# INHALED LEVOSALBUTAMOL VERSUS INHALED SALBUTAMOL IN ACUTE EXACERBATION OF ASTHMA

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**ABSTRACT**

**BACKGROUND**

Incidence of bronchial asthma has dramatically increased in last 2 to 3 decades. Inhalation therapy is the treatment of choice in acute exacerbation of asthma. Levosalbutamol (R-salbutamol) has been shown in different studies to be superior to racemic salbutamol (mixture of equal amount of (R) - and (S)- salbutamol). Thus, the present study was conducted to compare response of reversibility of bronchoconstriction and tolerability of inhaled levosalbutamol versus salbutamol.

**MATERIALS AND METHODS**

A study was done on 274 patients from November 2016 to September 2018. All patients received either salbutamol (2.5 mg) or levosalbutamol (0.63 mg) by nebulisation for 3 times at interval of 20 minute all parameters like FEV1, FVC, HR, RR, $SPO_2$, PEFR were recorded before starting treatment and after 1 hour of 1st nebulisation in both groups, and comparative study was done.

**RESULTS**

Both inhaled salbutamol and levosalbutamol were effective equally in bronchodilatation in acute exacerbation of Asthma. There was increase in heart rate in salbutamol inhalation but there was no significant change in HR in levosalbutamol group.

**CONCLUSION**

Both levosalbutamol and salbutamol showed significant improvement in acute exacerbation of bronchial asthma. There was increase in HR with salbutamol, but no significant change was observed in HR with levosalbutamol. Less dose of levosalbutamol produced the same effect and clinical improvement as compared to salbutamol.

**KEYWORDS**

Asthma, Levosalbutamol, Salbutamol, Nebulization, Bronchodilatation, Heart Rate.

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## BACKGROUND

Asthma is a heterogeneous disease, usually characterised by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.[1]

Exacerbation of asthma are episodes characterised by progressive increase in symptoms of shortness of breath, cough, wheezing or chest tightness and progressive decrease in lung function, i.e. they represent a change from the patient's usual status that is sufficient to require a change in treatment.[2]

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Symptoms of bronchial asthma can subside spontaneously or after treatment with medication. Patients of bronchial asthma may have episodic flare-ups (exacerbation) of asthma that may be dangerous to life and have a significant burden to patient himself and the society. Exacerbations usually occur in patient with a pre-existing bronchial asthma. But it may be the first presentation of bronchial asthma in some cases. Exacerbation of bronchial asthma usually presents after exposure to trigger agents (pollen, dust, mites, fumes, viral respiratory tract infection etc.) and /or poor compliance with medication. However, some patients may have episodes of exacerbation without exposure to any known trigger factor. Bronchial asthma affects 1 to 18% of population worldwide. The incidence of asthma has increased dramatically in last 2-3 decade. Inhalation therapy is the treatment of choice in acute exacerbation of Asthma. Salbutamol is most commonly used drug in treatment of acute exacerbation of Asthma. Commonly used formulation is racemic mixture of equal amount of (R)- and (S)- isomers (also known as enantiomer).[3]

These isomers are chemically identical, but they differ in conformation, being exact non-super imposable images of one another (mirror image).[4] R-Salbutamol has been shown

in different study to have a 2-times higher binding affinity than racemic salbutamol and a 100 times higher binding affinity than (S)-salbutamol for the $\beta_2$-adrenergic receptor.[5] The bronchodilator property of recemic (R, S)-salbutamol is attributed entirely to R-salbutamol. Different clinical studies especially in children have shown that levosalbutamol has a similar bronchodilator ability as racemic salbutamol even if given at one-half or one-fourth the dose.[6-11] It is shown in different studies that salbutamol given by nebulizer or pressurised metered dose inhaler with spacer produces same effect.[12]

**Aims and Objectives**

1. To study comparative response of Bronchodilatation (reversibility of bronchoconstriction) with inhaled Levosalbutamol versus Salbutamol.
2. To study tolerability of Levosalbutamol versus Salbutamol in acute exacerbation of Asthma.

