Original Article

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# Effects of Aerosolized Levosalbutamol Verses Salbutamol on Serum Potassium Level and Heart Rate in Children with Acute Exacerbation of Asthma

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## Abstract

**Background:** Aerosolized levosalbutamol (LEV) and Salbutamol are used commonly today in the management of acute exacerbation of childhood asthma and the complications and side effects with salbutamol and LEV therapy needs to be carefully studied. Published data shows that LEV will not cause much change in the serum potassium levels compared to salbutamol.

**Materials and Methods:** This prospective study conducted in a teaching hospital catering to the lower socioeconomic class. The study period was from December 2014 to May 2015. It included 60 known asthmatic children aged between 5 and 15 years who presented with acute exacerbation of childhood asthma were studied. Baseline clinical parameters were recorded before and after giving 3 back to back nebulization at 20 min apart in the 1st h of presentation. Respiratory rate (RR) heart rate (HR), oxygen saturation in room air $SpO_2$, forced expiratory volume in 1 s (FEV1) measured, asthma score and serum potassium level asthma score were monitored post nebulization.

**Results:** The present study Group-1 LEV cases were showing clinical improvement in terms of FEV1, asthma score and $SpO_2$ with reduced RR and there was not much statistically significant fall in the serum potassium level and HR at 60 min after nebulization as compared to the baseline. *P* - 0.0001. In Group 2 - Salbutamol cases were showing significant clinical improvement in $SpO_2$, FEV1, RR, and asthma score, but there were significant tachycardia and fall on serum potassium level after nebulization *P* = 0.0001. Among them 70% of children showing a drop of potassium level 0.5-0.8 mEq/L from the baseline values. The results were all found to be independent of extraneous factors like pH, prior use of inhaled steroids or bronchodilators and nutritional status.

**Conclusion:** The aerosolized LEV is superior medicine in the management of acute exacerbation of asthma in children and no side effects like increase in HR and hypokalemia.

**Key words:** Childhood asthma, Hypokalemia, Levosalbutamol, Salbutamol

## INTRODUCTION

Asthma is a common disease worldwide. It is the most common chronic disease in children.[1] The prevalence of asthma in childhood is 10-30%.[2,3] It is the leading cause of hospitalizations in children <15 years of age, and the leading cause of school absence.[4] In India, the estimated burden of asthma is believed to be more than 15 million.[5] Most children admitted to the hospital because of acute asthma do not require intensive care treatment.

The salbutamol and levosalbutamol (LEV) inhalation therapy are effective way of management of acute exacerbation of childhood asthma, but their uses are associated with undesirable side effects such as tachycardia and hypokalemia. Salbutamol, the most commonly used bronchodilator, is a chiral drug with R and S isomers. The commonly used formulation is a racemic mixture that contains equal amount of both R and S isomer. β2-agonist Racemic Salbutamol has been the mainstay of treatment for bronchial smooth muscle contraction since 1982.[6] β2-agonist are a racemic mixture that is composed

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of a 50:50 ratio of (R) and (S) isomers. "LEV" was approved by Food and Drug Administration in 1999 as a purified single isomer for clinical use in asthma patients.[1,7] The bronchodilator effects of salbutamol are attributed entirely to (R)-salbutamol (LEV), while (S)-salbutamol has been shown to possess bronchospastic and pro-inflammatory effects both *in vitro* and *in vivo* studies. LEV, the (R) enantiomer of salbutamol is currently available only in a liquid formulation for use via a nebulizer. LEV has approximately 2-fold greater affinity than the racemic salbutamol for the β2 adrenergic receptor and approximately 100 fold greater binding affinity than S-salbutamol. LEV elevates intracellular concentration of cylic adenosine monophosphate (cAMP) by activating adenyl cylase. In the airways, increased concentration of cAMP relaxes bronchial smooth muscle by reducing intracellular calcium and prevents contraction of hyperresponsive airways. Increased concentration of cAMP also inhibits the release of inflammatory mediators from mast cells and eosinophil.[8-12] There are several studies which demonstrate a significant decrease in serum potassium level after aeorosol therapy.[13,14]

In studies of outpatient asthma patients who were treated with LEV they experienced a significantly greater increase in forced expiratory volume in 1 s (FEV1), a longer duration of action and fewer side effects.[15-19] Though salbutamol is an effective treatment of acute exacerbation, its use is associated with undesirable side effects like tachycardia.[20.] The purpose of the present study is to evaluate the effects of LEV verses Salbutamol on serum potassium level and heart rate (HR).

