

A Prospective Study of Efficacy of Nebulized L-Adrenaline versus Salbutamol Comparison in Infants with Acute Bronchiolitis

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Abstract

Background: One of the most common baby illnesses, bronchiolitis necessitates hospitalisation for many infants, especially during the winter months. Respiratory syncytial virus (RSV) is the main pathogenic organism that causes the disease. Although none of the therapeutic techniques is specifically targeted, the major goal of management is to relieve symptoms. Salbutamol, adrenaline, anti-cholinergic medications, ipratropium bromide, and saline nebulization have all been used as bronchodilators with varied degrees of success.

Methods: To compare the effectiveness of nebulized salbutamol and adrenaline in treating bronchiolitis, this prospective study included 52 infants (2-12 months, male:female ratio 2:1) with bronchiolitis (with 1st episode of wheeze, previously healthy baby, physical findings with cough, running nose, fever, coryza, and inflation of lungs). The cases were randomly assigned to groups receiving nebulized salbutamol (n = 25) and nebulized adrenaline (n = 27). Three nebulizer treatments were administered following randomization, one every 20 minutes. Respiratory rate, MRDAI (Modified Respiratory Distress Assessment Instrument) score, and O₂ saturation were used to assess the effectiveness of the therapy.

Results: Cough (100%), respiratory discomfort (100%), feeding trouble (90.3%), running nose (98%) and wheeze (100%) were all observed in the study cases in both groups. Most of the cases are urban dwellers from non-smoking families. After three nebulizations, the salbutamol group's respiratory rate, MRDAI score, and O₂ saturation all significantly improved from their pre-nebulization values (RR-67.56.1, MRDAI score-14.61.3, SaO₂ 93.91.6) to their post-nebulization values (RR-52.54.9, MRDAI score-6.41.7, SaO₂-97.11.5). Respiratory rate, MRDAI score, and O₂ saturation all significantly increased after 3 nebulizations in the adrenaline group (pre-nebulization RR-64.95.9, MRDAI score-15.00.8, SaO₂-94.11.4, and post-nebulization RR-50.02.9, MRDAI score-7.71.0, SaO₂-97.91.5). Improvement was greater in the group taking adrenaline. Both groups' heart rates (salbutamol group-151.810.6 and adrenaline group-160.210.1) increased, with the adrenaline group experiencing a greater increase. Nebulized adrenaline therapy was shown to be considerably more effective than nebulized salbutamol therapy at relieving symptoms when comparative efficacy was assessed (p=.004).

Conclusion: According to the study, nebulized L-adrenaline is considerably more efficient than nebulized salbutamol at relieving symptoms in infants with bronchiolitis. Both nebulized salbutamol and nebulized L-adrenaline are beneficial.

Key words: Nebulized L-adrenaline, Nebulized Salbutamol, Acute Bronchiolitis.

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Background

A viral acute inflammatory lesion of the small airways called bronchiolitis. RSV (respiratory syncytial virus) is the culprit responsible for more than 70% of cases; additional pathogens include Parainfluenza virus, Adenovirus, Rhinovirus, Influenza virus, and *Mycoplasma pneumoniae*. The peak period is from midwinter to latespring. Almost all children contract bronchiolitis within the first three years of life, with the peak incidence occurring between 2 and 6 months of age [1]. Male newborns who have not been breastfed and who live in crowded conditions are more likely to get bronchiolitis. Most frequently, a family member who has a minor respiratory ailment is the cause of the viral infection.

Compared to infants of non-smoking moms, babies of smokers are more prone to get bronchiolitis. Where a heavy smoker stays with kids, the occurrence is more common [2]. Bronchitis causes more than 90,000 hospital admissions in the United States each year, with most patients being newborns under 90 days [3].

There have been recorded variations in bronchiolitis treatment. Various therapeutic techniques, such as bronchodilators, ribavirin, steroids, and antibiotics, are administered to hospitalised patients. These various treatment techniques have a considerable impact on the price and unfavourable hospital events [4].

