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Nebulized budesonide vs. ipratropium as an add-on to salbutamol in preschool wheeze – a randomized controlled trial

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ABSTRACT

Introduction and aim. Acute wheeze is common cause of emergency visits and hospitalization in preschool children. This randomized controlled trial directly compared nebulized budesonide versus ipratropium bromide as add-on therapy to salbutamol in children aged 1–5 years with moderate-to-severe acute wheeze.

Material and methods. This hospital-based randomized controlled trial included 84 children equally assigned to two groups. Group A received nebulized budesonide with salbutamol, and Group B received nebulized ipratropium bromide with salbutamol. The co-primary outcomes were the change in Pediatric Respiratory Assessment Measure (PRAM) score from baseline to 60 minutes and the PRAM score trajectory during the first 60 minutes.

Results. Baseline PRAM scores were comparable between groups. Group A showed significantly lower PRAM scores at 20, 40, 60 minutes, with greater mean PRAM reduction at 60 minutes ($p<0.05$). Mean time to achieve PRAM≤4 was shorter in Group A. Group A children had a significantly shorter hospital stay.

Conclusion: Nebulized budesonide as an add-on to salbutamol was associated with greater short-term improvement in PRAM scores and shorter hospital stay than ipratropium bromide; larger multicenter studies are needed.

Keywords. budesonide, child, ipratropium, preschool, salbutamol, wheezing

Introduction

Acute exacerbations of wheeze are among the most common reasons for emergency visits and hospital admissions among the children aged 1–5 years, contributing substantially to pediatric morbidity, health care utilization, and caregiver burden worldwide.[1] In early childhood, wheezing episodes are commonly triggered by viral respiratory infections and are associated with airway inflammation, mucosal edema, bronchoconstriction, and increased mucus secretion, leading to respiratory distress.[2] Because of smaller airway caliber and heightened inflammatory responses, young children are more vulnerable to severe manifestations and may require prompt treatment to prevent clinical deterioration.[3]

The mainstay of acute wheeze management is rapid reversal of bronchospasm and improvement in oxygenation, with nebulized salbutamol forming the cornerstone of therapy.[4] The bronchodilatory effect of salbutamol is through stimulation of β2 adrenergic receptors present in the bronchial smooth muscle. Salbutamol has limited effect on the underlying inflammatory process, and some children show suboptimal responses when treated with salbutamol alone.[5] For moderate-to-severe exacerbations, ipratropium bromide is frequently added because it blocks muscarinic receptors, reduces vagally mediated bronchoconstriction, and may improve clinical outcomes, especially in severe cases.[6,7] However, its action is largely bronchodilation and does not directly target airway inflammation.

This has led to increasing interest in early use of inhaled corticosteroids during acute wheezing episodes. Budesonide, a potent inhaled corticosteroid with high topical anti-inflammatory activity and a favorable safety profile, has been proposed as an adjunct to bronchodilator therapy.[8,9] Nebulized budesonide is particularly suitable for young children because it allows targeted pulmonary delivery with minimal systemic absorption and can be administered even in those unable to use inhaler devices effectively.[10] Previous studies suggest that early administration of inhaled corticosteroids may hasten symptom resolution, improve respiratory scores, and reduce the need for systemic corticosteroids and prolonged hospitalization.[11] Nevertheless, evidence remains inconsistent, particularly in children under 5 years, because of variations in study design, patient characteristics, dosing regimens, and outcome measures across trials.[12]

At present, there is no universal consensus regarding the best add-on therapy to salbutamol in preschool children with acute wheeze. Although ipratropium bromide is widely used in emergency care, its comparative efficacy against nebulized budesonide has not been adequately established in well-designed randomized controlled trials among children aged 1-5 years.[1,6] This question is clinically important because recurrent or inadequately treated wheeze in early childhood may increase the risk of recurrent hospitalizations, persistent airway hyperresponsiveness, and progression to chronic asthma.[8,9]

The Pediatric Respiratory Assessment Measure (PRAM) score is a validated tool used to assess the severity of wheeze and monitor response to treatment in children with acute respiratory distress.[2]

