Original article

Efficacy of Nebulized Ipratropium Bromide Versus Salbutamol in Infants with Acute Bronchiolitis

Md. Balayat Hossain Dhali,[1] Md. Shariful Islam,[2] Muhammed Anisur Rashid,[3] Mohammad Kamruzzaman,[4] Morshed Md. Moniruzzaman,[5] Abu Jafar Muhammad Kamrul Eman Rashed[6]

1. Assistant Professor
   Department of Paediatrics
   Chattogram Medical College
2. Professor and Head
   Department of Paediatrics
   Rangpur Medical College
3. Assistant Professor
   Department of Paediatrics
   Rangpur Medical College
4. Assistant Professor
   Department of Paediatrics
   Dinajpur Medical College
5. Assistant Professor
   Department of Paediatrics
   Shaheed M. Monsur Ali Medical College
   Sirajganj
6. Junior Consultant
   Department of Paediatrics
   Upazilla Health Complex
   Pirgacha, Rangpur

Correspondence to:
Md. Balayat Hossain Dhali
Assistant Professor, Department of Paediatrics
Chattogram Medical College
Chattogram, Bangladesh
E-mail: bhdhali1971@gmail.com

Submission Date : 02 Dec 2024
Accepted Date : 15 Jan 2025
Published Date : 30 March 2025
DOI: https://doi.org/10.3329/jrpmc.v10i1.81559

Abstract

Background:
Bronchiolitis, a common lower respiratory tract infection in infants, is primarily caused by respiratory syncytial virus (RSV). Management typically includes supportive care with oxygen therapy, hydration, and sometimes bronchodilators. However, the efficacy of bronchodilators remains debated.

Objective:
The study aimed to compare the effectiveness of nebulized ipratropium bromide and salbutamol in treating acute bronchiolitis in infants.

Methods:
An open-label, cross-sectional study was conducted at Chittagong Medical College Hospital from October 2008 to September 2009. Infants aged 2-12 months, presenting with their first episode of respiratory distress and clinical signs of viral respiratory illness (temperature ≥38°C and/or coryza), were included. The two groups (salbutamol and ipratropium bromide) were assessed at baseline and at 12, 24, 36, and 48 hours using the Modified Respiratory Distress Assessment Instrument (MRDAI) score. Clinical outcomes, including changes in MRDAI scores,drug side effects, and hospital length of stay (LOS), were recorded.

Results:
The study found no significant differences in MRDAI scores, LOS, or adverse effects between the two groups. Both salbutamol and ipratropium bromide were effective in relieving symptoms of acute bronchiolitis.

Conclusion:
Nebulized salbutamol and ipratropium bromide are equally effective in managing acute bronchiolitis in infants.

Keywords: Acute bronchiolitis, Ipratropium Bromide, Salbutamol, nebulized

Citation: Dhali MBH, Islam MS, Rashid MA, Mohammad Kamruzzaman M, Moniruzzaman MM, Abu Rashed JMKE. Efficacy of Nebulized Ipratropium Bromide Versus Salbutamol in Infants with Acute Bronchiolitis.J Rang Med Col. 2025 Mar;10(1):40-44. doi: https://doi.org/10.3329/jrpmc.v10i1. 81559

Introduction:

Bronchiolitis is a leading cause of lower respiratory tract infection in infants, primarily affecting children under two years, with peak incidence between 2-6 months of age. It typically presents coryzal symptoms, low-grade fever, wheezing, tachypnea, chest recession, and crepitations, often with radiological evidence of hyperinflation.[1] Respiratory syncytial virus (RSV) is the most common cause, responsible for approximately 50% of cases, while other etiologies include parainfluenza, adenovirus, influenza, and Mycoplasma pneumoniae.[2] The incidence of bronchiolitis peaks in winter and early spring,[3] with hospitalization rates reaching 6 per 1,000 children annually in the U.S. and significantly