While bronchodilators are frequently used to treat bronchiolitis, there is conflicting evidence regarding their effectiveness. The majority of studies have found no improvement in lung mechanics. In an empirical investigation, JD Kellner *et al.* noted that bronchodilators only cause

moderate short-term improvements in clinical scores [5].

Any type of steroid, particularly nebulized budesonide 1000 microgram/dose, is beneficial in treating bronchiolitis, according to a study by Arivolli Verappan and Ashir Kumar. Lepinephrine was effective and less expensive than other treatments for bronchiolitis, they add [6]. The only particular treatment for RSV infection in infants is ribavirin, a broad-spectrum antiviral medication¹. In a recent study, Ray and Singh came to the conclusion that nebulized salbutamol and epinephrine both significantly improved mean symptom scores and oxygenation. However, compared to the salbutamol group, the epinephrine group had a considerably greater improvement in the study parameters. "Adrenaline is more effective than salbutamol and is therefore a better, affordable and relatively safe alternative," they wrote in their conclusion [7].

A prospective research on the effectiveness of nebulized epinephrine versus salbutamol in hospitalised babies with bronchiolitis was conducted by Bertrand P *et al.* They observed that nebulized epinephrine reduced the bronchiolitis baseline clinical score more quickly than salbutamol.

Additionally, they came to the conclusion that nebulized epinephrine is both equally safe and more effective than salbutamol in the initial therapy of bronchiolitis [8].

The goal of the study was to compare the effectiveness of nebulized salbutamol and nebulized L-adrenaline in treating acute bronchiolitis.

Materials and Methods

The prospective, randomized, interventional study was conducted at Department of Pharmacology associated with Department of Pediatrics, Adesh Medical College and Hospital, Mohri, Shahbad, Kurukshetra, Haryana from November 2021 to March 2022.

In this study, infants (2–12 months old) who had previously been healthy and had their first wheezing episode along with physical symptoms of a viral infection, such as coryza, cough, fever, etc., as well as clinical and radiographic signs of pulmonary hyperinflation, were included. Patients with evidence of a prior attack that was comparable, asthma, a history of corticosteroid usage, atopy or allergy, congenital heart disease, or tuberculosis were excluded.

The cases were then randomly divided into two groups, A (salbutamol group) and B (adrenaline group), with one case going to the salbutamol group and the next case going to the adrenaline group (adrenaline group). Salbutamol was administered to Group A (the salbutamol group) in a dose of 0.15 mg/kg body weight (the minimum dose was 1 mg)⁷, diluted in normal saline to a final volume of 3 ml.

Cases in group B (the adrenaline group) were given nebulized adrenaline at a concentration of 0.1 ml per kilogramme of body weight (1 ampoule 1:1000 injection diluted with 9 ml of normal saline to make it 1 in 10000 solution) [7]. A additional 3 ml of the medication was combined with sterile saline. Each group received nebulization treatments spaced 20 minutes apart.

During this time, pulse oxymetry was performed, and SaO₂ readings were taken before and after nebulization. No other medications, such as antibiotics, steroids, intravenous fluids, etc., were administered during this time. In febrile cases only hydrotherapy was given. Respiratory rate,

MRDAI score, and oxygen saturation (by pulse oxymetry) were once more measured ten minutes after the final dose was administered to gauge the effectiveness of the treatment. On the basis of this assessment, the choice for continuing management was made.

After an hour of monitoring, oral medicine was given to children who had a sustained improvement in tachypnea and respiratory distress (wheezing and retractions) and were receiving it well. Children who did not get better were admitted to the hospital for additional treatment.

Supportive treatments were taken, including elevated positioning, fluids, nutrition, antibiotics (if needed), and counselling. Because the MRDAI score has completed validity and reliability testing in randomised controlled trials including patients with bronchiolitis, it was selected to evaluate the clinical outcome of nebulized salbutamol and adrenaline [4].

Utilizing suitable statistical tests including the paired and unpaired Student's "t" test, data were examined using SPSS statistical software.

