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# Role of Nebulized Epinephrine Versus Nebulized Hypertonic Saline in Moderate Bronchiolitis

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## ABSTRACT

**Objective:** To compare the nebulized epinephrine versus hypertonic saline solution in patients presenting with moderate bronchiolitis in terms of mean length of hospital stay. **Study Design:** Randomized Controlled Trial. **Duration and Place of Study:** This study was conducted at the Pediatrics Department of POF Hospital, Wah Cantt, from November 2023 to May 2024. **Methodology:** A total of 144 patients aged 1 day to 24 months with moderate bronchiolitis were randomized into two groups: Group I (nebulized racemic epinephrine) and Group II (3% hypertonic saline). Group I received 0.2 mL racemic epinephrine (USP 2.25%) diluted with 1.8 mL distilled water every 6 hours, while Group II received 2.0 mL hypertonic saline nebulization every 1–4 hours as needed. Vital signs, oxygen saturation, and adverse events were monitored, and length of hospital stay was documented. **Results:** Group I had a mean age of 10.06±6.98 months and Group II 12.50±6.97 months. The mean hospital stay was significantly shorter for Group I (3.943±0.14 days) compared to Group II (4.800±0.08 days, p=0.000). Stratification by feeding type revealed consistent trends favoring Group I, with breastfed patients showing stays of 3.956±0.15 days in Group I versus 4.800±0.09 days in Group II (p=0.000). Similarly, bottle-fed and other feeding types followed the same pattern. c**onclusion:** Nebulized epinephrine exhibits greater clinical efficacy in the management of pediatric bronchiolitis, resulting in significantly reduced hospital stays compared to hypertonic saline. These findings provide critical insights into pediatric respiratory care, highlighting the necessity of targeted therapeutic approaches for optimizing patient outcomes.

## INTRODUCTION

Bronchiolitis is the most frequent respiratory disease affecting infants and young children, characterized by inflammation and congestion of the bronchioles.[1] In most cases, it is usually caused by a viral infection, and among these, the leading cause is respiratory syncytial virus.[1] Other clinical features include wheezing, coughing, and difficulty breathing; when it gets to the moderate to severe state, treatment often calls for medical involvement.[2] Treatment is symptomatic mostly, as most viruses lack specific antiviral treatment. In moderate cases of bronchiolitis, interventions concerning nebulized medications or even other tactics have major roles to play in relieving obstructed air, dampening or toning down inflammation processes for improving oxygenation capability: therefore, they are main priority areas of research.[3]

Epinephrine is an alpha- and beta-adrenergic agonist bronchodilator whose use in the management of bronchiolitis has been extensively studied.[4] Nebulized epinephrine has the potential to reduce airway edema via alpha-adrenergic effects, while its beta-adrenergic actions cause relaxation of bronchial smooth muscles.[5] This dual action has made epinephrine a potential candidate in the management of moderate bronchiolitis where airway inflammation and obstruction are prominent. There are various studies that provide evidence for nebulized epinephrine providing temporary improvements in respiratory distress, though its use often remains open to debate due to limited evidence for its benefits and possible long-term side effects.[6]

Equally, comparison of treatment with other nebulized agents like hypertonic saline are important if the management is to be optimized. Another treatment approach for bronchiolitis is the use of hypertonic saline,

usually 3% or 5%, based on its effects of improving mucociliary clearance and reducing airway edema.[7] Hypertonic saline draws water into the airway lumen by nebulization, liquefying mucus and enhancing its expectoration, hence improving airflow.[8] It has a high degree of safety and may have benefits for shortening hospital stays among those with moderately severe bronchiolitis. Comparisons of hypertonic saline with epinephrine suggest that both have their merits.[9]

According to a study by Flores-Gonzalez et al., the length of hospital stay was significantly reduced in the epinephrine group as compared with the 3% hypertonic saline alone group (3.94 ±1.88 days vs. 4.82 ±2.30 days, P = 0.011).[10] Yasin et al. found that the mean length of stay for patients in the epinephrine group was 45 hours, while the mean length of stay for patients in the 3% hypertonic saline group was 74.3 hours.[11]

The study comparing nebulized epinephrine and hypertonic saline in moderate bronchiolitis is significant because it addresses a critical need for evidence-based management strategies for a common pediatric condition. Bronchiolitis is a leading cause of hospitalization in infants, and optimizing treatment can reduce respiratory distress, improve recovery, and shorten hospital stays.

