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Original Research Article

A comparative study on the effect of nebulized budesonide and levosalbutamol versus ipratropium bromide and levosalbutamol in the management of acute asthma in children aged 5-11 years

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ABSTRACT

Background: Asthma is a non-communicable chronic inflammatory condition of lung airways. The availability of new diagnostic methods, introduction of a number of drugs, both oral and inhaled has revolutionized management of asthma in children. Goal was to achieve maximum effect with least amount of medication and allowing infrequent use of quick relievers. The present study was, therefore, designed to compare the effectiveness of single dose nebulization with combination of nebulized budesonide and levosalbutamol (group A) versus commonly used ipratropium bromide and levosalbutamol (group B) in children (5-11 years) with mild-moderate exacerbation of asthma.
Methods: Was an observational comparative study involving 2 treatment groups of children in age group of (5-11) years, with mild-moderate exacerbation of asthma assessed by peak expiratory flow rate (PEFR) and pulmonary score (PS).
Results: Of 160 children analyzed, post nebulization mean predicted PEFR improved in both of the study groups, and the mean PS decreased in both the groups post nebulization which was statistically significant ($p<0.001$). But when comparing between the groups, the mean percentage of improvement in predicted PEFR and PS were almost similar.
Conclusions: Even though, both the groups gave the same end result the group in which budesonide was used had a higher recovery time with the least number of nebulization.

Keywords: Peak expiratory flow rate, Pulmonary score

INTRODUCTION

Asthma is a non-communicable chronic inflammatory condition of lung airways resulting in bronchial hyper-responsiveness and reversible episodic airway obstruction. Inflammation is the important component in the pathogenesis of asthma.[1]

Several epidemiological studies have shown that the prevalence of this condition is increasing in developing countries and India is of no exception and thus the prevalence has increased to nearly 20-30% in many parts of our country. The availability of new diagnostic methods, a better understanding of pathophysiology and introduction of a number of drugs, both oral and inhaled has revolutionized the management of asthma in children.

Levosalbutamol (selective beta-2 agonist) being a bronchodilator**,** it relaxes smooth muscles of airways from trachea to terminal bronchioles. Ipratropium bromide is an anticholinergic bronchodilator, inhibits bronchial secretions. Although ipratropium bromide is not usually employed as a first- line bronchodilator to treat chronic asthma, it is been used extensively in hospital emergency department as an adjuvant therapy for the emergency treatment of acute asthma exacerbation.

While, budesonide is an anti-inflammatory corticosteroid, classically suited for inhalation therapy. It acts by reducing bronchial hyper-activity, reduces mucosal

oedema and suppresses inflammatory response. Therefore, major components in the pathogenesis of asthma can be inhibited by budesonide with no known side effects with its short-term therapy. There have been remote reports of side effects such as dry mouth and ocular complications with repeated use of ipratropium bromide. No systemic side effects for both drugs in nebulized form. Onset of action almost similar for ipratropium bromide and budesonide (20-30 min).

Guidelines advocate use of short acting inhaled beta-2 agonist (SABA), anti-cholinergic and early administration of oral/IV corticosteroid as quick relievers in children experiencing an asthma exacerbation.[2]

Recently few studies have shown nebulization with budesonide in children with mild- moderate exacerbation of asthma is more effective as quick relievers in terms of prevention of progression of the illness.[3] But, no data currently available on the correct schedule for initiation of treatment with nebulized suspension of budesonide. Our goal was to achieve maximum effect with least amount of medication and allowing infrequent need of quick relievers.[4]

The present study was, therefore, designed to compare the effectiveness of a single dose nebulization with a combination of (budesonide and levosalbutamol) versus commonly used (ipratropium bromide and levosalbutamol) in children (5-11 years) with mild-moderate exacerbation of asthma.

METHODS

An observational study which was a non-experimental comparison of two treatment options as a part of standard treatment conducted in the out-patient department of pediatrics, DR. SMCSI medical college, Karakonam, Trivandrum, Kerala during the period from January 2015-July 2016 after getting ethical clearance from the institutional ethical committee. Children between age 5 and 11 years were included in the study.

Step 1 included all children presenting with acute asthma were being initially evaluated using pulmonary score and those with PS more than or equal to 3 or less than or equal to 6, being able to perform peak flow meter were included in the study.[5] Children treated with oral/inhaled/nebulized steroid in last 24 hours were excluded from the study. Written information of the study and consent forms were distributed to all the parents of children who fulfilled the inclusion criteria. Data was collected by detailed clinical examination and personal interview of the parent and the child using semi-structured questionnaire.