Despite widespread clinical use of both therapies, direct randomized comparisons between nebulized budesonide and ipratropium bromide as add-on treatment to salbutamol in preschool wheeze remain limited. Along with PRAM improvement, duration of hospital stay is a clinically meaningful outcome that reflects both recovery and healthcare resource use.[3,10-12]

Against this background, the present randomized controlled trial was designed to address the existing evidence gap by directly comparing nebulized budesonide plus salbutamol with ipratropium bromide plus salbutamol in children aged 1–5 years with moderate-to-severe acute exacerbations of wheeze. By directly comparing these two commonly used adjunctive regimens, the study aims to generate evidence on symptom resolution, PRAM score improvement, and hospital stay and thereby help guide evidence-based management of acute wheeze in young children. This study provides a direct head-to-head comparison of nebulized budesonide and ipratropium bromide as add-on therapies in preschool children, a population in which comparative evidence remains limited. Additionally, this study evaluates early response using serial PRAM scoring at short intervals, which has been inadequately explored in previous trials. Ipratropium bromide is widely used as an adjunct to salbutamol in moderate-to-severe acute wheeze; therefore, comparison with this commonly employed regimen was considered more clinically relevant than comparison with salbutamol alone.

Aim

The aim was to compare the efficacy of nebulized budesonide versus ipratropium bromide as add-on therapy to salbutamol in preschool children with moderate-to-severe acute wheeze

Co-primary objectives

1. To compare the change in Pediatric Respiratory Assessment Measure (PRAM) score from baseline to 60 minutes between treatment groups.
2. To compare the trajectory of PRAM scores during the first 60 minutes following treatment between treatment groups**.**

Secondary objectives

1. To compare the time required to achieve a PRAM score ≤4 between the two treatment groups.
2. To compare the duration of hospital stay between the two treatment groups.
3. To assess the need for additional bronchodilator or corticosteroid therapy following the initial treatment period.

Material and methods

Study design and setting

This hospital-based randomized controlled trial with a parallel-group design was carried out during the period from 2025 to 2026 in the Department of Pediatrics, SRM Medical College Hospital and Research Centre, a tertiary care teaching hospital. The participants were recruited from the pediatric emergency department and PICU, where children presenting with acute exacerbation of wheeze were routinely evaluated and managed. During the study period, participant recruitment, intervention administration, follow-up assessment, data collection and data analysis were carried out.

Study population

Children of age 1 to 5 years, presenting with acute exacerbation of wheeze, were screened for eligibility. The children were included if written informed consent was provided by a parent or legal guardian, children were aged 1 to 5 years, had clinically diagnosed wheeze, characterized by audible high-pitched whistling sounds predominantly during expiration, had moderate to severe exacerbation, defined by a Pediatric Respiratory Assessment Measure (PRAM) score of >4. The children presenting with life-threatening exacerbation of wheeze, had received systemic or inhaled corticosteroid therapy within the preceding 24 hours, had known cardiovascular disease, primary or secondary immunodeficiency, or chronic systemic illness, had mild exacerbation of wheeze, defined as a PRAM score of 0–4, were excluded.

Eligible participants were screened and enrolled at the time of presentation to the pediatric emergency department or PICU before initiation of the study intervention. Participants were recruited by consecutive sampling. All eligible children presenting to pediatric emergency department or PICU during the study period were assessed for eligibility and enrolled consecutively until the estimated sample size was attained. The sample size was estimated based on previously published studies evaluating nebulized budesonide in preschool wheeze. Assuming a two-sided α error of 0.05, a study power of 80%, and equal allocation between groups, the minimum required sample size was estimated as 42 participants per group (total n=84). The participants were equally allocated into treatment groups A and B, with 42 children in each treatment arm.

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of SRM Medical College Hospital and Research Centre (approval No.: SRMIEC-ST0724-1721). Written informed consent was obtained from parents or legal guardians. Parents were informed that participation was voluntary and they could withdraw their child from the study at any time without affecting the treatment. The study involved minimal risk and no invasive procedures beyond standard care. Patient confidentiality was strictly maintained throughout the study. The study was self-funded, and no external financial support or commercial sponsorship was involved.

