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ORIGINAL ARTICLE

Comparison of Inhaled Levosalbutamol vs Salbutamol in the Emergency Treatment of Severe Acute Asthma

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Abstract

Background: *This study was conducted to compare effectiveness of multidose regimen of levosalbutamol and salbutamol inhaler through a volumetric spacer device in adult patients with acute asthma.*

Materials & Methods: *The study was a randomized, single-blind, prospective study and was carried out in the emergency department of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka over a period of twelve months total 100 patients fulfilling the criteria of inclusions were included in this study and two groups are done in randomized manner. Study group received a multi-dose regimen of levosalbutamol by a metered dose inhaler through a spacer device and control group received salbutamol by metered dose inhaler through an identical spacer device. Clinical parameters, pulmonary functions, and side effects profile were recorded and results were analyzed by "unpaired 't' test".*

Result: *In this study there is no significant differences in respect to age, sex, heart rate and respiratory rate. The study demonstrated significant improvement in expiratory flow chart rate and better oxygenation and fewer side effects and less hospital admission rate in levsalbutamol to salbutamol group in maltidose inhalation form.*

Conclusion : *Our results indicate that repetitive doses of Levosalbutamol delivered by MDI through spacer device is an effective modality for management of patient with severe acute asthma.*

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Introduction

Bronchial asthma is a chronic inflammatory disorder of airways. It is a major public health problem and important cause of morbidity and mortality. It is widely distributed but variable in the prevalence. Around 300 million people in the world currently have asthma. It is estimated that there may be an additional 100 million people with asthma by 2025[1]

In Bangladesh, according to First National Asthma Prevalence Study[2] about 7 million- people (5.2% of population) are suffering from current asthma

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(at least three episodes of asthma attack in last 12 months). Unfortunately, majority of these patients are in 1-15 years of age group that is 7.4% of total pediatric population of our country is suffering from asthma[3].

The disease causes physical, emotional and financial sufferings for patients leading to deleterious effect on the overall socio-economic structure of the country[4].

The aims of treatments are, to abolish symptoms, to restore normal or best possible long-term airway function, to reduce the risk of severe attacks, to enable normal growth to occur in children, to minimize absence from school or, employment, patient and family participation, avoidance of identified causes where possible, use of lowest effective doses of convenient medications minimizing short-term and long-term side effects[5,6].

Currently the cornerstone of the therapy for acute asthma is the rapid reversal of the patients airways obstruction. The main stay therapy for severe acute asthma is nebulized B_2 agonist therapy. Salbutamol is a B_2 agonist and manufactured as a mixture containing 'R' Salbutamol and 'S' and Salbutamol 'R' salbutamol is responsible for its biological activity.[7,8]

Early in the course of treatment systemic corticosteroid should be administered to patient with moderate to severe acute asthma or to patient who fail to respond promptly and completely to inhaled b agonist[9]. In the emergency department theophylline is not recommended because it appear to provide no additional benefit to optimum inhaled B_2 agonist therapy and steroid and increase the adverse effect. It has narrow therapeutic index and frequently associated with adverse effect even in therapeutic. [10]

Despite the refinement in therapeutic strategy for acute asthma emergency department visit and hospitalization continue to account for predominant proportion of health care costs for asthma. These facts stress the need for the innovative emergency department based intervention.

Hypothesis

Levsalbutamol is superior to salbutamol for adult patient and with acute asthma.

Objectives

General objective:

To formulate an alternative effective first line therapy for adult patients with acute asthma.

Specific objective:

To compare effectiveness of multi-dose regime of levsalbutamol to salbutamol as a first-line therapy in adult patients with acute asthma.

Materials and Methods

Study population

Adult patient with acute asthma attending the emergency department of NIDCH during the above mentioned period were the study population.

Selection of patients

In this study of one hundred adult (18 to 50 years) patients with acute asthma attending the emergency department of NIDCH were selected. The diagnosis of acute asthma was done from history, examination and previous records of investigations (according to National Guideline for Asthma, Bronchiolitis and COPD).

The inclusion criteria for these patients were-

1. Established cases of bronchial asthma.
2. PEF 35%-50% of predictive value.
3. SO_2>90%
4. Adult patient (18-50 years)
5. Informed written consent of the patients.