## METHODOLOGY

This randomized controlled trial was conducted in the Pediatrics Department of POF Hospital, Wah Cantt, from November 2023 to May 2024. A total of 144 patients with moderate bronchiolitis, aged 1 day to 24 months, were included. Informed consent was taken from parents or guardians. The sample size of 72 per group was calculated using the WHO sample size calculator, based on expected hospital stay differences between the two treatment groups,[10] with 80% power and 5% significance level. Patients were randomly assigned into two groups using a random number table: Group I (nebulized racemic epinephrine) and Group II (3% hypertonic saline). Group I received 0.2 ml of racemic epinephrine (USP 2.25%) diluted with 1.8 ml distilled water every 6 hours as needed, while Group II received 2.0 ml of hypertonic saline, followed by nebulizations every 1–4 hours as required. Vital signs, oxygen saturation, and nebulization requirements were monitored every 4 hours, and adverse events such as tachycardia, sweating, pallor, or trembling were recorded. Patients were discharged upon showing clinical signs of mild illness, and their hospital length of stay was documented.

Data were analyzed using SPSS version 26.0. Categorical variables (gender, type of feed, adverse events) were presented as frequencies and percentages, while numerical variables (age, weight, duration of wheezy episodes, length of stay) were summarized as means and standard deviations. Independent sample t-tests were applied post-stratification to compare length of stay between groups, with $p \leq 0.05$ considered significant.

## RESULTS

Group I had a mean age of 10.06±6.98 months and weight of 8.29±2.31 kg, while Group II had a mean age of 12.50±6.97 months and weight of 9.11±2.02 kg. The mean duration of wheezy episodes was 5.01±1.37 days for Group I and 4.79±1.43 days for Group II. In Group I, 46 patients (63.9%) were male, and 26 (36.1%) were female, while in Group II, 42 patients (58.3%) were male, and 30 (41.7%) were female as shown in Table 1.

**Table 1**

*Mean±SD of patients according to age, weight and number of days with wheezy episode. n=144*

| Demographics | Group I n=72 Mean±SD | Group II n=72 Mean±SD |
|---|---|---|
| Age (months) | 10.056±6.98 | 12.500±6.97 |
| Weight (Kg) | 8.286±2.31 | 9.113±2.02 |
| Number of days with wheezy episode (days) | 5.014±1.37 | 4.792±1.43 |
| **Gender** | | |
| Male | 46 (63.9%) | 42 (58.3%) |
| Female | 26 (36.1%) | 30 (41.7%) |

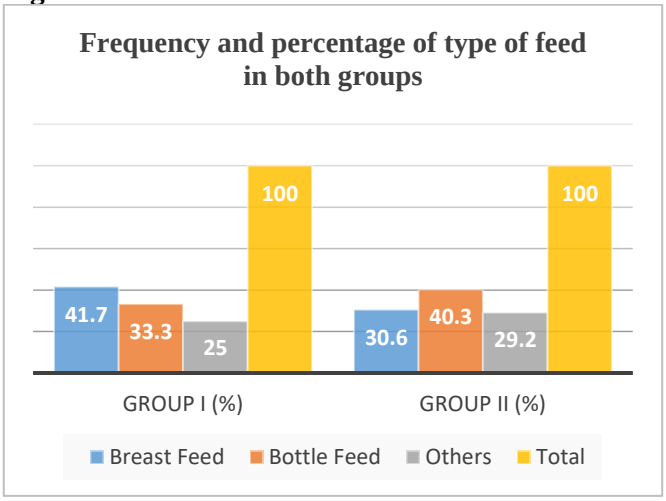
Regarding feeding types, 41.7% of patients in Group I were breastfed, 33.3% were bottle-fed, and 25% had other feeding types. In Group II, 30.6% were breastfed, 40.3% were bottle-fed, and 29.2% had other feeding types as shown in Table 2.

**Table 2**

*Frequency and percentage of type of feed in both groups.*

| Type Of Feed | n=72 Group I | n=72 Group II |
|---|---|---|
| 1 Breast Feed | 30 (41.7%) | 22 (30.6%) |
| 2 Bottle Feed | 24 (33.3%) | 29 (40.3%) |
| 3 Others | 18 (25%) | 21 (29.2%) |
| Total | 72 (100%) | 72 (100%) |

**Figure 1**



The mean length of hospital stay was significantly longer in Group II (4.800±0.08 days) compared to Group I (3.943±0.14 days) with a p-value of 0.000 as shown in Table 3.