Randomization and allocation

Randomization was performed using a computer-generated random sequence with a 1:1 allocation ratio. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes prepared by an independent investigator. Due to the nature of the intervention, blinding was not feasible. All randomized participants were included in the final analysis. The study utilized an open-label design owing to the nature of the interventions; however, outcome assessment via PRAM scoring adhered to standardized criteria to mitigate observer bias. PRAM assessments were performed by pediatric residents and consultants familiar with the PRAM scoring system and its standardized assessment criteria. All assessors received orientation regarding standardized PRAM assessment before study initiation. The same standardized PRAM assessment criteria were applied throughout the study to minimize inter-observer variability. However, formal certification using the online PRAM training module and assessment of inter-rater reliability were not performed.

Intervention

The enrolled participants were assigned to one of the following treatment groups:

Group A: Nebulized Salbutamol and Nebulized Budesonide

Group B: Nebulized Salbutamol and Nebulized Ipratropium Bromide

Dose: 1) Salbutamol: <20 kg – 2.5 mg; >20 kg – 5 mg

2) Ipratropium bromide: 250 µg for children <20 kg and 500 µg for children ≥20 kg, as per standard pediatric dosing guidelines

3) Budesonide: 0.5 mg

The study medications were administered according to standard pediatric dosing protocols. Each child received three consecutive nebulization cycles at 20-minute intervals during the first hour of treatment. Nebulization was administered using oxygen-driven jet nebulizers according to institutional protocol. Supportive care, including oxygen supplementation, was provided whenever required.

The study intervention consisted of three consecutive nebulization cycles administered during the first hour of treatment. Following completion of the study intervention, further management, including bronchodilator therapy, corticosteroid administration, oxygen supplementation, and discharge decisions, was provided according to the institutional treatment protocol and at the discretion of the treating pediatrician. No additional study-specific intervention was administered beyond the initial treatment period. Hospital admission and discharge decisions were made by the treating pediatric team according to institutional clinical protocols and physician judgment.

Outcome measures

The co-primary outcomes were (1) the change in Pediatric Respiratory Assessment Measure (PRAM) score from baseline to 60 minutes and (2) the PRAM score trajectory during the first 60 minutes following initiation of therapy. Secondary outcomes included time to achieve a PRAM score ≤4 and duration of hospital stay. Respiratory rate, heart rate, oxygen saturation, Glasgow Coma Scale, and need for additional therapy were monitored clinically but were not systematically retained for detailed secondary analysis.

Baseline demographic variables such as age and sex were also recorded. Laboratory parameters including complete blood count (CBC), eosinophil count, and C-reactive protein (CRP) were documented. Viral testing was not performed routinely and was undertaken only when clinically indicated using nasopharyngeal or throat swab RT-PCR testing. Therefore, viral identification was available only for a subset of participants. At presentation, all eligible children underwent detailed clinical evaluations, including history taking and physical examination. Baseline assessment included PRAM score, RR, HR, oxygen saturation, and GCS. After enrollment and randomization, the assigned nebulization regimen was administered. Participants were reassessed at 20, 40, and 60 minutes after nebulization using PRAM scores and vital parameters. Children were subsequently monitored until clinical stabilization and discharge. Data were collected using a standardized pro forma designed for the study.

Statistical analysis

Data were coded and entered into Microsoft Excel and analyzed using SPSS software version 28 (IBM, Armonk, NY, USA). Frequencies and percentages were used to express categorical variables, while mean and standard deviation were used for continuous variables. Inferential statistics included the chi-square test and Fisher's exact test for categorical variables. For the co-primary outcomes, the change in PRAM score from baseline to 60 minutes was compared between groups using the independent samples t-test, whereas the PRAM score trajectory during the first 60 minutes was analyzed using repeated-measures ANOVA. Post hoc pairwise comparisons with Bonferroni correction were performed where applicable. The p value of<0.05 was taken as statistical significance. No participants were lost to follow-up during the predefined observation period. Therefore, no imputation for missing outcome data was required.

