

## Original Research Article

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# Comparison of efficacy between levosalbutamol and levosalbutamol-ipratropium nebulization in mild to moderate childhood asthma

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## ABSTRACT

**Background:** The objective of the study was to compare the efficacy between levosalbutamol and ipratropium combination over levosalbutamol nebulisation in reversing airflow obstruction and improve oxygenation, evaluated using the pulmonary asthma score, SaO<sub>2</sub>, and PEFR in mild and moderate asthma.

**Methods:** A prospective, randomized, study was performed in RMMCH pediatric emergency department. Children between 6 and 12 years of age who presented with mild to moderate asthma exacerbations were enrolled in the study. They were randomly allocated into two different groups: one nebulised with levosalbutamol alone and another with addition of ipratropium bromide to levosalbutamol. Baseline Peak expiratory flow rate and Final absolute values or change from baseline 60-120 minutes after the inhalation are measured. Patients were evaluated using the pulmonary score.

**Results:** After treatment there is improvement in the mean pulmonary asthma scores and PEFR percentage in A+B group than A group, but it is not statistically significant (p value >0.05). There is statistically significant improvement in pulmonary asthma score and PEFR in each of the groups after nebulisation and pulmonary asthma score has a sensitivity of 66.7% and 65.6% in diagnosing severity of asthma in relation to PEFR.

**Keywords:** Ipratropium bromide, Levosalbutamol, Peak expiratory flow rate, Pulmonary asthma score

## INTRODUCTION

Asthma is a common chronic inflammatory disorder of the airways associated with airway hyper responsiveness. Asthma exacerbation is defined as an acute or subacute deterioration of symptom control that causes distress or risks health to the extent that a visit to a health care provider or treatment with systemic corticosteroids becomes necessary.<sup>1</sup> The most common trigger for asthma exacerbation in both younger and older children are viral respiratory tract infections. The other typical factors are exposure to allergens and a suboptimal control of asthma as a baseline.<sup>2</sup> Acute exacerbations are a frequent cause of emergency department visits.<sup>3,4</sup>

Children with acute asthma exacerbations frequently present to an emergency department with signs of respiratory distress. The most severe episodes are potentially life threatening. Effective treatment depends on the accurate and rapid assessment of disease severity at presentation. The use of evidence-based asthma guidelines can improve outcomes for children with asthma.<sup>5</sup>

The initial management of acute asthma exacerbations in children focuses on the rapid relief of bronchospasm with inhaled or nebulised bronchodilators.<sup>6,7</sup>

The administration of  $\beta_2$  agonists is the crucial element of therapy in status asthmaticus.<sup>8</sup> Children who are not responsive to bronchodilators require the addition of glucocorticoids.<sup>9,10</sup> Beta2 agonists are the most effective of the bronchodilators owing to their rapid onset of action and the extent of achieved bronchodilation.<sup>11,12</sup> Anticholinergic agents, such as ipratropium bromide and atropine sulphate have a slower onset of action and weaker bronchodilating effect than beta2 agonists but may relieve cholinergic bronchomotor tone and decrease mucousal edema and secretions.<sup>13,14</sup> Thus the combination of inhaled anticholinergics with beta2 agonists may yield enhanced and prolonged bronchodilation.

Several randomized controlled trials have examined the efficacy of the addition of anticholinergics to beta2 agonists for treating acute asthma in children.<sup>15,16</sup> Conflicting results from these trials were attributed to differences in the severity of the asthma, intensity (number of doses) of anticholinergic treatment, cointervention with glucocorticoids and study power.<sup>17</sup> Though current guidelines recommends the use of anticholinergics in acute severe or life threatening asthma, its role in mild to moderate asthma exacerbation is still inconclusive.

## METHODS

A prospective, randomized, study was performed in RMMCH pediatric emergency department between the

months of August 2016 and August 2018. The study was previously approved by the hospital ethics committee. Children between 6 and 12 years of age who presented with mild to moderate asthma exacerbations were enrolled in the study. They were randomly allocated into two different groups: one nebulised with levosalbutamol alone and another with addition of ipratropium bromide to levosalbutamol. Baseline Peak expiratory flow rate and Final absolute values or change from baseline 60–120 minutes after the inhalation were measured. Because the peak bronchodilator effect after the administration of anticholinergics occurs within 1-2 hours, it is reasonable to expect significant improvement during this time. Patients were evaluated using the pulmonary score.<sup>18</sup> The oxygen saturation (SaO<sub>2</sub>) was measured using a pulse oximeter. Peak expiratory flow rate was performed using a portable peak flow meter. The predicted PEF was adjusted for sex and height and the percentages of the PEFR before and after nebulisation was obtained.<sup>19,20</sup>