**Table 3**

*Comparison of mean length of hospital stay in both groups. n=144*

| | Group I n=72 | Group II n=72 | t | P-value |
|---|---|---|---|---|
| Length of Hospital Stay (days) | 3.943±0.14 | 4.800±0.08 | -44.258 | 0.000 |

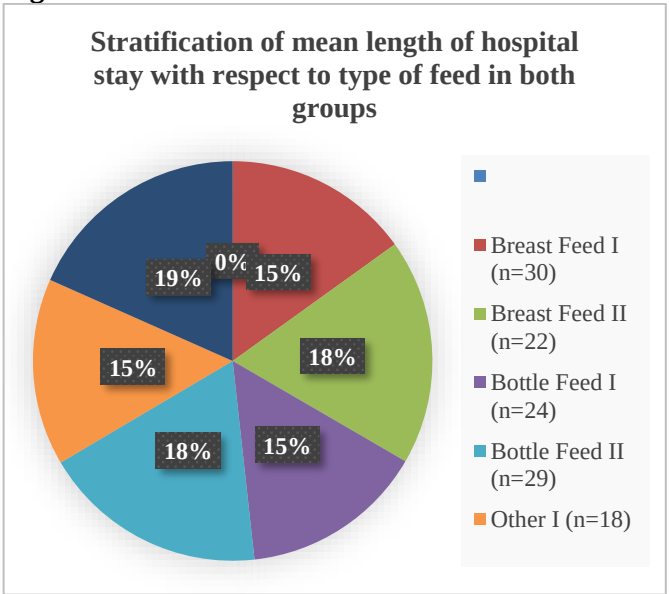
Breastfed patients in Group I had a mean hospital stay of 3.956±0.15 days compared to 4.800±0.09 days in Group II, with a p-value of 0.000. Bottle-fed patients in Group I had 3.904±0.13 days, while Group II had 4.789±0.07 days, with a p-value of 0.000. Patients with other types of feed in Group I had 3.972±0.12 days compared to 4.814±0.08 days in Group II, with a p-value of 0.000 as shown in Table 4.

**Table 4**

*Stratification of mean length of hospital stay with respect to type of feed in both groups.*

| Type of Feed | Group | Mean length of hospital stay (days) Mean | SD | p-Value |
|---|---|---|---|---|
| Breast Feed | I (n=30) | 3.956 | 0.15 | 0.000 |
| | II (n=22) | 4.800 | 0.09 | |
| Bottle Feed | I (n=24) | 3.904 | 0.13 | 0.000 |
| | II (n=29) | 4.789 | 0.07 | |
| Other | I (n=18) | 3.972 | 0.12 | 0.000 |
| | II (n=21) | 4.814 | 0.08 | |

**Figure 2**




## DISCUSSION

Apart from this study of pediatric respiratory interventions, multiple studies consistently highlight the nuanced efficacy of nebulized epinephrine and hypertonic saline in managing acute bronchiolitis. Our study provides crucial insights, demonstrating a statistically significant difference in hospital stay duration between nebulized epinephrine (Group I) and hypertonic saline solution (Group II) groups. Specifically, patients treated with nebulized epinephrine showed a shorter hospital stay of 3.943±0.14 days, compared to the hypertonic saline group's 4.800±0.08 days, with a p-value of 0.000. The pathophysiological mechanisms underlying these treatments are rooted in their distinct pharmacological properties. Epinephrine, a sympathomimetic agent, acts by stimulating β2-adrenergic receptors in bronchial smooth muscles, leading to bronchodilation and reduced airway resistance.[12] This mechanism explains its rapid onset of action in reducing respiratory distress. Hypertonic saline, conversely, works through mucociliary clearance enhancement and osmotic gradient principles, effectively reducing mucosal edema and improving mucus rheology. At the cellular level, hypertonic saline induces hydration of airway surfaces by creating an osmotic gradient, which helps mobilize thick, adherent mucus and reduces inflammatory mediator concentration. In a study by Uzma Abid at Holy Family Hospital demonstrated similar trends, with hypertonic saline significantly shortening hospital stays (45.92 ± 12.19 hours vs. 75.53 ± 43.87 hours) and reducing oxygen supplementation duration.[13] Our study's findings of shorter hospital stays with nebulized epinephrine align with investigations by Khandaker Tarequl Islam, which showed hypertonic saline's effectiveness in lowering clinical severity scores and accelerating recovery.[14] The immunomodulatory effects of these treatments are particularly noteworthy, with studies suggesting that both interventions can potentially modulate inflammatory responses in pediatric respiratory infections. The study by Simran Grewal et al. further focus the understanding by comparing nebulized 3% hypertonic saline combined with epinephrine, demonstrating statistically significant improvements in respiratory outcomes for infants with acute bronchiolitis.[15] Another study by Tareq Islam and Khadija Tarequl Islam consistently confirmed the benefits of hypertonic saline, highlighting reduced clinical severity, shorter oxygen therapy duration, and abbreviated hospital stays.[14] Our current study not only endorse these previous findings but also provides a unique contribution to the understanding of treatment efficacy in acute bronchiolitis. The results collectively underscore the potential of both nebulized epinephrine and hypertonic saline in pediatric respiratory care, emphasizing the importance of nuanced treatment strategies tailored to individual patient characteristics and clinical presentations.