Results

A total of 96 children were evaluated for eligibility, with 84 satisfying the inclusion criteria and subsequently randomized into two equal groups (n=42 each). No participants were lost to follow-up, and all randomized participants were included in the final analysis.

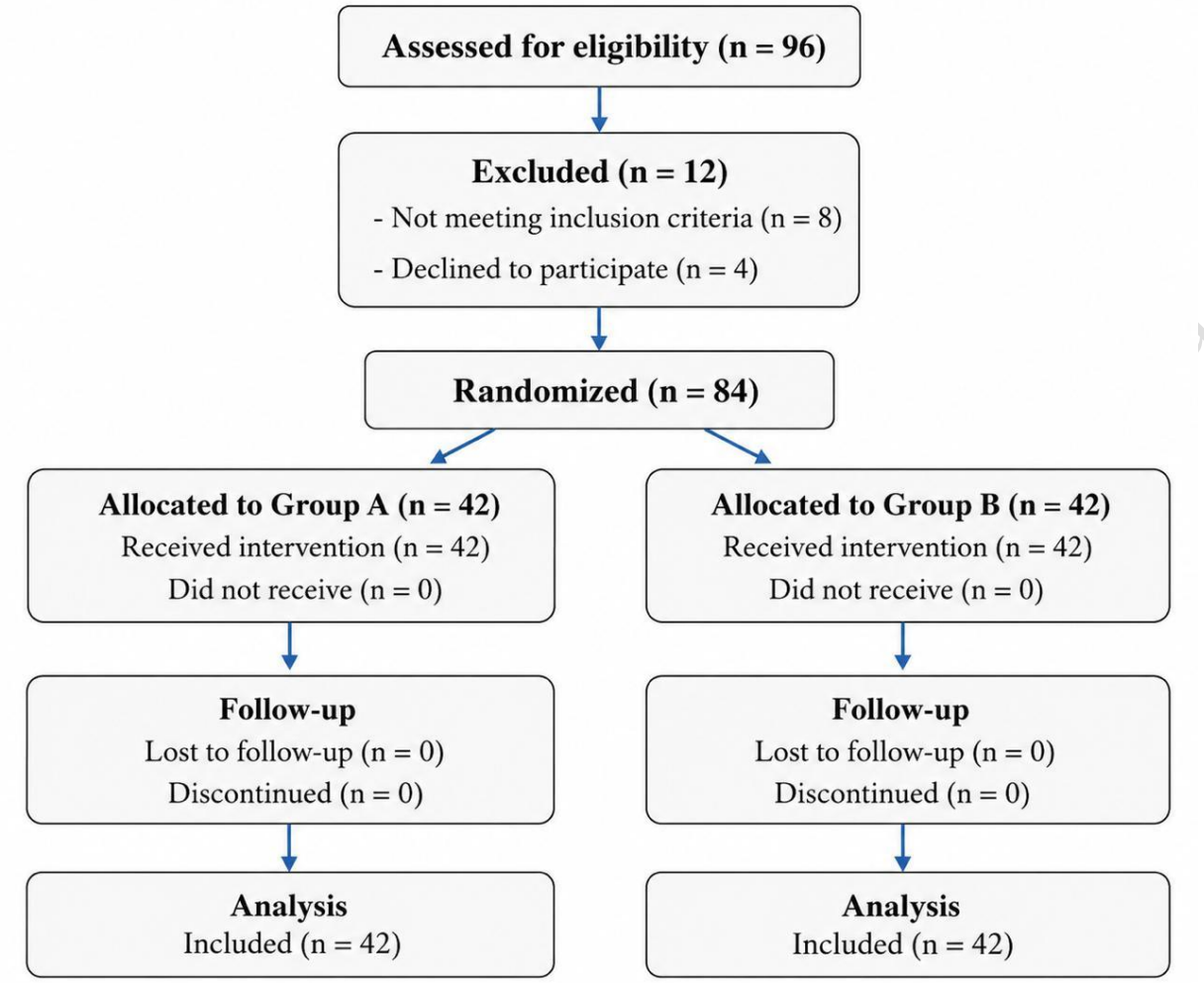

Fig. 1. CONSORT flow diagram showing participant recruitment, randomization, follow-up, and analysis

The baseline demographic and clinical characteristics, treatment response, and outcome measures were analyzed and compared between the nebulized budesonide plus salbutamol group and the nebulized ipratropium bromide plus salbutamol group.

