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Assessment of the Efficacy of Nebulized 3% Hypertonic Saline versus Nebulized Adrenaline in Infants with Acute Bronchiolitis

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Authors' contributions

This work was carried out in collaboration among all authors. Author NEAGE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MBH and RMGES managed the analyses of the study. Author RMGES managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The aim of the work was to assess the efficacy of nebulized 3% hypertonic saline versus nebulized adrenaline in treatment of acute bronchiolitis in infants as supportive therapy with conventional therapy.
Place and Duration of Study: Pediatric Pulmonology Unit (PPU), Tanta University Hospital (TUH), was applied during the period from April 2019 to April 2020.
Methodology: We included ninety infants with moderate to severe acute bronchiolitis were selected, enrolled in the study and randomized into 3 groups: Group A: thirty patients were received nebulized 3% hypertonic saline plus conventional therapy. Was started from first day of admission till RADI score became 4. Group B: thirty patients were received nebulized adrenaline plus conventional therapy. Was started from first day of admission till RADI score became 4. Group C: thirty patients were received conventional therapy. Was started from first day of admission till RADI score became 4. They were subjected to history taking, clinical assessment and

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investigations (CXR, ECHO, CBC and CRP). Follow up done in Chest Clinic four day after discharge.

Results: There was statistically significant difference between studied groups as mean duration of O2 supplementation was significantly shorter in group B than in group A than in group C (p-value<0.05). On admission, mean RR in group B was significantly higher than those in groups A and C (p-value=0.05), On 5th day, mean RR in group B was significantly lower than those in groups A and C (p-value= 0.05). On admission, mean HR in group B was significantly higher than those in groups A and c (p-value =0.05) On 5th days, mean HR in group B was significantly lower than those in groups A and C (p-value= 0.05), with no statistically significant difference between groups A and C. length of hospitalization in studied groups group B showed significantly shorter need for hospital stay than that in groups A and C, with no statistically significant difference between group A and C.

Conclusion: When comparing between inhalation of adrenaline and hypertonic saline 3% in acute bronchiolitis adrenaline improve RD, oxygenation and decrease length of hospitalization.

Keywords: Respiratory syncytial virus; viral bronchiolitis; adrenaline; hypertonic saline 3%; respiratory distress; length of hospitalization.

1. INTRODUCTION

Bronchiolitis is an acute inflammation of the bronchioles in infant that leads to small airway edema, necrosis, and increased mucus production [1].

The most common cause is the respiratory syncytial virus (RSV) with the highest incidence occurring between December and March. Ninety percent of children are infected with RSV in the first 2 years of life and up to 40% of them will have lower respiratory infection. Other viruses identified are human metapneumo virus, influenza and adenovirus and Para influenza [2].

Acute bronchiolitis is largely a disease of the first year of life; 2-3% of infants aged <1 year are admitted each year with bronchiolitis caused by RSV. The RSV “season” in the UK extends from November to March [3].

Risk factors for bronchiolitis are male gender, a history of prematurity, young age (being born in relation to the RSV season), pre-existing disease such as bronchopulmonary dysplasia, underlying chronic lung disease, neuromuscular disease, congenital heart disease, exposure to environmental tobacco smoke, high parity, young maternal age, short duration of breastfeeding, maternal asthma and poor socioeconomic factors [4].

Diagnosis of acute bronchiolitis is mainly clinical [1]. Bronchiolitis often starts with rhinorrhea and fever, thereafter gradually increasing with signs of a lower respiratory tract infection including tachypnea, wheezing and cough. Very young children, particularly those with history of prematurity, may appear with apnea as their major symptom. Feeding problems are common [5].

Treatment of bronchiolitis is mostly supportive and includes suctioning of secretions, encouraging feeding and maintaining hydration. Other treatments include bronchodilators, corticosteroids; epinephrine inhalation and nebulized hypertonic saline are controversial [1].

The study of Sakulchit and Goldman [6] showed that Nebulized epinephrine in hospitalized children with moderate to severe disease had lack of effect to decrease of length of hospitalization.

On the other hand Sit SP et al. [7] showed that analysis of results revealed that the children with moderate to severe acute bronchiolitis showed significant improvement of respiratory distress and length of hospitalization.

The study reported by Zhang L et al. [8] used hypertonic saline for treatment of acute bronchiolitis showed that nebulized hypertonic saline may reduce hospital stay.

In the study did by Grewal S [9] demonstrate no improvement in respiratory distress in the hypertonic saline group.

2. MATERIALS AND METHODS

The study was applied during the period from April 2019 to April 2020 in Pediatric Pulmonology Unit (PPU), Tanta University Hospital (TUH).