The severity of the asthma crisis was classified according to the pulmonary asthma score as mild (score 5-7 and PEF >70% of the predicted value according to the age and sex); moderate (score 8-11) and PEF 50-70% or FEV<sub>1</sub> 60-80% of the predicted value) and severe (score 12-15) and PEF <50% or FEV<sub>1</sub> <60% of the predicted value). The pulmonary asthma score was the main criteria to rank severity of asthmatic crisis.

**Table 1: Assessment of severity of asthma exacerbations by Pulmonary Asthma Score.**

Component score	0	1	2	3
Respiratory rate	14-20	21-26	27-30	>31
Oxygen saturation	>98% at room air	95-97% on room air	90-94% on room air	<90% on room air
Auscultation	Normal breath sounds	End expiratory wheezing	Expiratory wheezing	Inspiratory and expiratory wheeze
Retractions	None	Intercostal	Intercostal and substernal	Intercostal and substernal and supraclavicular
Dyspnea	Speaks in complete sentences	Speaks in short sentences, coos, and babbles	Speaks in partial sentences, short cry	Speaks in single words, short phrase/grunting

## RESULTS

Group A- levosalbutamol

Group A+B - levosalbutamol + ipratropium bromide.

Out of 50 children participated in the study, 25 children were allotted to A group and 25 children were allotted to A+B group. Out of 50 children, 37 children were above 8 years of age and 13 children were less than 8 years of age.

Children were classified based on the severity of asthma exacerbation at the time of presentation as mild and moderate exacerbation using a clinical scoring system, Pulmonary asthma score. Based on PAS classification of disease severity, both groups contained an equal proportion of mild and moderate cases before nebulisation. Hence two groups were adequately matched based upon severity of exacerbation.

Comparison of heart rate before and after nebulisation indicates that there is no significant tachycardia following

nebulisation. There is improvement in respiratory rate and oxygen saturation in both groups following nebulisation. And also there is a significant improvement in PAS and PEFR after nebulisation with both the treatment regimes.

**Table 2: Age group and name of the medication used cross tabulation.**

Age range	Name of the medication used		Total	P value
	A	A+B		
6-8 yrs	8	5	13	0.260
>8yrs	17	20	37	
Total	25	25	50	

**Table 3: Comparison of pulmonary asthma score before nebulisation in two groups.**

PAS classification	Name of the medication used		Total	P value
	A	A+B		
Mild	10	8	18	0.509
Moderate	15	17	32	
Total	25	25	50	

**Table 4: Comparison of asthma severity based on baseline PEFR between two groups.**

	Name of the Medication Used		Total	P value
	A	A+B		
Pefr %	Mild	10	8	18
	Moderate	15	17	32
	Total	25	25	50

There is no significant difference in PEFR after nebulisation between A+B and A group. Hence the addition of ipratropium bromide nebulisation doesn't significantly improve PEFR than the levosalbutamol alone group.

There is no significant difference in improvement of PAS after nebulisation between A+B group and A group. Hence the addition of ipratropium bromide nebulisation doesn't significantly improve PAS than the levosalbutamol alone group.

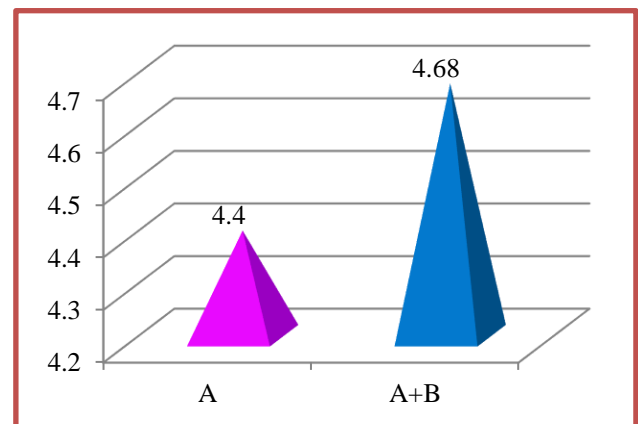
**Table 5: Comparison of means of HR, RR, SPO<sub>2</sub>, PAS AND PEFR before and after nebulization.**

