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ORIGINAL ARTICLE

PEAK EXPIRATORY FLOW RATE WITH SALBUTAMOL PLUS IPRATROPIUM BROMIDE VERSUS SALBUTAMOL ALONE IN ACUTE ASTHMA IN CHILDREN IN LAHORE, PAKISTAN: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Paediatric asthma usually presents with acute exacerbation and requires hospital admission and emergency management. The objective of this study was to compare the peak expiratory flow rate (PEFR) with salbutamol plus ipratropium bromide versus salbutamol alone in acute asthma in children in Lahore, Pakistan.

Material & Methods: This randomized controlled trial was undertaken at The Children's Hospital and The Institute of Child Health, Lahore, Pakistan from 14-04-2017 to 17-10-2017. One hundred children with acute asthma with age 2-12 years were enrolled. Fifty patients each were randomly assigned to experimental and control groups by lottery method. At presentation, PEFR was measured by using a peak flow meter. Experimental group received three doses of 2.5 mg salbutamol and 500 mcg of ipratropium at 20 minutes intervals. Control group received three doses of 2.5 mg salbutamol alone. PEFR was again measured after 60 minutes.

Results: Mean age in experimental group was 9.60±2.86 years, whereas it was 8.68±3.28 years in control group, almost similar. Mean weight in experimental group was 29.50±8.26 kg, whereas it was 28.24±10.07 kg in control group, almost similar. Baseline mean PEFR% was 43.18±4.25 in experimental, while it was 42.48±4.82 in control group. Mean PEFR% at 60 minutes after intervention was 82.88±7.54 in experimental, while it was 60.04±6.05 in control group. PEFR% was higher in experimental group showing its better effect than the control group ($p<.00001$).

Conclusion: The peak expiratory flow rate was higher with salbutamol plus ipratropium bromide versus salbutamol alone in acute asthma in children in Lahore, Pakistan.

KEY WORD: Peak Expiratory Flow Rate; Children; Asthma; Salbutamol; Ipratropium Bromide.

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1. INTRODUCTION

1.1 Background: Asthma has become a common disease in this industrialized era and results in frequent emergency visits requiring hospital admissions and aggressive management. The paediatric age group with relatively smaller airways is more prone to exacerbations and emergency visits.[1,2] Airway hyper-responsiveness is the underlying etiology and inhaled corticosteroids have been used along with beta-2 agonists to control the

symptoms of asthma.[3,4]

Viral respiratory tract infections are the commonest cause of exacerbation in asthmatic patients, especially in the paediatric age group. In comparison to 50-75 percent of adults, 80 percent of children presenting with wheezy chest are due to viral infections.[5] In extreme cases, ventilatory care and ICU management may be needed in acute severe asthma.[6] Physicians should be trained enough to identify the severity of asthma and provide prompt treatment.[7]

Salbutamol is a short-acting beta-2 agonist and is used as an emergency bronchodilator. It is commonly used in racemic mixture form which contains an equal concentration of R and S isomers.[8] Salbutamol provides the same bronchodilator effect when used in combination with an inhaled corticosteroid.[9]

When salbutamol is given in combination with ipratropium, the bronchodilator effect is synergistically enhanced as shown by PEFR and forced expiratory flow rates as compared to children receiving salbutamol alone.[10] One trial reported that even after one hour, the mean increase in peak flow was 94.44±33.70% in the combination group (n=40), while 62.57±29.26% in the salbutamol group (n=40) (p=<.0001).[11] But other studies did not demonstrate a significant advantage in PEFR with salbutamol along with ipratropium bromide or alone.[12-13]

It is seen that asthma exacerbation is the third most common cause of hospital admission in children and frequently requires paediatric ICU care. In the modern age, the prevalence, as well as morbidity and mortality of asthma have risen. In Pakistan, also affected by environmental change, asthma has become a common respiratory problem.[14-15]

1.2 Research objective: To compare the peak expiratory flow rate with salbutamol plus ipratropium bromide versus salbutamol alone in acute asthma in children in Lahore, Pakistan.