The study was Randomized controlled trial by Screening of all infants admitted with wheezy chest to PPU during the period of the study and from them 90 infants with moderate to severe acute bronchiolitis were selected, enrolled in the study and randomized into 3 groups:

Group A: Thirty patients were received nebulized 3% hypertonic saline in the dose of 3 ml irrespective of weight and age with o_2 flow 1oL/Minute every 6 hours plus conventional therapy. Was started from first day of admission till RADI score became 4.

Group B: Thirty patients were received nebulized adrenaline 1 ml/amp (1:1000 dilutions) in the dose of .5 ml/kg during each nebulization with 3 ml normal saline on o_2 flow 10 ml/Minute every 6 hours plus conventional therapy. Was started from first day of admission till RADI score became 4.

Group C: Thirty patients were received conventional therapy i.e Oxygen and fluids therapy. Was started from first day of admission till RADI score became 4.

Inclusion criteria were: Infants with clinical diagnosis of acute bronchiolitis aged of two months to 2 years and first episode of wheezing.

Exclusion criteria were: Wheezing children < 2 month or > 2 yrs, Infants with recurrent wheezy, Complicated cases with acute bronchiolitis e.g. bronchopneumonia or heart failure or progressive respiratory failure requiring mechanical ventilation, Infants with family history of asthma and Infants with finding concomitant with other lung pathology, infants with congenital heart disease or chronic lung diseases or Infants with evident Gastroesophegeal Reflux Disease (GERD).

For all infants admitted with wheezy chest to PPU by history, clinical, radiology and laboratory.

1- History:

Detailed history taking with special emphasis on Demographic data: Age, sex. Detailed of present illness, past history of recurrent wheezy chest, family history for asthma and allergic diseases (dermatitis, conjunctivitis and rhino sinusitis) were excluded. Previous history of admission in NICU was excluded, History of CHD and History of GERD.

2- Clinical:

Thorough clinical examination with special emphasis on:

a) Respiratory rate on admission

Table 1. Normal RR according to age [10]

Age	Respiratory rate
<1 year	30-40
1-2 years	25-35
2-5 years	25-30
5-12 years	20-25
>12 years	12-20

b) Chest examination: RDAI score (wheezy chest/crackles and retractions) on admission.
c) The major outcome parameters was studied to find out the efficacy of treatment with improvement in respiratory distress by Respiratory Distress Assessment Instrument (RDAI score) in the first day of admission [11].

RDAI score assessment of respiratory distress by auscultation of wheezy/crackles and each phase took score during expiration, during inspiration or lung field involved and retractions also assessed either supraclavicular, intercostal or subcostal and each one took score .and according to total scores the patient took score on admission to show degree of respiratory distress.

Score analysis: < 4 mild acute bronchiolitis, 5-10 moderate acute bronchiolitis, 11-17 severe acute bronchiolitis.

3-Imaging:

a) Plain X ray chest done for all cases on admission in Radiology department Tanta University using x ray device (SIEMENS SN3312554) for exclusion of pneumonia, other lung pathology and congenital heart diseases (CHD).
b) ECHO done for all cases on admission by GE vivid 7 in Pediatric cardiology unit.
c) Fluoroscopy done for cases with history of vomiting on admission in Radiology unit in Teaching Hospital.

4-Laboratory:

a) CBC and CRP on admission for exclusion of bacterial pneumonia.

Table 2. RDAI [11]

Symptoms	Scores					Maximum scores
	0	1	2	3	4	
Wheeze/crackles						
During expiration	None	End only	1/2 phase	3/4phase	throughout	4
During inspiration	None	Partial	Throughout			2
Lung field involved	None	<2of 4	>3of 4			2
Retractions						
Supraclavicular	None	Mild	Moderate	Marked		3
Intercostal	None	Mild	Moderate	Marked		3
Subcostal	None	Mild	Moderate	Marked		3
Total						17

2.1 Statistical Analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and IQR. Significance of the obtained results was judged at the 5% level. Chi-square test, Fisher's Exact or Monte Carlo Correction for chi-square when more than 20% of the cells have expected count less than 5, Student t-test For normally distributed quantitative variables, to compare between two studied groups, F-test (ANOVA) For normally distributed quantitative variables, to compare between more than two groups and Post Hoc test (Turkey) for pairwise comparisons, Paired t-test For normally distributed quantitative variables, to compare between two periods and Kruskal Wallis test For abnormally distributed quantitative variables, to compare between more than two studied groups and Post Hoc (Dunn's multiple comparisons test) for pairwise comparisons. Power of significance was evaluated as Probability level (P-value) (≤ 0.05) is significant, P-value (> 0.05) not significant, P-value (< 0.01) is highly Significant.