	N	Mean	Std. deviation
Before			
B-HR	50	130.84	23.191
B-RR	50	35.74	8.799
B-SPO <sub>2</sub>	50	94.5000%	3.01865%
B-PAS	50	6.52	2.443
B-PEFR	50	65.6800%	9.29437%
After			
A-HR	50	128.40	23.181
A-RR	50	29.44	7.843
A-SPO <sub>2</sub>	50	96.2800%	2.57967%
A-PAS	50	4.54	2.451
A-PEFR	50	77.8200%	7.93003%

**Table 6: Comparison of mean PAS after nebulisation between two groups.**

Name of the Medication Used	N	Mean	Std. Deviation	T value	P value
PAS	A	25	4.40	2.449	-0.40 0.691
	A+B	25	4.68	2.495	

According to PEFR before nebulisation, 18 patients had mild and 32 had moderate exacerbations and there is no significant differences in severity in both groups based on PEFR. Hence PEFR grading correlates with asthma severity based on PAS.



**Figure 1: Comparison of PAS after nebulisation between two groups.**

**Table 7: Comparison of mean PEFR after nebulisation in two groups.**

	Name of the medication used	N	Mean	Std. deviation	T value	P value
% of Predicted PEFR after neb	A	25	77.1600%	8.80663%	-0.585	0.562
	A+B	25	78.4800%	7.06588%		

## DISCUSSION

Both groups were matched for age, sex, oxygen saturation and asthma severity. Based on PEF, out of 50 children, 36% had mild exacerbation and 64% had moderate exacerbation of asthma respectively.

Chi square test was used for statistical analysis, paired and unpaired T test were used for comparison between two groups.

There is statistically significant improvement in pulmonary asthma score and PEF in each of the groups after nebulisation and pulmonary asthma score has a sensitivity of 66.7% and 65.6% in diagnosing severity of asthma in relation to PEF. After nebulisation there is significant improvement in respiratory rate and oxygen saturation in each of the groups but there is not much difference between two groups.

After treatment there is improvement in the mean pulmonary asthma scores and PEF percentage in A+B group than A group, but it is not statistically significant (p value >0.05). This may be attributed to small sample size in both groups. Yet the effects of Ipratropium with levosalbutamol seems to be equal to the levosalbutamol alone group.

In a study of 125 children with severe asthma, by Quershi et al, found that (FEV1) improved to a greater extent in children receiving salbutamol and ipratropium than in those receiving salbutamol placebo, but there is no effect on overall rates of hospitalisation. In a subgroup analysis of children in whom FEV1 was less than 30 percent of the predictive value, the hospitalisation rate among those receiving the combination therapy was significantly lower than the rate with salbutamol alone.<sup>21</sup>

In a study of 434 children by Schuh et al with moderate and severe asthma exacerbation showed that the addition of ipratropium bromide had a significant effect on improvement of asthma score, but there was no significant improvement of PEF.<sup>22</sup>

In a study done in India by Sharma A et al in 2004 showed that frequent combined nebulisation with salbutamol and ipratropium significantly improved percentage of PEF starting at 30 minutes and lasting for 4 hours in 50 children (6-14years) with moderate exacerbation.<sup>23</sup>

Ricardo Iraman et al.<sup>24</sup> In their study found that Ipratropium +Salbutamol group presented a significantly greater improvement in clinical parameters (PAS+SPO<sub>2</sub>) and in lung function(PEF) than children in salbutamol group. But this study differed from our study in including children with moderate to severe asthma crisis. In our study acute severe asthma cases were excluded due to

their inability to perform peak expiratory flow and forceful expiration may aggravate bronchospasm.

In a study of 298 participants by Francine et al, showed that no increased bronchodilation was associated with addition of ipratropium bromide compared to placebo. No group differences were observed in oxygen saturation, corticosteroid use, patient disposition and relapse status.<sup>25</sup>

In a study of 477 children by Joseph J. Zorc et al, ipratropium group subjects had 13% shorter treatment time and required fewer total albuterol doses, but admissions rates did not differ significantly.<sup>26</sup>

## CONCLUSION

Ipratropium combination therapy has a definitive role in severe asthma crisis. But its role in mild to moderate asthma exacerbation is still inconclusive. Statistical significance has not been obtained in our study due to relatively smaller number of cases in each group. Pulmonary asthma score holds good in assessing the severity of asthma exacerbation and hence can be used for rapid clinical evaluation of acute asthma in emergency settings and also to assess the response to treatment and to decide on hospital admission.

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