control group (P>0.05). In addition, the total satisfaction of family members in the research group was 95.53%, which was equivalent to that of the control group (P>0.05).

Prognostic recurrence

Finally, in the 6-month follow-up survey, we successfully tracked all the subjects. The recurrence rate of bronchopneumonia at 6 months was 6.67% in the research group and 11.11% in the control group, with no statistical significance (P>0.05, fig. 4).

DISCUSSION

In this study, we found that Acetylcysteine combined with diphylline is remarkably effective and is expected to become a new treatment option for bronchopneumonia.

First of all, the number of cured children was markedly greater in the research group (P<0.05), suggesting that compared with the single use of diphylline, its combination of Acetylcysteine can achieve more significant therapeutic effects.

Table 1: Comparison of clinical data

Group (n=45)	Age	Sex		Disease duration (d)	family disease history	
		Boys	Girls		Have	None
Control	5.20±1.74	30 (66.67)	15 (33.33)	10.62±3.37	6 (13.33)	39 (86.67)
Research	5.47±1.55	27 (60.00)	18 (40.00)	11.47±3.44	5 (11.11)	40 (88.89)
t (or χ^2)	0.769	0.431		1.177	0.104	
P	0.444	0.512		0.243	0.748	

Table 2: Comparison of clinical efficacy

Group (n=45)	Clinical efficacy				Time to symptom relief		
	Cured	Effective	Ineffective	Total effective rate	Wheezing	Coughing	Expectoration
Control	18 (40.00)	21 (46.67)	6 (13.33)	86.67	4.24±0.86	6.18±1.05	4.71±0.92
Research	28 (62.22)	14 (31.11)	3 (6.67)	93.33	3.51±0.99	5.62±0.94	4.13±0.97
χ^2 (or t)	4.447	2.291	1.111	1.111	3.754	2.648	2.903
P	0.035	0.130	0.292	0.292	<0.001	0.010	0.005

Table 3: Comparison of adverse effects

Group (n=45)	Rash	Vomiting	Diarrhea	Insomnia	Headache	Adverse reaction
Control	1 (2.22)	1 (2.22)	2 (4.44)	0 (0.00)	1 (2.22)	11.11
Research	1 (2.22)	2 (4.44)	2 (4.44)	2 (4.44)	0 (0.00)	15.56
Fisher's exact (or χ^2)	-	-	-	-	-	0.385
P	1.000	1.000	1.000	0.494	1.000	0.535

Table 4: Comparison of treatment compliance rate and satisfaction of family satisfaction

Group (n=45)	Treatment compliance		Family satisfaction			
	Yes	No	Very satisfied	Satisfied	Dissatisfied	Total satisfaction (very satisfied + satisfied)
Control	40 (88.89)	5 (11.11)	30 (66.67)	12 (26.67)	3 (6.67)	93.33
Research	41 (91.11)	4 (8.89)	33 (73.33)	10 (22.22)	2 (4.44)	95.56
χ^2	0.124					0.212
P	0.725					0.645

At the same time, the research group had a shorter time to recovery from symptoms ($P<0.05$), indicating that Acetylcysteine combined with diphylline can improve the clinical symptoms of children with bronchopneumonia more rapidly and play a role in quickly alleviating the progression of bronchopneumonia. After the onset of bronchopneumonia, the airway undergoes structural remodeling under inflammatory stimulation and oxidative stress under various pathological conditions, and the balance between airway secretion and clearance is disrupted, resulting in sputum retention and increased sputum viscosity, which is also one of the main pathological changes in the progression of bronchopneumonia (Li *et al.*, 2021; Dilworth *et al.*, 2022). Relying solely on the respiratory dilation effect of diphylline may not achieve a complete cure for the pathological damage caused by bronchopneumonia.

