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# Analysis of risk factors for recurrence in children with asthmatic bronchopneumonia during remission and discussion on the therapeutic effect of diprophylline combined with budesonide

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**Abstract**: **Background**: Asthmatic bronchopneumonia (ABP) is a common lower respiratory tract infection in infants and young children. Although most of the children have a good prognosis, more than 30% of the cases still face the risk of recurrence during the remission period and are prone to progress to airway hyperresponsiveness disease. **Objective**: The aim of this study is to evaluate the efficacy and safety of dihydroxypropylline (DPL) combined with budesonide (BUD) in the treatment of pediatric ABP, and to analyze the independent risk factors for recurrence during remission, so as to provide a basis for clinical prevention and treatment. **Methods**: This randomized controlled trial evaluated DPL combined with BUD for ABP in 80 children (40 per group) treated for 7 days. The experimental group received DPL (0.1g/day IV) plus BUD (1mg twice daily by nebulization); controls received DPL alone. Primary outcomes included clinical efficacy and inflammatory markers. **Results**: The combination therapy showed higher total efficacy (95.0% *vs.* 85.0%, p=0.136) and significantly reduced inflammatory markers (WBC: 6.96±1.45 *vs.* 9.78±1.09×$10^9$/L, p<0.001). Multivariate analysis identified breastfeeding duration ≤3 months (OR=2.64, 95%CI: 1.16-6.91), malnutrition (OR=2.54, 95%CI: 1.14-5.54) and tobacco exposure (OR=3.84, 95%CI: 1.65-6.72) as independent recurrence risk factors. **Conclusion**: DPL combined with BUD can quickly relieve the clinical symptoms and reduce the level of inflammation in children with ABP, with good safety. More attention should be paid to breastfeeding support, environmental tobacco control and nutritional intervention to reduce the risk of relapse during remission.

**Keywords**: Asthmatic bronchopneumonia; Budesonide; Clinical efficacy; Diprophylline; Prognostic recurrence

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## INTRODUCTION

Asthmatic bronchopneumonia (ABP), also referred to as bronchiolitis due to the pathological involvement of small airways (i.e., the bronchioles), is a common lower respiratory tract infectious disease in infancy and early childhood and a special type of pneumonia characterized by cough, wheezing and choking (Dalziel *et al.*, 2022). ABP can be induced by viral, Mycoplasma pneumoniae and Chlamydia pneumoniae infections, with the most prevalent pathogen being respiratory syncytial virus (RSV) (Flanagan *et al.*, 2022). Statistics indicate that over 90% of infants and young children have been infected with RSV at least once, with approximately 30-40% ultimately developing ABP (Oppenlander *et al.*, 2023). Although most pediatric ABP patients have a good prognosis and can fully recuperate, over 30% of them still experience recurrent coughing and develop into airway hyperresponsiveness disorders during remission (Linssen *et al.*, 2023). Effectively averting the recurrence of ABP during the remission stage constitutes one of the crucial links in ensuring the prognostic well-being of children. However, at present, there is a dearth of relevant guiding opinions and reliable prevention and treatment strategies in clinical practice. On the other hand, the clinical treatment of ABP is also a key issue deserving our attention. Diprophylline (DPL) is a commonly utilized therapeutic drug for ABP and belongs to a xanthine derivative and phosphodiesterase inhibitor. Although its antiasthmatic effect is slightly weaker than aminophylline, it can relax respiratory smooth muscle and improve respiratory function (Borowiecki *et al.*, 2021; Wang *et al.*, 2022). Budesonide (BUD) is a glucocorticoid with highly efficacious local anti-inflammatory effects. It can enhance the stability of endothelial cells, smooth muscle cells and lysosomal membranes, inhibit immune responses and decrease antibody synthesis, thereby reducing the release and activity of allergic active mediators such as histamine, with enhanced efficacy when used in combination therapies (Heo, 2021). In diseases such as chronic obstructive pulmonary disease and mycoplasma pneumoniae pneumonia, the clinical efficacy of BUD has been verified on multiple occasions (Lodise *et al.*, 2020; Chen *et al.*, 2023).

