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Original Articles

Bronchodilator Response to Salbutamol Delivered by Metered Dose Inhaler with Spacer and Dry Powder Inhaler in Acute Asthma In Children: A Comparative Study

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Abstract:

Background: *Salbutamol inhalation is the mainstay of treatment for acute exacerbation of asthma. A number of delivery systems for asthma medication have been developed for children, each having its own advantages and disadvantages. This study was done to compare the bronchodilator effect of salbutamol inhalation delivered through metered dose inhaler (MDI) with spacer and dry powder inhaler (DPI) in children presenting with mild and moderate acute asthma.*

Methodology: *Children of 6 to 15 years of age with mild or moderate acute exacerbation of asthma were assessed primarily and randomly distributed into two groups having equal number of patients and received 400micro-gram of salbutamol delivered by either MDI with spacer or DPI device. The primary outcome variable was peak expiratory flow rate (PEFR) and secondary outcome variables were percent predicted PEFR, heart rate, respiratory rate, oxygen saturation, wheezing and accessory muscle scores. Changes in primary and secondary outcome variables, before and after drug intervention were recorded and subjected to statistical tests for significance. Separate analyses were done for mild and moderate asthma patients.*

Results: *The changes in primary outcome variable (PEFR) in both groups before and after intervention was 179.19 ± 33.27 vs. 197.52 ± 57.01 liters/min and 184.81 ± 59.65 vs. 202.83 ± 64.76 liters/min respectively, which was statistically highly significant (P= 0.001). Similar significant changes were also observed in case of secondary outcome variables.*

Conclusion: *Bronchodilator response to salbutamol in mild or moderate acute asthma in children is similar when equal amount of drug is delivered either through an MDI with spacer or a DPI.*

Key words: *acute asthma, exacerbation, salbutamol, PEFR*

Introduction:

Asthma is a chronic inflammatory disorder of lower airway with significant mortality and morbidity. Around 300 million people in the world currently have asthma.[1] About 7 million people in Bangladesh are suffering from current asthma (at least three episodes of asthma attack in the last 12 months) which is about 5.2% of total population of our country and 7.4% of total pediatric population of our country is suffering from asthma.[2]

Currently the corner stone of management of acute asthma exacerbation is the rapid reversal of air way obstruction. Inhalation route is the corner stone of therapy for asthma according to the major international guidelines of asthma management[3]. Different inhalation systems are available for delivering salbutamol in acute asthma in children. Pressurized

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metered dose inhalers are popular and most widely used method for administration of inhaled aerosols to the lower airways[4] but a number of problems are still associated with their use. Failure to synchronize between inhaler actuation and inspiration is the most important drawback of this system [5]. The use of a spacer device may eliminate the need for hand to lung co-ordination but addition of this extra device makes the system more bulky, more costly and less portable, hence less preferred by young asthmatic children. Metered dose inhalers (MDIs) contain lubricants that may cause bronco-constriction[6]. Moreover, MDI suspensions contain chlorofluorocarbons (CFC) which is harmful for environment[7]. Non CFC metered dose inhalers have been developed but this increase the cost of medication. Dry powder inhalers (DPI) could be an attractive and more convenient alternative to pressurized metered dose inhalers without the attending problems of MDI. Hand-lung co-ordination is not needed in this system. It is cost effective and there is less chance of drug misuse or wastage. Due to small size of the device it is easily portable, hence more preferred delivery system for children. Moreover it is environment friendly and bio-equivalent to MDI [8].

Limited number of studies exists to compare the clinical efficacy of MDI with spacer and DPI in the treatment of acute asthma in children. So this study was done to compare the efficacy of theses two inhalation systems for salbutamol treatment in mild and moderate acute exacerbation of asthma in children.

Methodology:

This comparative study was done in outpatient department of paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka and National Asthma Center, National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka during the period of May 2007 to April 2008. The study protocol was approved by institutional Ethical Committee.

Children of either sex between six to fifteen years of age, presented to the place of study with mild or moderate acute asthma were enrolled in the study. Mild acute asthma was defined as presence of cough and wheezing without any form of distress, cyanosis, increased respiratory rate (R/R). Patients were able to speak in full sentence between breaths and PEFR was >80% of predicted value. Moderate acute asthma was defined as presence of cough and wheezing, use of accessory muscles, increased respiratory rate(R/R), inability to speak in full sentences between breaths and PEFR was < 80% of predicted value[9].

After proper clinical assessment, PEFR was done by using Wrights' mini peak flow meter with adequate demonstration to the patient. The best of the three results was accepted. Respiratory rate was counted for full one minute. Heart rate (H/R) and oxygen saturation (SaO_2) were recorded from digital display of pulse oxymeter. Wheezing and accessory muscle scores were recorded as per guideline[10.] Children were then randomized to be assigned in either MDI with spacer group or DPI group to take salbutamol treatment. Children of MDI with spacer group received four puffs of salbutomal (each puff contains 100 microgram of salbutamol) through commercially available spacer with valve. It was ensured that the child took five deep breaths from one actuation. Children assigned to the DPI group received 2 cozy caps (each cozy cap contains 200 microgram of salbutamol) through a DPI device (cozyhaler).Children performed five maximum inspiratory_maneuver as per demonstration after taking one cozycap. Thirty minutes after salbutamol treatment children were re-evaluated and changes in study parameters were recorded. Results were expressed as mean ±SD.

