ORIGINAL ARTICLE

COMPARISON OF BRONCHODILATORY EFFICACY POTENTIAL OF RACEMIC SALBUTAMOL AND LEVOSALBUTAMOL IN PATIENTS WITH MILD TO MODERATE PERSISTENT ASTHMA

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ABSTRACT

Introduction: The World Health Organization has estimated that 15 million disability-adjusted life years (DALYs) are lost annually due to asthma, representing 1% of the total global disease burden. Racemic Salbutamol and Levo Salbutamol both have potent broncho-dilatory effect and therefore, both are used in the treatment of Asthma. The study was conducted to compare bronchodilatory efficacy potential of Salbutamol with Levo-Salbutamol.

Methodology: The present study was conducted among 100 patients at a tertiary care hospital mild to moderate persistent asthma. Patients were divided in two groups, 50 subjects in each group. After performing baseline spirometry, group A and group B subjects were given 2.5 mg salbutamol and 1.25 mg levosalbutamol, respectively, through nebulizer (continuous, compressor type of nebulizer with drug particle size 0.5-5 micron and average nebulization rate 0.2ml/min.). After 20 minutes, repeat spirometry was performed to measure bronchodilatory response.

Results: Two groups are comparable for base line characteristics, as there is no age & sex wise and symptom wise significant difference in the distribution of patients ($p > 0.05$ for all variables). Overall picture is suggestive of no significant statistical difference in bronchodilatory potential between Salbutamol and Levo-Salbutamol. Positive raise in FEV1, FEV1/FVC% and PEFR is statistically not significant in both groups ($P > 0.05$ for all three).

Conclusion: Salbutamol and Levo-Salbutamol had isoeffective bronchodilatory potential in bronchial asthma patients when used at equipotent doses.

Keywords: Racemic Salbutamol, Levosalbutamol, Bronchodilator, Asthma

INTRODUCTION

Asthma is a problem worldwide, with an estimated 300 million affected individuals.[1,2] The World Health Organization has estimated that 15 million disability-adjusted life years (DALYs) are lost annually due to asthma, representing 1% of the total global disease burden. Annual worldwide deaths from asthma have been estimated at 250,000 and mortality does not appear to correlate well with prevalence.[1]

The term asthma comes from the ancient Greek word for panting or gasping. It was Hippocrates (460-357 BC), the Greek physician, who first described asthma and its resulting "spasms". Galen (130-201 BC), a Greco-Roman doctor, discovered that asthma was due to bronchial obstruction. He treated it with owl's blood in wine. Camel and crocodile droppings were the asthma treatments of choice in Ancient Egypt. In 1901, a Japanese scientist, Jokici Takamine, purifies adrenaline, found in the suprarenal glands of sheep (discovered in 1898) and develops the first effective bronchodilator. In the 1960s, asthma researchers discovered that asthma is an inflammatory disease, not just constriction of the airways, and that asthma sufferers have a sensitive immune system which reacts to airborne allergens. The first inhaled anti-inflammatory medication is born. In 1972, inhaled corticosteroids hit the market.

Although from the perspective of both the patient and society the cost to control asthma seems high, the cost of not treating asthma correctly is even higher. The clinical spectrum of asthma is highly variable, and different cellular patterns have been observed, but the presence of airway inflammation remains a consistent feature. Factors that influence the risk of asthma can be divided into those that cause the development of asthma and those that trigger asthma symptoms; some do both. The former include host factors (which are primarily genetic) and the latter are usually environmental factors. However, the mechanisms whereby they influence the development and expression of asthma are complex and interactive. For example, genes likely interact both with other genes and with environmental factors to determine asthma susceptibility.[3,4] In addition, developmental aspects—such as the maturation of the

immune response and the timing of infectious exposures during the first years of life—are emerging as important factors modifying the risk of asthma in the genetically susceptible person.