3. RESULTS

Table 3: Comparison between the three studied groups according to demographic data.

Regarding age gender in studied groups, there was no statistically significance difference between the 3 studied groups (p- Value >0.05).

Table 4: Comparison between three studied groups according to bronchiolitis severity and duration of o_2 supply. Showed that no statistically significance difference between studied groups according to bronchiolitis severity (p-value >0.05).

According to duration of O_2 supplementation, a statistically difference between studied groups as mean duration of O_2 supplementation was significantly shorter in group B than in group A than in group C (p-value<0.05).

Table 5: Comparison between & within each of three studied groups according to respiratory rate (cycle/min) where: On admission, mean RR in group B was significantly higher than those in groups A and C (p-value=0.05), with no statistically significant difference between groups A and C.

After 48 hours, no statistically significant difference between three studied groups regarding RR.

On 5th day, mean RR in group B was significantly lower than those in groups A and C (p-value= 0.05), with no statistically significant difference between groups A and C.

On comparison within each of the three studied groups between means of RR either on admission or after 48 houre or after 5 days of therapy ,the mean RR was significantly lower after 5 days of therapy than that after 48 hours than that on admission in each of studied groups (p-value <0.05).

Table 6: Comparison between & within each of three studied groups according to HR (beat /min) On admission, mean HR in group B was significantly higher than those in groups A and c (p-value =0.05), with no statistically significant difference between groups A and C.

After 48 hours, mean HR in groups A and B were significantly lower than that in group C (p-value= 0.05), with no statistically significant difference between groups A and B.

On 5th days, mean HR in group B was significantly lower than those in groups A and C (p-value= 0.05), with no statistically significant difference between groups A and C.

On comparison within each of the three studied groups between means of HR either on admission or after 48 hours or after 5 days of therapy, the mean HR was significantly lower after 5 days of therapy than that after 48 hours than that on admission in each of the studied groups (p-value <0.05).

Table 7: Comparison between & within each of three studied groups according to oxygen saturation (%)On admission, mean oxygen saturation in group A and B were significantly lower than they in group C (p-value=0.05), with no statistically significant difference between groups A and B.

After 48 hours and on 5th day, mean oxygen saturation in group B was significantly higher than that in groups A and C and also significantly higher in group C when compared with group A.

On comparison within each of the three studied groups between means of oxygen saturation either on admission or after 48 hours or after 5 days of therapy, the mean oxygen saturation was significantly higher after 5 days of therapy than that after 48 hours than that on admission in each of the studied groups 9 (p-value <0.05).

Table 8: Comparison between the three studied groups according to RDAI score during admission and on chest clinic follow up on admission, there was no statistically difference between studied groups, however after 48 hours and on 5th day, mean RDAI in group B was significantly lower than that in group A and C, with no statistically significant difference between groups A and C.

After discharge and on follow up in chest clinic after 1 week, mean RDAI in group B was significantly lower than that in groups A and C, with no statistically significant difference between groups A and C (p-value <0.05).

Table 9: Comparison between the three studied groups according to length of hospitalization days. Group B showed significantly shorter need for hospital stay than that in groups A and C, with no statistically significant difference between group A and C.

Table 3. Comparison between the three studied groups according to demographic data

Variable	Group A (n = 30)		Group B (n = 30)		Group C (n = 30)		Test of Sig.	P
	No.	%	No.	%	No.	%		
Gender								
Male	26	86.7	19	63.3	20	66.7	$\chi 2$=	0.092
Female	4	13.3	11	36.7	10	33.3	4.763	
Age (months)								
Min. – Max.	2.0 – 18.0		3.0 – 15.0		4.0 – 10.0		H=	0.053
Mean ± SD.	6.97 ± 4.19		7.83 ± 3.35		5.67 ± 1.52		5.861	
Median (IQR)	6.0 (5.0-8.0)		9.0 (4.0-9.0)		6.0 (4.0–6.0)			
Sig. bet. grps.	p1=,p2=,p3=							

Table 4. Comparison between three studied groups according to bronchiolitis severity and duration of o_2 supply

	Group A (n = 30)		Group B (n = 30)		Group C (n = 30)		Test of sig.	P
	No.	%	No.	%	No.	%		
Bronchiolitis severity								
Moderate	25	83.3	18	60.0	21	70.0	χ^2=4.002	0.135
Severe	5	16.7	12	40.0	9	30.0		
Duration of o_2 supply (days)								
Min. – Max.	3.0 – 6.0		2.0 – 4.0		3.0 – 6.0		H=53.505*	<0.001*
Mean ± SD.	4.80 ± 0.76		2.67 ± 0.76		4.07 ± 0.74			
Median (IQR)	5.0 (4.0–5.0)		2.50 (2.0 – 3.0)		4.0 (4.0 – 4.0)			
Sig. bet. grps.	p_1<0.001*, p_2=0.006*, p_3<0.001*							

