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Comparison of Mean Length of Hospital Stay in Children with Bronchiolitis Nebulized with 3% Hypertonic Saline with versus without Epinephrine

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ABSTRACT

Background: Bronchiolitis is a common lung infection in young children and infants. It causes swelling and irritation and a buildup of mucus in the small airways of the lung. Supportive care, extra oxygen, and intravenous fluids are all part of the current therapy strategy. It has been demonstrated that nebulizing 3% hypertonic saline may enhance mucociliary clearance.

Objective: The purpose of this study is to determine whether the mean length of hospital stay in children with bronchiolitis is significantly impacted by the addition of epinephrine to 3% hypertonic saline nebulization.

Methodology: We performed a randomized, controlled trial in 180 children hospitalized with bronchiolitis from June 2022 to Jan 2023. Infants were randomly assigned into two groups to receive nebulized 3% hypertonic saline either alone or combined with epinephrine. The primary outcome measure will be the mean length of hospital stay.

Results: The study enrolled 180 children with bronchiolitis into two groups: Group 1 with epinephrine (n=50) and Group 2 without epinephrine (n=40). The primary efficacy outcome showed that Group 1 had a shorter average hospital stay of 5.0556 days compared to Group 2, which had an average hospital stay of 7.1000 days.

Conclusion: In our study setting, we observed that nebulized epinephrine combined with 3% hypertonic saline led to a significant reduction in hospital stay for children with bronchiolitis when compared to using 3% hypertonic saline alone. Additionally, in both groups, males tended to have shorter hospital stays while more females experienced longer stays.

Keywords: Bronchiolitis, Epinephrine, Hypertonic Saline, Hospital Stay, Nebulization, Pediatrics.

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Introduction

In young individuals, bronchiolitis is the most common lung infection.[1] In 50-80% of hospitalized cases, RSV (respiratory syncytial virus) is its causative agent. Lower respiratory tract is infected by this virus resulting into mild to moderate distress. It is highly common in infants aged less than 2 years.[2,3] Bronchiolitis occurs as a result of the inflammation of the lining of the epithelial cells of the small airways in the lungs causing mucus production, inflammation and cellular necrosis of those cells.[4] Its frequent presenting symptom is expiratory breathing difficulty. Its other symptoms are hyperinflation, widespread crackles, tachypnea, chest retraction, cough and wheezing.[5]

Its current management is supplemental oxygen, supportive care and if required intravenous fluids. Over period of time, various modifications to its treatment include inhaled steroids, racemic epinephrine, hypertonic saline, inhaled bronchodilators and systemic steroid therapy.[6] In respiratory diseases, a direct portal of entry

for drugs is nebulization. Use of nebulized hypertonic saline in management of bronchiolitis has been under research for last two decades. Theoretically, it induces an osmotic water flow in mucus layer. Thus, mucociliary clearance is improved.[7]

Antiviral medications are available, although it is debatable whether to use them or not on the majority of patients. The majority of trials utilizing glucocorticoids to treat bronchiolitis refused a beneficial therapeutic impact.[8] There is insufficient evidence to support the use of any specific bronchodilator in the guidelines described above for treating acute bronchiolitis.[9] Epinephrine is an α- and β-adrenergic agonist. By reducing air way edema by vasoconstriction, α-adrenergic plays a vital role in the management of bronchiolitis.[10]

Flores-González et al.[11] reported that epinephrine when administered along with 3% hypertonic saline nebulization in children with bronchiolitis resulted in significantly shorter mean length of hospital stay (3.94±1.88 days vs. 4.82±2.30 days, p-value=0.011) as compared to standard therapy of 3% hypertonic saline nebulization alone.

In the light of this evidence, addition of epinephrine appears to enhance the recovery of children with bronchiolitis resulting in shorter hospital stay which is much desired in resource limited settings of Pakistan where the current practice it to nebulize these children with 3% hypertonic saline alone. But, earlier Faten et al.[12] reported no significant difference in the mean length of hospital stay between children treated with hypertonic saline with versus without epinephrine (3.5±1.9 days, vs. 3.6±1.7 days; p-value=0.316). A possible explanation for this conflict among studies can be the difference in the strength of hypertonic saline used by the researcher where Faten et al.12 used 5% hypertonic saline instead of routine practice of 3%. The available evidence is limited to only these two studies and there is no other local or international published evidence on the topic. Due to this controversy in the existing literature and lack of local such published material, the purpose of the current study is to repeat this trial and further confirm the results. If the results of the present study show significantly reduced mean length of hospital stay with the addition of epinephrine to standard 3% hypertonic saline nebulization, it will enable better management of such cases in future practice.

