

Comparison of Efficacy of Epinephrine to Salbutamol and Ipratropium Bromide Combined in Acute Bronchiolitis

AHSAN IQBAL DANISH¹, QAISER SHEHZAD HUMAYOUN², ASAD SHABBIR³, ISRAR LIAQUAT⁴, MUHAMMAD HAFEEZ⁵, IBRAHIM⁶

¹Medical Officer Pediatrics, Tehsil Headquarter Hospital, Jand

^{2,3,4}Assistant Professor Pediatrics, Holy Family Hospital, Rawalpindi

⁵Senior Registrar Pediatrics Holy Family Hospital, Rawalpindi

⁶Assistant Professor Paeds Medicine, Swat Medical College / Swat Medical Complex Teaching Hospital Saidu Sharif, Swat

Corresponding author: Asad Shabbir, Email: dr.Asadshabbir@gmail.com, Cell: +923345512956

ABSTRACT

Background: Epinephrine, an alpha receptor agonist, has been suggested to be a supreme bronchodilator. A biologically active drug name Ipratropium bromide is helpful for the treatment of bronchiolitis among infants and improves on the signs and symptoms of bronchiolitis.

Objective: To compare effectiveness of combined nebulized salbutamol with nebulized adrenaline and ipratropium bromide in bronchiolitis affected children in terms of mean improvement in RDAI score.

Methodology: After approval from ethical committee this randomized control trial of 6 month duration is carried out by Randomization of patients in 2 groups. Group A received salbutamol (0.15mg/kg) combined with ipratropium bromide (250 micrograms per dose) with isotonic sodium chloride solution 0.9% (2 mL) and Group B received a dose of epinephrine (0.5mg/kg in concentration of 1:1000(max 5 mg), distributed by nebulizer with the help of a face mask with continuous oxygen flow at 6L/min Prior to each drug administration and at 30 mins, the researcher evaluated the condition of infant's and records the respiratory rate, RDAI score⁹, heart rate and SaO₂.

RESULTS: Comparison of effectiveness of combined nebulized salbutamol with nebulized adrenaline and ipratropium bromide in bronchiolitis affected children in terms of mean improvement in RDAI score shows that at baseline in Group-A it was 10.73±1.59 and 10.98±1.42, p value was 0.27, it was reduced after 30 minutes of treatment in Group-A 3.23±0.52 and 2.67±0.47 in Group-B, pvalue was 0.001.

Conclusion: We concluded that Epinephrine is better than salbutamol and ipratropium combined in terms of mean improvement in RDAI score

Keywords: Bronchiolitis, children, salbutamol and ipratropium Bromide, Epinephrine.

INTRODUCTION

Bronchiolitis is a communal ailment in <2 years of age children and is the important reasons of hospitalization in infants. Acute bronchiolitis, considered by acute wheezing in children or infants and related with respiratory tract infections signs, is the utmost communal etiology of respiratory syncytial virus.¹ Rhinovirus adenoviruses, bocaviruses and metapneumoviruses are currently the etiology of bronchiolitis.² Respiratory viral syncytial virus. The RSV in Pakistan has seen a marked increase in the winter. Significant increases in positive RSV infection by 30-50% were recorded from December to February.³ In Pakistan, especially, respiratory infections are responsible for 20-30% of all child deaths.⁴

The meta-analysis showed that bronchodilators, like salbutamol or albuterol, do not reduce hospitalization after outpatient treatment, do not improve saturation of oxygen, do not condense the hospital stay duration, and do not shorten the recovery time after illness at home. Epinephrine therapy was first proposed by Wohl and Chernick in 1987. A recent study by Kadir et al found that both L-epinephrine and the combination

Salbutamol and ipratropium bromide were effective in acute bronchiolitis, but L-adrenaline was more effective.⁶

However, other studies in patients with acute bronchiolitis treated with nebulized epinephrine or salbutamol showed a comparable decrease in RDAI scores over the 1st 48 hours. group A (ipratropium bromide) 2.0 ± 0.7, group B (epinephrine) 2.2 ± 0.6 (p-value 0.000), group A mean and standard deviation 2.000 ± 0.77615, and in group B 2.2934 ± 0.61420.8. Therefore, the ideal management of bronchiolitis remains undecided. No additional local work done. Therefore, this study rationale is to do the comparison of two drugs for the emergency bronchiolitis treatment. This study results will assist in selecting the suitable drug that can alleviate the disease symptoms and provide local management data.

The Original Study

Objective: To compare effectiveness of combined nebulized salbutamol with nebulized adrenaline and ipratropium bromide in bronchiolitis affected children in terms of mean improvement in

RDAI score.

Operational Definition

Acute bronchiolitis: Clinical indication of lower airway obstruction (chest wall retractions and physical findings of wheezing) succeeding an URTI in children upto the 18th months of life.

Moderately ILL: Having modified RDAI score 8-15 (see attached annexure)

Improvement: Change in RDAI score was measured at baseline and 30 min post treatment

Hypothesis: Epinephrine is better than salbutamol and ipratropium combined in terms of mean improvement in RDAI score.