Table 5. Comparison between & within each of three studied groups according to respiratory rate (cycle/min)

Respiratory rate (cycle/min)	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	Test of significance	P –value
On admission					
Min. – Max.	25.0 – 53.0	32.0 – 56.0	27.0 – 52.0	F=11.089*	P:<0.001*
Mean ± SD.	37.40 ± 8.30	44.83 ± 8.96	35.93 ± 5.97		p_1=0.001*
Median (IQR)	36.50 (32.0–43.0)	49.0 (35.0–52.0)	36.0 (34.0–36.0)		p_2=0.750, p_3<0.001*
After 48 hour					
Min. – Max.	25.0 – 45.0	20.0 – 37.0	25.0 – 45.0	F=1.984	P:0.144
Mean ± SD.	32.27 ± 6.36	29.97 ± 5.60	32.50 ± 4.13		
Median (IQR)	30.50 (26.0–38.0)	28.0 (26.0–36.0)	32.0 (30.0–34.0)		
After 5 days					
Min. – Max.	23.0 – 35.0	20.0 – 30.0	25.0 – 35.0	F=8.581*	P:<0.001*
Mean ± SD.	28.93 ± 3.85	26.10 ± 2.58	28.80 ± 2.31		p_1=0.001*
Median (IQR)	29.0 (25.0–31.0)	25.0 (25.0–28.0)	30.0 (27.0–30.0)		p_2=0.984 p_3=0.002*
F	27.704	174.938	52.019		
p-value	P:<0.001* p_1<0.001* p_2<0.001* p_3=0.001*	P:<0.001* p_1<0.001* p_2<0.001* p_3<0.001*	P:<0.001* p_1<0.001* p_2<0.001* p_3<0.001*		

Table 6. Comparison between & within each of three studied groups according to HR (beat /min)

HR (beat/min)	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	Test of sig.	P –value
On admission					
Min. – Max.	128.0 – 150.0	120.0 – 152.0	130.0 – 155.0	F=3.124*	P:0.049*
Mean ± SD.	135.80 ± 7.31	140.27 ± 8.51	139.57 ± 6.36		p_1=0.058
Median (IQR)	133.5(130.0– 140.0)	141.0 (135.0– 150.0)	140.0 (135.0– 142.0)		p_2=0.129 p_3=0.930
After 48 hour					
Min. – Max.	112.0 – 145.0	110.0 – 140.0	112.0 – 145.0	F=9.637*	P:<0.001*
Mean ± SD.	125.60 ± 7.42	122.87 ± 8.79	131.93 ± 8.35		p_1=0.405
Median (IQR)	125.0 (122.0– 128.0)	123.0 (120.0– 130.0)	135.0 (128.0– 135.0)		p_2=0.010* p_3<0.001*
After 5 days					
Min. – Max.	100.0 – 135.0	90.0 – 120.0	98.0 – 135.0	F=64.840*	P:<0.001*
Mean ± SD.	121.90 ± 6.77	103.27 ± 7.82	124.97 ± 9.19		p_1<0.001*
Median (IQR)	120.0 (120.0– 125.0)	100.0 (98.0– 110.0)	128.0 (120.0– 130.0)		p_2=0.302 p_3<0.001*
F	62.562	293.298	103.902		
P value	P:<0.001* p_1<0.001* p_2<0.001* p_3=0.020*	P:<0.001* p_1<0.001* p_2<0.001* p_3<0.001*	P:<0.001* p_1<0.001* p_2<0.001* p_3<0.001*		

Table 7. Comparison between & within each of three studied groups according to oxygen saturation (%)