impacting pediatric admissions in developing countries.[4,5] In low-resource settings, the burden is even greater, with acute respiratory infections (ARI) accounting for 27% of deaths in children under five in Bangladesh.[6] Management is primarily supportive, focusing on oxygen therapy, hydration, and monitoring for respiratory distress. The use of bronchodilators, particularly salbutamol and ipratropium bromide, remains controversial. Although widely used, meta-analyses suggest limited effectiveness in reducing hospital stay or improving clinical outcomes.[7] Salbutamol, a β 2-agonist, is commonly administered to relieve bronchospasm, but studies indicate minimal benefit in bronchiolitis, which primarily involves airway inflammation rather than bronchoconstriction. Ipratropium bromide, an anticholinergic, has been suggested as an alternative due to its bronchodilator effects and fewer reported side effects.[8,9] However, international guidelines remain inconsistent regarding its use. Given the high disease burden and ongoing debate over treatment strategies, this study aimed to evaluate whether nebulized ipratropium bromide is more effective than nebulized salbutamol in managing acute bronchiolitis. Understanding their comparative effectiveness may help guide clinical decision-making and improve patient outcomes.[10] The aim of the study was to compare the efficacy of nebulized salbutamol and ipratropium bromide in the management of acute bronchiolitis in hospitalized infants.

Methods:

This open-label, cross-sectional comparative study was conducted in the Pediatric Inpatient Department of Chittagong Medical College Hospital (CMCH) from October 2008 to September 2009. A total of 100 infants (aged 2-12 months) admitted with their first episode of respiratory distress, wheezing, and clinical signs of viral respiratory illness (temperature ≥38°C and/or coryza) were enrolled. Data collection was done using a structured questionnaire, and written consent was obtained from the patient's mother or guardian. A detailed history, general examination, and systemic assessment were performed. Disease severity (moderate or severe bronchiolitis) was assessed using the Modified Respiratory Distress Assessment Instrument (MRDAI) scoring system (Table-1), which included respiratory rate, nasal flaring, wheezing, chest recession, and general status.[11] Antibiotics were given as per WHO guidelines[12] or consultant recommendations in severe cases. The scoring system was slightly modified to align with WHO ARI protocols.[13-15] Patients were randomly assigned into two groups based on alternating registration numbers: Group A (Salbutamol group) and Group B (Ipratropium group). Group A received nebulized salbutamol (0.15 mg/kg, minimum 1 mg) diluted in 3 mL normal saline every 4 hours,[10,11] while Group B received nebulized ipratropium bromide (250 µg in 3mL normal saline) every 6 hours.[10,11] Supportive care, including airway clearance, oxygen therapy, hydration, and feeding, was provided. Patients were clinically evaluated at 12, 24, 36 48 hours and at discharge using the MRDAI score[10] (Table-I). Changes in MRDAI score, and hospital stay were recorded. Data were analyzed using SPSS version 15.0, employing Chi-square tests, Fisher's exact test, and Student's t-test, with $p<0.05$ at 95% CI considered statistically significant. Results were presented in tables and compared with previously published studies.

Table-I: Modified respiratory distress assessment instrument (MRDAI) scoring system

Score	Respiraion/ min	Retraction	Nasal flaring	Wheezing	General status
0	<40	No	No	No	Normal
1	40- <50	Intercostal	Mild/rare	Heard only in exp. with stethoscope	Uneasy/ occasional crying
2	50- <60	Intercostal, sub- costal and supraclavicular	Moderate/ Intermittent	Heard in both insp. & exp. with stethoscope	Very uneasy/ continuous crying
3	>60	Abdominal respiration accompanying	Severe/ continuous	Heardwithout stethoscope	Lethargic

Results:
Table-II showed the distribution of age and sex in both groups. Most cases were ≤ 6 months, with a male predominance. No significant differences were observed between the groups (p >0.05).