## CONCLUSION

Nebulized epinephrine shows superior clinical efficacy in managing pediatric bronchiolitis, demonstrating significantly shorter hospital stays compared to hypertonic saline. These findings contribute valuable insights to pediatric respiratory treatment strategies, emphasizing the importance of precise therapeutic interventions.

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## REFERENCES

1. Jartti T, Smits HH, Bønnelykke K, Bircan O, Elenius V, Konradsen JR, et al. Bronchiolitis needs a revisit: distinguishing between virus entities and their treatments. Allergy. 2019;74(1):40-52. https://doi.org/10.1111/all.13624.
2. Alharbi AS, Al-Hindi MY, Alqwaiee M, Al-Shamrani A, Alharbi S, Yousef A, et al. Saudi initiative of bronchiolitis diagnosis, management, and prevention 2024 updated consensus on the prevention of respiratory syncytial virus. Ann Thorac Med. 2024;19(3):190-200. https://doi.org/10.4103/atm.atm_69_24.
3. Gatt D, Martin I, AlFouzan R, Moraes TJ. Prevention and treatment strategies for respiratory syncytial virus (RSV). Pathogens. 2023;12(2):154. https://doi.org/10.3390/pathogens12020154.
4. Pereira RA, Oliveira de Almeida V, Zambrano M, Zhang L, Amantéa SL. Effects of nebulized epinephrine in association with hypertonic saline for infants with acute bronchiolitis: a systematic review and meta-analysis. Health Sci Rep. 2022;5(3):e598. https://doi.org/10.1002/hsr2.598.
5. Deeney BT, Cao G, Orfanos S, Lee J, Kan M, Himes BE, et al. Epinephrine evokes shortening of human airway smooth muscle cells following $\beta_2$ adrenergic receptor desensitization. Am J Physiol Lung Cell Mol Physiol. 2022;323(2):L142-L151. https://doi.org/10.1152/ajplung.00444.2021.
6. Cahill AA, Cohen J. Improving evidence based bronchiolitis care. Clin Pediatr Emerg Med. 2018;19(1):33-9. https://doi.org/10.1016/j.cpem.2018.02.003.
7. Baron J, El-Chaar G. Hypertonic saline for the treatment of bronchiolitis in infants and young children: a critical review of the literature. J Pediatr Pharmacol Ther. 2016;21(1):7-26. https://doi.org/10.5863/1551-6776-21.1.7.
8. Máiz Carro L, Martínez-García MA. Nebulized hypertonic saline in noncystic fibrosis bronchiectasis: a comprehensive review. Ther Adv Respir Dis. 2019;13:1753466619866102. https://doi.org/10.1177/1753466619866102.
9. Liu L, Pan M, Li Y, Tan G, Yang Y. Efficacy of nasal irrigation with hypertonic saline on chronic rhinosinusitis: systematic review and meta-analysis. Braz J Otorhinolaryngol. 2020;86(5):639-46. https://doi.org/10.1016/j.bjorl.2020.03.008.
10. Flores-González JC, Matamala-Morillo MA, Rodríguez-Campoy P, Pérez-Guerrero JJ, Serrano-Moyano B, Comino-Vazquez P, et al. Epinephrine improves the efficacy of nebulized hypertonic saline in moderate bronchiolitis: a randomised clinical trial. PLoS One. 2015;10(11):e0142847. https://doi.org/10.1371/journal.pone.0142847.
11. Yasin F, Afridi ZS, Mahmood Q, Khan AA, Condon S, Khan RA. Role of nebulized epinephrine in moderate bronchiolitis: a quasi-randomized trial. Ir J Med Sci. 2021;190(1):239-42. https://doi.org/10.1007/s11845-020-02293-5.
12. Ring J, Klimek L, Worm M. Adrenaline in the acute treatment of anaphylaxis. Dtsch Arztebl Int. 2018;115(31-32):528-34. https://doi.org/10.3238/arztebl.2018.0528.
13. Abid U, Afzal A, Zaman N. Comparing treatment with nebulized 3% hypertonic saline versus nebulized 0.9% saline in patients with acute bronchiolitis: a double-blind randomized controlled trial. JRMC. 2024 Mar;28(1):440-4. https://doi.org/10.37939/jrmc.v28i1.2335.
14. Islam KT, Mollah AH, Matin A, Begum M. Comparative efficacy of nebulized 3% hypertonic saline versus 0.9% normal saline in children with acute bronchiolitis. Bangladesh J Child Health. 2018;42(2):130-7. https://doi.org/10.3329/bjch.v42i3.39264
15. Grewal S, Ali S, McConnell DW, Vandermeer B, Klassen TP. A randomized trial of nebulized 3% hypertonic saline with epinephrine in the treatment of acute bronchiolitis in the emergency department. Arch Pediatr Adolesc Med. 2009;163(11):1007-12. https://doi.org/10.1001/archpediatrics.2009.196.