Original Articles

Metered Dose Inhaler with Spacer Versus Dry Powder Inhaler for Delivery of Salbutamol in Acute Exacerbations of Asthma: A Randomized Controlled Trial

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Manuscript received: January 29, 2003, Initial review completed: April 8, 2003, Revision accepted: June 20, 2003.

Background: *Delivery of various drugs by aerosol inhalation is the mainstay of treatment of asthma. Many delivery systems have been developed for children, each having its own advantages and disadvantages. Studies comparing the clinical efficacy of metered dose inhalers (MDI) and dry powder inhalers (DPI) in the treatment of acute exacerbations of asthma in children are limited. We conducted a study to compare the response to salbutamol inhalation delivered by metered dose inhaler with a spacer versus rotahaler (DPI) in children presenting with mild or moderate acute exacerbations of asthma.* ***Methods****: Children in the age group of 5-15 years who presented with a mild or moderate acute exacerbation of asthma were randomized to receive 400 µg salbutamol by either a MDI with spacer or a DPI. The changes in the wheezing and accessory muscle scores, SaO_2, and PEFR were recorded and subjected to statistical tests for significance.* ***Results:*** *One hundred and fifty three children were studied; 78 were assigned to the MDI-spacer group and 75 to rotahaler (DPI) group. After receiving treatment, the PEFR improved by about 11% in both the groups. The oxygen saturation increased by 2% in both the groups. Within each group, the improvement in PEFR, SaO_2, wheeze and accessory muscle score after the treatment was statistically significant. In both the groups the children co-operated equally well.* ***Conclusion:*** *Metered dose inhaler with spacer and dry powder inhaler have equal efficacy in delivering salbutamol in therapy of mild to moderate acute exacerbations of bronchial asthma in children between 5-15 years of age.*

Key words: *Asthma, Acute exacerbation, Metered dose inhaler, Rotahaler, Spacer*.

ASTHMA is a clinical syndrome characterized by increased responsiveness of the tracheobronchial tree to a variety of stimuli, airway inflammation and airway obstruction that is reversible either spontaneously or with treatment. Aerosol inhalation has long been recognized as the mainstay of treatment of asthma(1). The success of therapy and subsequent relief of symptoms depends upon the deposition of adequate amount of drug in the lungs. This depends to a large extent upon the delivery system. Many delivery systems have been developed for children, each having its own unique advantages and disadvantages. Prominent among them are pressurized metered dose inhalers (MDI) with or without spacers, dry-powder inhalers (DPI) and

nebulizers. Studies comparing the clinical efficacy of MDI and DPI in the treatment of asthma in children are limited and none about comparison in acute exacerbations. Therefore, we conducted a study to compare the response to salbutamol inhalation delivered by metered dose inhaler with a spacer versus rotahaler (a DPI) in children presenting with mild or moderate acute exacerbation of asthma.

Subjects and Methods

The study was conducted in the Pediatric Chest Clinic of a tertiary care hospital in north India. The study subjects were children in the age group of 5-15 years who presented with a mild or moderate acute exacerbation of asthma(2) and were cooperative enough to use a peak flow meter to measure the peak expiratory flow rate (PEFR). Mild exacerbation was defined by presence of cough and wheezing without any form of distress, cyanosis, increased respiratory rate, or impairment of activity; ability to speak in full sentences in between breaths, with PEFR >80% of predicted value. Moderate exacerbation was defined as cough, wheezing, with use of accessory muscles, increased respiratory rate, and inability to talk in full sentences, and PEFR 60-80% of predicted. For inclusion, other than clinical features of mild or moderate acute exacerbation, the PEFR had to be more than 60-80% of the values predicted for the height(3). Children with features of severe acute exacerbation or PEFR less than 60% of the predicted value or a lower respiratory tract infection were excluded. In addition, children who had received a bronchodilator within the last 6 hours of presentation were excluded.

The children were then randomized by using a random number table to receive salbutamol by either a MDI with spacer or a DPI. One of the authors examined the child to record the wheezing and accessory muscle scores(4), oxygen saturation (SaO_2) and PEFR using Wright's mini peak flow meter. The child was then administered 400 µg of salbutamol by either a MDI with spacer or a DPI (Rotahaler) by another author unaware of the baseline characteristics. Children assigned to the MDI group received four 100 µg puffs of salbutamol using a 750 mL commercially available spacer with valve (Cipla Ltd., Mumbai, India). It was ensured that the patients took 5 deep breaths following one actuation of the MDI into the spacer. Children assigned to rotahaler (Cipla Ltd., Mumbai, India) group received 2 rotacaps (Cipla Ltd., Mumbai, India) each of 200 µg salbutamol. Children performed 5 maximum inspiratory maneuvers after each dose. Thirty minutes after treatment, the children were reevaluated.

Baseline parameters were compared for the two groups. The changes in the wheezing and accessory muscle scores, SaO_2, and PEFR were recorded and subjected to statistical tests for significance. Statistical package STATA 7.00 (Stata Corp, TX, USA) was utilized for this purpose.

Results

One hundred and fifty three children were studied. Seventy-eight children were assigned to the MDI-spacer group and 75 to Rotahaler group. The baseline characteristics are shown in *Table I*. The proportion of boys was significantly more in the MDI-spacer group. Percent predicted PEFR in both the groups were similar. Children in the MDI-spacer group had a higher accessory muscle use score.