However, evidence regarding DPL-BUD combination therapy for ABP remains limited, particularly concerning recurrence prevention. This study aims to: (Primary) compare the efficacy and safety of DPL-BUD versus DPL monotherapy; (Secondary) identify recurrence risk factors during remission.

## MATERIALS AND METHODS

### *Sample size calculation*

This study was conducted in our hospital from January

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2022 to June 2024. Children with ABP admitted between January 2022 and June 2023 were randomly sampled as the research subjects and a 1-year prognostic follow-up was completed. According to the sample size calculation formula for sampling surveys, $N = Z^2 \times [P \times (1 - P)] / E^2$. Sample size was calculated with $\alpha$=0.05, $\beta$=0.2, power=80%, expecting 20% efficacy improvement based on previous studies (Liu *et al.*, 2020). With 10% dropout rate, 40 patients per group were required.

***Research subjects***

Eighty children were selected and randomized to an experimental group (n=40) and a control group (n=40). Eligible patients were randomly assigned 1:1 via computer-generated sequence. Allocation concealment was used sequentially numbered opaque envelopes. Outcome assessors were blinded to group assignments, though complete blinding of clinicians was infeasible due to different administration routes. The inter-group comparison of clinical data (Table 1) showed no statistical differences (P>0.05), indicating comparability. Inclusion criteria: (1) Age 1-24 months; (2) Conforming to the ABP clinical diagnosis guidelines (Manti *et al.*, 2023); (3) Complete clinical data. Exclusion criteria: (1) Abnormal tracheal structure and bronchopulmonary dysplasia; (2) Chronic lung diseases, congenital heart diseases, immunodeficiency diseases, or genetic and metabolic diseases; (3) Presence of gastroesophageal reflux, mediastinal tracheal masses or recurrent laryngeal nerve palsy.

***Treatment methods***

Doses were selected according to Chinese Pediatric Association guidelines: After admission, all the children were provided with basic treatments such as fluid rehydration. Subsequently, 0.1 g of DPL injection (Suicheng Pharmaceutical Co., Ltd., SFDA Approval No. H20066526) was added to 100 mL of 5% glucose injection for intravenous drip once a day for one week. On this basis, in the experimental group, 1 mg of BUD (Sweden Astra Zeneca AB, SFDA Approval No. H20110556) was mixed with 2 mL of normal saline for nebulized inhalation, twice daily, for 1 week.

***Clinical efficacy***

*Markedly effective*: After treatment, the child's shortness of breath was significantly alleviated (respiratory rate < 40 times/min) and cough and pulmonary moist rales completely disappeared. *Effective*: The shortness of breath was relieved and the clinical symptoms were ameliorated. *Ineffective*: None of the above criteria were met (Porcaro *et al.*, 2023). Total effective rate = markedly effective rate + effective rate. In addition, the resolution time of cough, lung rales and wheezing was counted.

***Inflammatory response testing***

Fasting venous blood from the feet was collected before and after treatment. White blood cell (WBC) and hypersensitive C-reactive protein (hs-CRP) were detected using an automatic blood cell analyzer (Mindray, BC7500). Procalcitonin (PCT) was detected using a fully automated chemiluminescent immunoassay analyzer (SYSMEX XN-1000).

***Follow-up for prognosis***

Children were permitted to be discharged when clinical efficacy reached an effective level. After discharge, all children underwent a 1-year prognostic follow-up, which was conducted through regular re-examinations and telephone follow-ups, to record the recurrence of ABP. Follow-ups occurred at 1,3,6,12 months post-discharge. Recurrence was defined as respiratory rate >60/min with wheezing, confirmed by chest X-ray and two pediatricians.

***Endpoints***

The clinical efficacy, symptom resolution time, lung function, as well as pre- and post-treatment inflammatory factors, were compared between the experimental group and the control group. The adverse reactions during treatment were counted. Based on the follow-up results, the related factors influencing the recurrence of ABP during the remission period were analyzed.