Additionally, Acetylcysteine can stimulate ciliary movement and increase the clearance function of mucosal cilia, thus achieving the therapeutic purposes of relieving airflow obstruction and preventing pulmonary infections (Papi *et al.*, 2024). Therefore, in this study, we observed better clinical efficacy and shorter symptom relief time in the research group. At the same time, Wei J *et al.* pointed out that Acetylcysteine can also inhibit glutathione, antagonize the toxicity of bivalent aldehydes, reduce the pool of protein sulfhydryl system, limit the release of cytokines in the initial stage of immune proliferation, and reduce the activity of nuclear factor-κB, so as to play a role in inhibiting oxidative stress and inflammatory responses, enhance the protective ability of airway mucosa, and alleviate inflammation and pathological changes (Wrotek *et al.*, 2024). This is confirmed by the fact that the inflammatory response is lower and lung function is better after treatment in the two groups of children in this study. In addition, in a study by Khalatbari Mohseni G et al. on the treatment of multiple sclerosis with Acetylcysteine, it was also found that the use of Acetylcysteine not only helps to improve clinical therapeutic effects, but also improves prognostic lung function (Khalatbari Mohseni *et al.*, 2023), which is consistent with our research results.

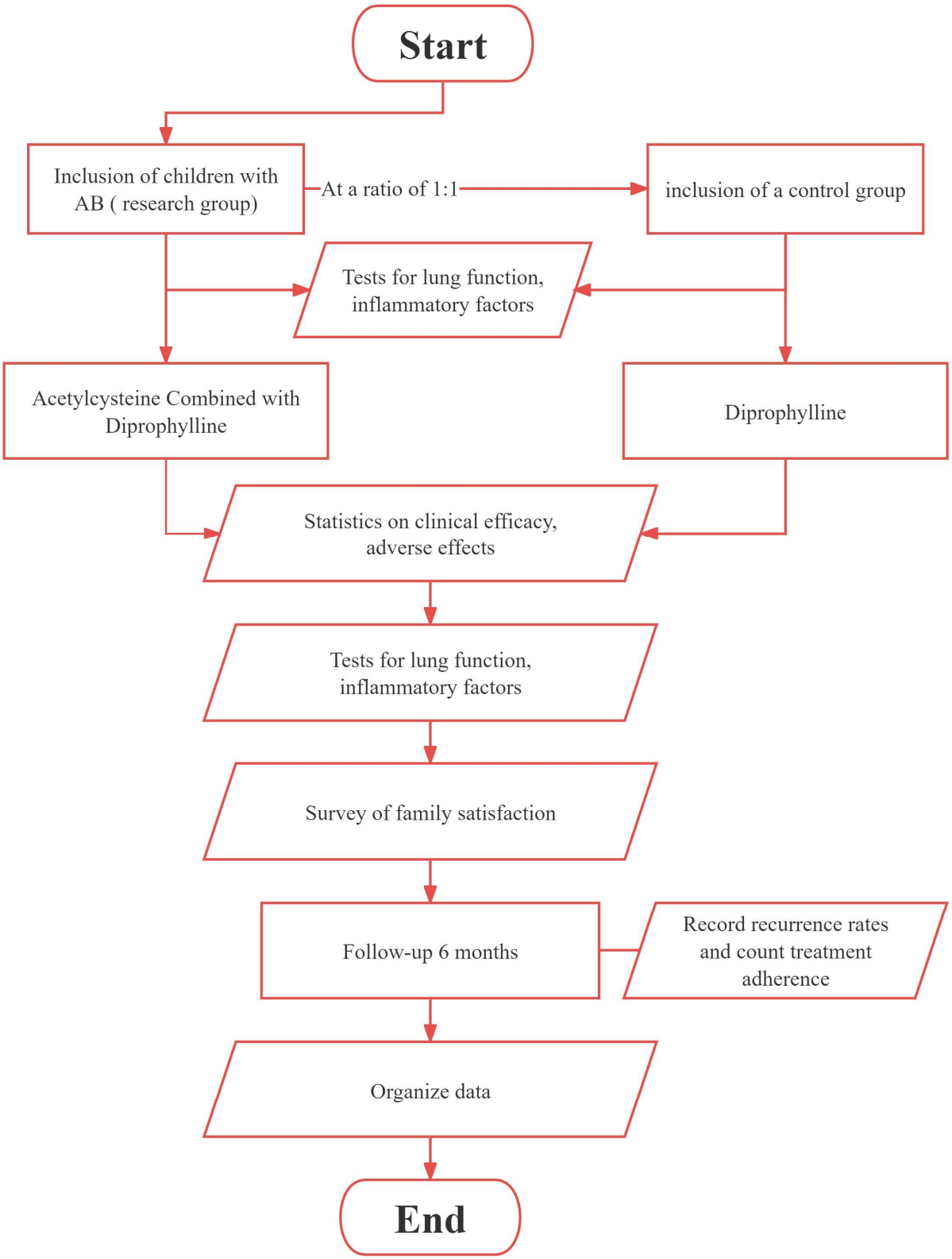

Fig. 1: Flow chart of this study.