After receiving treatment, the PEFR improved by about 11% in each of the groups (*Table II*). The oxygen saturation increased by 2% in both the groups. The accessory muscle use scores were significantly less in the

TABLE I–*Baseline Characteristics of Study Population*

Parameter	MDI-spacer group (n = 78)	Rotahaler group (n = 75)	P value
Male:Female	55:23	40:35	0.03
Age in years*	9 (8-10)	10 (9-11)	0.28
PEFR (liters/min)*	190 (170-210)	199 (170-207)	0.71
Percent predicted PEFR*	77.5% (73-83.9)	74.25% (71-78.1)	0.17
SaO_2 (%)*	96 (95-96)	96 (95-96)	0.76
Wheeze score*	2 (1-2)	1(1-2)	0.19
Accessory muscle score*	1 (0-1)	0 (0-1)	0.04

*median (95% confidence interval).

TABLE II–*Post-treatment Characteristics in the Two Groups*

Parameter	MDI-Spacer group (n = 78)	Rotahaler group (n = 75)	P value
PEFR (Liters/min)*	217.5 (189.2-237.4)	210 (191.9-244.1)	0.11
Percent predicted PEFR*	87.7 (81.8-92.2)	83.3 (77.9-86.4)	0.09
% increase in PEFR after treatment*	11.2 (9.3-13.3)	11.1 (8.1-12.5)	0.63
SaO_2 (%)*	97 (97-97)	98 (97-98)	0.09
Increase in SaO_2 (%) after treatment*	2.06 (1.04-2.08)	2.08 (1.05-2.1)	0.13
Wheeze score*	1 (0-1)	1 (0-1)	0.14
Accessory muscle score*	0 (0-0)	0 (0-0)	0.02

* median (95% confidence interval).

rotahaler group. However, the wheeze scores were comparable.

Within each group, the improvement in PEFR, SaO_2, wheeze and accessory muscle score after the treatment were statistically significant. In both the groups the children co-operated equally well.

Discussion

Delivery of drugs as aerosols, particularly via metered dose inhalers, has been a major breakthrough in the treatment of asthma, as it allows adequate drug deposition in the lower respiratory tract without any significant systemic side effects. However, despite adequate tuition many patients are unable to use a pressurized inhaler efficiently, especially children. Failure to co-ordinate inhaler actuation with inspiration is the most important error(1,5-7). Also they contain lubricants that may cause broncho-constriction(8). The use of a spacer device eliminates the need for any breath-hand co-ordination. But the side-effects of

Key Message

- Metered dose inhaler with spacer and dry powder inhaler have equal efficacy in delivering salbutamol in therapy of mild to moderate acute exacerbation of bronchial asthma in children 5-15 years of age.

propellants and lubricants are not eliminated. Static electricity accumulates on many poly carbonate and plastic spacers attracting drug particles that become charged when they are produced by the MDI. Spacer made of anti-static material and washing them before use may reduce this problem(9).

Dry powder inhalers (DPIs) provide an alternative formulation for drug delivery to the airways without the attendant problems of MDIs and are bioequivalent to them(10). There is no need for any breath-hand actuation. But the need for a minimum level of inspiratory flow for a DPI to be useful still exists.

We observed that efficacy of salbutamol in mild or moderate acute exacerbation of asthma was similar when the drug is delivered by MDI-spacer or a dry powder inhaler. The increase in PEFR in the two groups was about 11%. We used PEFR values predicted for height to calculate the decrease in PEFR. While it is preferable to establish baseline PEFR values for a child, the same can be done only by repeated measures of PEFR. Most patients do not monitor PEFR on a regular basis at home. So we did not use this parameter for our study and relied up on percent predicted PEFR for categorization. Accessory muscle scores were higher in MDI group than Rotahaler group at baseline, while other parameters to assess severity were comparable. There was significant improvement in the scores in both the groups; however, the difference between two groups persisted. This discrepancy may be avoided by use of composite scores for assessment of severity(11).

A number of studies have been done to compare the efficacy of the many inhalational systems available among adults. Most of them have shown that salbutamol administered by a DPI is as efficacious as that by MDI(12-14). Two studies(15,16) found DPI to be more effective.

There are no studies to show the clinical efficacy of rotahaler in children with acute exacerbations of asthma. Two studies evaluated changes in the lung function tests after administering the drug by either rotahaler or a MDI alone. Kemp, *et al*.(17) studied two groups of children with asthma. In first group, the changes in lung function were studied after administration of a single dose of 100 µg or 200 µg of salbutamol and no significant differences were found. In the second group, the children received 200 µg of salbutamol for 12 weeks. While there were no significant differences between and pre- and post-treatment lung function tests, the children in the MDI group had higher number of acute exacerbations. The authors explained this by the fact that the children in the MDI group had significantly lower mean baseline FEV_1 when compared with the rotahaler group. In another study on 44 children, Bronksy, *et al*. (18) observed that the two devices (rotahaler and MDI) were equally efficacious in delivering salbutamol in exercise-induced asthma(18).

Alwarez, *et al.*(19) in an analysis of 10 RCTs observed that in stable asthma in children, salbutamol administered via pMDI is as effective as DPIs. No additional clinical benefit was found in either case. Singh and Kumar compared the clinical efficacy of a transparent, DPI (transparent Rotahaler) with MDI and spacer in moderate persistent childhood asthma(20). The two groups of children received both inhaled steroids and bronchodilators through either of the devices for 6 weeks and then were crossed over to the other group. Comparisons made on weekly symptom scores, PEFR at interval visits, PEFR variability, additional bronchodilator use and acute exacerbations of asthma did not reveal any statistically significant differences during the two treatment periods.

We studied the efficacy of the two devices in only acute exacerbations and only for bronchodilators. Based on our findings and review of literature, we conclude that metered dose inhaler with spacer and dry powder inhaler have equal efficacy in therapy of bronchial asthma in children

Contributors: RL, SKK designed and coordinated the study and prepared the manuscript. GG, BPB, RN were involved in collection of data. GG and BPB were also involved in preparation of manuscript. SKK will act as the guarantor of the study.

Funding: None.

Competing interests: None stated.

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