Baseline demographic and clinical characteristics

The mean age was 2.93 years (SD 1.42) in Group A and 3.21 years (SD 1.50) in Group B. Although the distribution across age categories showed some imbalance between groups despite randomization, the mean ages were broadly similar. Sex distribution and weight were also comparable between groups.

All children in both groups had no cyanosis. Chest radiograph findings, viral profile, and mode of oxygen supplementation were broadly comparable between the two groups. Viral testing was available only for a subset of participants because testing was performed when clinically indicated.

Table 1. Baseline demographic and clinical characteristics of study participants*

S. No	Variable	Category	Group A	Group B
1	Age group	1 to 2 years	6 (14.3 %)	10 (23.8 %)
		2 to 3 years	22 (52.4 %)	10 (23.8 %)
		3 to 5 years	14 (33.3 %)	22 (52.4 %)
	In years	Mean (SD)	2.93 (1.42)	3.21 (1.50)
2	Sex	Male	16 (48.5%)	17 (51.5%)
		Female	26 (51%)	25 (49%)
3	Weight (kg)	Mean (SD)	12.3 (2.8)	13.6 (3.08)
4	Cyanosis	Absent	42 (100%)	42 (100%)
5	Chest x ray	Normal	29 (48.3%)	31 (51.7%)
		Hyperinflation	13 (54.2%)	11 (45.8%)
6	Throat swab	Positive	7 (46.7%)	8 (53.3%)
		Negative	35 (50.7%)	34 (49.3%)
7	Virus type	Influenza	5 (50%)	5 (50%)
		RSV	2 (40%)	3 (60%)
		NA	35 (50.7%)	34 (49.3%)
8	Oxygen mode	HFNC	7 (46.7%)	8 (53.3%)
		Simple O2	35 (50.7%)	34 (49.3%)

* Data are presented as number (%) or mean±SD, HFNC – high flow nasal cannula, viral testing was performed only when clinically indicated; percentages are based on available data

Comparison of PRAM scores at different time intervals

For the first co-primary outcome**,** baseline PRAM scores were similar between Group A (6.64±1.428) and Group B (6.71±1.312; p=0.291). At 20 minutes, PRAM scores were lower in Group A (5.05±1.67) compared to Group B (6.14±1.28; p=0.048). At 40 minutes, PRAM scores were lower in Group A (3.76±1.68) compared to Group B (5.76±1.36; p=0.034). At 60 minutes, PRAM scores were lower in Group A (2.50±1.50) compared to Group B (5.26±1.43; p=0.038).

PRAM scores decreased more rapidly in Group A compared to Group B at all post-treatment time points.

Table 2. Comparison of PRAM scores between groups at different time intervals*

Time point	Group A (n=42)	Group B (n=42)	p
Baseline	6.64±1.428	6.71±1.312	0.291

20 minutes	5.05±1.667	6.14±1.280	0.048
40 minutes	3.76±1.679	5.76±1.358	0.034
60 minutes	2.50±1.502	5.26±1.432	0.038
Change at 60 minutes	4.14±0.647	1.45±0.889	0.006

* Data are presented as mean±SD

For the second co-primary outcome, repeated measures ANOVA demonstrated a statistically significant time × group interaction ($p < 0.05$) (Fig. 2), indicating that the reduction in PRAM scores over time differed between groups.