Table-II: Distribution of age and sex among study groups(n=100)

Category	Group-A no.(%)	Group-B no. (%)	Total	p-value
Age ≤6 Months	28(56.0)	30(60.0)	58(58.0)	>0.05*
Age >6 Months	22(44.0)	20(40.0)	42(42.0)	
Male	42(84.0)	40(80.0)	82(82.0)	
Female	8(16.0)	10(20.0)	18(18.0)	

*not significant

Among the subjects of the two groups, 46 cases (22 of Group-A and 24 of Group-B) were with moderate bronchiolitis (MRDAI score, 4-8) and 54 cases 28 of Group-A and 26 of Group-B were with severe bronchiolitis (MRDAI score >8) (p>0.05) (Table-III).

Table-III: Grading and Statistics of MRDAI Score at Admission Among Study Groups (n=100)

Grading of MRDAI Score at Admission	Group-A no.(%)	Group-B no. (%)	N	Mean±SD	Median	Range	p-value
Moderate (4–8)	22(44.0)	24(48.0)	50	6.86±1.39	9	6–11	>0.05*
Severe (>8)	28(56.0)	26(52.0)	50	9.20±1.14	9	7–11	
Total	50(100.0)	50(100.0)	100	8.94±1.29	9	6–11	

*not significant

The mean MRDAI scores at admission in Group-A were 8.68±1.39 and Group-B were 8.80±1.14. The follow up MRDAI scores of group-A and group-B after 12, 24, 36 and 48 hours of treatment and at discharge showed that mean MRDAI scores has significantly reduced in both groups in comparison to mean MRDAI scores before treatment in both groups. Both groups improved over time, with Group A consistently having slightly higher scores. At discharge, Group A had a lower mean score (2.28) than Group B (2.68). Overall, both groups showed similar improvements (Table-IV).

Table-IV: Statistics of MRDAI score at admission, follow-ups (12, 24, 36, and 48 Hours) and discharge among the study Groups

MRDAI Score	N	Mean	sd	Median	range	p-value
At admission						
Group A	50	8.68	1.39	9	6–11	>0.05*
Group B	50	9.20	1.14	9	7–11	
12 hours						
Group A	50	6.84	0.84	7	6–9	>0.05*
Group B	50	6.44	0.76	6	5–8	
24 hours						
Group A	50	5.84	0.62	6	5–7	> 0.05*
Group B	50	5.48	0.71	5	4–7	
36 hours						
Group A	50	4.96	0.67	5	4–6	>0.05*
Group B	50	4.60	4.60	5	3–6	
48 hours						
Group A	50	4.04	0.60	4	4–5	>0.05*
Group B	50	3.84	0.62	4	3–5	
At discharge						
Group A	50	2.28	0.45	2	2–3	>0.05*
Group B	50	2.68	0.47	3	2–3	

*not significant

There was no statistically significant difference between the two groups regarding the mean MRDAI score reduction after 48 hours of treatment (p>0.05) (Table-V).

Table-V: MRDAI score reduction after 48 hours among study group

	N	Mean sd	p-value
Group A	50	4.64±0.79	>0.05*
Group B	50	5.36±0.52	

*not significant

No significant difference was found in the length of hospital stay between the two groups (Table-VI).

Table-VI: Length of hospital stay among study groups

Days	Group A	Group B	p-value
Mean ± SD	3.60±0.76	3.64±0.63	
Median	4.00	4.00	>0.05
Range	2–5 days	3–5 days	

*not significant

Discussion:

Acute bronchiolitis is a significant lower respiratory tract infection (LRTI) in children under six months, often resembling asthma due to rhinorrhea, wheezing, and tachypnea. This similarity has led to the common use of bronchodilators and corticosteroids.[11] As half of all bronchiolitis cases later develop reversible airway disease, numerous studies have examined the efficacy of bronchodilators.[16] The role of sympathomimetics (salbutamol) and anticholinergics (ipratropium bromide) remains debated. This study aimed to evaluate and compare the benefits of B2-specific agonists (salbutamol) and anticholinergics (ipratropium bromide) in children experiencing their first episode of bronchiolitis- related wheezing and respiratory distress. A total of 100 cases were studied: 50 in Group-A (salbutamol) and 50 in Group-B (ipratropium bromide). Male infants were more affected (M: F=4.5:1) compared to previous studies (Bulent K et al: 1.5:1).[15] The mean age in our study was 5.62±2.69 months, consistent with Uyan A P et al (6.9±3.4 months) and Bulent K et al (5.1±2.7 months).[8,11] Most cases (58%) were under six months, with 42% aged 6-12 months.