1.3 Null hypothesis: The peak expiratory flow rate with salbutamol plus ipratropium bromide is the same as with salbutamol alone in acute asthma in children in Lahore, Pakistan.

1.4 Operational definition: In the current study, acute asthma is defined as a respiratory condition assessed by difficulty in breathing, wheezing and PEFR<50% on the peak flow meter.

2. MATERIALS AND METHODS

2.1 Design, setting and duration: It was a randomized controlled trial conducted at The Children's Hospital and The Institute of Child Health, Lahore, Pakistan from 14-04-2017 to 17-10-2017. Ethical approval was granted by the Institutional Ethical Committee. Consents of the parents/guardians were sought before inclusion in the trial.

2.2 Sampling: One hundred children fulfilling the selection criteria were enrolled in the study from the emergency section of The Children Hospital Lahore. Fifty patients each were then randomized into two equal groups by lottery method to experimental group and control group.

2.3 Selection criteria: All children presenting with acute severe asthma with age 2-12 years were eligible. Those with congenital malformations (cerebral palsy, muscular dystrophy) and those already given salbutamol therapy (from the medical record) were excluded.

2.4 Equipment, procedure and intervention: At the presentation, PEFR was measured by using a peak flow meter. Experimental group received three doses of 2.5 mg salbutamol and 500 mcg of ipratropium at 20 minutes intervals. The control group received three doses of 2.5 mg salbutamol alone. PEFR was again measured after 60 minutes.

2.5 Data collection plan: Sex (boys/girls), weight in kg and baseline PEFR % were matching variables. PEFR % at 60 minutes was a single research variable. Sex was measured at nominal, while all other variables were measured on ratio scale.

2.6 Data analysis plan: Sex was evaluated in terms of count and percentage. The mean and standard deviation of weight in kg and PEFR in percentage were calculated. An independent samples t-test with an alpha of .05 was used to test the null hypothesis for the comparison of the two groups. The mean and standard deviation of the two groups, as well as their difference, confidence interval of their difference, t-value, degrees of freedom, and significance (2-tailed), were generated through IBM SPSS Statistics for Windows, v.21.0, released 2012 (IBM Corp., Armonk, NY).

3. RESULTS

3.1 Descriptive analysis: Fifty children in experimental group included 31 (62%) boys and 19 girls (38%), while 50 children in control group included 30 (60%) boys and 20 (40%) girls; almost similar in proportion.

The mean age was 9.60±2.86 years in experimental group, while it was 8.68±3.28 years in control group; both were closely similar. The mean weight was 29.50±8.26 kg in experimental group, while it was 28.24±10.07 kg in control group; again both were almost similar.

The baseline mean PEFR % was 43.18±4.25 in experimental group, while it was 42.48±4.82 in control group; almost similar.

The mean PEFR % at 60 minutes after intervention/manipulation was 82.88±7.54 in experimental group, while it was 60.04±6.05 in control group.

Table 1: Peak expiratory flow rate (PEFR) with salbutamol plus ipratropium bromide versus salbutamol alone in acute asthma in children in Lahore, Pakistan

Groups	Sample size	Mean	SD	Difference of means	95%CI of difference		t value	d.f.	p-value
					Lower	Upper			
Experimental	n1=50	82.88	7.54	22.84	20.13	25.55	16.71	49	< .00001
Control	n2=50	60.04	6.05						

3.2 Hypothesis testing: Mean PEFR percentages were compared between the two groups using independent samples t test at alpha .05. As p-value <.00001 was lower than alpha level of .05, hence H_0 was verified to be false and hence rejected, showing statistically significantly higher value for experimental group. (Table 1)

4. DISCUSSION

In our study, the mean PEFR% at 60 minutes after intervention/ manipulation was 82.88±7.54 in experimental group, while it was 60.04±6.05 in control group. Significantly higher PEFR % was achieved with salbutamol plus ipratropium bromide than with salbutamol alone in acute asthma in children in Lahore, Pakistan (p<.00001).