MATERIAL AND METHODS

Study Design: Randomized Controlled Trial

Setting: Department of pediatrics Benazir Bhutto Hospital, Rawalpindi. The department is 95 bedded unit of a tertiary hospital affiliated with Rawalpindi Medical College

Duration of Study: The study was finished in six months' time after institution approval 30th August, 2019 to 29th February, 2020

Sample Size: Sample size was taken using Open EPI calculator taking Confidence Interval 95%, Power of test 80%, Mean and SD of Group A 2.000±0.77615⁸ mean and SD of Group B 2.2934±0.61420⁸, Sample size is 90 in each group (total of 180)

Sample Selection:

Inclusion Criteria:

1. Acute bronchiolitis
2. Moderate degree of illness
3. Age: 2-18 months

Exclusion Criteria:

1. RDAI score >15, requiring resuscitation
2. Previous use of bronchodilators
3. Previous pulmonary (bronchopulmonary dysplasia) or cardiac disease
4. Family H/o asthma, H/o 2 or more respiratory distresses

Data Collection Procedure: First, approval from the hospital's ethics committee was obtained. Infants who met the criteria of inclusion were selected for the study and guardian or parent of the

child gave the written informed consent. Respiratory rate, Weight, heart rate and SaO₂ (assessed by pulse oximetry) were documented for each infant.

Patients receiving epinephrine or salbutamol in combination with ipratropium were randomized using a random number table prepared by pharmacists, and the children were divided into 2 groups. Group A received ipratropium bromide (250 micrograms per dose) and salbutamol (0.15 mg / kg) together with isotonic sodium chloride solution 0.9% (2 ml), and group B received a dose of epinephrine (0.5 mg / kg) with 1:1000 concentration (max. 5 mg) is administered via a nebulizer with a face mask with 100% oxygen at continuous flow with rate of 6 L / min.

Neither the investigator, nor parents nor carers were present during the preparation and administration of the drug. The researcher never disclosed the drug identities of either party. Thus, both sides remained blind and study drug was given. Before and 30 minutes after each drug administration, the researcher evaluated the condition of the infant's and documented the RDAI (the most commonly used severity tool), respiration rate, SaO₂ and heart rate.

Patients stayed in the Emergency Department for minimum 150 mints. At the end, the investigator who was blinded govern the necessity for hospitalization grounded on the infant's condition and clinical assessment.

Double blind was used to avoid observer bias. All data was collected in a Performa specially designed by the researcher.

Data Analysis Procedure: The data analysis was done with SPSS 16.0. Mean SD was calculated for quantitative variables (age, weight, vital signs, RDAI score at baseline and 30 minutes). The independent t-test was used to compare the mean RDA score. A p value of <0.05 was regarded significant. It is controlled by age, gender, weight, and stratification.

RESULTS

A total of 180 cases (90 in each group) fulfilling the selection criteria were enrolled to compared efficacy of combined nebulized salbutamol with nebulized adrenaline and ipratropium bromide in children with bronchiolitis in rappsorts of mean RDAI score improvement.

Age distribution shows that 71.11%(n=64) in Group-A and 82.22%(n=74) in Group-B were between 2-12 months of age whereas 28.89%(n=26) in Group-A and 17.78%(n=16) in Group-B were between 13-18 months of age, mean+sd was calculated as 9.58+4.12 months in Group-A and 8.63+4.19 months of age in Group-B. (Table No. 1)

Gender distribution shows that 53.33%(n=48) in Group-A and 84.44%(n=49) in Group-B were male whereas 46.67%(n=42) in Group-A and 45.56%(n=41) in Group-B were females. (Table No. 2) Mean weight of the patients was calculated as 7.37+1.81 kgs in Group-A and 6.9+1.96 kgs in Group-B. (Table No. 3)

Table 1: age distribution (n=180)

Age (in months)	Group-A(n=90)		Group-B(n=90)	
	No. of patients	%	No. of patients	%
2-12	64	71.11	74	82.22
13-18	26	28.89	16	17.78
Total	90	100	90	100
Mean+SD	9.58+4.12		8.63+4.19	

Table 2: gender distribution (n=180)

Gender	Group-A(n=90)		Group-B(n=90)	
	No. of patients	%	No. of patients	%
Male	48	53.33	49	54.44
Female	42	46.67	41	45.56
Total	90	100	90	100

Comparison of efficacy of combined nebulized salbutamol with ipratropium bromide and nebulized adrenaline in children with bronchiolitis in terms of mean improvement in RDAI score shows that at baseline in Group-A it was 10.73+1.59 and 10.98+1.42, p value was 0.27, it was reduced after 30 minutes of treatment in

Group-A 3.23+0.52 and 2.67+0.47 in Group-B, p value was 0.001. (Table No. 4)

The data was stratified for age, weight and gender in Table No. 5-7.