Various clinical scoring systems assess bronchiolitis severity. Uyan A P et al used a system including respiratory rate, nasal flaring, wheezing, and general status.[11] Other systems incorporated factors like oxygen saturation, retraction, and auscultation findings.[17] In our study, the MRDAI score (Modified Respiratory Distress Assessment Instrument) was used due to its non- invasive nature and low inter-observer variation. Moderate bronchiolitis (MRDAI 4-8) accounted for 46% of cases, while 54% had severe bronchiolitis (≥29). On admission, MRDAI scores ranged from 6-11 in Group-A and 7-11 in Group-B, with mean MRDAI score was 8.68±1.39 vs 9.20±1.14; respectively, p>0.05) and after 12, 24, 36 and 48 hours of treatment (6.84±0.84 vs 6.44±0.76; 5.84±0.62 vs 5.48±0.71; 4.96±0.67 vs 4.60±0.76; and 4.04±0.60 vs 3.84±0.62 respectively, p>0.05). After 48 hours, score reductions were 4.64±1.17 (Group-A) and 5.06±0.80 (Group-B), which was statistically insignificant. The primary outcome was assessed based on MRDAI score reduction and hospital length of stay (LOS). LOS was also similar (3.60±0.76 vs. 3.64±0.63 days, p>0.05) (14,24). Studies by Uyan A P et al and King et al found no significant difference between salbutamol and ipratropium bromide groups regarding clinical scores and hospitalization duration.[11,18] Bronchodilators are widely used worldwide, though their efficacy is debated. In Canada, 78% of bronchiolitis cases receive bronchodilators, whereas in the U.S., pediatric allergists and pulmonologists recommend them in 86% of cases.[11] WHO Division of Child Health and Development reported that bronchodilators help only one-third of cases, while Suzanne S. et al. found a 60% response rate.[19,20] Some studies show improved oxygenation and respiratory effort with ipratropium bromide[11,16], whereas others report no significant benefits.[21] Our study found both drugs equally effective in reducing MRDAI scores and LOS (p>0.05). Side effects were minimal, with tremors in four salbutamol cases (resolved spontaneously). Prior studies noted salbutamol related side effects, including tremor, hyperactivity, and hypokalemia, but no adverse effects from ipratropium bromide.[8,11]

Conclusion:

Acute bronchiolitis is a common lower respiratory tract disease in infants, with most children affected by age two. Despite the limited role of antibiotics and steroids, they are frequently used in treatment. Bronchodilators like salbutamol and ipratropium bromide are widely used globally, but local studies are scarce. The role of sympathomimetics and anticholinergics in acute bronchiolitis remains debated. Nebulized ipratropium bromide is a safe option for symptom relief with minimal side effects and may be preferred over salbutamol. Larger multicenter trials are needed to confirm these findings.

References:

1. Kabir ML, Haq N, Hoque M, Ahmed F, Amin R, Hossain A, et al. Evaluation of hospitalized infants and young children with bronchiolitis - a multi centre study. Mymensingh Med J. 2003 Jul;12(2):128-33.
2. Kabir ARML, Mollah AH, Anwar KS, Rahman