Results

52 cases were enrolled in the study, 25 (male-15, female-09) were treated with nebulized salbutamol, and 27 (male-17, female-10) were treated with nebulized adrenaline. 42 babies (salbutamol group 21; adrenaline group 21) were delivered normally, making up the majority of instances (salbutamol group 25; adrenaline group 24) in both groups. The cases' body weights varied from 4.5 kg to 13 kg (mean-6.7kg). The majority of infants in the salbutamol (17/25; 68%) and adrenaline (17/27; 63%) groups were nursed exclusively until they were 4 months old. In both groups, only 2 cases combined complementary and breast feeding.

Six instances (6/25; 24%) in the salbutamol group received just supplemental feeding, as opposed to eight cases (8/27; 29.6%) in the adrenaline group.

Twenty (20/25; 80%) of the salbutamol group's cases and 23 (23/27; 85%) of the adrenaline group's cases reside in urban areas, while five cases (five/25; 20%) of the salbutamol group's cases and four cases (4/27; 15%) of the adrenaline group's patients do. The majority of the cases (adrenaline group-23/27; 85%; salbutamol group-19/25; 76%) reside in a typical environment.

Salbutamol group 6/25, or 24% of patients, and adrenaline group 4/27, or 15% of cases, both live in congested environments. The majority of cases (groups 21/25 for salbutamol; 84%; and group 24/27 for adrenaline; 89%) reside in well-ventilated rooms. The rest of the families had insufficient ventilation. Family members who smoked were 12 (11/25) (44%) in the salbutamol group and 6 (6/27; 22.2%) in the adrenaline group. Most of the family members (34) were nonsmokers (13/25; 52% in the salbutamol group and 21/27; 77.8% in the adrenaline group).

Table 1: Distribution of Resident of the family, crowded living and ventilation status

		Salbutamol Group (n=25) No. (%)	Adrenaline Group (n=27) No. (%)
Residence	Urban	20(80%)	23(85.2%)
	Rural	5(20%)	4(14.8%)
Crowded living	Present	6(24%)	4(14.8%)
	Absent	19(76%)	23(85.2%)
Ventilation	Good	21(84%)	24(89%)
	Poor	4(16%)	3(11%)

Table 2: Clinical Presentation of both groups

	Salbutamol Group (n=25) No. (%)	Adrenaline Group (n=27) No. (%)
Cough	25(100%)	27(100%)
Fever	16(64%)	16(59.3)
Respiratory distress	25(100%)	27(100%)
Feeding difficulties	21(84%)	26(96.3%)
Running nose	24(96%)	27(100%)

All individuals had a cough, however 98% of cases also had a runny nose (adrenaline group 27/27, 100%; salbutamol group 24/25, 96%).

In 21 (84%) of the salbutamol group's patients and 26 (96%) of the adrenaline group's patients, difficulty swallowing was a presenting symptom. Only 16 instances (salbutamol group-16/25; 64%; and adrenaline group-16/27; 59%) in both groups showed signs of fever (98^oF-103^oF).

All the cases were presented with wheeze and respiratory distress.

When the lungs were examined, 10 (19.2%) patients had palpable spleens, while 33 (63.5%) patients had no notable auscultatory findings. Only 9 (17.3%) families had a member with an atopic condition, such as asthma, eczema, or allergic rhinitis.

The mean respiratory rate (52.9±4.9), oxygen saturation (97.1±1.5), and RDAI score (6.4±1.7) were all considerably higher

after salbutamol medication when compared to the pre-nebulization values (67.5±6.1, 93.9±1.6, and 14.6±1.3, respectively) (p.001 for all parameters). Additionally, nebulization significantly raised heart rate (151.8± 10.6 vs. 109.4± 0.4; p =.004).

Mean respiratory rate (50.0±2.9), oxygen saturation (97.9±0.8), and RDAI score (7.5±0.1) all significantly improved after nebulized adrenaline therapy (p<0.001 in all parameters). These improvements were in contrast to respiratory rate (64.9±5.9), oxygen saturation (94.11±2.9), and RDAI score (15.04±0.8) prior to nebulization. Following nebulization, the mean heart rate jumped considerably (160±10.1 vs 105 ±10.04; p <0.001).