The exclusion criteria were-

1. Long history of smoking, COPD. Chronic cough, old TB, fever (>38^0C).
2. Co-morbidity-CCF, CRF, CLD malignancy.
3. Age <18 years.
4. Pregnancy.
5. Unable to blow PEF meter.
6. SO_2<90% inspite of treatment with O_2 and drugs.

Study design

1. In this single-blind, randomized controlled study, adult patients with acute asthma was

selected consecutively from emergency department.

2. After selection of patients, a written consent was taken from the participants.
3. Patient's demographic data, total duration of acute exacerbation total asthma suffering period and pre-medication taken to control asthma were noted in a protest questionnaire.
4. These patients were divided into two groups 'A' and 'B' with the use of a computerized random number table. Randomly selected group 'A' was enrolled in study and group 'B' was enrolled as control.
5. Study group received levosalbutamol delivered by a metered dose inhaler (MDI) into a volumetric uptech spacer device in a dose of five puffs at 10 minutes interval. The randomly selected another group received five puffs of salbutamol (100 mgm/puff) at 10 minutes interval by the same measure and same device.
6. High flow oxygen was given when SO_2 had fallen below 92%
7. Variables were measured immediately before starting treatment and at 20 minutes interval thereafter for one hour in each patient.
8. Peak expiratory flow (PEF, saturation of oxygen (SO_2), respiratory rate (R/R), heart rate (HR), accessory muscles used, dyspnoea, wheeze were the variables that were recorded in a preformed questionnaire form (appendix-I)
9. At the end, each patient was asked for nausea, palpitation, tremor, anxiety, headache, dry mouth and if present was noted.
10. At the end every patient was assessed and those improved and PEFR > 60% of predictive value were discharged with oral prednisolone and bronchodilators.

Results

Out of 100 patients 50 patients were enrolled in levosalbutamol group and 50 patients were in salbutamol group.

Age of Levsalbutamol (study) group was 31.9±11.3 (mean±SD) and control group was 32.5±7 (mean±SD). The difference was not statistically significant (P=0.82). Among the study group the highest percentage of patients (50%) was in the age group 21-30 years followed by 32% in the age group 31-40 years, 18% in the age group 41-50 years and below 20 age group. Similar age pattern was found in the control group patients with highest percentage (52%) in the age group 31-40 years followed by 28% in the age group 21-30 years and also below 20 age group, the lowest in the age group 41-50 years (16%).

At the end of protocol, every patient was assessed clinically & PFT and those improved and PEF >60% of predictive value was discharged with oral prednisolone and bronchodilators. 6% patients in levosalbutamol group and 20% patients in control group don't fulfilling the criteria for discharge were admitted into the hospital. This difference is statistically significant (P<0.05).

At the end of study, each patient was asked for any adverse effect and 24% patients in control group 16% patients in study group had tremor. Palpitation nausea and headache occur in almost equal number of patients in both groups. This side-effect profile had no significant statistical difference between these two groups.

Table-I

Sex distribution of the patients.

	Levosalbutamol group		Salbutamol group		Significance
	No.	%	No.	%	
Male	31	62. %	30	60%	Not Significant
Female	19	38. %	20	40%	

Table-II

Educational status in two groups of patients in study population.

Level of education	Group I		Group II		Total		Significance
	No.	%	No.	%	No.	%	
Below SSC	28	56	32	64	60	60	Not Significant
SSC passed	10	20	11	22	21	21	
HSC passed	10	20	5	10	15	15	
Graduate & above	2	4	2	4	4	4	

Table-III

Changes of Respiratory rate before and after intervention in two groups of patients in studied population.

	Group A Mean Res±SD	Group B Mean Res±SD
Pre-treatment	31.20±1.56	31.20±1.49^{NS}
After 20 minutes	28.80±1.32	28.93±1.95^{NS}
After 40 minutes	26.83±1.49	27.40±2.11^{NS}
After 60 minutes	25.73±1.23	26.13±1.85^{NS}

^{NS} - Not significant
P<0.05 in unpaired 't' test

Table-IV

Changes of Heart rate before and after intervention in two groups of patients in studied population.