**MATERIALS AND METHODS**

**Study Duration**- November 2016 to September 2018.

**Inclusion Criteria-** Cases of bronchial asthma of age 20-40yrs. attending NMCH.

**Exclusion Criteria**

1. Patient already on oral steroid.
2. Known case of hypersensitivity to salbutamol or levosalbutamol
3. Patients having cardiac disease
4. Any other chronic lung disease.
5. Pregnant Female.
6. Hemodynamic unstable patient.

Patient with acute exacerbation of bronchial asthma visiting NMCH, Jamuhar were enrolled in our study after taking informed consent from them. A detailed clinical history was taken from all such patient & all required investigations were done in all such patients. A base line PFT (FEV1, FVC and PEFR) was done in all patients. $SPO_2$, HR & RR were also taken in every patient. This was a double-blind randomized study and the patients were randomly divided into two groups: -

1) Levosalbutamol group (R-Salbutamol 0.63mg) -134 cases (M -65 & F -69).
2) Salbutamol group (Racemic salbutamol 2.5 mg) -140 cases (M - 66 & F - 74).

The patients accordingly received either salbutamol or levosalbutamol usually on alternate basis (i.e. if 1st patient received salbutamol then 2nd will receive levosalbutamol and so on) by nebulizer. After 1st nebulization, the 2nd nebulization was done with the same medicine after 20 min. of 1st dose. It was followed by 3rd nebulization after 20 min. of 2nd nebulization with same medicine in same patient. After one hour of 1st nebulization, PFT was repeated again and PEFR, $SPO_2$, FEV1, FVC, HR and RR were recorded.

**Abbreviations**

FEV1-Forced expiratory volume in one second. FVC-Forced vital capacity. HR- Heart rate. RR- Respiratory rate. $SPO_2$-peripheral capillary oxygen saturation. PEFR- peak expiratory flow rate, L- Litre.

**RESULTS**

134 cases (M-65 & F-69) received levosalbutamol and 140 cases (M-66 & F-74) received Racemic salbutamol by nebulizer. All the cases were of age group 20 to 40 years and both the group were comparable (Table-1) levosalbutamol and salbutamol were found to be equally effective and caused significant changes in different parameters as shown in Table-3. The changes were comparable in both the groups except the HR which increases significantly in salbutamol group only (Table-2).

| Parameters | Levosalbutamol | Salbutamol | P Value |
|---|---|---|---|
| RR (per minute) | 28.8±5.22 | 29.6±4.86 | 0.1901 |
| HR (per minute) | 108±17.98 | 106±18.02 | 0.358 |
| $SPO_2$ (%) | 90.56±13.86 | 91.23±14.08 | 0.69 |
| PEFR (L/minute) | 196.44±26.46 | 195.24±25.08 | 0.7002 |
| FEV1 (% of predicted value) | 65.42±9.08 | 67.02±8.76 | 0.1388 |
| FVC (% of predicted value) | 55.52±7.86 | 54.48±8.12 | 0.2827 |

***Table 1. Pre-Treatment Mean Value (Baseline)***

Baseline (pre-treatment) data for all above parameters were comparable between levosalbutamol and salbutamol groups (Table 1) P value being insignificant (P>0.05).

| Parameters | Levosalbutamol | Salbutamol | P Value |
|---|---|---|---|
| RR (per minute) | 25.42±4.86 | 26.42±5.02 | 0.0952 |
| HR (per minute) | 106.42±18.04 | 122.42±23.24 | <0.0001 |
| SPO2 (%) | 98.24±12.84 | 96.98±13.02 | 0.42 |
| PEFR (L/minute) | 275.42±27.02 | 273.32±28.03 | 0.53 |
| FEV1 (% of predicted value) | 85.24±10.11 | 86.68±9.96 | 0.23 |
| FVC (% of predicted value) | 88.24±9.76 | 86.82±10.16 | 0.23 |

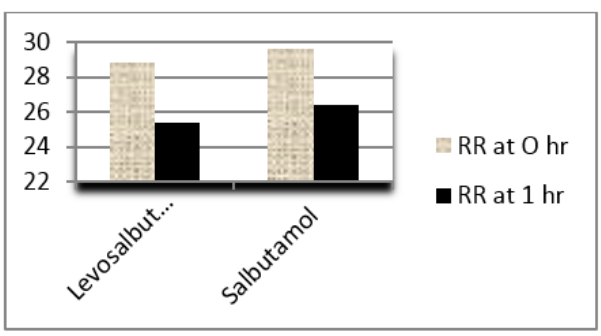
***Table 2. Post-Treatment Mean Value after One Hour***

Post-treatment values for all above parameters (except HR) between Levosalbutamol and Salbutamol group were comparable, but there was a significant increase in HR in Salbutamol group (P value <0.0001). This study shows that levosalbutamol and salbutamol are producing equal therapeutic response in acute exacerbation of bronchial asthma.