Adrenaline was found to be substantially more effective than salbutamol in every parameter compared between the two treatment modalities, with the exception of the MRDAI score following nebulization, where the p value was 0.08. After the third nebulization, however, the respiratory rate (p=.03), oxygen saturation (p=.03), and MRDAI score reduction (0.004) were all considerably better in the adrenaline group.

Only 4 (16.0%) of the 25 patients (48%) in both groups whose nasal swabs were tested for RSV antigen were found to be positive. Differences between the groups are not displayed here.

Table 3: Comparison of response to therapy with nebulized salbutamol vs adrenaline (Before therapy)

	Salbutamol Group (n=25) No. (%) Mean±SD	Adrenaline Group (n=27) No. (%) Mean±SD	p-value
Respiratory rate	67.5±5.4	64.9±5.9	0.12
Heart rate	104.4±5.4	105.4±10	0.17
Oxygen saturation	93.6±1.6	94.1±1.4	0.63
RDAI score	14.6±1.3	15±0.8	0.13
RDAI score reduction			

Table 4: Comparison of response to therapy with nebulized salbutamol vs adrenaline (After therapy)

	Salbutamol Group (n=25) No. (%) Mean±SD	Adrenaline Group (n=27) No. (%) Mean±SD	p-value
Respiratory rate	52.5±4.9	50±2.9	0.03
Heart rate	151.8±10	160.2±10.2	0.005
Oxygen saturation	97.1±1.5	97.9±0.8	0.03
RDAI score	6.4±1.7	7.7±1.0	0.08
RDAI score reduction	6.12±1.7	7.33±1.1	0.004

Discussion

52 cases were included in the current investigation, with 25 (males: 15; females: 9) receiving nebulized salbutamol and 27 (males: 17; females: 10) receiving nebulized adrenaline. In both groups, bronchiolitis most commonly affects male infants [7-10].

Most of the cases in both categories were routinely delivered at term births. The cases' body weights varied from 4.5 kg to 13 kg (mean-6.5 kg). The average age in an Indian study was 5.6 months [7]. Up to four months, the majority of cases in both the

salbutamol and the adrenaline groups were breastfed exclusively. In both groups, only 2 instances received mixed feeding. Six individuals in the salbutamol group and eight cases in the adrenaline group received only supplemental feeding.

The current study revealed that breastfed newborns also have bronchiolitis, despite the fact that breastfeeding has a preventive effect against infection. Only a few cases—20 cases (80%) in the salbutamol group and 23 cases (85.2%) in the adrenaline group—live in rural areas. In this case, newborns in urban areas are disproportionately afflicted, and bronchiolitis is assumed².

The majority of cases reside in typical environments with good ventilation. Despite living in a well-ventilated room, the majority of cases suffered bronchiolitis attacks. Only four mothers work outside the home, leaving 47 mothers as stay-at-home moms. Compared to 6, only 12 family members in the salbutamol group smoked. The majority of the families in both categories did not smoke. Smoking, especially maternal smoking, is a known risk factor for bronchiolitis [11,12].

Running nose, cough, wheezing, fever, and trouble eating were the most common presenting symptoms in both groups in the current study (Table-2). 94% of cases in the current study's cases had runny noses and 100% of cases had coughs. In 75% of the instances involving salbutamol and nearly all of the cases involving adrenaline, difficulty feeding was a presenting symptom.

Only 16 instances in total, across the two groups, had fever (up to 103.0F). According to one investigation, clinical manifestations were nearly identical to those in our study¹⁰. Spleen palpability was shown to be present in 42% of cases by L. Kabir *et al.*, but only 19% in the current study [10].

Out of a total of 52 cases, only 25 samples of nasal swabs were examined for RSV, and only four patients' nasal swabs tested positive for RSV antigen. An earlier investigation revealed cases of anti-RSV antibody (IgM) positivity of 45.0%¹⁰. According to a research conducted in England, 60% of cases exhibited RSV antigen in their nasal swabs that was positive [13].