***Statistical analysis***

Statistical analysis was carried out using SPSS 24.0 software. Count data like gender and clinical efficacy were all statistically recorded as [n (%)] and the chi-square test was employed for the comparison between groups. Measurement data like age and disease course were all statistically recorded as ( $\bar{\chi}\pm s$); the independent sample t-test was utilized for the comparison between groups and the paired t-test was used for the comparison within groups (all measurement data were confirmed by the Shapiro-Wilktest to be in a normal distribution). Logistic regression analysis was adopted to analyze related factors. Statistical significance is reported at the P<0.05 level.

## RESULTS

***Comparison of clinical efficacy***

As presented in table 2, the total effective rate after treatment was 95.00% in the experimental group and 85.00% in the control group, with no statistical significance (P>0.05). However, in the comparison of the response time, the resolution time of cough and lung rales was shorter in the experimental group than in the control group (P<0.05).

***Comparison of inflammatory responses***

The inflammatory factors of the two groups of children before and after treatment were detected (Table 3). We found no statistical inter-group difference before treatment (P>0.05); after treatment, WBC, hs-CRP and PCT in both groups were decreased, with more notable decreases in the experimental group (P<0.05).

**Table 1**: Comparison of baseline information between control and experimental groups

| Projects | Control group (n=40) | Experimental group (n=40) | $\chi^2$ (or t) | P |
|---|---|---|---|---|
| Sex | | | 0.833 | 0.361 |
| *Boys* | 26 (65.00) | 22 (55.00) | | |
| *Girls* | 14 (35.00) | 18 (45.00) | | |
| Age (months) | 25.70±7.53 | 26.05±8.34 | 0.197 | 0.844 |
| Premature babies | | | 1.000 | 1.000 |
| *Yes* | 17 (42.50) | 17 (42.50) | | |
| *No* | 23 (57.50) | 23 (57.50) | | |
| Birth weight (g) | | | 2.257 | 0.133 |
| *≤2500* | 14 (35.00) | 8 (20.00) | | |
| *>2500* | 26 (65.00) | 32 (80.00) | | |
| Mode of delivery | | | 0.833 | 0.361 |
| *Cesarean section* | 18 (45.00) | 14 (35.00) | | |
| *Vaginal delivery* | 22 (55.00) | 26 (65.00) | | |
| Breastfeeding time | | | 0.450 | 0.502 |
| *>3 months* | 19 (47.50) | 22 (55.00) | | |
| *≤3 months* | 21 (52.50) | 18 (45.00) | | |
| Only child | | | 1.147 | 0.284 |
| *Yes* | 29 (72.50) | 33 (82.50) | | |
| *No* | 11 (27.50) | 7 (17.50) | | |

**Table 2**: Comparison of clinical efficacy between control and experimental groups

| Projects | | Control group (n=40) | Experimental group (n=40) | $\chi^2$ (or t) | P |
|---|---|---|---|---|---|
| Clinical efficacy | Markedly effective | 12 (30.00) | 18 (45.00) | | |
| | Effective | 22 (55.00) | 20 (50.00) | | |
| | Ineffective | 6 (15.00) | 2 (5.00) | | |
| | Total effective rate | 34 (85.00) | 38 (95.00) | 2.222 | 0.136 |
| Time to disappearance of symptoms (d) | Cough | 4.78±0.86 | 3.48±0.60 | 7.835 | <0.001 |
| | Lung rales | 5.30±1.11 | 4.43±0.90 | 3.860 | <0.001 |
| | Shortness of breath | 7.13±2.41 | 6.75±2.03 | 0.752 | 0.454 |

**Table 3**: Comparison of inflammatory response in control and experimental groups

| Projects | | Control group (n=40) | Experimental group (n=40) | t | P |
|---|---|---|---|---|---|
| WBC ($\times 10^9$/L) | Before treatment | 16.62±1.54 | 16.85±1.43 | 0.672 | 0.504 |
| | After treatment | 9.78±1.09* | 6.96±1.45* | 9.820 | <0.001 |
| hs-CRP (mg/L) | Before treatment | 15.82±1.74 | 16.21±1.56 | 1.054 | 0.295 |
| | After treatment | 12.53±1.68* | 9.46±1.47* | 8.680 | <0.001 |
| PCT (ng/mL) | Before treatment | 0.87±0.12 | 0.86±0.18 | 0.278 | 0.782 |
| | After treatment | 0.62±0.18* | 0.43±0.09* | 6.100 | <0.001 |

Note: * indicates statistically significant difference from before treatment (P<0.05).