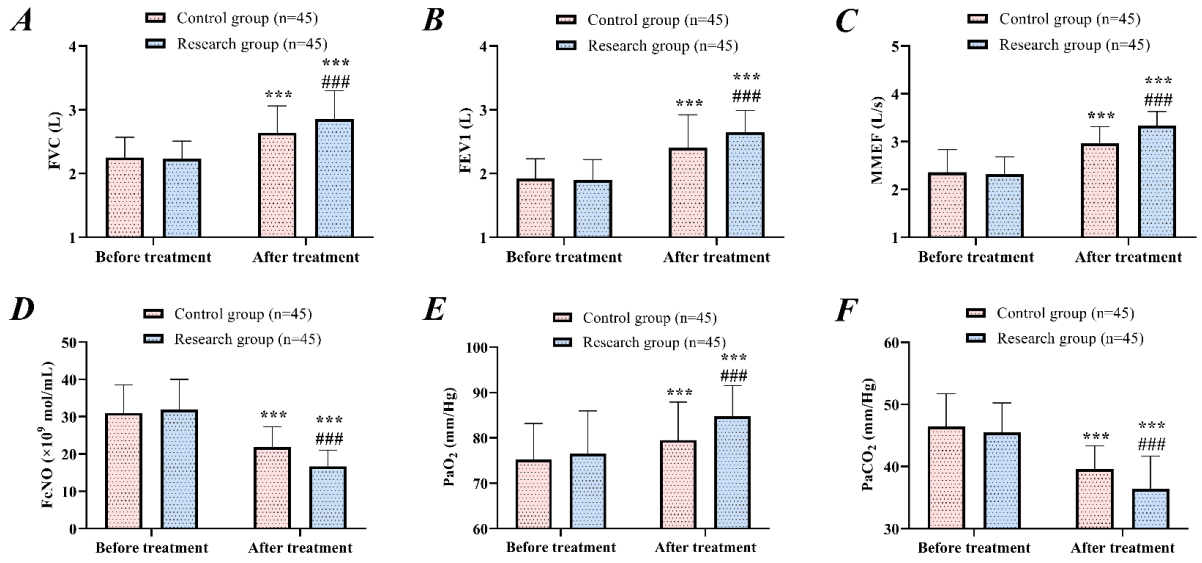

Fig. 2: Comparison of lung function. A) change in FVC before and after treatment, B) change in FVC1 before and after treatment, C) change in MMSE before and after treatment, D) change in FeNO before and after treatment, E) change in PaO_2 before and after treatment, F) change in $PaCO_2$ before and after treatment. Comparison with before treatment ***P<0.001, comparison with control group ####P<0.001.