Oxygen saturation (%)	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	Test of sig.	P
On admission					
Min. – Max.	88.0 – 95.0	85.0 – 98.0	89.0 – 96.0	F=15.466*	P:<0.001*
Mean ± SD.	91.60 ± 1.69	90.60 ± 2.84	93.73 ± 2.0		p_1,= 0.197
Median (IQR)	92.0 (90.0– 93.0)	90.0 (90.0– 92.0)	95.0 (92.0– 95.0)		p_2=0.001*
					p_3<0.001*
After 48 hour					
Min. – Max.	90.0 – 95.0	93.0 – 99.0	90.0 – 96.0	F=24.103*	P:<0.001*
Mean ± SD.	92.73 ± 1.48	95.77 ± 1.99	94.27 ± 1.55		p_1<0.001*
Median (IQR)	92.0 (92.0– 93.0)	95.0 (94.0– 97.0)	95.0 (93.0– 95.0)		p_2=0.002*
					p_3=0.003*
After 5 days					
Min. – Max.	92.0 – 96.0	95.0 – 99.0	92.0 – 99.0	F=61.660*	P:<0.001*
Mean ± SD.	94.43 ± 1.19	97.93 ± 1.14	95.60 ± 1.38		p_1<0.001*
Median (IQR)	95.0 (94.0– 95.0)	98.0 (98.0– 99.0)	95.0 (95.0– 96.0)		p_2=0.001*
					p_3<0.001*
F	78.097*	78.097*	78.097*		
p-value	P:<0.001*	P:<0.001*	P:<0.001*		
	p_1<0.001*	p_1<0.001*	p_1=0.001		
	p_2<0.001*	p_2<0.001*	p_2<0.001*		
	p_3<0.001*	p_3<0.001*	p_3<0.001*		

Table 8. Comparison between the three studied groups According to RDAI score during admission and on chest clinic follow up

RDAI	Group A	Group B	Group C	F	p
On admission					
Min. – Max.	6.0 – 11.0	6.0 – 12.0	6.0 – 11.0	2.164	0.121
Mean.	8.0	9.0	8.0		
Median (IQR)	8.0 (7.0 - 8.0)	8.0 (7.0 - 10.0)	7 (6.0 - 10.0)		
After 48 hours					
Min. – Max.	6.0 – 8.0	4.0 – 8.0	6.0 – 8.0	19.365*	P:<0.001*
Mean.	7.0	6.0	7.0		p1<0.001*
Median (IQR)	7.0 (7.0 - 8.0)	6.00 (5.0 - 7.0)	6.0 (6.0 - 7.0)		p2=0.122
					p3<0.001*
After 5 days					
Min. – Max.	4.0 – 8.0	4.0 – 4.0	4.0 – 6.0	4.015*	P:0.023*
Mean.	5.0	4.0	5.0		p_1=0.018*
Median (IQR)	5.0 (4.0 - 6.0)	4.0 (-)	5.0 (5.0 - 5.0)		p_2=0.905
					p_3=0.036*
Follow up in chest clinic by RDAI					
Min. – Max.	2.0 – 4.0	2.0 – 3.0	1.0 – 4.0	11.585*	P:<0.001*
Mean.	3.0	2.0	3.0		p_1<0.001*
Median (IQR)	3.0 (2.0 – 4.0)	2.0 (2.0 – 2.0)	3.0 (2.0 – 4.0)		p_2=0.893
					p_3=0.001*

Table 9. Comparison between the three studied groups according to length of hospitalization days

Variable	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	F	P
Length of hospitalization (days)					
Min. – Max.	4.0 – 7.0	2.0 – 5.0	5.0 – 7.0	70.161*	<0.001*
Mean ± SD.	5.77 ± 0.77	3.27 ± 1.14	5.27 ± 0.58		
Median (IQR)	6.0 (5.0 - 6.0)	3.0 (2.0 - 5.0)	5.0 (5.0 - 5.0)		
Sig. bet. grps.	p_1<0.001*, p_2=0.070, p_3<0.001*				

4. DISCUSSION

As regard to demographic data (gender and age) according to age the present study conducted on infants from 2 months to 2 years and according to gender there were no statistical significance difference between group A, group B and group C (p-value >0.05).

This is agreement to a study by Asin F et al. [12] who aimed to explore the role of nebulized epinephrine and hypertonic saline 3% in moderate bronchiolitis the study population consisted of eighty cases below 2 years divided into two groups for first group who nebulized adrenaline and other group nebulized hypertonic saline, they reported that the demographics of two groups were not significantly different according to age and gender.

This agreed also with Del Giudice et al. [13] who aimed to explore the Effectiveness of Nebulized Hypertonic Saline and Epinephrine in Hospitalized Infants with Bronchiolitis. The study included seventy cases below 2 years divided into two groups one group nebulized adrenaline and other nebulized hypertonic saline, they showed that no statistically significance difference between two groups according to age and gender.

The present study showed that group B who nebulized adrenaline had statistically significance decrease of duration of oxygenation when compared with group A who nebulized HS or group C with conventional therapy (p-value <0.05).

The study done by Sit SP, et al. [7] showed that analysis of results revealed that the children in both groups had similar clinical profile at the time of inclusion in the study. After three doses of nebulization, the adrenaline group showed significant improvement in oxygen saturation. And decrease need for oxygenation so duration of oxygenation in adrenaline group showed statistically significance decrease when compared with others.