Step 2 included respiratory function test was measured by PEFR before giving the drug. Intervention consisted of one-time nebulization with either group A or group B. Those children assigned to group A received budesonide (1 mg) and levosalbutamol (1.25 mg) and those children assigned to group B received ipratropium bromide (250 mcg) and levosalbutamol (1.25 mg).[6-8]

Step 3 involved reassessment of the treated subject was done 20 minutes after the 1st nebulization by assessing: PS and PEFR. Total 160 subjects were taken up for the study of which 80 subjects as group A and 80 as group B. The outcome measured were, difference in clinical score and PEFR**,** repeated number of nebulization required and difference in proportion of patients requiring IP treatment.

PS was assessed by 3 variables-respiratory rates, wheeze and use of accessory muscle.[5] Each variable is awarded 4 scores- 0, 1, 2, 3 summed up to 9. Patient with PSI ≥3 or ≤6 considered as mild-moderate category.

PEFR was measured in subjects fulfilling these criteria using mini-wright peak flow meter before starting treatment and best of the 3 readings considered.[9] Observed PEFR was expressed as, the percentage of normal PEFR which was taken based on the PEFR nomogram.[9]

Statistical analysis

Data was collected and entered in Microsoft excel and analyzed using SPSS software version 22. All qualitative variables expressed as proportions and quantitative variables as mean and standard deviation. Chi square test was done for statistical test of significance. Mean PEFR and mean PS values before and after treatment in each treatment group was compared using paired t test, and unpaired t test was done measure the significant improvement in PEFR and PS post treatment between the study groups.

RESULTS

Of 160 subjects who satisfied the inclusion criteria majority 43% were in the age group of 5-11 years with mean age of 7.9 years. 56% constituted males and 44% were females, with male:female ratio 1.3:1. 53% of cases were persistent asthmatics and 47% of cases had intermittent episodes.

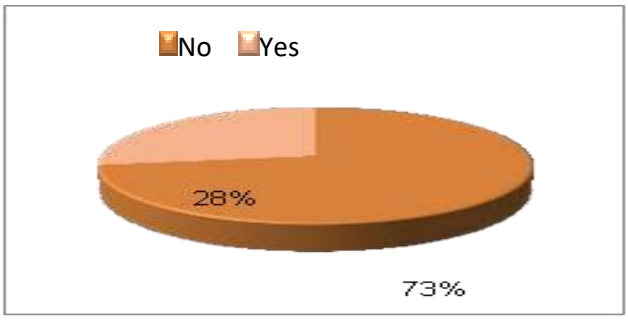

Figure 1: Repeat number of nebulization required group-A.

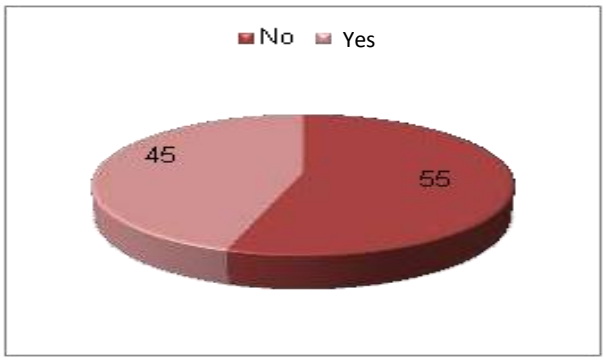

Figure 2: Repeat number of nebulization required group-B.

The mean PEFR improved in group A (budesonide and levosalbutamol) with treatment from 51.09 to 72.25% of predicted (calculated by PEFR nomogram) and the difference 21.16% was statistically significant using paired t test (p<0.001).The mean pulmonary score was observed to be decreased from 4.7 to 2.23 in group A after treatment and the difference (2.4) was found to be statistically significant using paired t test (p<0.001).

The mean PEFR improvement in group B (bromide and levosalbutamol) with treatment was 21.72 from 50.48 to 72.2% of predicted (calculated by PEFR nomogram) which was statistically significant using paired t test (p<0.001).[9] The mean pulmonary score was observed to be decreased from 5.2 to 2.3 in group B and the difference (2.9) was found to be statistically significant using paired t test (p<0.001).

On comparison of PEFR between groups after treatment there was no statistically significant difference in mean PEFR value between the groups (p=0.60) (Table 1). and there was no statistically significant difference in mean pulmonary score between the groups (p=0.327) (Table 2).

Table 1: Comparison of PEFR between groups after treatment.

PEFR	Mean PEFR	Standard deviation	Standard error of mean	P value (test of significance) unpaired t test
Group A (budesonide and levosalbutamol)	137	31.5	3.5	0.60
Group B (ipratropium bromide and levosalbutamol)	134	30.6	3.4	

Table 2: Comparison of PS between groups after treatment.

