COMPARISON OF SALBUTAMOL ALONE WITH SALBUTAMOL PLUS IPRATROPIUM BROMIDE IN THE TREATMENT OF ACUTE ASTHMA IN CHILDREN

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ABSTRACT

Introduction: Asthma is one of the most common chronic diseases in children and worldwide its prevalence has increased dramatically in the last three decades. Nebulized wet aerosol delivery of salbutamol is still considered the main therapeutic option in the management of acute wheezing episodes in children in the emergency departments.

Objective: To compare the efficacy of salbutamol alone with salbutamol plus ipratropium bromide in the treatment of acute asthma in children under 2 years of age

Study Design and Setting: This Randomized Controlled Trial study was conducted at the department of pediatrics, Lady Reading Hospital, Peshawar, (from1st November 2013 to30th April, 2014).

Subjects and Methods: This study comprised of 41 participants in each group, between the age of 6 month to 2 years selected by table of random numbers. Self constructed questionnaire including the variables under study was used.

Results: In this study, 82 patients were divided in two Groups equally. All children were between 6 to 24 months of age. 23 males and 18 females were included in while in group B there were 24 males and 17 females. The efficacy was significant in both the groups with p-value=0.024.

Conclusion: The comibination use of salbutamol plus ipratropium bromide Nebulization is effective for the treatment of children with acute asthma in the emergency department.

KEY WORDS: Asthma, Salbutamol, Ipratropium bromide, Efficacy.

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways characterized by episodic wheeze and reversible airway obstruction. An exacerbation of bronchial asthma is one of the common presenting complaints in an emergency medicine ward of a hospital and is a major economic and health burden. Precipitating factors include allergens to which he/she is sensitized, pulmonary infections especially those caused by viruses, cold, physiological stress, exercise and inhaled irritants[2,7]1,2. Worldwide, approximately 2,55,000 deaths annually are attributable to asthma and are largely preventable, frequently being related to poor management[8]3.

Although there is little evidence to support the use of inhaled bronchodilators, they remain one of the first-line treatment choices for acute asthma. In mild to moderate acute asthma, beta2 agonists may be equally as effective from a metered-dose inhaler/spacer combination compared with nebulizer for control of acute symptoms[9]4. The foundations of the treatment of acute asthma are bronchodilators, corticosteroids and oxygen. Inhaled β2-agonists constitute first-line therapy in acute asthma. Treatment with an inhaled short-acting β2-agonist (SABA) bronchodilator should be started as early as possible[10]5. The combination of the nebulized anti-cholinergic, Ipratropium Bromide (IP), with a nebulized β2-agonist has been shown to result in greater bronchodilatation than a β2-agonist alone[12]6. The most severely affected patients benefit the most, and IB should be considered in combination with inhaled β2- agonists in the more severe forms of asthma, especially early in the acute attack[10]5.

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SUBJECTS AND METHOD

The study was conducted after approval from hospital ethical & research committee. All children from 6 months to 2 years of age presenting with moderate to severe asthma were diagnosed according to operational definition and were included in the study through EDCC. The purpose and benefits of the study were explained to parents/guardians of the children and they were assured about the risks and benefits involved and that the study is done purely for research and data publication and if agreed upon a written informed consent were obtained.

All the children were checked with detailed history and clinical examination. All children were randomly allocated in two groups by lottery method. Children in group A were subjected to salbutamol nebulization (5mg/ml solution) ½ ml + 3 ml normal saline repeated

every hour and slowly decreasing the dose over next 6 hours and children in group B were subjected to salbutamol plus ipratropium bromide Nebulization i.e. salbutamol (5mg/ml) ½ ml + 3ml normal saline plus ipratropium bromide (0.25mg/ml) ½ ml + 3 ml normal saline given every hour and slowly decreasing over next 6 hours. All the children under treatment were closely monitored for heart beat, respiration and feeding. Finally a check examination was done at 6th hour of initiation of therapy to see the efficacy of either treatment.

A strict exclusion criterion was followed and Information including name, age, gender and address were recorded in a pre designed proforma. Data collected were analyzed in SPSS version 10. Mean + SD were calculated for numerical variables like age of the child. Frequency and percentages were calculated for categorical variables like gender and efficacy. Chi square test was used to compare the efficacy of both the groups while keeping p value of < 0.05 as significant.

RESULTS

A total of 82 patients of of acute asthma in children under 2 years of age were observed, which were divided in two equal groups. Patients in group A were managed by salbutamol plus ipratropium bromide Nebulization and another group B of patients were going through salbutamol nebulization.

Gender wise distribution shows that 23(56.1%) were male and 18(43.9%) were female in Group A with male to female ratio was 1.28:1 while Group B contains 24(58.5%) were male and 17(41.5%) were female with male to female ratio was 1.41:1. Overall Male to female ratio was 1.34:1. Sex distribution among the groups was insignificant with p-value=0.500 (Table 1).

Average age was 15.24 months +6.26SD in Group A and 13.39 months +6.32SD, with age distribution as shown in table 2. The age distribution among the group was also insignificant with p-value 0.311 (Table 2).

Efficacy wise distribution shows that Group A shows efficacy in 37(90.2%) patients and 4(9.8%) patients have no efficacy while Group B have efficacy in 29(70.7%) patients and no efficacy in 12(29.3%) patients which shows that efficacy was highly significant in both the treatments with p-value=0.024. (Table 3).