The goal of asthma treatment, to achieve and maintain clinical control, can be reached in a majority of patients[5] with a pharmacologic intervention strategy developed in partnership between the patient/family and the doctor. For most classes of controller medications, improvement begins within days of initiating treatment, but the full benefit may only be evident after 3 or 4 months.[5,6]. In severe and chronically undertreated disease, this can take even longer.[7] Rapidly acting β-2 agonists play the central role in the treatment. Salbutamol has one asymmetric (chiral) carbon atom and therefore it exists as a pair of enantiomers. Racemic Salbutamol and Levo Salbutamol both have potent broncho-dilatory effect. So, both can be used in the treatment of Asthma.

The study conducted to compare bronchodilatory efficacy potential of Salbutamol with Levo-Salbutamol.

METHODOLOGY

The present study was conducted on adult patients attending at a tertiary care hospital of Jamnagar city in Gujarat, India. All patients having bronchial asthma attending chest clinic (OPD) during the study period of 6 month were enrolled in the study. Ethical clearance was taken from the ethical committee of the institute. Written consent of eligible patients were taken after explaining the study objectives. Total 100 eligible patients with mild to moderate persistent asthma were enrolled in the study.

All patients were enquired about their asthma symptoms, severity, precipitating factors, past history, family history and personal history in detail. A thorough general and systemic examination was performed then. Basic investigations included haemogram (with AEC in some patients), chest radiograph, sputum routine/microbiological examination and ECG.

Spirometry with reversibility was done in all 100 patients. All patients were subjected for spirometry using ST-90 Futuremed (Japan) machine. 100 patients were divided in two groups - Group A & Group B having 50 subjects in each group. Patients were advised to stop all anti-asthma medications 24 hours prior to spirometry combined with bronchial reversibility test. After performing baseline spirometry, group A and group B subjects were given 2.5 mg salbutamol and 1.25 mg levosalbutamol, respectively, through nebulizer (continuous, compressor type of nebulizer with drug particle size 0.5-5 micron and average nebulization rate 0.2ml/min.). After 20 minutes, repeat spirometry was performed to measure bronchodilatory response (An increase of at least 12% in FEV1% and 200 ml in absolute FEV1 was considered a positive reversibility test).

Data were entered in to Microsoft excel and analysed using epi info. Appropriate statistical tests were applied.

OBSERVATIONS

In this study we divided the total 100 patients in two equal groups. Patients of Group A had treatment with Salbutamol where as patients of Group B had treatment with Levo-Salbutamol. Study results were as follow.

Table 1: Age and Sex wise Distribution of Patients

Age group	Group A (n=50)		Group B (n=50)		Total
	Male (%)	Female (%)	Male (%)	Female (%)	
18-20	0 (0.0)	1 (6.67)	1(2.78)	0(0.00)	2 (2.0)
21 – 30	10 (28.57)	4 (26.67)	11 (30.56)	5 (35.71)	30 (30.0)
31 – 40	**17 (48.57)**	2 (13.33)	**15 (41.67)**	1 (7.14)	**35 (35.0)**
41 – 50	5 (14.29)	**7 (46.67)**	7 (19.44)	**7 (50.00)**	26 (26.0)
51 – 60	2 (5.71)	0 (0.00)	0 (0.00)	1 (7.14)	3 (3.0)
61 – 70	0 (0.00)	1 (6.67)	2 (5.56)	0 (0.00)	3 (3.0)
> 70	1 (2.86)	0(0.00)	0 (0.00)	0 (0.00)	1 (1.0)
Total	**35 (100.0)**	**15 (100.0)**	**36 (100.0)**	**14 (100.0)**	**100 (100.0)**

Table 1 shows age and sex wise distribution of patients. Maximum patients (35%) were from age group of 31 to 40 years of age. As we had included adult patients only, there was no patients age less than 18 years. Total number of male was 35 in group A and 36 in group B. Total number of female was 15 in group A and 14 in group B. Maximum number of male in group A (48.57%) and in group B (41.67%) was from 31 to 40 years of age and maximum number of female in group A (46.67%) and in group B (50%) was from 41 to 50 years of age.

There was no any gross difference in age and sex wise distribution between two groups. As more than 20% of cell values are less than 5 and 9 cells are having cell value of zero, p-Value cannot be calculated.