### Objective

To study the effects of LEV versus sabutamol nebulization on serum potasium level and HR in children with acute exacerbation of asthma aged between 5 and 15 years.

## MATERIALS AND METHODS

This is a prospective study done on 60 children aged 5-15 years attending the pediatric emergency Department of Kannur Medical College, Anjarakkandy, and were grouped into children receiving LEV (Group I-30 cases) and those receiving salbutamol (Group II, 30 cases). The studied medicines nebulized salbutamol (2.5 mg) or LEV (0.63 mg) was diluted in 2.5 ml NS and was nebulized over a period of 7-10 min, 3 times in an hour. After 60 min, HR and serum potassium levels were measured.

### Inclusion Criteria

Patient aged between 5 and 15 years presenting with acute exacerbation of asthma.

### Exclusion Criteria

Age >15 and <5 years, severe asthma, children already on preventive therapy (inhaled steroids or long-acting bronchodilator), patients on treatment diuretics, aminoglycosides, bicarbonates, acute gastroenteritis, the presence of baseline hypokalemia, congenital heart diseases and patients with hepatic, pre-existing renal disease.

### Data Collection and Evaluation

Parents were given a detailed briefing about the purpose of the study. After obtaining permission from the head of the Institute and taking informed consent from parents of the children/guardian, they were enrolled in the study. Ethical clearance was obtained from Institutional Ethical Committee. Data were entered and analyzed using excel spread sheet. Nebulized salbutamol (2.5 mg) diluted in 2.5 ml NS was administered 3 times during the 1st h in Group I and LEV (6.3 mg) diluted in 2.5 ml NS to Group II. The following parameters were recorded initially and after giving 3 nebulizations at 20 min interval in the 1st h of presentation-respiratory rate (RR), HR, oxygen saturation in room air SPO2, FEV1, asthma score and serum K+ level. Clinical asthma severity score includes 5 parameters (tachypnea, hypoxia, retractions, wheeze and dyspnea) (Table 1).[6] Each parameter was scored from 0 to 3 (maximum total score was 15). A score of more than 7 was considered as severe. All the values were expressed as mean ± standard deviation (SD) for pre- and post-treatment effects. Comparative analysis of baseline parameters of two groups and within the groups and percentage of improvement between these two groups before and after treatment was done using unpaired "*t*" test. All the statistical analysis was performed using SPSS package 21 version.

Complete blood count, serum creatinine, serum electrolytes, ABG and X-ray of chest were studied when it was required. All the patients were monitored by continuous electrocardiography, and arterial oxygen saturation by pulse oximetry with a finger oximeter. The baseline peak expiratory flow rate was measured. An intravenous (IV) line for repeated blood sampling was established. After the third administration of back to back LEV or salbutamol nebulization in 20 min apart total three doses (60 min), RR and serum potassium levels were assessed. The mean and SD were calculated for baseline and subsequent measure of potassium. Serum potassium level was monitored at 0 h and 60 min post nebulization.

## RESULTS

To study the effects of medicines following parameters were recorded pre and post nebulizations that there was

a statistically significant fall in the serum potassium level at 60 min as compared to the baseline level of potassium in the group - Salbutamol after back to back nebulization.

. After (Group 1) LEV nebulization, there was a signifi cant increment in FEV1 and SPO2 with a decrease in tachypnea and asthma score ($P$ = 0.0001) while no significant difference was found in pre- and post-treatment HR and serum K+ levels (Table 4). In the salbutamol (Group 2), there was a clinical improvement in terms of FEV, oxygen saturation and asthma score, but a signifi cant tachycardia and decrease in potassium levels ($P$ = 0.0001) (Table 5). Of 70% of children and showed a fall of 0.2-0.6 mEq/L from the baseline values. Serum potassium concentration decreased signifi cantly (3 mEq/L) in one patient in the continuous salbutamol nebulization; however, this patient had inadvertently been given IV maintenance fl uids without potassium chloride. Supplemental potassium chloride (20 mEq/L) was added to her IV fl uids and the hypokalemia resolved without any adverse consequences. The results were all found to be independent of extraneous factors like pH, Prior use of inhaled steroids or bronchodilators and nutritional status.