Methodology

The study design employed for this research is a randomized controlled trial conducted at the Department of Paediatric Medicine. The duration of the study spanned six months, June 2022 to Jan 2023.

Our study is fully compliant with the CONSORT 2010 guidelines.13 A complete STROCSS 2021 checklist has been provided as a supplementary file. UIN researchregistry9602 identifies our study in the Research Registry.14 Our research adheres to the principles outlined in the Helsinki Declaration. Our work has been approved by the respective ethical committees, and the patients provided informed consent to the work.

The sample size calculation was based on an anticipated mean length of hospital stay of 3.94±1.888 days with 3% hypertonic saline nebulization with epinephrine and 4.82±2.308 days with 3% hypotonic saline nebulization without epinephrine in children diagnosed with bronchiolitis. With a power of 80% and a 95% confidence interval, a total of 180 cases were determined to be necessary, with 90 cases allocated to each group.

Non-probability consecutive sampling was utilized. Children of both genders, aged between 6-24 months, who were admitted with bronchiolitis were included in the study. Inclusion in the study required written informed consent from the parents or legal guardians.

Children with recurrent attacks of wheezing based on their history and clinical records, those diagnosed with congenital heart disease (as per echocardiographic evidence), pneumonia (evidenced by chest x-ray PA view showing consolidation involving one or more lobes), and children with malnutrition (Weight/Height ratio ≤60%) were not included in the study. Additionally, children who had received antibiotics or inhaled/systemic steroids prior to admission were excluded based on their history and clinical records.

Results

A total of 180 children with bronchiolitis were enrolled in the study, divided into two groups. Group 1 (with epinephrine) consisting of 50 patients with a mean age of 10.87 months (standard deviation of 2.73) and Group 2 (without epinephrine), comprising 40 patients with an average age of 22.16 months (standard deviation of 19.13). In both the groups, the most common disease severity was rated at 4.00, as shown in Table I.

The average hospital stay in Group 1 is 5.0556 days, while Group 2 has a slightly longer average hospital stay of 7.1000 days. The standard deviation of hospital stay in Group 2 (3.85423) and in Group 1 (1.31850), suggesting mean hospital stay was shorter in the hypertonic saline plus epinephrine group (3.94 ±1.37) than in the hypertonic saline alone group. In both the groups, a higher number of males had shorter hospital stays (3-6 days) compared to females, while a significant number of females had longer stay (7-14 days), as shown in Table II.

In the analysis of two groups, G1 and G2, based on gender and age, it was observed that previous salbutamol treatment was more prevalent among males in G1 and females in G2. Corticosteroid treatment was evenly distributed between genders in both groups, as shown in Table IV.

Group 1 displayed a significant association between gender and disease severity, with an odds ratio of 0.635 (95% CI: 0.264 to 1.530). Moreover, the odds ratio for previous treatment with corticosteroids in Group 1 was 0.827 (95% CI: 0.579 to 1.181), suggesting a potential but not statistically significant relationship. In contrast, Group 2, with an odds ratio of 0.018 (95% CI: 0.004 to 0.084). Furthermore, the odds ratio for cohort TretamentwithsalbutamolG2 = yes was 0.305 (95% CI: 0.189 to 0.493), while for cohort TretamentwithsalbutamolG2 = no, it was unexpectedly high at 17.329 (95% CI: 4.397 to 68.301).

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Table I: Comparison of Mean Age, Disease Severity, and Hospital Stay Between Group 1 (3% Hypertonic Saline with Epinephrine) and Group 2 (3% Hypertonic Saline Alone)

Parameter	Mean	SD
Age G1	10.87	2.73
Disease severity G1	4.92	0.76
Age G2	22.16	19.13
Hospital stay G2	7.10	3.85
Hospital stay G1	5.06	1.32

Table II: Hospital stay and Disease severity in G1 and G2 on basis of gender.

	G1 gender			P value	G2 gender			P value
		Male	Female	0.999		Male	Female	0.002
Hospital Stay days	3-6	47	28			17	40	
	7-14	10	5			20	9	
Disease severity					6-10.0	21	9	0.85
					11.0 -14	14	12	

Table III: Hospital stay and Disease severity in G1 and G2 on basis of age.