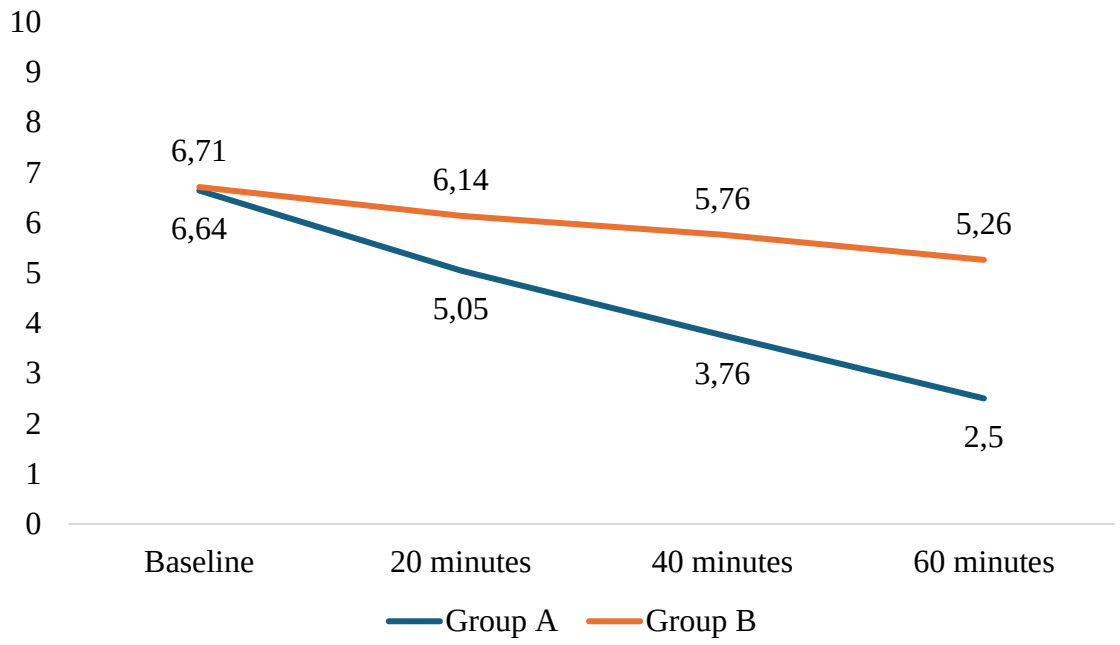

Fig. 2. Comparison of PRAM scores at different time intervals

Comparison of time to achieve PRAM≤4

The mean time to achieve a PRAM score ≤ 4 was shorter in group A compared to group B (38.45±3.351 minutes vs. 52.40 ± 3.883 minutes; p=0.011).

Table 3. Comparison of time to achieve PRAM ≤ 4*

	Study group	**N**	**Mean**	**SD**	**p**
Time to PRAM≤ 4	Group A	42	38.45	3.351	0.011
	Group B	42	52.40	3.883	

***** Data are presented as mean±SD

Comparison of duration of hospital stay

The hospital stay was found to be significantly lower in group A than in group B (2.414±0.2581 vs 3.495±0.2793 days; p=0.007).

Table 4. Comparison of duration of hospital stay*****

	Study group	n	Mean	SD	p
Hospital stay days	Group A	42	2.414	0.2581	0.007
	Group B	42	3.495	0.2793	

***** Data are presented as mean±SD

Respiratory rate, heart rate, oxygen saturation, and Glasgow Coma Scale were monitored clinically during patient management but were not systematically retained for detailed secondary analysis

Adverse events

No adverse events were observed in either group during the study period.

Discussion

This randomized controlled trial compared two commonly used add-on nebulized regimens given with salbutamol in children aged 1–5 years presenting with moderate-to-severe acute exacerbation of wheeze. The principal finding was that nebulized budesonide plus salbutamol (group A) was superior to nebulized ipratropium bromide plus salbutamol (group B) for both co-primary outcomes, namely the change in PRAM score from baseline to 60 minutes and the PRAM score trajectory during the first 60 minutes. This was accompanied by a shorter time to achieve PRAM ≤4 and a reduced hospital stay.