AKMF, Amin R, Rahman ME. Management of bronchiolitis without antibiotics: a multicentre randomized control trial in Bangladesh. Acta Paediatrica. 2009 Sep; 98(10): 1593-1599.doi: https://doi.org/10.1111/j.1651-2227.2009.01389.x
3. Kabir ARML, Amin MR, Morshed AKMA, Shirin M. Viral bronchiolitis: an update on a recent epidemic. ORION. 2002 May; 12:9-10.
4. Yousif TK, Khaleq BA. Epidemiology of ARI among children under five years old attending Tikrit General Teaching Hospital. Middle East J Fam Med. 2006;4(3):1.
5. Talukder MQK, Das DK. Nutritional status and acute respiratory tract infection. Bangladesh J Child Health. 1987;11(4):149-53.
6. Khan MR, Mola M, Rahman ME. Acute Respiratory Infections (ARI) in children. Journal of IPGMR, 1987 Vol 2(1): 4-6.
7. Garrison MM, Christakis DA, Harvey E, Cummings P, Davis RL. Systemic corticosteroids in infant bronchiolitis: A meta-analysis. Pediatrics. 2000 Apr;105(4): E44. doi: 10.1542/peds.105.4.e44.
8. Karadag B, Ceran O, Guven G, Dursun E, Ipek IO, Karakoc F, et al. Efficacy of salbutamol and ipratropium bromide in the management of acute bronchiolitis-a clinical trial. Respiration. 2008;76(3):283-7. doi: 10.1159/000111817.
9. Schuh S, Johnson D, Canny G, Reisman J, Shields M, Kovesi T, et al. Efficacy of adding nebulized ipratropium bromide to nebulized albuterol therapy in acute bronchiolitis. Pediatrics. 1992 Dec;90(6):920-3.
10. Absar SM, Jahan S, Khanum S. Efficacy of nebulized ipratropium bromide versus salbutamol in infants with acute bronchiolities. Bangladesh Med Res Counc Bull. 2008 Dec;34(3):112. doi: 10.3329/bmrcb.v34i3.1861.
11. Uyan AP, Ozyurek H, Keskin M, Afsar Y, Yilmaz E. Comparison of two different bronchodilatorsin the treatment of acute bronchiolitis. The internet journal of pediatrics and neonatology, 2003; 3(1).
12. Kabir ARML, Amin MR, et al. Magnitude of respiratory disorders in under-5 children attending different hospitals of Bangladesh. Research report ICMH. March 2009.
13. Asthma Association, Bangladesh. National guidelines—asthma, bronchiolitis and COPD. 3rd ed. Dhaka: Asthma Association; 2005 May. p. 137-43.
14. Azad AK. Effects of steroid in acute bronchiolitis [MD thesis]. Chittagong: Chittagong University, Chittagong Medical College; 2007.
15. CARI Project, DGHS, Government of Bangladesh. A manual for the management of the young children with an acute respiratory infection. Geneva: World Health Organization; 1993. (WHO/IARI/93).
16. Wang EE, Milner R, Allen U, Maj H. Bronchodilators for treatment of mild bronchiolitis: a factorial randomised trial. Arch Dis Child. 1992 Mar;67(3):289-93. doi: 10.1136/adc.67.3.289.
17. Berger I, Argaman Z, Schwartz SB, Segal E, Kiderman A, Branski D, et al. Efficacy of corticosteroids in acute bronchiolitis: short-term and long-term follow-up. Pediatr Pulmonol. 1998 Sep;26(3):162-6. doi: 10.1002/(sici)1099-0496(199809)26:3<162::aid-ppul2>3.0.co;2-n.
18. King VJ, Viswanathan M, Bordley WC, Jackman AM, Sutton SF, Lohr KN, et al. Pharmacologic treatment of bronchiolitis in infants and children: a systematic review. Arch Pediatr Adolesc Med. 2004 Feb;158(2): 127-37. doi: 10.1001/ archpedi. 158.2.127.
19. World Health Organization. Management of the young child with an acute respiratory infection. Supervisory skills training module. Geneva, World Health Organization, revised 1991[unpublished document; WHO Division of Child Health and Development (CHD)].
20. Schuh S, Coates AL, Binnie R, Allin T, Goia C, Corey M, Dick PT. Efficacy of oral dexamethasone in outpatients with acute bronchiolitis. J Pediatr. 2002 Jan;140(1): 27-32. doi:10.1067/mpd. 2002. 120271.
21. Hay WW, Levin MJ, Soudheimer JM, Deterding RR. Current diagnosis and treatment in pediatrics. 18th ed. New York: McGraw-Hill; 2007. p. 506-7, 1106-8.