Table 2: Distribution of Respiratory Symptoms (Multiple Responses)

Symptom	Group A (%) (n=50)	Group B (%) (n=50)
Cough	50 (100.0)	50 (100.0)
Expectoration	41 (82.0)	46 (92.0)
Dyspnoea	44 (88.0)	40 (80.0)
Chest pain/ Tightness in chest	21 (42.0)	18 (36.0)
Haemoptysis	1 (2.0)	2 (4.0)

p-Value – 0.9039

Cough was the universal symptom, present in 100% patients followed by dyspnoea, expectoration of variable amount and quality. Subjective sensation of chest pain or chest tightness was present in 42% patients in group

A and 36% of patients in group B, where as haemoptysis was present only small number of patients.
Table 2 also shows that there was no significant difference in distribution of patients between two groups according to respiratory symtoms. (p-Value > 0.05)
Average (mean of the positive increase in FEV1% of all subjects in respective group) bronchodilator reversibility was 13.8% in group-A and 14.3% in group-B. There is no difference of reversibility potential between these drugs in asthmatics (p>0.05). Average increase in FEV1/FVC% was 11.7% and 12.2% in group-A and group-B respectively, which is also shows only marginal difference. Increase in PEFR was 23.3% in group-A and 24.7% in group-B which is not significant (p>0.05).

Table 3: Comparision of Bronchodilatory Efficacy of Two Drugs

Positive reversibility	Group-A (n=50) (Salbutamol)	Group-B (n=50) (Levosalbutamol)
Mean positive increase in FEV1%	13.8%	14.3%
Mean positive increase in FEV1/FVC%	11.7%	12.2%
Mean positive increase in PEFR	23.3%	24.7%

Table 4: Subjective Reversibility

Subjective reversibility	Group-A (N=50) (Salbutamol)	Group-B (N=50) (Levosalbutamol)
Present (% of pts)	78%	81%
Absent (% of pts)	22%	19%

The presence of subjective reversibility also showed a very marginal difference between two groups with 78% in group-A and 81% in group-B.

DISCUSSION

The present study was aimed to compare bronchodilatory efficacy potential of Salbutamol with Levo-Salbutamol. For that we had enrolled total 100 eligible patients with mild to moderate persistent asthma and divided them in two equal groups of which one group received the treatment of Salbutamol and the other received the treatment of Levo-Salbutamol.

Table 1 and 2 show that two groups are comparable as there is no age & sex wise and symptom wise significant difference in the distribution of patients. After that patients were advised to stop all anti-asthma medications 24 hours prior to spirometry combined with bronchial reversibility test. After performing baseline spirometry, group A and group B subjects were given 2.5 mg salbutamol and 1.25 mg levosalbutamol, respectively, through nebulizer (continuous, compressor type of nebulizer with drug particle size 0.5-5 micron and average nebulization rate 0.2ml/min.). After 20 minutes, repeat spirometry was performed to measure bronchodilatory response.

This shows that average (mean of the positive increase in FEV1% of all subjects in respective group) bronchodilator reversibility was 13.8% in group-A and 14.3% in group-B. There is no significant statistical difference of reversibility potential between these two drugs in asthmatics (p>0.05). Average increase in FEV1/FVC% was 11.7% and 12.2% in group-A and group-B respectively, which is also showing only marginal difference. Increase in PEFR was 23.3% in group-A and 24.7% in group-B which is not significant (p>0.05). Thus, overall picture is suggestive of no significant statistical difference in bronchodilatory potential between Salbutamol and Levo-Salbutamol.

These study findings are comparable with Lotvall et al who stated that LEV/RAC potency ratios for local and systemic effects are similar suggesting a comparable therapeutic ratio in asthmatic patients.[7]

Our study findings are in contrast with Maiti R et al. who found Levosalbutamol to be superior compared to recemic salbutamol in mild persistent asthma.[8]

CONCLUSION

Salbutamol and Levo-Salbutamol had isoeffective bronchodilatory potential in bronchial asthma patients when used at equipotent doses.

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