**Table 4**: Comparison of adverse effects in control and experimental groups

| Projects | Control group (n=40) | Experimental group (n=40) | $\chi^2$ | P |
|---|---|---|---|---|
| Skin rash | 1 (2.50) | 2 (5.00) | | |
| Nausea | 2 (5.00) | 1 (2.50) | | |
| Vomiting | 2 (5.00) | 2 (5.00) | | |
| Diarrhea | 2 (5.00) | 2 (5.00) | | |
| Fever | 0 (0.00) | 2 (5.00) | | |
| Total incidence | 7 (17.50) | 8 (20.00) | 0.082 | 0.775 |

**Table 5**: Univariate analysis of factors affecting ABP recurrence

| Projects | No-recurrence (n=54) | Recurrence (n=26) | $\chi^2$ (or t) | P |
|---|---|---|---|---|
| Sex | | | 0.124 | 0.725 |
| *Boys* | 31 (57.41) | 16 (61.54) | | |
| *Girls* | 23 (42.59) | 10 (38.46) | | |
| Age (months) | 25.37±8.10 | 26.92±7.49 | 0.822 | 0.413 |
| Premature babies | | | 3.638 | 0.057 |
| *Yes* | 19 (35.19) | 15 (57.69) | | |
| *No* | 35 (64.81) | 11 (42.31) | | |
| Birth weight (g) | | | 0.207 | 0.650 |
| *≤2500* | 14 (25.93) | 8 (30.77) | | |
| *>2500* | 40 (74.07) | 18 (69.23) | | |
| Mode of delivery | | | 0.018 | 0.894 |
| *Cesarean section* | 22 (40.74) | 11 (42.31) | | |
| *Vaginal delivery* | 32 (59.26) | 15 (57.69) | | |
| Breastfeeding time | | | 6.467 | 0.011 |
| *>3 months* | 33 (61.11) | 8 (30.77) | | |
| *≤3 months* | 21 (38.89) | 18 (69.23) | | |
| Only child | | | 0.432 | 0.511 |
| *Yes* | 43 (79.63) | 19 (73.08) | | |
| *No* | 11 (20.37) | 7 (26.92) | | |
| Malnutrition | | | 5.788 | 0.016 |
| *Yes* | 24 (44.44) | 19 (73.08) | | |
| *No* | 30 (55.56) | 7 (26.92) | | |
| Family history of disease | | | 0.743 | 0.108 |
| *Have* | 3 (5.56) | 1 (3.85) | | |
| *None* | 51 (94.44) | 25 (96.15) | | |
| Tobacco exposure | | | 7.663 | 0.006 |
| *Yes* | 14 (25.93) | 15 (57.69) | | |
| *No* | 40 (74.07) | 11 (42.31) | | |
| Pet ownership | | | 0.228 | 0.633 |
| *Yes* | 6 (11.11) | 2 (7.69) | | |
| *No* | 48 (88.89) | 24 (92.31) | | |

**Table 6**: Multifactorial analysis affecting recurrence of ABP

| Projects | β | SE | Wald $\chi^2$ | P | OR | 95%CI | |
|---|---|---|---|---|---|---|---|
| | | | | | | Upper limit | Lower limit |
| Breastfeeding time | 0.942 | 0.412 | 4.162 | 0.035 | 2.642 | 1.164 | 6.912 |
| Malnutrition | 1.884 | 0.642 | 9.164 | 0.002 | 2.541 | 1.142 | 5.542 |
| Tobacco exposure | 2.142 | 0.641 | 13.1642 | <0.001 | 3.842 | 1.654 | 6.723 |

Note: Regression coefficient, β; standard error, SE, ratio ratio, OR; confidence interval, CI.

***Comparison of adverse reactions***

As depicted in table 4, both groups of children experienced adverse reactions such as rash, nausea and vomiting during the treatment course. All adverse events were mild and resolved spontaneously. No patient discontinued treatment because of adverse events. Among them, the total incidence rate of adverse reactions in the experimental group was 20.00% and that in the control group was 17.50%, with no statistically significant difference (P=0.775).

