

# COMPARISON OF EFFICACY OF IPRATROPIUM BROMIDE VERSUS EPINEPHRINE IN ACUTE BRONCHIOLITIS IN INFANTS

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## ABSTRACT

**Background:** Bronchiolitis, viral infection of lower respiratory tract of infants is the leading cause of infants morbidity and hospitalization. Yearly up to 30% of healthy infants are hospitalized for Bronchiolitis resulting in an estimated 12,000 hospitalization. The effects are not limited to the acute illness episode because 40-50% of children diagnosed with Bronchiolitis suffer from subsequent wheezing and air way reactivity Asthma. Attempts to address the burden of disease via vaccine development have largely been unsuccessful and treatment is purely supportive rather than curative. Furthermore the medical therapies for acute Bronchiolitis in young infants are controversial. Anti cholinergic agent ipratropium bromide has been shown to reduce the work of breathing in infant of Bronchiolitis in controlled clinical trials.

**Objectives:** Comparison of efficacy of ipratropium bromide verses epinephrine in Acute Bronchiolitis in infants.

**Materials and Methodes:** The efficacy of ipratropium and epinephrine in acute Bronchiolitis were compared in the department of Paediatrics, Hayatabad Medical Complex, Peshawar through double blinded randomized controlled study. The study started on March 12,2014 and ended on 11 August -2014, the peak season for Bronchiolitis. A total of 334 infants under 12 months were randomly allocated in two groups. Group A infants were subjected to nebulized ipratropium and infants of group B were given nebulized epinephrine. A standardized respiratory distress assessment instrument (RDAI) was used to measure the improvement of symptoms. The assessment was done on initial arrival (base line) and 24 hours after the initiation of therapy.

**Result:** The mean age of the infants in group A was 7.47 2.7 months while in group B it was 6.9 2.5 months (P value 0.085). The mean follow up RDAI score in group A was 2.0 0.7 while group B it was 2.2 0.6 ( P value 0.000). The overall efficacy in group A was 70.1% and in group B it was 62.3% (P value 0.133).

**Conclusion:** Ipratropium bromide is equally effective as epinephrine in the treatment of acute Bronchiolitis in children below 12 months of age.

**Key Words:** Acute Bronchiolitis, Ipratropium bromide, epinephrine, respiratory distress assessment instrument.

## INTRODUCTION:

The most common etiology of Bronchiolitis is respiratory syncytial virus (RSV) with highest incidence of infection occurring between December and march. Acute Bronchiolitis is recognized by constellation of clinical signs and symptoms including a viral upper respiratory prodrome followed by increased respiratory effort and wheezing in children less than 2 years.

Since no definitive treatment for the specific virus exists, therapy is directed toward symptomatic relief. The role of bronchodilator has been subjected to many studies and evidence-based reviews of the literature

since 1950s. Bronchodilator is common now a days but its efficacy is not accepted universally.

Epinephrine an alpha receptor agonist is suggested to be an ideal bronchodilator. Ipratropium bromide an anti cholinergic used to treat infants of Bronchiolitis is biologically active and have effects on symptoms. The efficacy of nebulized ipratropium bromide have been studied in multi centered multiple trials and its use appeared to be beneficial. But the efficacy of nebulized ipratropium bromide is not well studied among Pakistan infants. This study aims to study the efficacy of nebulized ipratropium and compare it with a well studied bronchodilator i-e nebulized epinephrine and if found efficacious will be included in a ward protocol for the treatment of Bronchiolitis.

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## MATERIAL & METHODS

This study was conducted in Paediatric A ward, Hayatabad Medical Complex, a tertiary care hospital in Peshawar. The study protocol was approved by the hospital ethics committee and informed consent was obtained from each parent before entering the child into the study.

All healthy infants 2-12 months old presented with first episode of wheezing or wheezing with crackles were eligible for enrolment.

Infants with recurrent wheezing, infants with cardio pulmonary disease and immune deficiency, infants ever diagnosed with Asthma or those who had taken any bronchodilator or steroids during 24 hours prior to admission were all excluded from the study.

All those patients, who qualify the inclusion criterion, were divided into two groups. Consecutive non probability sampling technique was used for assigning patients to either group i-e group A and group B. First patient was entered randomly on lottery basis. Patients in group A were given nebulized ipratropium and patient in group B were given nebulized epinephrine. children in both group received periodic doses 6 hourly of either ipratropium (nebulized 250 ug with 3 ml of saline) or epinephrine (1: 1000, 0.5 ml /kg subject to a max 2.5 ml with 3 ml saline ) via a nebulizer along with oxygen.

Treatment success was defined as improvement of one or more of severity score calculated in modified RDAI. Changes in heart rate (HR), oxygen, saturation (SPO2), respiratory rate (RR) and respiratory distress assessment instrument (RDAI) were assessed at the time of admission and 24 hours after admission.