This is explained by adrenaline had a combined alpha-adrenergic and beta-adrenergic agonist, was postulated to offer better benefit with its effect of reducing the mucosal edema and achieving satisfactory bronchodilatation [14].

On contrast to our study Sakulchit and Goldman [6], showed that Nebulized epinephrine in hospitalized children with moderate to severe disease (markedly increased respiratory rate, retractions and decreased oxygen saturation) had lack of effect to decrease duration of oxygenation although mixed α- and β-adrenergic agonist and explained it as The α-adrenergic action is responsible for vasoconstriction and reduction of airway edema inspite this the main pathology of acute bronchiolitis.

In our study we explore nebulized of adrenaline in group B showed statistically significance improved of symptoms of acute bronchiolitis than group A & C (p-value <0.05).

But studied performed by Sakulchit T and Goldman RD [6], found that every winter they see infants with flu like symptoms and wheezing and diagnosed them as bronchiolitis based on their presenting symptoms. And they nebulized epinephrine as routinely used in infants with bronchiolitis. It is an option to consider in those with severe symptoms. They found that there were no symptoms and signs of improvement.

On the other hand studies done by Sit SP, et al. [7] supported our study as showed that analysis of results revealed that the children in both the groups had similar clinical profile at the time of inclusion in the study. After three doses of nebulization, the adrenaline group showed significant improvement in symptoms of acute bronchiolitis.

In our study adrenaline group B showed statistically significance in decrease in the mean of HR, the mean of RR, the RDAI score and increase in mean of o_2 saturation of moderate to severe cases of acute bronchiolitis than group A &C (p-value <0.05).

The study done by Sit SP, et al. [7] showed that analysis of results revealed that the children in both groups had similar clinical profile at the time of inclusion in the study. After nebulization, the adrenaline group showed significant improvement in mean respiratory rate, RDAI score as well as oxygen saturation. However, these changes were significantly more marked in the adrenaline group as compared to other group for all parameters. Not only were the mean scores and mean SpO_2 levels better in the adrenaline group, but also the oxygen saturation were higher in adrenaline group. This benefit in clinic physiologic profile was also reflected in the need for hospitalization as the admission rate was significantly lower in the adrenaline group. Thus, both drugs showed good efficacy with L-adrenaline.

Also Studied cases by Sakulchit T and Goldman RD [6] in both the groups presented with cough (100%), respiratory distress (100%), feeding difficulty (90.3%), running nose (98%) and wheeze (100%) that inhaled adrenaline reported that nebulized adrenaline therapy was significantly superior to relive symptoms and signs like HR, RR, o_2 saturation and hospital stay and this with our study.

The study agreed by Shanmuga Priyadharshini T [15], about treatment of acute bronchiolitis is mainly supportive. Various bronchodilators have been used in the treatment. There was improvement in all the 3 Groups in terms of HR, RR and RDAI. GROUP B had significant improvement compared to other Groups. Group B drug was found to be adrenaline. Group B that is use of nebulized adrenaline brought about symptomatic improvement in the decrease in tachycardia, tachypnea and RDAI score and the difference was significant. Hence Group B, nebulized adrenaline was found to be effective in acute control of symptoms.

On contrast to our study the study by Usman S et al. [16] total 66 patients with 33 in each group between ages of 2-months to 3-years admitted with the diagnosis of bronchiolitis, were included in the study. Children in the group 1 were patients treated with salbutamol nebulization 0.15 mg/kg with 3 ml normal saline every six hourly. Children in the group 2 received adrenaline nebulization 0.1 ml/kg of 1:1000 dilutions with 3 ml normal saline every six hourly. Both the groups were given similar supportive management that included oxygen therapy, intravenous fluids, and antipyretics. Data was collected in the form of age, gender, heart rate, respiratory rate, SpO2 and RDAI score at admission, 6 hr, 24 hr and 48 hr after admission, duration of hospital stay and duration of oxygen therapy. There was no significant difference in the values of RDAI, heart rate, respiratory rate, SPO2 at admission and subsequently after 6 hrs, 24 hrs, and 48 hrs. So there was no significant difference in RDAI scores between the two groups recorded at different time intervals.

In our study regarding to length of hospitalization group B showed statistically significance decrease in length of hospitalization than group A&C (p-value <0.05).