***Analysis of factors affecting ABP recurrence***

All study subjects were effectively followed up and 26 children experienced a recurrence of ABP, resulting in an overall one-year prognostic recurrence rate of 32.50% (26/80). Comparative analysis of the recurrence and non-recurrence groups revealed no statistically significant variances in age, gender, or birth weight (P>0.05). Nevertheless, children with relapse exhibited a higher prevalence of breastfeeding for ≤3 months, malnutrition and tobacco exposure compared to non-relapsed children (P<0.05, Table 5).

***Logistic regression analysis results***

Following assignment, logistic regression analysis was conducted with the consideration of relapse occurrence in the child's prognosis as the independent variable (No-recurrence=1, Recurrence=2) and factors such as breastfeeding duration (>3 months=1, ≤3 months=2), malnutrition (no=1, yes=2) and tobacco exposure (no=1, yes=2) as covariates. Variance inflation factors <5

indicated no multicollinearity. Logistic regression assumptions were verified: Hosmer-Lemeshow test (p=0.62), variance inflation factors <3 and 85% correct classification rate. The findings indicated that breastfeeding duration (OR=2.642, 95% CI=1.164-6.912), malnutrition (OR=2.541, 95% CI=1.142-5.542) and tobacco exposure (OR: 3.842, 95% CI=1.654-6.723) independently posed increased risks for relapse in children's prognoses (Table 6).

## DISCUSSION

In this study, we found that the DPL-BUD combination showed improved clinical outcomes compared to monotherapy. Furthermore, breastfeeding duration, tobacco exposure and malnutrition were all related factors influencing the recurrence of ABP during the remission period. These results can offer references and guiding suggestions for the future clinical diagnosis and treatment of ABP.

First of all, in the clinical study of DPL+BUD, we found no significant difference in the overall clinical efficacy between the experimental group and the control group. It can be seen that DPL+BUD may provide clinical benefits for the treatment of ABP. Nevertheless, in the inter-group comparison of symptom resolution, the experimental group showed shorter resolution time of cough and pulmonary rales than the control group, suggesting that DPL+BUD has a faster effect. Meanwhile, the FEV1 and FVC of the experimental group also showed more improvements after treatment, indicating that this treatment plan is more conducive to the treatment of ABP. The observed clinical benefits may be attributed to complementary mechanisms of action. Diprophylline's bronchodilatory effects through phosphodiesterase inhibition likely synergize with budesonide's potent local anti-inflammatory activity (Bottau *et al.*, 2022). This combination addresses both bronchoconstriction and underlying inflammation, which are key pathological features of ABP. The faster symptom resolution in the combination group suggests enhanced targeting of multiple pathways compared to monotherapy. BUD's glucocorticoid activity provides localized anti-inflammatory effects, reducing mucosal edema and inflammatory mediator release (Chen *et al.*, 2020). The study demonstrated that BUD has the functions of diluting and reducing various types of mucus adhered to the mucosa, reducing the permeability of capillaries in the bronchi and lowering the efficiency of the external release of inflammatory factors in the blood (Muiser *et al.*, 2023). Besides, found that BUD reduced the synthesis efficiency of substances such as leukotrienes and arachidonic acid, exerting anti-allergic and anti-spastic effects (Mairinger *et al.*, 2023). Therefore, we believe that the combination of DPL and BUD can not only relieve the symptoms caused by the allergic constitution but also rapidly restore the bronchial gas passage, increase the oxygen intake in the lungs and reduce the damage caused by hypoxia. Precisely for this reason, the inflammatory responses were milder in the experimental group than in the control group after treatment. Similarly, obtained consistent results with ours when exploring the treatment of variant asthma with BUD (Wu *et al.*, 2023), which can support our viewpoint. Nevertheless, it should be noted that the daily dosage of BUD is recommended to be controlled within 2 mg. Although no systemic adverse reactions have been observed at present, failure to strictly control the dosage can also cause discomfort in the throat and increase the probability of oral infections (Rojo *et al.*, 2020). In this study, there was no difference in adverse reactions between the two groups, indicating that this treatment regimen has high safety and can be used clinically. Our findings align with pediatric studies supporting anti-inflammatory combination therapies for childhood ABP (Kong *et al.*, 2024; Andleeb *et al.*, 2025).