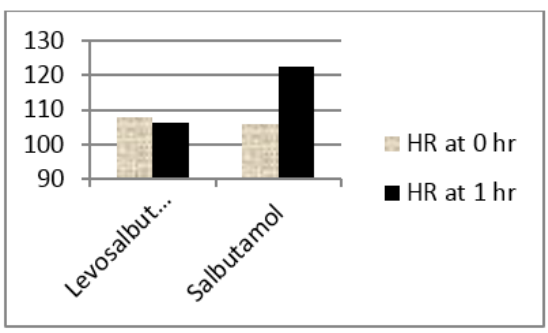
| Parameters | Levosalbutamol | | | Salbutamol | | |
|---|---|---|---|---|---|---|
| | Pre-Treatment | Post-Treatment | P Value | Pre-Treatment | Post-Treatment | P value |
| RR (per minute) | 28.8±5.22 | 25.42±4.86 | <0.0001 | 29.6±4.86 | 26.42±5.02 | <0.0001 |
| HR (per minute) | 108±17.98 | 106.42±18.04 | 0.46 | 106±18.02 | 122.42±23.24 | <0.0001 |
| $SPO_2$ (%) | 90.56±13.86 | 98.24±12.84 | <0.0001 | 91.23±14.08 | 96.98±13.02 | .0005 |
| PEFR (L/minute) | 196.44±26.46 | 275.42±27.62 | <0.0001 | 195.24±25.08 | 273.32±28.03 | <0.0001 |
| FEV1 (% of predicted value) | 65.42±9.08 | 85.24±10.11 | <0.0001 | 67.02±8.76 | 86.68±9.96 | <0.0001 |
| FVC (% of predicted value) | 55.52±7.86 | 88.24±9.70 | <0.0001 | 54.48±8.12 | 86.82±10.16 | <0.0001 |

***Table 3. Pre and Post-Treatment Observations***

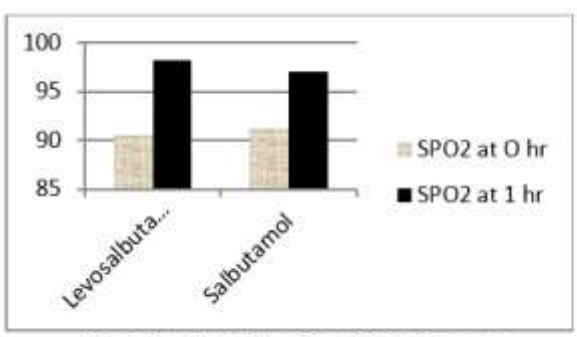
Changes in all parameters in both the groups were significant (P<0.05) except in heart rate in case of Levosalbutamol group where there is no significant change in heart rate (P value >0.05). Thus, this study shows that levosalbutamol produces lesser clinical side effect as compared to racemic salbutamol.