PEFR	Mean	Standard deviation	Standard error mean	P value
Group A	2.24	0.83	0.09	0.327
Group B	2.35	0.59	0.06	

22 subjects in group A and 36 subjects in group B required repeat nebulization shown in Figure 3 and 4. On comparison between groups 62.1% required repeat nebulization in group B and only 37.9% required repeat nebulization in group A, which was statistically significant (p=0.016) (Table 3).

Table 3: Comparison of requirement of repeat nebulization between groups.

Repeat nebulization	Group A (%)	Group B (%)
No	58 (56.9)	44 (43.1)
Yes	22 (37.9)	36 (62.1)
Total	80	80

Table 4: Rate of IP admission.

Required IP admission	Group A (%)	Group B (%)
Yes	25 (31)	32 (40)
No	55 (69)	48 (60)
Total	80	80

40% of subjects in group B and 31% (n=25) subjects in group A required hospitalization which was not statistically significant (p=0.16) (Table 4).

DISCUSSION

In our hospital based observational comparative study among 160 children who presented with mild to moderate acute exacerbation of asthma, primary outcome was analyzed by the change in peak expiratory flow rate and pulmonary score. The importance of clinical scoring systems has been demonstrated by a number of studies.[10,11]

In the study group A (budesonide and levosalbutamol), post nebulization the mean predicted PEFR improvement was 21.16% of predicted when compared to pre-treatment, which was statistically significant (p<0.001). Similar studies done in India by Singhi and in Turkey by Nuhoglu et al were of similar opinion to ours with respect to showing the additional effect of nebulization with budesonide to beta 2 agonist in increasing PEFR in children with acute asthma.[3,12] Post-nebulization mean pulmonary score in group A decreased by 2.4 (from 4.7

to 2.23) which was statistically significant (p<0.001). Singhi, Nuhoglu, and Volvovitz et al however, in their studies observed similar improvement in pulmonary score index with respect to ours.[3,12,13]

In the study group B (ipratropium bromide and levosalbutamol), post nebulization the mean predicted PEFR improvement was 21.72% of predicted when compared to pre-treatment, which was statistically significant (p<0.001). Our results are in consistent with the results of the studies by Rodrigo, Chakraborti and Qureshi et al in which there was significant improvement in PEFR values post nebulization.[14-16] Post nebulization mean pulmonary score decreased by 2.9 (from 5.28 to 2.33) which was statistically significant (p<0.001). Goggin and Amitabh et al in their studies published, showed similar improvement in clinical score following treatment, with respect to ours.[15,17]

After nebulization with budesonide and ipratropium bromide along with a beta 2 agonist respectively in group A and B, primary outcome results were analyzed between groups and showed there was no statistically significant difference in mean PEFR (p=0.60) and pulmonary score (p=0.327) between groups post nebulization.

Analyzing the secondary outcome measures, such as repeat number of nebulization required between the groups, 62% subjects who received nebulization with ipratropium bromide and levosalbutamol underwent repeat nebulization and only 37.9% subjects who received budesonide and levosalbutamol required repeat nebulization (p=0.016) which was statistically significant. Georgia et al in their study concluded with a similar opinion.[18]

Another, secondary outcome measured was the admission rates between groups. Higher hospitalization rate (40%) was seen in subjects who received nebulization with ipratropium bromide and levosalbutamol and only (31%) patients in group A (i.e. those received budesonide and levosalbutamol nebulization) required hospitalization. But this difference did not reach statistical significance (p=0.16). This, result can be justified by certain studies such as by Sano pointed out that budesonide treatment for acute asthma crisis is followed by reduced hospital admissions when compared to Ipratropium bromide. Plotnick et al observed in their study that no reduction in hospitalization with use of a single dose of ipratropium bromide. However, addition of multiple doses of the drug reduced that hospital admission by 30%.[19,20]

Budesonide has a very rapid onset of action, due to its acute anti-inflammatory effect and may therefore have an additive effect in decreasing admission rates.[21, 22]

CONCLUSION

In my study the following findings were concluded from the analysis.

The highest frequency of asthma was found in the age group of 5-7 years with male preponderance (56%). Most of the study subject (53%) were persistent asthmatics. The PEFR and pulmonary score values improved significantly in both the groups post-nebulization (p<0.001), but when comparing in between groups the result was not statistically significant, to know the best outcome (p>0.05). Even though, both the groups gave the same end result the group in which budesonide was used had a higher recovery time with the least number of nebulization.

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