The primary out come variable was the changes PEFR and secondary out come variables were the changes in percent predicted PEFR, H/R, R/R and SaO_2, wheezing and accessory muscle scores. Initially the primary and secondary out come variables of two groups were compared. Then the changes in variables at half an hour after salbutamol therapy were recorded and subjected to statistical tests for significance using SPSS 12.0 for windows software. Children with mild and moderate acute asthma in both groups were analyzed separately.

Results:

Total 106 children were study sample among which 53 were in MDI-spacer group and 53 in DPI group. The base line characteristics (age, sex, height and weight, family history of asthma, smoking history of parents, duration of sufferings from asthma) were almost same in two groups and non significant statistically ($p>0.05$).

Changes in out come variables of both groups before salbutamol inhalation were statistically non significant

as p>0.05(Table-I). Similarly, changes in out come variables of both groups after salbutamol inhalation were also statistically non significant (Table-2) during inter group observation but highly significant (p<0.001) changes observed when intra group observation were done.

But statistically highly significant (p<.01) changes observed in both primary and secondary outcome variables before and after salbutamol inhalation when within group observation was done as shown in table-III & IV.

The changes in mean PEFR within groups before and after salbutamol inhalation for patients with mild and moderate acute asthma were also statistically significant (p=.001) which is shown in table-V.

Figure-1 shows clinically significant changes in wheezing and accessory muscle scores before and after drug intervention

Table- I

Changes in outcome variables of both groups before Drug intervention

Variable	Group		t value#	df	p value
	Gr-A (MDI with spacer) n=53	Gr-B (DPI) n=53			
PEFR (liters/min)	179.19 ± 33.27 (100 - 310)	184.81 ± 59.65 (90 - 330)	-.512	104	0.610
PEFR (% of predicted)	73.66 ± 6.82 (61- 82)	72.37 ± 8.10 (60 - 81)	.889	104	0.376
Heart rate (beats/min)	111.90 ± 13.39 (88 -142)*	116.85 ± 13.87(96 -160)	-1.867	104	0.065
Respiratory rate (breaths/min)	31.72 ± 7.67(20 - 50)	33.32 ± 8.45 (20 - 52)	-1.023	104	0.308
SaO_2 (%)	96.11 ± 1.37 (92 - 98)	95.58 ± 1.57(91 - 98)	1.844	104	0.068

*Mean ± SD, # unpaired t test was done

Table- II

Changes in outcome variables of both groups after Drug intervention

Variable	Group	t value #	df	p value	
	Gr A (MDI with spacer)n = 53	Gr B (DPI)n = 53			
PEFR (liters/min)	197.53 ± 57.02(110 - 350)	202.83 ± 64.76 (100 - 360)	-.447	104	.656
PEFR (% of predicted)	80.88 ± 6.60(62.5 - 90)	79.34 ± 8.42(64 - 94)	1.046	104	.298
Heart rate (beats/min)	98.42 ± 7.38* (82 -120)	100.0 ± 9.47(80 -122)	-.961	104	.339
Respiratory rate (breaths/min)	21.17 ± 2.56(16 - 30)	21.79 ± 3.16 (16 - 32)	-1.115	104	.268
SaO_2 (%)	97.87 ± .79(95 - 99)	97.58 ± .98 (95 - 99)	1.631	104	.106

*Mean ± SD, # unpaired t test was done

Table-III

Comparison of parameters before and after intervention of the patients of Group-A

Variable	Group A (MDI with spacer) n=53		t value#	df	p value
	Before intervention	After intervention			
PEFR (liters/min)	179.19 ± 33.27(100 - 310)	197.53 ± 57.02(110 - 350)	- 4.455	52	.001
PEFR (% of predicted)	73.66 ± 6.82 (61 - 81)	80.88 ± 6.60(62.5 - 90)	- 15.624	52	.001
Heart rate(beats/min)	111.90 ± 13.39* (88 -142)	98.42 ± 7.38 (82 -120)	10.166	52	.001
Respiratory rate (breaths/min)	31.72 ± 7.67(20-50)	21.16 ± 2.55(16 - 30)	11.225	52	.001
SaO_2 (%)	96.11 ± 1.37 (92 - 98)	97.86 ± .78(95 - 99)	-12.115	52	.001

*Mean ± SD, # Paired t test was done

Table- IV

Comparison of parameters before and after intervention of the patients of Group-B

Variable	Group B (DPI)n = 53		t value#	df	p value
	Before intervention	After intervention			
PEFR (liters/min)	184.81 ± 59.65* (90 - 330)	202.83 ± 64.76 (100-360)	-13.701	52	0.001
PEFR (% of predicted)	72.37 ± 8.10 (60 - 91)	79.34 ± 8.43(64 - 94)	-15.832	52	0.001
Heart rate (beats/min)	116.85 ±13.87(96 -160)	100.0 ± 9.47(80 -122)	12.543	52	0.001
Respiratory rate (breaths/min)	33.32 ± 8.45 (20-52)	21.79 ± 3.16(16-32)	11.754	52	0.001
SaO_2 (%)	95.58 ±1.57 (92- 98)	97.58 ± .98(95 - 99)	-12.374	52	0.001

*Mean ± SD, # paired t test was done.