Baseline comparability between the two groups was largely acceptable. Although age-group distribution differed between groups, mean age and baseline PRAM scores were comparable. Nevertheless, the possibility of residual confounding related to age cannot be completely excluded. This age profile is close to preschool wheeze cohorts studied by Razi et al.[13] and Razi and Andiran et al.[14] whereas studies by Upham et al.[15] and Wyatt et al.[16] included broader pediatric age groups and therefore greater phenotypic heterogeneity. Thus, the present study reflects a preschool-aged population presenting with acute wheezing, although wheezing phenotypes were not systematically characterized. Sex distribution was balanced, consistent with prior studies.[13,15] Mean weight was also comparably similar to other studies.[13,14] The absence of cyanosis in both groups further indicates that the cohort represented moderate-to-severe wheeze without overt cyanotic respiratory failure, and therefore the findings are most applicable to this clinical spectrum,

comparable to other studies.[13,15] Chest X-ray findings, throat swab results, virus type, and oxygen support mode were similar between groups.

Both co-primary outcomes, namely change in PRAM score from baseline to 60 minutes and PRAM score trajectory, favored nebulized budesonide. Baseline PRAM scores were similar, but group A (nebulized salbutamol and budesonide) showed significantly lower PRAM scores at 20, 40 and 60 minutes, with greater overall reduction at 60 minutes. This indicates a more rapid and sustained clinical response with nebulized budesonide plus salbutamol. These findings are consistent with studies showing benefit from early nebulized budesonide in acute asthma or wheeze. Chen et al. demonstrated better early lung function recovery and higher remission rates with high-dose budesonide.[17] Razi et al. also reported improved clinical scores and lower hospitalization rates in preschool children receiving nebulized budesonide.[13] Murphy et al. similarly concluded that early nebulized budesonide may reduce symptom severity and hospitalization in children aged ≤5 years.[9] However, not all studies have shown benefit. Upham et al. found no difference in early asthma score improvement or admission rates,[15] and Razi and Andiran et al. reported no difference in length of stay in hospitalized wheezing children.[14] These differences may be due to variations in severity, dosing, and concurrent systemic corticosteroid use.

The shorter time to achieve PRAM ≤4 in group A (nebulized salbutamol and budesonide) is clinically meaningful because it reflects earlier stabilization and may reduce repeated nebulization, prolonged monitoring, and escalation of care. This is comparable to findings from Razi et al., who reported shorter discharge time with budesonide,[13] and Chen et al., who found earlier remission.[17] Although ipratropium-containing regimens have shown benefit in some studies, particularly when compared with salbutamol alone,[19,21] the present study suggests that budesonide was superior to ipratropium bromide as an add-on to salbutamol. Nevertheless, ipratropium bromide remains an effective adjunct bronchodilator in acute wheeze and has demonstrated clinical benefit when combined with salbutamol, particularly in moderate-to-severe exacerbations.

A further important finding was the significantly shorter hospital stay in group A. This suggests early improvement being translated into a downstream service benefit. Similar reductions in hospitalization burden with budesonide have been reported previously,[13,18] although some studies did not find a significant length-of-stay advantage.[14,16] These results should be interpreted with caution due to the limited sample size, single-center design, and baseline age distribution imbalance.

All enrolled children were admitted for observation according to institutional protocol because they presented with moderate or severe wheezing requiring repeated nebulization. Discharge decisions were based on clinical stability, oxygen independence, adequate oral intake, and caregiver readiness. Therefore, duration of hospitalization may have been influenced not only by clinical response but also by institutional discharge practices. Consequently, differences in hospital stay should be interpreted as exploratory findings rather than definitive measures of treatment efficacy.

Study strengths and limitations

Randomized equal allocation improved internal validity. The study focused on preschool children, a clinically important age group with limited comparative evidence. Serial PRAM scoring at fixed intervals captured early response objectively. Clinically relevant outcomes such as time to PRAM≤4 and hospital stay increased practical applicability to emergency and inpatient pediatric care.

Despite randomization, age-group distribution differed between treatment groups at baseline. Since younger children may have different wheezing phenotypes and treatment responses compared with older preschool children, residual confounding cannot be excluded.