Table 3: mean weight of the patients(n=180)

Weight(grams)	Group-A(n=90)		Group-B(n=90)	
	Mean	SD	Mean	SD
	7.37	1.81	6.9	1.96

Table 4: Comparison Of Efficacy Of Combined Nebulized Salbutamol With IpratropiumBromide And Nebulized Adrenaline In Children With Bronchiolitis In Terms OfMean Improvement In Rdai Score (n=180)

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	10.73	1.59	10.98	1.42	0.27
30 minutes after treatment	3.23	0.52	2.67	0.47	0.001

Table 5: stratification for age(n=180)

Age: 2-12 months

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	10.80	1.58	11.08	1.50	0.28
30 minutes after treatment	3.27	0.54	2.73	0.45	0.0001

Age: 13-18 months

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	10.58	1.65	10.50	0.89	0.86
30 minutes after treatment	3.15	0.46	2.38	0.50	0.0001

Table 6: stratification for weight (n=180)

Upto 5 kgs

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	11.06	1.34	11.72	1.65	0.18
30 minutes after treatment	3.19	0.54	2.72	0.46	0.005

>5 kgs

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	10.66	1.64	10.69	1.22	0.90
30 minutes after treatment	3.24	0.52	2.65	0.48	0.0001

Table 7: Stratification For Gender (n=180)

Male

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	10.58	1.64	11.37	1.59	0.01
30 minutes after treatment	3.19	0.53	2.65	0.48	0.0001

Female

RDAI score	Group-A(n=90)		Group-B(n=90)		P value
	Mean	SD	Mean	SD	
At baseline	10.90	1.54	10.51	1.03	0.17
30 minutes after treatment	3.29	0.51	2.68	0.47	0.0001

DISCUSSION

The communal bronchiolitis etiology is respiratory syncytial virus (RSV), with the peak frequency of infections between December and March. Acute bronchiolitis is diagnosed by a combination of clinical symptoms, including increased respiratory effort and wheezing, following the viral prodrome of the upper respiratory tract infection in children < 2 years.

Epinephrine, an alpha receptor agonist, has been suggested to be a supreme bronchodilator. An anticholinergic drug called Ipratropium bromide is helpful to treat bronchiolitis affected infants,

is active biologically and improve the symptoms.

Therefore, this study rationale is to do the comparison of two drugs for the emergency bronchiolitis treatment. This study results will assist in selecting the suitable drug that can alleviate the disease symptoms and provide local management data.

In our study, 71.11% (n = 64) in group A and 82.22% (n = 74) in group B were between 2 and 12 months of age, while 28.89% in group A (n = 74) n = 26) and 17.78% (n = 74). = 16) Between 13-18 months in Group B, mean + standard deviation is 9.58 + 4.12 months in Group-A and 8.63 + 4.19 months in Group-B % Calculated as 53.33 (n = 48). In group A 84.44% (n = 49) were men, in group A 46.67% (n = 42), and in group B 45.56% (n = 41) were women. Comparison of effectiveness of combined nebulized salbutamol with nebulized adrenaline and ipratropium bromide in bronchiolitis affected children in terms of mean improvement in RDAI score shows baseline values of 10.73 + 1.59 and 10.98 + 1.42, p 0.27 in the group A. After 30 minutes of treatment, it decreased to 3.23 + 0.52 in group A and 2.67 + 0.47 in group B, the p-value was 0.001.

The results of our study are consistent with the study showing similar efficacy in both control studies in patients with acute bronchiolitis treated with ipratropium bromide nebulized compared to epinephrine. 2.2 0.6 (p-value 0.000), the mean and standard deviation were 2000 + 0.77615 in group A and 2.2934 + 0.61420.8 in group B.

Dr. Syama Prasad Sit et al. compared the effectiveness of nebulized L-adrenaline with salbutamol in infants with bronchiolitis. They found that both salbutamol and L-adrenaline suggestively improved the oxygenation and mean symptom score. Though, the group of adrenalines displayed greater development in study parameters than the group of salbutamol. More adrenaline given group of children can be sent home after treatment in emergency. They concluded that both l-adrenaline and nebulized salbutamol were operative in relieving symptoms in bronchiolitis affected infants and that nebulized l-adrenaline was significantly better than nebulized salbutamol.⁹

Another randomized clinical trial in 72 infants with moderately severe bronchiolitis in three equal groups found that both nebulized salbutamol and epinephrine reduced respiratory failure and enhanced oxygenation compared to normal saline. L-epinephrine was much active than salbutamol in nebulizing in improving oxygen saturation and relieving respiratory distress, and reduced hospitalization need. However, based on the results of our

study and other studies, the hypothesis of our study that "epinephrine is better than the combination of salbutamol and ipratropium in terms of mean improvement in RDAI score" is confirmed.

In addition, our study was based on one center, which should be confirmed in the future by further multi-center studies.

CONCLUSION

We concluded that Epinephrine is better than salbutamol and ipratropium combined in terms of mean improvement in RDAI score.

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