	Group A Mean HR±SD	Group B Mean HR±SD
Pre-treatment	123.13±5.76	125.13±5.36^{NS}
After 20 minutes	124.87±5.32	126.27±5.11^{NS}
After 40 minutes	125.93±5.27	128.13±4.82^{NS}
After 60 minutes	127.60±5.21	129.93±4.64^{NS}

^{NS} - Not significant
P<0.05 in unpaired 't' test

Table-V

Changes of SO_2 before and after intervention in two groups of patients in studied population.

	Group A Mean SO_2±SD	Group B Mean SO_2±SD
Pre-treatment	93.80±1.28	93.15±1.04^{NS}
After 20 minutes	95.33±1.54	94.07±1.03^{NS}
After 40 minutes	97.10±0.88	95.00±1.15^{NS}
After 60 minutes	97.80±0.53	96.60±0.84^{NS}

^{NS} - Not significant
P<0.05 in unpaired 't' test

Table-VI

Changes of PEFR before and after intervention in two groups of patients in studied population.

	Group A Mean PEFR±SD	Group B Mean PEFR±SD
Pre-treatment	205.83±40.61	203.17±31.91^{NS}
After 20 minutes	235.67±41.14	214.50±31.47*
After 40 minutes	264.50±45.04	229.67±35.21*
After 60 minutes	287.00±44.38	253.17±36.23*

^{NS} - Not significant; *Significant
P<0.05 in unpaired 't' test

Discussion:

Bronchial asthma is a major public health problem. Around 300 million people in the world have current asthma. An effective management is essential to control the disease and as well as disease prevention. The aim of the present study was to findout an effective therapy for adult patients with acute asthma. This prospective study was conducted in National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka, for a period of one year starting from December 2006 to November 2007. Total 100 patients were treated during this period, and two groups were made from a computerized random table. Socio-demographic and clinical variables were measured in each patient. The present study demonstrated that levosalbutamol produced significant bronchodilation in asthmatic patients. This study failed to demonstrate significant differences in heart rate, respiratory rate and oxygen saturation.

Sociodemographic data of the study subjects were evaluated. Mean age of the study subject was 31.9 + 11.3 years and that of the control group was 32.5 + 13.7 years and the highest proportion of the study

subjects (50%) were below 30 years. Analysis revealed that no statistically significant mean age difference was found between patients of study and control group (P > 0.05). This meen age of patients was consistent with the finding of Nowalk et al (2004)[11] who conducted a pilot study comparing the effect of levsalbutamol and racemic salbutamol.

Analysis of the patients in respect to sex showed male predominance with a male : female ratio 1.6:1 in study group and 1.5:1 in control group and there was no statistically significant sex difference in between the study and control group (P > 0.05). This finding correlated with the finding of NAPS (1999)[12], where male : female ratio was 1.03:1. The male predominance may be explained by greater prevalence rate of male for the disease and differences in health care seeking behavior between men and women.

Educational status of the patients were evaluated. The highest number of patients in the study group had below S.S.C level of education (56%), S.S.C and H.S.C passed subjects were 40%. In control group below S.S.C level was 60%, S.S.C and H.S.C passed subjects were 36%. This educational status of the patients was consistent with the study of Kabir et al (1999)[2]. He showed that 67.7% asthmatic patients received below S.S.C level of education and 21.06% patients were S.S.C passed. This reflects the educational status of the people of Bangladesh.

Analysis of the duration of acute attack was evaluated. The mean duration of acute asthma attack in study group was 118.8+ 77.8 hours. In control group it was 104.7 + 60.1 hours. Analysis revealed that there was no statistically significant difference in two groups (P > 0.05). This analysis is consistent with the study Kabir et al (1999)[2] of Bangladesh. He showed that mean duration of acute attack was 108.6 + 65.3 hours.

Premedications taken by asthmatic patients before attending the emergency department of National Institute of Diseases of the Chest and Hospital was evaluated. In study group 96% patients were treated with inhaled salbutamol and 56% treated with inhaled steroid. In the control group 98% patients recived inhaled salbutamol and 68% patients received inhaled steroids. This scenario differs from Kabir et al (1999)[2]. In National Asthma Prevalence study of Bangladesh (NAPS) he showed that 22% asthmatic people in the community used inhalation therapy. This difference might be explained that before attending Emergency Department, they received inhalation therapy in different places.