The respiratory rate and O₂ saturation significantly improved when salbutamol was nebulized compared to adrenaline, and the difference in improvement between the two groups after the third nebulization was statistically significant. Nebulized salbutamol and adrenaline therapy was also found to greatly reduce symptoms in a research conducted in a neighbouring country, and nebulized adrenaline was found to be significantly more effective than salbutamol⁷. Nebulized salbutamol and adrenaline [14] did not significantly differ from one another, according to Menon *et al.* The mean O₂ saturation before nebulization in the salbutamol and adrenaline groups in the current study (Table-3) was 93.9% and 94.1%, respectively. Following nebulization, the mean oxygen saturation increased to statistically significant levels of 97.1% and 97.8% in the salbutamol and adrenaline groups, respectively. In a research identical to ours, SaO₂ before nebulization in the salbutamol and adrenaline groups, respectively, was 91.1% and 90.6%, and after nebulization, these scores increased to 93.9% and 98.0%, respectively [7].

When compared with salbutamol before and after nebulization against adrenaline, there was no significant improvement in O₂ saturation in a trial conducted in Canada [14]. Adrenaline is not more effective than regular saline, according to Ainiune AA *et al.*'s comparison of the two treatments' efficacy [13]. The maximal effect of nebulized epinephrine appeared in 30

minutes and continued for 60–90 minutes, according to a previous study on croupy infants [15]. The maximum change in SaO₂ was observed in both groups in this investigation after the second nebulization, or roughly 30 minutes after the start of nebulization, despite the fact that the effects of the medicines persisted after the third dose. This could possibly be the reason why some authors who utilised a single dose of adrenaline failed [16].

In our study, the reduction in MRDAI (Respiratory Distress Assessment Instrument) score was 6.1 and 7.3 in the salbutamol and adrenaline groups, respectively. An earlier Indian study where the mean score decrease was 8.8 and 5.9 in the adrenaline and salbutamol groups, respectively [7], also demonstrated that the reduction of MRDAI score in the adrenaline group is considerably superior to the salbutamol group. According to a Canadian study, the MRDAI score was reduced by 7.5 and 6.6 points in the salbutamol and adrenaline groups, respectively, but neither result was statistically significant [14]. Ainine AA has also demonstrated that there is no discernible difference in RDAI score reduction between saline and adrenaline nebulization [13].

To evaluate the respiratory functional status and level of distress in our study, we combined the MRDAI score and oxygen saturation. These scores are easy to evaluate in the OPD setup, non-invasive, and have little inter-observer variation. The best objective criterion for determining a child's level of distress has been suggested as arterial oxygen saturation measured by pulse oxymetry [17].

The children in both groups had comparable clinical profiles at the time of participation in the trial, according to analysis of the current study. Both the adrenaline and salbutamol groups considerably improved after three consecutive times of nebulization,

although the improvement in the adrenaline group was more pronounced than it was in the salbutamol group across the board. Not only were the average score and average SaO₂ levels higher in the adrenaline group, but more patients in the adrenaline group experienced substantial improvements in their clinical scores and oxygen saturation as well ($p < 0.03$).

The cardiac side effects of medications utilised were also investigated because the chronotropic action of adrenergic agents on the heart is often a source of concern. Both salbutamol and adrenaline significantly raised heart rate, with the adrenaline group experiencing a greater increase. However, there were no unfavourable clinical outcomes in this trial, including increased irritability, tremors, facial blanching, arrhythmia, congestive heart failure, or any kid requiring drug withdrawal, tachycardia management, or any other intervening measures. Both generic (adrenaline) and specific bronchodilators (salbutamol, for example) can help with bronchiolitis symptoms relief and oxygenation.

Conclusion

Salbutamol and L-adrenaline are both effective at easing symptoms and enhancing oxygenation in bronchiolitis, according to the study's findings. Nebulized L-adrenaline was shown to be more effective than nebulized salbutamol in treating bronchiolitis when comparative efficacy was assessed. Adrenaline nebulized can be administered without any significant risks to relieve bronchiolitis symptoms. To validate the findings of our investigation, larger, multicenter, double blind, randomised controlled studies are needed.

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