Larger studies with stratified randomization according to age are warranted. The study did not systematically characterize wheezing phenotypes, including recurrent wheeze history, atopic status, family history of asthma, or allergic sensitization. Information regarding previous hospitalization for wheeze, environmental tobacco smoke exposure, fever, and detailed atopic history was not systematically collected and therefore could not be analyzed. Therefore, subgroup analyses according to wheezing phenotype could not be performed, and differential treatment responses among specific phenotypic subgroups cannot be excluded. The sample size was modest, and the study was conducted in a single center, limiting generalizability. PRAM scoring may be subject to observer variation. Although PRAM scoring followed standardized criteria and assessors received orientation regarding PRAM assessment, formal assessor certification and inter-rater reliability testing were not conducted. Respiratory rate, heart rate, oxygen saturation, and Glasgow Coma Scale were monitored clinically but were not systematically retained for detailed secondary analysis. Systemic corticosteroid administration after the initial study intervention was not systematically recorded and may have influenced later outcomes, including duration of hospitalization. Viral categorization was limited, and the observed reduction in hospital stay may have reflected institutional discharge practices in addition to treatment response; therefore, hospital stay should not be interpreted as a measure of treatment efficacy alone. Outcome assessors were not blinded to treatment allocation because of the open-label design. Although PRAM scoring was performed using standardized criteria and assessors received orientation regarding PRAM assessment, the open-label design could have influenced subjective clinical assessment, and observer bias cannot be excluded. Criteria for treatment failure and initiation of rescue systemic corticosteroids were based on institutional clinical protocols and physician judgment rather than predefined study-specific criteria.

Although the study achieved the planned sample size, detailed assumptions underlying the original sample size calculation, including the expected treatment effect and standard deviation, were unavailable from archived study records. Therefore, the adequacy of statistical power should be interpreted cautiously. Treatment failure was not predefined as a study outcome. Escalation of therapy was determined by the treating pediatrician according to institutional clinical protocols.

Clinical implications

The findings suggest that nebulized budesonide as an add-on to salbutamol may provide faster symptom relief, earlier stabilization, and shorter hospitalization in moderate-to-severe wheeze. This can improve bedside decision-making, reduce escalation of care, optimize bed utilization, and lessen caregiver burden. PRAM also proved useful as a practical monitoring tool in acute settings. The regimen associated with faster PRAM improvement and shorter hospital stay may be considered as an add-on therapy to salbutamol in similar clinical settings; however, these findings require confirmation in larger multicenter randomized trials before routine clinical implementation. PRAM should be monitored at regular short intervals. Non-responding by 40–60 minutes should be reassessed early. Standardized discharge criteria, oxygen weaning, and correct nebulization techniques should be ensured.

Future directions

Large multicenter randomized trials are needed to confirm these findings. Future studies should use stratified randomization by age and severity, standardize co-interventions, and assess additional outcomes such as recurrence of wheezing episodes, emergency department revisit rates, subsequent systemic corticosteroid therapy, oxygen weaning time, and cost-effectiveness. Subgroup analyses according to viral status, atopy, and recurrent wheeze may improve individualized treatment selection.

Conclusion

In this randomized direct comparison, nebulized budesonide as an add-on to salbutamol was associated with greater short-term improvement in PRAM scores and shorter hospital stay than nebulized ipratropium bromide as an add-on to salbutamol in children aged 1–5 years presenting with moderate or severe wheezing. Larger multicenter studies with detailed phenotypic characterization of preschool wheezing are needed to confirm these findings and determine the patient subgroups most likely to benefit. These findings may help optimize the acute management of preschool wheeze pending confirmation in larger multicenter randomized trials.

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Declarations

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Author contributions

Conceptualization, V.V.; Methodology, R.A.; Investigation, R.A.; Data curation, R.A.; Writing – original draft, R.A.; Writing – review & editing, V.V., A.R., S.S.; Supervision, S.S.

Conflicts of interest

The authors declare no competing interests.

Data availability

The datasets are available from the corresponding author on reasonable request.

Ethics approval

The study was approved by the Institutional Ethics Committee of SRM Medical College Hospital and Research Centre (Approval No: SRMIEC-ST0724-1721). Written informed consent was obtained from the parents or legal guardians of all participating children.

Use of AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist with language refinement and manuscript polishing. After using these tools, the authors reviewed and edited all content as needed and take full responsibility for the content of the published article.

Trial registry

CTRI/2025/04/085680 (registered on 25/04/2025).

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