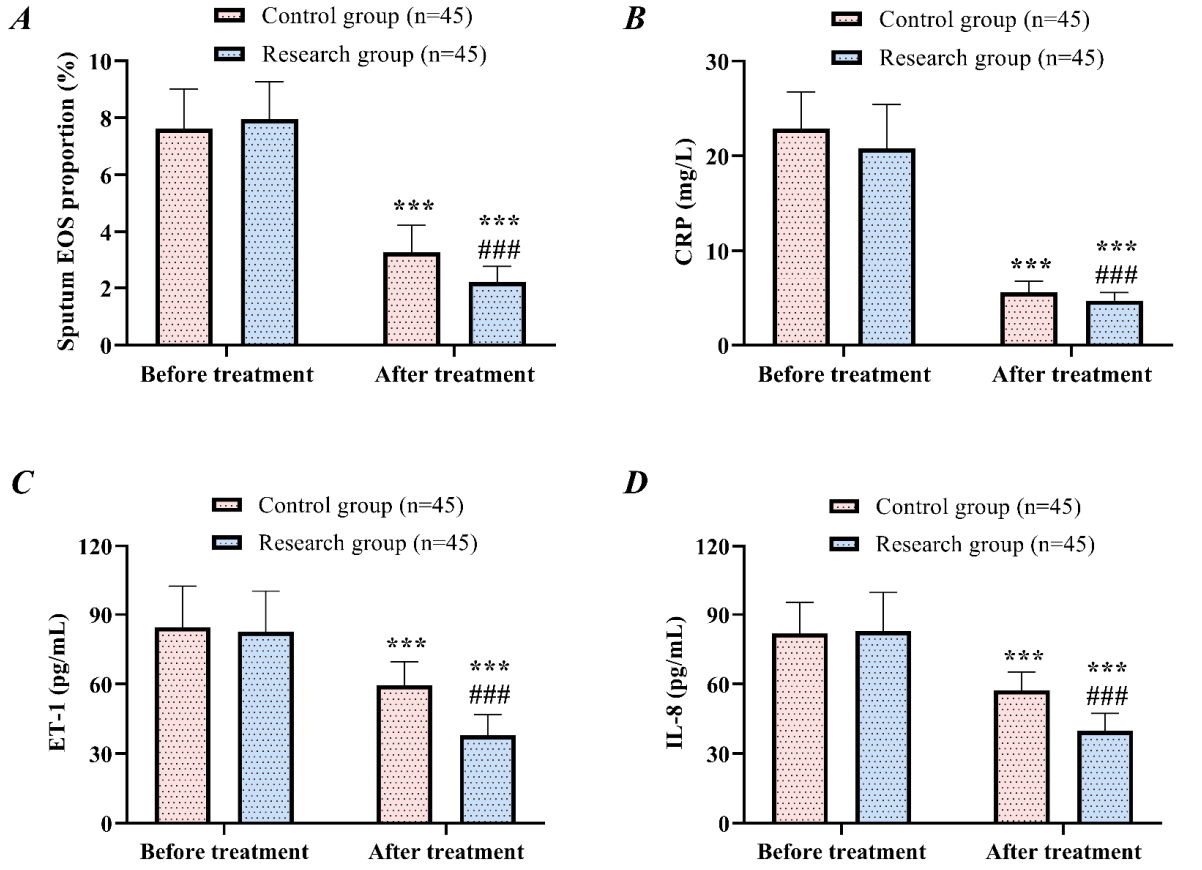

Fig. 3: Comparison of inflammatory responses. A) change in sputum EOS proportion before and after treatment, B) change in CRP before and after treatment, C) change in ET-1 before and after treatment, D) change in IL-8 before and after treatment. Comparison with before treatment ***P<0.001, comparison with control group ####P<0.001.

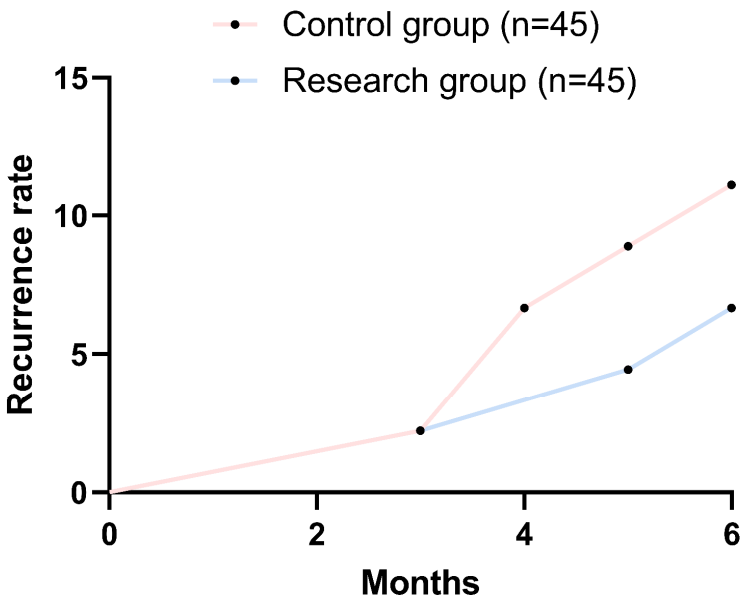

Fig. 4: Comparison of prognostic recurrence rates.