This is in agreement to a study by studied cases by Yasin F et al. [17] carried on infants with moderate bronchiolitis, from October 2013 to March 2014. Out of eighty cases, 16 in HS and 18 in Racemic Epinephrine groups were enrolled. At the time of admission, 0.2 ml of Racemic Epinephrine added to 1.8 ml of distilled water was nebulized to Racemic Epinephrine group, as compared with 2 ml of 3% HS in nebulized form. Racemic Epinephrine was re-administered if needed on 6 h in comparison with 3% HS at the frequency of 1 to 4 h. The LOS in Racemic Epinephrine group ranged between 18 and 160 h (mean 45 h), while in HS group, LOS was 18.50–206 h (mean 74.3 h). The LOS was significantly short in Racemic Epinephrine group (p value 0.015) which was statistically significant. SO racemic epinephrine nebulization as first-line medication may significantly reduce the length of hospital stay in infants with moderate bronchiolitis in comparison with nebulized HS.

The study by Usman S et al. [16] total 66 patients with 33 in each group between ages of 2-months to 3-years admitted with the diagnosis of bronchiolitis, were included in the study. The study concluded that there was a significant reduction in duration of hospital stay in patients who received adrenaline nebulization then those nebulized with salbutamol.

On contrast to our study Florin TA et al. [18] assessed length of hospital stay for infants up to 12 months of age who were admitted with a first

episode of acute respiratory tract infection and wheezing. Infants receiving nebulized epinephrine confirmed the lack of epinephrine effect on length of hospital stay among 404 infants with moderate to severe bronchiolitis.

Other study from Australia reported by Wainwright et al. [19] showed healthy infants with a first episode of wheezing and a clinical diagnosis of bronchiolitis after administration of nebulized epinephrine or placebo, there was no difference found in length of hospital stay and a recent Cochrane review by Oymar K et al. [20] concludes that inhaled (racemic) adrenaline does not improve important clinical outcomes such as length of hospital stay or the use of supportive care in moderate to severe bronchiolitis inpatients. This is supported by a recent large Norwegian randomized controlled trial (RCT) of 404 infants.

The studied carried by Shanmuga Priyadharshini T [15] about acute bronchiolitis is the most common condition in children with rapid respiration, chest retractions, and wheezing. RSV is the most common cause for acute bronchiolitis. Up to 3% of all children are hospitalized with acute bronchiolitis in their first year of life. Despite the high prevalence of acute bronchiolitis, little consensus exists on the optimal management of the disease. Management of acute bronchiolitis is mainly supportive. Various bronchodilators have been used in the treatment. Group B, nebulized adrenaline was found to be effective in acute control of symptoms. However, saturation and duration of hospital stay did not vary between the groups.

In contrast to our study the study reported by Wainwright et al. [19] used hypertonic saline for treatment of acute bronchiolitis showed that Nebulized hypertonic saline may reduce hospital stay by 10 hours in comparison to other line for infants admitted with acute bronchiolitis. Infants who received hypertonic saline also had statistically significant lower post inhalation clinical scores. Nebulized hypertonic saline may also reduce the risk of hospitalization by 14% among children treated as outpatients or in the emergency department. We found only minor and spontaneously resolved adverse effects from the use of nebulized hypertonic saline when given with treatment to relax airways (bronchodilators). Nebulized hypertonic saline appears to be safe and widely available at low cost.

Other contrast study reported by Hsieh CW et al. [21] using hypertonic saline for nebulizing treatment in children with bronchiolitis showed significantly improve the severity of respiratory distress, shorten the LOS and increase the children's night-time sleep quality, The study included 4186. Compared to the control group, the HS group exhibited significant reduction of severity of respiratory distress, included studies used the Clinical Severity Score.

5. CONCLUSION

In conclusion, findings of our study suggest that of nebulized adrenaline is better in terms of reducing clinical severity (HR, RR, O_2 saturation), duration of O_2 supplementation, length of hospital stay in children with moderate to severe acute bronchiolitis in comparison to 3% hypertonic saline.

The study revealed that:

There was statistically significance increase risk of acute bronchiolitis in male more than female.

There was statistically significance improvement of HR, RR, O_2 saturation, decrease RDAI score and decrease in duration of O_2 supplementation in infants who nebulized adrenaline when compared with infants nebulized hypertonic saline 3%.

There was statically significance increase length of hospitalization in hypertonic saline 3% group in relation to adrenaline.

Results of the study showed no difference in groups regarding the severity of bronchiolitis according to the RDAI score, as well as the obvious supremacy of nebulised adrenaline in treating the disease. However, groups were "not the same", according to the initially higher RR and HR in group B, compared with group A and group C. The mentioned fact adds to the supremacy of adrenaline over hypertonic saline and conventional therapy alone. Despite initially higher RR and HR in group B, adrenaline was more effective in treating the disease.