Table V

Comparison of changes in PEFR within groups for mild and moderate asthma patients

	Mean ±SD		
	Before treatment	After treatment	p value*
Group A			
• Mild (n=18)	188.44 ± 48.14	200.83 ± 50.1	0.001
• Moderate·	167.23 ± 57.98	195.83 ± 60.89	0.001
• (n=35)			
Group B			
• Mild (n=14)	198.07 ± 51.08	211.54 ± 54.01	0.001
• Moderate·	180.5 ± 61.61	199.74 ± 69.12	0.001
• (n=39)			

• Paired t test was done

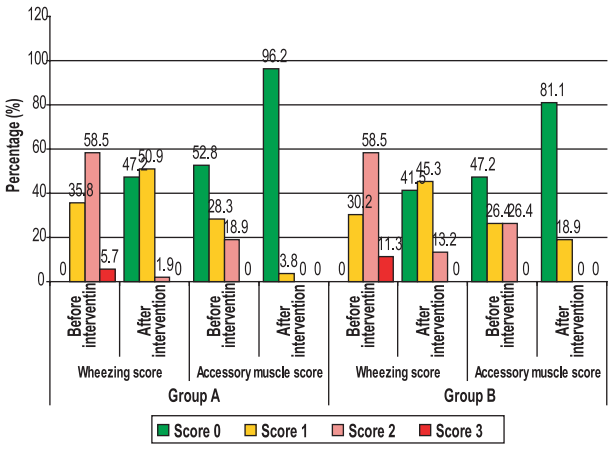

Fig.-1: *Changes in wheezing and accessory muscle scores before and after salbutamol treatment*

Discussion:

Salbutamol is the mainstay of treatment for acute exacerbation of asthma. Inhalation route is widely preferred for prompt relief of bronco- constriction with very minimum systemic effects. A number of devices are available for salbutamol inhalation in children with acute asthma, each having some advantages and disadvantages. Pressurized MDI using spacer is the conventional and most widely used drug delivery system for children. Dry powder inhalers are the newer alternatives to MDIs with same clinical efficacy.

To compare the efficacy of different inhalation systems available for the management of asthma, a number of studies have been done among the adults and most of them have shown that administration of salbutamol through a DPI device is as efficacious as that by

MDI[11].Two studies found DPI to be more effective[12]. Studies comparing the clinical efficacy of MDI and DPI in the treatment of asthma in children are limited. Lodha et al. [13] studied two groups of children with mild and moderate acute exacerbation asthma receiving salbutamol through either MDI with spacer or a DPI and found equal efficacy which is almost similar to the result of the present study.

In this study, the base line characteristics between two groups were similar and statistically non-significant. But 30 minutes after salbutamol inhalation there were significant changes in PEFR, percent predicted PEFR, wheeze score, accessory muscle score, H/R, R/R and SPo2. In group-A, before intervention mean PEFR was 179.19 ± 33.27 liters/min and percent predicted PEFR was 73.66±6.82 percent. But after intervention the two parameters were 197.52 ± 57.01litres/min and 80.87 ± 6.57 percent respectively. The increase in both parameters were statistically highly significant (p=0.001). Similarly in group-B, mean PEFR and percent predicted PEFR, before and after intervention were 184.81±59.65 vs. 202.83±64.76litres/min and 72.37±8.10 vs. 79.34±8.43 percent respectively and these changes were also highly significant (P=0.001). Changes in all other parameters, before and after intervention were also statistically significant.

Bronsky et al.[14] observed that the two devices were equally efficacious in delivering salbutamol in exercise induced asthma in children, supports the finding of the present study.

Regarding the analysis of primary outcome variable (PEFR) according to severity of asthma (mild or moderate acute asthma),the changes in PEFR was not significant when between group analysis was done as p> .05 for both groups but highly significant changes in mean PEFR observed when within group analysis was done (p = .001) Sing et al [15] compared the clinical efficacy of a transparent DPI with MDI plus spacer in moderate persistent asthma in children with a result of having equal efficacy in delivering anti-inflammatory therapy of bronchial asthma. It is also consistent to the present study.

Callaghan et al [16] also found similar clinical efficacy when salbutamol was delivered by these two devices with more acceptability of DPI among the paediatric patients. However the present study did not compare the acceptability of these two devices

Conclusion:

Inhalation route is widely preferred for rapid relief of airway obstruction in acute asthma with very minimum systemic effects. Different inhalation systems are available for delivering salbutamol in acute asthma in children. From this study it can be concluded that bronchodilator response to salbutamol in mild and moderate acute asthma in children is similar when equal amount of drug is delivered either through an MDI with spacer or DPI.

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