Similar results are reported by Joiya, et al.[16] from Multan, Pakistan in 2017-18 in an RCT with 52 patients each in salbutamol alone and salbutamol plus ipratropium bromide. They found higher mean PEFR% in combination group 87.12±17.10 than the salbutamol alone group 68.69±18.64 (p=<.0001).

Memon, et al.[13] from Karachi, Pakistan enrolled 100 patients each in salbutamol only and salbutamol plus ipratropium groups in 2012-13. They used Bentur Clinical Scores (BCS) for post-intervention analysis. There was no difference for BCS at 15 minutes after the last dose between the two groups (4.9±2.1 vs. 4.4±2.4, p=>.05).

Singh, et al.[17] from India examined the bronchodilator effects of salbutamol and ipratropium bromide in 30 patients of bronchial asthma; pre and post exercise. Salbutamol showed improvement in PEFR by 15.96% from basal values, whereas Ipratropium bromide showed improvement by 13.01%. Salbutamol was found to be a better drug among smokers, those with a family history of bronchial asthma, and in younger age groups. Ipratropium bromide performed better in adults over the age of 40 years and those with eosinophilia.

Hossain, et al.[11] from Bangladesh documented in acute severe asthma patients that a 60-minute increase in peak flow was about 32% greater in the salbutamol plus Ipratropium combination group (n=40) as compared to salbutamol alone group (n=40) (94.44±33.70% vs. 62.57±29.26%, p<.0001) and the percentage predicted peak flow reached 60% for the combination group while not for salbutamol group.

Children getting the nebulized drug in combination showed up to 25-75% improvement in percent-predicted PEFR and forced expiratory flow when compared to children nebulized with salbutamol alone. A synergistic effect was seen when ipratropium was given with salbutamol via a meter dose inhaler with a spacer for acute asthma exacerbation.[10]

Sharma, et al.[18] from Rohtak, Haryana, India concluded that combined nebulization with Ipratropium and salbutamol is helpful in moderate severity of asthma. Significantly better results were seen 80% of PEFR starting at 30 minutes and lasting about 4 hours in the combination groups.

Watanasomsiri, et al.[12] from Pathumthani, Thailand, from September 2001 to February 2003 on 74 paediatric asthma patients demonstrated clear advantage of using ipratropium with salbutamol. Asthma clinical score and PEFR were used to assess improvement. It was seen that a greater number of subjects in the treatment group showed PEFR of 100 percent or above when compared with the control group. Moreover, there were no additional side effects on heart rate, respiratory rate and blood pressure when ipratropium nebulizations were added to salbutamol. The results obtained were not significant but the favourable response of adding ipratropium bromide to the salbutamol regimen was demonstrated and consistent with other studies.

A study from the European zone comprising 434 children with severe asthma demonstrated that FEV-1 improved significantly in the combination group as compared to the salbutamol alone group. The same study concluded that adding anti-cholinergic to beta-2 agonists significantly reduces the hospitalization rate in patients (27.4% vs 36.5%) presenting with severe exacerbation of asthma.[19]

O'Driscoll, et al.[20] performed a double-blind study of nebulized bronchodilator treatment in

56 asthma and 47 COPD patients. Peak flow rate (PFR) was measured before and one hour after the treatment. PFR increased by a mean of 31% in 23 asthmatic patients given salbutamol alone one hour after treatment, but by a mean of 77% in 33 similar patients given combination treatment (95% confidence interval for the difference 8-84%). The immediate PFR response to a combination of salbutamol and ipratropium bromide was better in acute asthma than the response to nebulized salbutamol alone. Both drugs were equally beneficial to COPD patients.

5. CONCLUSION

In our study, the peak expiratory flow rate (PEFR) was higher with salbutamol plus ipratropium bromide versus salbutamol alone in acute asthma in children in Lahore, Pakistan.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

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Conception or Design:	MAB, MAAB
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Manuscript Writing & Approval:	MAB, MAAB, SS, MMA, BTH, SMS

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.