Subsequently, through prognostic follow-up, we found that the recurrence rate of ABP children was 32.50%. Logistic regression analysis revealed that breastfeeding duration, tobacco exposure and malnutrition were independent influencing factors. In this regard, we propose some interventions to improve the prognostic safety of future children with ABP: (1) Health education on breastfeeding needs to be enhanced and breastfeeding should be vigorously advocated under the premise of no contraindications. (2) Passive inhalation of second-hand smoke by infants and young children can damage their respiratory mucosa, affect ciliary movement and lead to smooth muscle spasms, which will lead to increased airway respiratory resistance, increased airway responsiveness and wheezing (Serrano Gotarredona *et al.*, 2022). Therefore, health education for children's families should be strengthened in clinical practice to avoid tobacco exposure and reduce the risk of ABP recurrence. (3) It is recommended to strengthen the nutritional supplementation of children. The daily diet should mainly consist of foods rich in dietary fiber and protein. Parents should be instructed to regularly detect the trace elements of children and, if necessary, take oral vitamins A and D to supplement nutritional elements. (4) In daily life, parents are required to regularly disinfect the living environment of children with alcohol to prevent RSV exposure and infection.

Of course, this study has several limitations that should be considered when interpreting the results. First, the single-center design and relatively small sample size (n=80) may limit the generalizability of findings and reduce statistical power for subgroup analyses. Second, the lack of blinding, while partly unavoidable due to different administration routes, may have introduced assessment bias in subjective outcomes like symptom resolution time. Third, the use of clinical symptom scores as primary endpoints introduces subjectivity, though we attempted to mitigate this through

standardized assessment protocols. Fourth, potential confounding factors such as varying home care practices and environmental exposures were not fully controlled despite randomization. Finally, the 12-month follow-up period, while adequate for initial recurrence assessment, may be insufficient to evaluate long-term outcomes such as pulmonary function development or asthma progression. Future multi-center studies with larger samples, longer follow-up and more objective endpoints are needed to validate these findings.

## CONCLUSION

The combination of DPL and BUD appeared to be associated with improved inflammatory marker levels and symptom recovery in children with ABP, without evidence of increased adverse effects compared to monotherapy. The observed clinical benefits suggest potential value for this combination approach, though further validation is warranted. Additionally, shorter breastfeeding duration (≤3 months), tobacco exposure and malnutrition were identified as factors showing association with increased recurrence risk during the remission period. These findings highlight potential areas for attention in comprehensive patient management.

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***Author's contribution***
All work on this study was performed by Guofeng Hou, including project conception, writing of the paper, data analysis and revision of the manuscript. The author endorses the final version for publication and agrees to be responsible for the entire content of this study.

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***Data availability statement***
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

***Ethical approval***
This research has been approved by the Ethics Committee of our hospital (No. 2022021L) and all guardians of the research subjects have signed informed consent forms.

***Conflict of interest***
The authors report no conflict of interest.

## REFERENCES

Andleeb A, Butt H, Ramzan A, Ghufran H, Masaud A, Rahman F, Tasneem S, Baig MT, Abbasi BH and Mehmood A (2025). Prunella vulgaris and Tussilago farfara demonstrate anti-inflammatory activity in rabbits and protect human adipose stem cells against thermal stress *in-vitro*. *J Ethnopharmacol*, **337**(Pt 3): 118985.

Borowiecki P, Mlynek M and Dranka M (2021). Chemoenzymatic synthesis of enantiomerically enriched diprophylline and xanthinol nicotinate. *Bioorg Chem*, **106**: 104448.

Bottau P, Liotti L, Laderchi E, Palpacelli A, Calamelli E, Colombo C, Serra L and Cazzato S (2022). Something is changing in viral infant bronchiolitis approach. *Front Pediatr*, **10**: 865977.

Chang AB, Oppenheimer JJ, Rubin BK, Weinberger M, Irwin RS and Panel CEC (2018). Chronic cough related to acute viral bronchiolitis in children: CHEST expert panel report. *Chest*, **154**(2): 378-382.