When efficacy was stratified among the gender in both the groups it showed insignificance in both the groups. (Table 4).

DISCUSSION

The treatment of acute asthma consist of beta agonists and systemic/inhaler steroids. Majority of patients responds to this treatment and can be managed as outpatients. It has been observed that addition of anticholinergic drugs to salbutamol improves FEV1 and reduces hospital admission[7-11]. Use of anticholinergic drug is based on premise that cholinergic pathways play an important role in the pathogenesis of asthma due to upper respiratory infection, (URI) which is responsible for 50%-60% of acute asthma in childeren[12-13].

Ipratropium bromide alone does not lead to much improvement but its use with salbutamol demonstrates significant improvement in FEV1 and decreased hospitalization rate in children with acute asthma[7-11].

Results of our randomized controlled trial study declared that addition of ipratropium to salbutamol in children having acute asthma causes statistically significant greater improvement.

Beck et al[14] conducted study in children adding single dose of ipratropium to salbutamol. The medications were delivered using a nebulizer. The author observed significant improvement in FEV1 at 60 minutes in ipratropium group 20.6% vs 3.5% ($p<0.05$) but at 40 minutes there was no statistically significant improvement. Similer result was observed by Agarwal et al that there is no benefit of combination of ipratropium to salbutamol[15].

There are some studies that have evaluated the effect of multiple doses of ipratropium. Goggin et al[16] and Rayner et al[17] did not report any benefit with the use of ipratropium. On the other hand, Quireshi et al[11], Zorc et al[18] and Hossain AS et al [19] observed better response in the combination group.

Aaron SD conducted a systematic review to clarify the issue of efficacy of addition of anticholinergics in treatment of acute asthma.[20] He observed that there was no definite improvement in adult population, but in pediatric asthma patients there was a statistically significant difference in efficacy of addition of ipratropium to salbutamol without adverse effects and results in reduction in need of hospitalization[20].

Throughout our study, an asthma clinical pathway was used, thus ensuring consistency in management of patients in all groups. In addition, a standard clinical assessment scale and pulmonary index were used to titrate treatment, in particular the frequency of nebulized salbutamol. The pulmonary index[21] has sensitivity of 88% and specificity of 77% in childhood asthma. Thus, it is likely that our findings reflect real differences in outcome between treatment groups. We didn't use Peak Flow Meter and its data didn't collected, as peak flow is not reproducible in children younger than 4 years and in very sick children of all ages[22]. Oxygen was titrated to maintain a SaO2 above 93%, so oxygen need rather than SaO2 was the variable indicating desaturation in this study. The importance of supplemental oxygen therapy to correct the hypoxia caused by severe asthma has been highlighted in many studies and suggested as a common reason for hospitalization of children[23].

Hypoxia can therefore be considered a useful

Table No 1: Gender Wise Comparison of Both the Groups

		Group		Total	p-value
		Group A	Group B		
Gender	Male	23	24	47	0.500
		56.1%	58.5%	57.3%	
	Female	18	17	35	
		43.9%	41.5%	42.7%	
Total		41	41	82	
		100.0%	100.0%	100.0%	

Table No 2: Age Wise Distribution in Both The Groups

		Group		Total	p-value
		Group A	Group B		
Age (in months)	<= 10.00	14	21	35	0.311
		34.1%	51.2%	42.7%	
	11.00 - 15.00	3	1	4	
		7.3%	2.4%	4.9%	
	16.00 - 20.00	15	14	29	
		36.6%	34.1%	35.4%	
	21.00+	9	5	14	
		22.0%	12.2%	17.1%	
Total		41	41	82	
		100.0%	100.0%	100.0%	
Mean +SD		15.24 months+ 6.26	13.39 months +6.32	14.32 months +6.32	

Table No 3: Efficacy Wise Distribution in Both the Groups

		Group		Total	p-value
		Group A	Group B		
Efficacy	Yes	37	29	66	0.024
		90.2%	70.7%	80.5%	
	No	4	12	16	
		9.8%	29.3%	19.5%	
Total		41	41	82	
		100.0%	100.0%	100.0%	

Table No 4: Gender Wise Distribution of Efficacy in both the Groups

	Group								
	Group A				Group B				
	Efficacy				Efficacy				p-value
	Yes		No		Yes		No		
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %	
Gender Male	21	91.3%	2	8.7%	18	75.0%	6	25.0%	0.2719
Female	16	88.9%	2	11.1%	11	64.7%	6	35.3%	0.1927

measure of disease severity and a part of criteria for discharge from hospital after discontinuation of oxygen therapy in patients presented acute exacerbation of childhood asthma[18,23,24]. In our study the majority of children who received salbutamol plus ipratropium bromide had their oxygen therapy ceased at 12 hours post-randomization, compared with only 54% those receiving salbutamol alone. This earlier reduction in oxygen therapy is consistent with the more rapid clinical improvement seen in those children who received combination therapy, resulting in this group patients being ready for discharge home earlier.

In conclusion, we demonstrated that in children with acute asthma, the addition of an ipratropium bromide with salbutamol to frequent nebulized and systemic steroids produced a more rapid clinical improvement, resulting in earlier discharge from the hospital compared to salbutamol only nebulized patients. The combination of frequent nebulized ipratropium and intravenous salbutamol/nebulized salbutamol provide additional benefit over the salbutamol alone. We advocate the early use of a combination dose salbutamol and ipratropium bromide.

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