## RESULTS

The study comprised a total of 334 infants between 02 to 12 months of age. 167 infants in group A were subjected to nebulized ipratropium while 167 infants in group B were subjected to nebulized epinephrine. The mean age of the infants in group A was 7.47 2.7 months, while in group B it was 6.9 2.5 months (Table 1).

While distributing the sample with regard to gender, in group A, there were 56.9% male infants and 43.1% female infants, while in group B there were 50.3 % male infants and 49.7 % female infants.

Both the groups were followed according to their therapy guidelines and final assessment was done 24 hours after computation of the last dose of the therapy. In group A, the follow up mean RDAI score was 2.00.7 while in group B, the follow up mean RDAI score observed was 2.2 0.6 mean. RDAI score at follow up of the two groups was statistically significant after applying T test for comparing mean (Table 2). But the efficacy of treatment, which was defined as improvement of at least 1 RDAI score from baseline was 70.1 % in group A, while 62.3% in group B. the difference was statistically not significant after applying chi square test with a P value of 0.133 (Table 3).

## DISCUSSION

Ipratropium bromide is an anti cholinergic bronchodilator, with no superior efficacy for RSV Bronchiolitis. Treatment of Bronchiolitis is mainly supportive and the role for bronchodilator is still controversial in the latest guideline release by the American Academy of Paediatrics. The Cochrane review of the use of bronchodilator for Bronchiolitis showed short term improvement in clinical score, with no improvement in the measures of oxygenation or in the length of hospital stay. Wohl and Chernick postulated that, since mucosal edema is an important component of air way obstruction in infants with Bronchiolitis, a logical approach to therapy might be to use a combined  $\alpha$ -adrenergic and  $\beta$ -adrenergic agonist, such as epinephrine.

Analysis of the present study also revealed that the infants in both the group shows improvement in their mean RDAI score but the response to treatment

### Modified RADI

Clinical Parameter	Score 0	Score 1	Score 2	Score 3
Respiratory rate (per minute)	< 40	40-60	60-70	>70
Use of Accessory Muscles	None	1 accessory muscles used	2 accessory muscles used	≥ 3 accessory muscle used
Clour/cyanosis	Pink room air/no cyanosis	Cyanosed when crying	Pink with oxygen or cyanosed in room air	Cyanosed with oxygen or cardio respiratory arrest
Ascultatory finding	Normal	Decreased air entry no Rhonchi heard	Decreased air entry Rhonchi heard	Silent chest

**Table No.1: Comparison of Mean age of both groups (n=167 each)**

	N	Mean	Std. Deviation	Std. Error Mean
Age of the Infant(Months) Ipratropium Group	167	7.4784	2.78434	.21546
Epinephrine Group	167	6.9743	2.54431	.19688

**Table No.2: Comparison of Mean follow up RDAI Score of Both Groups ( n=167 each)**

		N	Mean	Std. Deviation	Std. Error Mean					
Follow up RDAI Ipratropium		167	2.0000	.77615	.06006					
Group Score Epinephrine Group		167	2.2934	.61420	.04753					
Independent Sample Test										
		Levene's Test for equality of variances		t-test for equality of Means						
		F	Sig.	T	Df	Sig. (2-tailed)	Mean Difference	Std Error Difference	95% Confidence interval of the difference	
									Lower	Upper
Follow up RDAI score	Equal variances assumed	2164.	.142	-3.83	332	.000	-.29341	.07659	-.4408	-.1427
	Equal variances not assumed			-3.83	315.34	.000	-.29341	.07659	-.44411	-.1427

**Table No.3: Comparison of Mean follow up RDAI Score of Both Groups ( n=167 each)**

	Group of the infant		Total		
	Ipratropium Group	Epinephrine Group			
Yes Count	117	104	221		
Efficacy of % within group of Treatment the infant	70.1%	62.3%	66.2%		
Group No Count	50	63	113		
% within group of the infant	29.9%	37.7%	33.8%		
Total Count	167	167	334		
% within group of the infant	100.0%	100.0%	100.0%		
Chi-Square Tests					
	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.260	1	.133	.165	.083
Continuity Correction	1.926	1	.165		
Likelihood Ratio	2.264	1	.132		
Fisher's Exact Test					
Linear-by-Linear Association	2.254	1	.133		
N of Valid cases	334				

in either group was not statistically significant failing to reject the null hypothesis. Among 321 infant in six research studies, there was no significant difference in the length of hospital stay between ipratropium bromide and placebo, and no significant difference between the combination of nebulized ipratropium bromide and beta 2 agonist compared with a beta 2-agonist alone. However combined ipratropium bromide and beta 2-agonist therapy did show significantly improved clinical score at 24 hours compared with placebo, and parents preferred ipratropium bromide over placebo for relief of their children's symptoms at home.

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