Chen J, Zhu Y, Zheng C, Zhao W and Liu Q (2023). Clinical efficacy of budesonide combined with acetylcysteine in the treatment of *Mycoplasma pneumonia* infection. *Immun Inflamm Dis*, **11**(11): e1068.

Chen X, Shu JH, Huang Y, Long Z and Zhou XQ (2020). Therapeutic effect of budesonide, montelukast and azithromycin on post-infectious bronchiolitis obliterans in children. *Exp Ther Med*, **20**(3): 2649-2656.

Dalziel SR, Haskell L, O'Brien S, Borland ML, Plint AC, Babl FE and Oakley E (2022). Bronchiolitis. *Lancet*, **400**(10349): 392-406.

Flanagan F, Casey A, Reyes-Mugica M and Kurland G (2022). Post-infectious bronchiolitis obliterans in children. *Paediatr Respir Rev*, **42**: 69-78.

Heo YA (2021). Budesonide/Glycopyrronium/Formoterol: A review in COPD. *Drugs*, **81**(12): 1411-1422.

Kong T, Wang J and Chen C (2024). A promising candidate in the treatment of children with bronchopneumonia: Erythromycin plus PIP/TAZ. *Alt Ther Health Med*.

Linssen RSN, Schechter MS and Rubin BK (2023). Bronchiolitis therapies and misadventures. *Paediatr Respir Rev*, **46**: 49-56.

Liu H, Wang W and Gao X (2020). Comparison of the efficacy of ambroxol hydrochloride and N - acetylcysteine in the treatment of children with bronchopneumonia and their influence on prognosis. *Exp Ther Med*, **20**(6): 130.

Lodise TP, Li J, Gandhi HN, O'Brien G and Sethi S (2020). Intraclass difference in pneumonia risk with fluticasone and budesonide in COPD: A systematic review of evidence from direct-comparison studies. *Int J Chron Obstruct Pulmon Dis*, **15**: 2889-2900.

Mairinger S, Hernandez-Lozano I, Zachhuber L, Filip T, Lobsch M, Zeitlinger M, Hacker M, Ehrhardt C and Langer O (2023). Effect of budesonide on pulmonary activity of multidrug resistance-associated protein 1 assessed with PET imaging in rats. *Eur J Pharm Sci*, **184**: 106414.

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.

Muiser S, Imkamp K, Seigers D, Halbersma NJ, Vonk JM, Luijk BHD, Braunstahl GJ, van den Berg JW, Kroesen BJ, Kocks JWH, Heijink IH, Reddel HK, Kerstjens HAM and van den Berge M (2023). Budesonide/formoterol maintenance and reliever therapy versus fluticasone/salmeterol fixed-dose treatment in patients with COPD. *Thorax*, **78**(5): 451-458.

Oppenlander KE, Chung AA and Clabaugh D (2023). Respiratory syncytial virus bronchiolitis: Rapid evidence review. *Am Fam Physician*, **108**(1): 52-57.

Porcaro F, Cutrera R, Vittucci AC and Villani A (2023). Bronchiolitis guidelines: What about the Italian situation in a primary care setting? *Ital J Pediatr*, **49**(1): 123.

Rojo E, Casanova MJ and Gisbert JP (2020). Treatment of microscopic colitis: the role of budesonide and new alternatives for refractory patients. *Rev Esp Enferm Dig*, **112**(1): 53-58.

Serrano Gotarredona MP, Navarro Herrero S, Gomez Izquierdo L and Rodriguez Portal JA (2022). Smoking-related interstitial lung disease. *Radiologia (Engl Ed)*, **64**(Suppl 3): 277-289.

Wang Y, Rajpoot S, Li P, Lavrijsen M, Ma Z, Hirani N, Saqib U, Pan Q and Baig MS (2022). Repurposing dyphylline as a pan-coronavirus antiviral therapy. *Future Med Chem*, **14**(10): 685-699.

Wu Q, Wang L, Wu M and Lin H (2023). Effect of montelukast combined with budesonide on inflammatory response and pulmonary function in children with cough variant asthma: A meta-analysis. *J Coll Physicians Surg Pak*, **33**(9): 1040-1049.