Furthermore, we found that Acetylcysteine combined with diphylline also has high safety. However, this is inconsistent with the findings of Chen H *et al.* (Chen *et al.*, 2023), who used Acetylcysteine injection to treat chronic obstructive pulmonary disease and found obvious dizziness and vomiting in patients, possibly related to the effect of Acetylcysteine on gastrointestinal peristalsis (Tang *et al.*, 2023). In this study, Acetylcysteine was administered by nebulization inhalation, which can directly act on the bronchial mucosa and exert a therapeutic effect through mucosal absorption and high-concentration action, usually without causing obvious adverse reactions. Of course, this may also be related to the small number of cases in this study, as we also observed no significant difference in the prognostic recurrence rate between the two groups of children in the follow-up results.

Unlike adults, children with bronchopneumonia are not mentally mature and may have greater rebellious tendencies, which can greatly affect treatment compliance (Todd K *et al.*, 2023). In this study, the treatment compliance of both groups of children reached more than 98%. We believe that by conducting health education for children and their families and comprehensively explaining knowledge about diseases, treatment, and nursing, their disease awareness can be improved, which helps to obtain their cooperation. Besides, conducting psychological care, diverting their attention, and using various non-verbal communication skills to reduce children's negative psychology can effectively reduce or avoid non-compliance during nebulization treatment. In terms of environmental care, providing children and their families with a good treatment and hospitalization environment can also improve their physiological comfort. Through these measures, children and their families can be in a good physical and mental state, and a harmonious nurse-patient relationship can be established with children and their families, contributing to an enhancement in compliance and satisfaction of children and their families.

There are some limitations in this paper that cannot be ignored. For example, smaller number of cases, shorter study period. Also, we need to add more objective clinical indicators to evaluate the effect of Acetylcysteine combined with diphylline on Bronchopneumonia, such as immunoglobulins. Finally, we also need to compare the therapeutic effect of Acetylcysteine combined with diphylline with other therapeutic options to provide a more comprehensive clinical reference.

CONCLUSION

Acetylcysteine combined with diphylline provides rapid relief of coughing and wheezing and improves lung function in children with Bronchopneumonia. At the same time, this program can also effectively inhibit the inflammatory response of the children, which has a high clinical application value.

Conflicts of interest

The authors report no conflict of interest.

Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Acknowledgements

Not applicable

REFERENCES

Adikusuma W, Chou WH, Lin MR, Ting J, Irham LM, Perwitasari DA, Chang WP and Chang WC (2022). Identification of Druggable genes for asthma by integrated genomic network analysis. *Biomedicines.*, **10**(1): 113.

Baillie EJ, Merlo G, Magin P, Tapley A, Mulquiney KJ, Davis JS, Fielding A, Davey A, Holliday E, Ball J, Spike N, FitzGerald K and van Driel ML (2022). Antibiotic prescribing for upper respiratory tract infections and acute bronchitis: A longitudinal analysis of general practitioner trainees. *Fam. Pract.*, **39**(6): 1063-1069.

Morina N, Haliti A, Iljazi A, Islami D, Bexheti S, Bozalija A and Islami H (2018). Comparison of effect of leukotriene biosynthesis blockers and inhibitors of phosphodiesterase enzyme in patients with bronchial hyperreactivity. *Open Access Maced. J. Med. Sci.,* **6**(5): 777-781.

Calverley P, Rogliani P and Papi A (2021). Safety of N-acetylcysteine at high doses in chronic respiratory diseases: A Review. *Drug. Saf.*, **44**(3): 273-290.

Chen H, Zhou H, Luo C, Zong K, Fu Y, Li W, Luo C, Xue G, Jiang E, Duan Y, Luo T and Jiang Y (2023). Efficacy of treatment with N-acetylcysteine inhalation for AECOPD: A propensity-score-matched cohort study. *Clin. Respir. J.*, **17**(10): 1038-1047.

Dilworth TJ, Hietpas K, Kram JJF and Baumgardner D (2022). Impact of geodemographic factors on antibiotic prescribing for acute, uncomplicated bronchitis or upper respiratory tract infection. *J. Am. Board. Fam. Med.*, **35**(4): 733-741.