Analysis of heart rate of the patients were evaluated. The base line mean heart rate was 4.47 in study group and 4.6 in control group. Analysis revealed that there was no statistically significant difference in heart rate (P > 0.05). The mean change of heart rate was consistent with the finding of Nelson et al (1998)[12] who showed that mean change of heart rate after study was 10.6 in levsalbutamol group and 10.8 in salbutamol group. This was not statistically significant (P>0.05).

Analysis of respiratory rate was evaluated. In study group mean reduction in respiratory rate was 5.47 in study group and in control group it was 5.07. The analysis was not statistically significant. Analysis of respiratory rate was consistent with Schreck et all (2005)[13]. He carriedout a study comparing levsalbutamol and salbutamol in the emergency department of a teaching hospital. He showed that mean change of respiratory rate in levsalbutamol group was 4.6 and in salbutomol group it was 5.4. It was not significant (P > 0.05).

Analysis of percentage saturation of oxygen was evaluated. In study group the mean difference before and after treatment was 4.0 and in control group it was 3.45. The result was not significant. Schreck et al (2005)[13] in the previously mentioned study showed that the mean change of percentage saturation of oxygen was 3.2 in levsalbutamol group and 3.1 in salbutomol group. It was not statistically significant. (P > 0.05).

Analysis of expiratory flow rate (PEFR) was evaluated. In study group mean PEFR was 81.39 and in control group it was 50.0. The analysis was statistically significant (P <0.05). Hardley et al (2000)[14] showed that the average increase in PEF for 1.25 mg of levsalbutamol was 88% grater than 2.5mg of racemic salbutamol. The difference was statistically significant. (P<0.05)

Hospitalization rate after treatment was evaluated and this study demonstrated that hospitalization following treatment with levsalbutamol was 6% and after treatment with salbutamol was 20%. The difference was statistically significant. Carl et al (2003)[15] demonstrated hospitalization rate was significantly lower in levsalbutamol group (36%) than in the racemic salbutamol group (45%, P<0.05). This finding was consistent with the present study.

The present study demonstrated that there side effects like palpitation, nausea, vomiting, dry mouth nervousness were similar in both groups. Nelson et al (1998)[12] showed that palpitation, nausea, vomiting, dry mouth nervousness were similar following administration of levsalbutamol 1.25 mg and salbutamol 2.5 mg. These finding were similar to present study.

In spite of all these facts the study had some limitations such as studied population was small. Only 100 patients were included in this study. So, study results might be reevaluated by further large-scale study. FEV_1 was not measured, though it was an important parameter. Pediatric patients those were most frequently affected by asthma but these patients were not considered here. Very sever acute asthmatics (PEFR <35%) were excluded from this study for ethical issue. Baseline theophylline and steroid level were not measured here due to lack of logistics. So, these might influence study results. This was a single blind study. So, there was a chance of bias in spite of taking all types of measure to prevent it.

All these evidences revealed that levsalbutamol in multi-dose inhalation form was effective in bronchodilation and reduction of hospital admission of acute asthmatics in adults, thereby reduce the overall cost of treatment and reduce loss of working period of the productive age group patients which was very important for a developing country like Bangladesh. This was first time in Bangladesh that levsalbutamol was used in inhaler form with multiple dose regime in emergency department for treatment of severe acute asthma. It demands further evaluation regarding its doses schedule through a large scale double blind study.

Conclusion:

Repetitive doses of Levosalbutamol delivered by MDI through spacer device is an effective modality for management of patient with severe acute asthma. It is well tolerated by most of the patients. It is convenient and user-friendly procedure easily understood by patients and their attendants. It is a cheap method which does not involve technical equipment like nebulizer and is not dependent on external source of energy. The procedure is easily applicable in domestic environment and low facility emergency or outpatient department particularly in rural settings. In addition, it can play a crucial role till arrival of rescue services like ambulance as well as during transport of the patient to hospital.

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