The majority of cases were aged between 9 and 11 years, 25 cases (42%) followed by 21 (35%) cases age between 12 and 15 years and 14 (23%) children belong to 5-8 years (Table 2). Among them 28 (58%) males and 32 (42%) cases were females who presented with acute exacerbation of childhood asthma (Table 3).

All the values for pre- and post-treatment parameters are expressed as mean ± SD. Comparison done using unpaired '*t*' test at 5% level of significance. All the statistical analysis was performed by SPSS 21 version (Tables 4 and 5).

Mean baseline FEV1 52.2 ± 0.53/min (range 80-120%). Serum potassium levels decreased significantly from 4.46 ± 0.61 (baseline) to 3.643 ± 0.35 mEq/L (60 min) ($P$ = 0.0001) and HR increased from 101.80 ± 8.2 (baseline) to 124.6 ± 6.8 beats/min post salbutamol nebulization ($P$ = 0.0001) (Tables 6 and 7).

In Group 1 patients, the effects of LEV nebulization will not cause the hypokalemia and tachycardia. $P$ = 0.0001.

## DISCUSSION

Asthma is the most common chronic disease of children.[1-3] It contributes significantly to the number of cases in pediatric emergency. Acute exacerbation of asthma was the 3rd most common diagnosis most common diagnosis (5.2%) after acute diarrhea and seizures.4-8 No clinical study data available and all study done with comparative effects of LEV verses salbutamol on potassium and HR in acute exacerbation of asthma only one data available that Singhi et al.,[12] study was done two decade ago and they observed that after salbutamol nebulization the serum potassium level decreased marginally from 3.9 ± 0.5 mEq/L to 3.7 ± 0.5 mEq/L ($P$ < 0.05). A decrease in serum potassium concentration was noted in 26 (56.5%) and hypokalemia (serum potassium < 0.005). Recently, a randomized, double-blind clinical study comprising 84 asthmatic children admitted at 11 different centers over 3 years was conducted in Bangladesh.[1,10],

Another study done by Punj et al.,[2] in India among children aged 5-18 years presenting in the ED with acute exacerbation of asthma. The patients had initial mean PEFR < 0.01) and better tolerability, less tachycardia and less hypokalemia compared to salbutamol ($P$ < 0.01).[2,14] Our study result shows that both have same therapeutic effect with less signifi cantly less side effects like tachycardia and hyokalemia in the Levosalbutamol Group 1 ($P$ - 0.0001 < 0.05). The study conducted by Punj et al.,[2,15] they observed that LEV has equally good effect with salbutamol in improving FEV1, SpO2 and asthma score in the treatment of acute exacerbation of asthma in children but better tolerability in terms of tachycardia and hypokalemia compared to salbutamol. A similar study done by Rahman et al.,[1,16] concluded that LEV has similar therapeutic effects with salbutamol in acute exacerbation of asthma but has no side effects such as tachycardia and hypokalemia. Ralston et al.,[14,16,17] compared LEV with a combination of salbutamol and ipratropium bromide in children between 6 and 18 years presenting with acute asthma and reported that LEV was associated with less tachycardia but showed no other advantage of associating RAC with ipratropium bromide. Our study underlines the fact that while having similar effects with Sabutamol group 2 alone, levosalbutamol Group 1 does not cause either tachycardia or hypokalemia.[9,10,20]

**Table 1: CASS (6)**

| Score | RR | Room air saturation* | Auscultation (wheeze) | Retractions | Dyspnea |
|---|---|---|---|---|---|
| 0 | <30 | 97-100 | None | None | None |
| 1 | 31-45 | 94-96 | End expiration | ± | Full sentences |
| 2 | 46-60 | 91-93 | All expiration | ++ | Partial sentences |
| 3 | >60 | <91 | Inspiration and expiration without stethoscope | +++ | Single word/grunt |