Fu M, Wushouer H, Hu L, Li N, Guan X, Shi L and Ross-Degnan D (2021). Outpatient prescribing pattern for acute bronchitis in primary healthcare settings in China. *NPJ. Prim. Care. Respir. Med.*, **31**(1): 24.

Ghazaly MMH, Abu Faddan NH, Raafat DM, Mohammed NA and Nadel S (2021). Acute viral bronchiolitis as a cause of pediatric acute respiratory distress syndrome. *Eur J Pediatr.*, **180**(4): 1229-1234.

Hoerr FJ (2021). The Pathology of Infectious Bronchitis. *Avian. Dis.*, **65**(4): 600-611.

Khalatbari Mohseni G, Hosseini SA, Majdinasab N and Cheraghian B (2023). Effects of N-acetylcysteine on oxidative stress biomarkers, depression, and anxiety symptoms in patients with multiple sclerosis. *Neuropsychopharmacol Rep.*, **43**(3): 382-390.

Li J, Chen Y, Yu X, Xie Y, Li X, Diagnosis and Treatment Guideline for Chinese Medicine on Acute Trachea-Bronchitis working team RDBoCAoCMRDBoCMAoM (2021). Diagnosis and treatment guideline for Chinese medicine on acute trachea-bronchitis. *J. Evid. Based. Med.*, **14**(4): 333-345.

Manti S, Staiano A, Orfeo L, Midulla F, Marseglia GL, Ghizzi C, Zampogna S, Carnielli VP, Favilli S, Ruggieri M, Perri D, Di Mauro G, Gattinara GC, D'Avino A, Becherucci P, Prete A, Zampino G, Lanari M, Biban P, Manzoni P, Esposito S, Corsello G and Baraldi E (2023). UPDATE - 2022 Italian guidelines on the management of bronchiolitis in infants. *Ital. J. Pediatr.*, **49**(1): 19.

Todd K, Luchtman-Jones L, Blackmore A, Hennessey C, McGrady ME (2023). Barriers to medication adherence in children, adolescents, and young adults prescribed anticoagulation. *Pediatr. Blood Cancer.,* **70**(2): e30076.

Papi A, Alfano F, Bigoni T, Mancini L, Mawass A, Baraldi F, Aljama C, Contoli M and Miravitlles M (2024). N-acetylcysteine Treatment in Chronic Obstructive Pulmonary Disease (COPD) and Chronic Bronchitis/Pre-COPD: Distinct Meta-analyses. *Arch. Bronconeumol.*, **60**(5): 269-278.

Patel N, Patel M, Inja R, Krvavac A and Lechner AJ (2021). Plastic bronchitis in adult and pediatric patients: A review of its presentation, diagnosis and treatment. *Mo. Med.*, **118**(4): 363-373.

Rodriguez-Herrera C, Lopez-Jimenez JJ, Del Toro-Valero A, Torres-Carrillo NM, Torres-Carrillo N, Godinez-Pena CA, Mendez-Magana AC, Herrera-Godina MG and Fletes-Rayas AL (2021). The Newcastle satisfaction with nursing scales in a Mexican oncology hospital. *Afr. Health Sci.*, **21**(1): 60-66.

Simpson JL, Phipps S and Gibson PG (2009). Inflammatory mechanisms and treatment of obstructive airway diseases with neutrophilic bronchitis. *Pharmacol. Ther.*, **124**(1): 86-95.

Tang W, Zhu D, Wu F, Xu JF, Yang JP, Deng ZP, Chen XB, Papi A and Qu JM (2023). Intravenous N-acetylcysteine in respiratory disease with abnormal mucus secretion. *Eur. Rev. Med. Pharmacol Sci.*, **27**(11): 5119-5127.

Taylor A, Zerfas I, Le C, D'Amico F, Heath FR and Baumgartner M (2022). Treatment of acute bronchitis and its impact on return emergency department visits. *J. Emerg. Med.*, **63**(1): 10-16.

Wrotek A, Badyda A and Jackowska T (2024). Molecular mechanisms of N-acetylcysteine in rsv infections and air pollution-induced alterations: A scoping review. *Int. J. Mol. Sci.*, **25**(11): 6051.