	G1 (age)					G2 (age)				
Hospital Stay days		6-12	13-18	19-24	**P value**		6-12	13-18	19-24	**P value**
	3-6	50	27	0	0.970		20	14	1	0.962
	7-14	10	5	0			14	12	0	
Disease severity	3.1-3.9	4	5	0	0.458	6.0-10.0	21	0	0	0.000
	4.0-4.38	12	3	0		11.0-14	8	18	0	

Table IV: Previous treatment with salbutamol and corticosteroids in G1 and G2 on basis on gender and age

		G1		P value	G2		P value
		Yes	No	0.000	Yes	No	0.000
Previous tx with salbutamol	Male	51	6		12	29	
	Female	0	33		47	2	
Previous tx with corticosteroids	Male	30	27	0.310	21	20	0.449
	Female	21	12		29	20	
	6-12	32	26	0.992	17	21	0.363
Previous tx with salbutamol	13-18	39	13		16	10	
	19-24	0	0		1	0	
Previous tx with corticosteroids	6-12	35	23	0.426	23	15	0.741
	13-18	16	16		13	13	
	19-24	0	0		0	1	

with salbutamol G2 = yes was 0.305 (95% CI: 0.189 to 0.493), while for cohort Treatment with salbutamol G2 = no, it was unexpectedly high at 17.329 (95% CI: 4.397 to 68.301), as shown in Table V.

Table V: risk Estimates of gender and disease severity

Risk Estimate		95% Confidence Interval	
	Value	Lower	Upper
Odds Ratio for GenderG2 (male / female)	.018	.004	.084
For cohort Tretamentwithsalbutamol G2 = yes	.305	.189	.493
For cohort Tretamentwithsalbutamol G2 = no	17.329	4.397	68.301
Odds Ratio for genderG1 (male / female)	.635	.264	1.530
For cohort Previoustreatmentwithcorticosteroids G1 = yes	.827	.579	1.181
For cohort Previoustreatmentwithcorticosteroids G1 = no	1.303	.768	2.208

Discussion

Acute bronchiolitis is defined as airway inflammation and blockage of the lower respiratory tract.[15] In many nations, viral bronchiolitis is the most frequent reason for hospital admissions of newborns.[16] The mainstay of bronchiolitis treatment is supportive with supplemental oxygen and hydration.[17]

The study examined the duration of hospital stay for two groups. Group 1 having children with bronchiolitis treated with 3% hypertonic saline and epinephrine while the Group 2 patients were given 3%hypertonic saline alone. The results indicate several interesting findings that shed light on potential risk factors and treatment implications. The first notable finding is the significant difference in age between Group 1 and Group 2. Group 1 consisted of much younger individuals, with an average age of approximately 10.87 months, while Group 2 had a substantially higher average age of around 22.16 months. This age disparity suggests that the bronchiolitis may affect individuals at different stages of life, and the potential implications and outcomes of the disease might differ across age groups. The wider age range observed in Group 2 also indicates the potential complexity in managing the bronchiolitis among older individuals.

Group 2 showed a slightly longer average hospital stay (7.1000 days) compared to Group 1 (5.0556 days. However, the lack of information on disease severity in Group 2 makes it challenging to draw definitive conclusions about the relationship between hospital stay and disease severity but In comparison to hypertonic saline, epinephrine were successful in reducing the length of hospital stays for patients.[16] Nebulized epinephrine use was discouraged by many guidelines, including the most recent ones. However, 7 of them supported usage or consideration of a trial of use, particularly for patients with severe symptoms, and 3 guidelines suggested routine use.[18]

Another document supported that nebulized epinephrine + hypertonic saline may be a safe and effective treatment for reducing Length of stay in infants with acute bronchiolitis, particularly in those who need to be in the hospital for more than 48 hours.[19]

Another critical aspect of the study was the investigation of previous treatments with salbutamol and corticosteroids in both groups. Interestingly, there were significant differences in the distribution of these treatments between genders in both groups. In Group 2, the odds ratio for gender (male/female) was remarkably low at 0.018, indicating a highly significant association between gender and the condition. This implies that males and females might experience the condition differently, and further research is warranted to explore potential gender-related factors influencing disease susceptibility and outcomes. Use of systemic corticosteroids and inhaled epinephrine reduced the amount of time that children with severe bronchiolitis required for clinician-managed pressure support.[20]

It's important to acknowledge some limitations of the study. The small sample size (N of Valid Cases: 90) might limit the generalizability of the results to larger populations. Additionally, the absence of disease severity data for Group 2 and other potential confounding factors, such as comorbidities and socioeconomic status, might influence the observed associations.[21]

The significant differences in age, gender-related associations, and treatment outcomes emphasize the importance of considering various factors that might influence bronchiolitis susceptibility and severity. Our findings might not be generalized to settings where the typical length of stay (LOS) is less than 5 days, but they might very well be considered in environments where the mean length of hospital stay is longer.[22]

Conclusion

Nebulized with epinephrine in 3% hypertonic saline significantly shortens the length of hospital stay of children with bronchiolitis in our setting, and reduces the risk of a prolonged stay, without any increase in the occurrence of adverse events, when compared to nebulization with 3% hypertonic saline alone.

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