*Off oxygen for 5 min or until saturation drops <91%. CASS: Clinical asthma severity score, RR: Respiratory rate

**Severity assessment**

| | Mild | Moderate | Severe |
|---|---|---|---|
| Asthma score | 5-7 | 8-11 | 12-15 |
| % FEV1 | <80 | 50-65 | <50 |

FEV1: Forced expiratory volume in 1 s

**Table 2: Age distribution**

| Age in years | Group 1 LEV | Group 2 Salbutamol | Percentage |
|---|---|---|---|
| 5-8 | 06 | 08 | 23 |
| 9-11 | 13 | 12 | 42 |
| 12-15 | 11 | 10 | 35 |
| Total | 30 | 30 | 100 |

LEV: Levosalbutamol

**Table 3: Gender wise distribution**

| Index | Male | Female | Total |
|---|---|---|---|
| Number of cases | 28 | 32 | 60 |
| Percentage | 58 | 42 | 100 |

**Table 4: Pre-treatment observations**

| Parameters | Pre-treatment LEV | Pre-treatment salbutamol |
|---|---|---|
| RR | 29.79±0.73 | 28.20±0.61 |
| HR | 100.6±7.1 | 101.8±8.2 |
| SPO2 | 94.76±0.59 | 94.76±0.59 |
| FEV1 | 52.20±0.53 | 56.4±0.73 |
| Serum potassium level mEq/L | 4.46±0.79 | 4.26±0.36 |
| Asthma score | 6.60±0.55 | 6.6±0.75 |

RR: Respiratory rate, HR: Heart rate, FEV1: Forced expiratory volume in 1 s, LEV: Levosalbutamol

**Table 5: Post-treatment observations**

| Parameters | Post treatment LEV | Post treatment salbutamol |
|---|---|---|
| RR | 21.7±1.6 | 22.6±1.25 |
| HR | 106.2±8.1 | 124.6±6.8 |
| $SpO_2$ | 98.33±2.99 | 97.93±1.95 |
| FEV1 | 68.98±12.21 | 67.13±1.77 |
| Serum potassium level MEq/L | 4.43±0.60 | 3.64±0.35 |
| Asthma score | 5.0±1.31 | 5.2±0.82 |

RR: Respiratory rate, HR: Heart rate, FEV1: Forced expiratory volume in 1 s, LEV: Levosalbutamol

**Table 6: Pre-treatment observations of LEV versus salbutamol**

| Parameters | LEV | Salbutamol | *P* value |
|---|---|---|---|
| HR | 100.6±7.1 | 101.8±8.2 | 0.5469 (>0.05) |
| Serum potassium | 4.46±0.66 | 4.26±0.36 | 0.1505 (>0.05) |

HR: Heart rate, LEV: Levosalbutamol

**Table 7: Post-treatment observations of LEV and salbutamol**

| Parameters | LEV | Salbutamol | *P* value |
|---|---|---|---|
| HR | 106±8.1 | 124.6±6.8 | 0.0001 (<0.05) |
| Serum potassium | 4.43±0.60 | 3.64±0.35 | 0.0001 (<0.05) |

HR: Heart rate, LEV: Levosalbutamol

## CONCLUSIONS

All previous study was assessed the efficacy of levosalbutamol versus salbutamol in the management of acute exacerbation of asthma. Presnt study shows that the effects of aerosolized LEV (Group 1)is the superior and safer drug in the treatment of acute exacerbation of asthma and no effect on Serum potassium level in 30 children who were admitted in the Paediatric Emergency department. It was concluded that there was not much significant fall in serum potassium and heart rate in children with acute exacerbation of asthma after using aerosolized LEV. when compared to aerosolized salbutamol there was a change in serum potasium level from 0.5 to 0.8 mEq/L and heart rate increased from 25 to 30 beats per minute post nebulisation the most significant fall occurring at 60 minutes.

A significant hypokalemia occurred only 3.3% but extra caution needs to be taken when subjecting patients with gastroenteritis ,on oral steroids,diuretics,underlying renal or hepatic disease,cardiac cases etc.who are more prone for to develop the electrolyte imbalances to nebulized salbutamol.

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