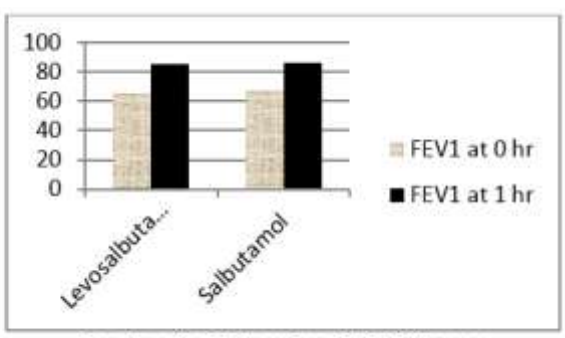

***Bar Graph 1. Showing RR Changes***



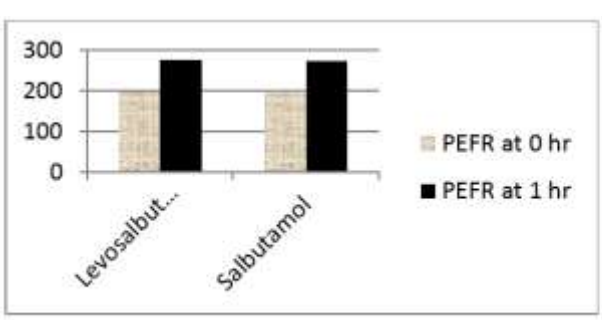

***Bar Graph 2. Showing HR Changes***



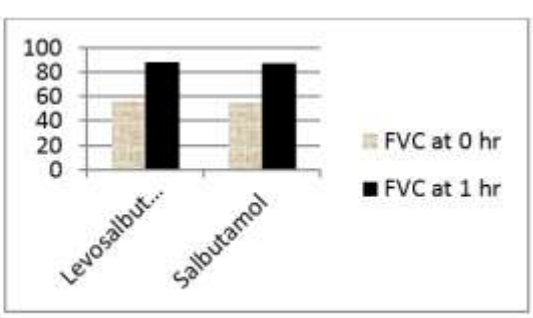

***Bar Graph 3. Showing SPO2 Changes***




***Bar Graph 4. Showing FEV1 Changes***




***Bar Graph 5. Showing PEFR Changes***




***Bar Graph 6. Showing FVC Changes***

## DISCUSSION

Total 312 patients enrolled in our study out of which 38 patients could not complete the study due to unstable hemodynamic state and thus they were excluded from study. Remaining 274 patients were included in the study. Out of 274 cases, 140 cases received nebulization with salbutamol (racemic salbutamol) and other 134 patients received nebulization with levosalbutamol (R-salbutamol). To compare the effect of salbutamol and levosalbutamol, both baseline value (HR, RR, $SPO_2$, FEV1, PEFR, FVC) at zero minute and value after 1 hour of first nebulization was compared. After analysing the table, it was found that both salbutamol and levosalbutamol were significantly effective in bronchodilatation and clinical improvement in acute exacerbation of bronchial asthma. The changes in all the parameters except in HR were similar in both the groups. There was no significant change in heart rate in levosalbutamol group whereas in salbutamol group heart rate increased significantly. Several studies[13,14] have shown that levosalbutamol causes lesser clinical side effects and no significant increase in heart rate in contrast to racemic salbutamol. This was similar to the findings of our study also. Salbutamol is a racemic mixture of equal amounts of (R) - and (S) - isomer (enantiomers) having similar physical and chemical properties but different receptor specificity leading to different physiological and pharmacological effects. The bronchodilator properties of racemic salbutamol have been entirely attributed to the (R)-isomer. Clinical studies have demonstrated that (R)-isomer is responsible for bronchodilatation whereas (S)-isomer is being inert. This supports our observation in this study in which only one-fourth dose (0.63mg) of levosalbutamol had produced the same clinical improvements (as evident from changes in different parameters) as compared to racemic salbutamol (2.5mg). Some studies have suggested that (S)-salbutamol might antagonize the action of airway muscle relaxation caused by (R)-salbutamol, by increasing intracellular $Ca^{2+}$ levels, by enhancing airway hyper responsiveness to spasmogens and by increasing the production of histamine.[15,16,17,18] Thus administration of only (R)-salbutamol (levosalbutamol) would have a better therapeutic index than racemic salbutamol. Some clinical studies have shown a greater bronchodilatation effect with levosalbutamol compared to racemic salbutamol when given as a long-term therapy in case of bronchial asthma.[8]

Another study from a Jantikar et all showed similar bronchodilator response between levosalbutamol and salbutamol,[19] but increase in heart rate was similar in both groups in their study.

## CONCLUSION

Both levosalbutamol and salbutamol produce significant bronchodilatation and clinical improvement in acute exacerbation of bronchial asthma. There was a significant increase in HR with salbutamol but no increase in HR with levosalbutamol. Lesser dose (0.63mg) of levosalbutamol produced the same effect as compared to salbutamol (2.5mg). Thus, it can be concluded from this study that levosalbutamol could be preferred over salbutamol in acute exacerbation of bronchial asthma.

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