CONSENT AND ETHICAL APPROVAL

Written informed consent was obtained from all parents or guardians of the children. The study was approved by the Ethical Committee of Faculty of Medicine, Tanta University. Permission number is 32775/11/18.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical practice guideline: The diagnosis, management and prevention of bronchiolitis. Pediatrics. 2014;134:1474-502.
2. Greenough A, Cox S, Alexander J, et al. Health care utilization of infants with chronic lung disease. Arch Dis Child. 2001;85:463-8.
3. Jha A, Jarvis H, Fraser C, et al. Respiratory syncytial virus. NCBI. 2017;5.
4. Abraha HY, Lanctot KL, Paes B. Risk of respiratory syncytial virus infection in preterm infants: Reviewing the need for prevention. Expert Review of Respiratory Medicine. 2015;9:779-99.
5. Zorc JJ, Hall CB. Bronchiolitis, recent evidence on diagnosis and management. Pediatric. 2010;125:342-9.
6. Sakulchit T, Goldman RD. Nebulized epinephrine for young children with bronchiolitis. Can Fam Physician. 2016;62:991–3.
7. Sit SP, Pal PS, Kant M, et al. Adrenaline versus salbutamol in infants with bronchiolitis. IOSR Journal of Dental and Medical Sciences. 2016;15:41-4.
8. Zhang L, Mendoza-Sassi RA, Wainwright C, et al. Nebulised hypertonic saline solution for acute bronchiolitis in infants. Cochrane Database of Systematic Reviews. 2017;12:1858-465.
9. Grewal S, Ali S, McConnell DW, et al. 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;163:1007-12.
10. O'Leary F, Hayen A, Lockie F, et al. Defining normal ranges and centiles for heart and respiratory rates in infants and children: A cross-sectional study of patients attending an Australian tertiary hospital paediatric emergency department. Archives of Disease in Childhood. 2015;100:733-7.
11. Verma IP, Garg P, Karnawat BS, et al. Study of therapeutic effects of nebulized adrenaline alone, nebulized adrenaline plus injectable dexamethasone (in combination) and nebulized 3% hypertonic saline alone in clinically diagnosed cases of bronchiolitis. International Journal Contemporay Pediatrics. 2017;4:1414-9.
12. Asin F, Afridi ZS, Mahmood Q, et al. Role of nebulized epinephrine in moderate bronchiolitis: A quasi-randomized trial. Ir J. Med Sci.; 2020. DOI:https://doi.org/10.1007/s11845-020-02293-5
13. Del Giudice, Saitta F, Leonardi S, et al. Effectiveness of nebulized hypertonic saline and epinephrine in hospitalized infants with bronchiolitis. International Journal of Immunopathology and Pharmacology. 2012;25:485-91.
14. Guo C, Sun X, Wang X, et al. Network meta-analysis comparing the efficacy of therapeutic treatments for bronchiolitis in children. Journal of Parenteral and Enteral Nutrition. 2018;42:186-95.
15. Shanmuga Priyadharshini T. Comparison of nebulised adrenaline, nebulised salbutamol and nebulised budesonide in the treatment of bronchiolitis. A double blinded randomized trial. Doctoral Dissertation, Government Mohan Kumaramangalam Medical College, Salem; 2017.
16. Usman S, Zareen A, Gillani A, et al. Comparison of adrenaline and salbutamol nebulization in treatment of children with bronchiolitis. The Professional Medical Journal. 2019;26:1434-9.
17. Yasin F, Afridi ZS, Mahmood Q, et al. Role of nebulized epinephrine in moderate bronchiolitis: A quasi-randomized trial. Irish Journal of Medical Science. 2020;1: 4.
18. Florin TA, Plint AC, et al. Viral bronchiolitis. The Lancet. 2018;389:211-24. Iskander IF, Gamaleldin R, El Houchi S, El Shenawy A, Seoud I, El Gharbawi N, e al. Serum bilirubin and bilirubin/albumin ratio as predictors of bilirubin encephalopathy. Pediatrics. 2014;134(5): 1330-9.
19. Wainwright C, Zhang L, Mendoza-Sassi RA, et al. Nebulised hypertonic saline solution for acute bronchiolitis in infants. Cochrane Database of Systematic Reviews. 2017;12:1858-465.
20. Oymar K, Skjerven HO, Mikalsen IB. Acute bronchiolitis in infants, a review. Scandinavian Journal of Trauma,

Resuscitation and Emergency Medicine. 2014;22:23.
21. Hsieh CW, Chen C, Chen KH, et al. Exploring the efficacy of using hypertonic saline for nebulizing treatment in children with bronchiolitis: A meta-analysis of randomized controlled trials. BMC Pediatrics. 2020;20:434.

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