

Research Article

A comparative study of safety and efficacy of tiotropium bromide with salbutamol in moderate persistent bronchial asthma in a tertiary care hospital

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ABSTRACT

Background: The objective of this study was to compare the safety and efficacy of tiotropium bromide with salbutamol in moderate persistent cases of bronchial asthma at tertiary care hospital.

Methods: This was an open label, randomized parallel group study done in Government General Hospital, Srikakulam for a period of 12 weeks. Group-1 was given tiotropium bromide metered dose inhalational therapy 18mcg once daily in 50 patients. Group-2 was given salbutamol metered dose inhalational therapy 100mcg thrice daily in 30 patients.

Results: Symptomatic improvement was observed in 1 two groups. At end point, mean FEV₁ in tiotropium bromide treatment group improved by 149.96% compared with 135.16% salbutamol treatment group. At end point, mean FVC value in tiotropium bromide treatment group improved by 145.71% compared with 122.34% in salbutamol group. Mean FEV₁ / FVC also improved by 155.41% in tiotropium bromide group compared with 105.41 % in salbutamol group.

Conclusion: The present study proved tiotropium provide superior safety and efficacy relative to control drug in bronchial asthma patients in both clinical assessment score and spirometrically.

Keywords: Tiotropium bromide, Salbutamol, FEV₁, FVC, FEV₁ / FVC and moderate persistent asthma

INTRODUCTION

Asthma is derived from the Greek word meaning “to stay in order to breathe or difficulty in breathing”.¹ Bronchial asthma is a condition of the lungs characterized by widespread narrowing of the airways due to spasm of the smooth muscle, edema of the mucosa, and the presence of mucus in the lumen of the bronchi and bronchioles. It is caused by the local release of spasmogens and vasoactive substances in the course of an allergic reaction.² According to World Health Organization (WHO-2010) 300 million people worldwide were affected by asthma leading to approximately 250,000 deaths per year.³ It is the most common chronic illness in

childhood and is one of the most common causes of admission to the hospital among children and adults.⁴

Salbutamol is a fairly selective beta-2 agonist with relaxant effects on smooth muscles of bronchi and uterus. Being a non-catecholamine it is not metabolized by COMT and thus exhibits longer duration of action than isoprenaline. For immediate relief of asthma it is given by oral inhalation from a metered dose inhaler, 100 micro grams in a single dose. It can also be given orally, intra muscularly or by slow I.V injection. Sustained release tablets are also available. Inhalation causes fewer side effects than systemic administration. Tiotropium bromide has longer duration of action and shows some selectivity

for M₁ and M₃ receptors, with lower affinity for M₂ receptors and thus less presynaptic effect on acetylcholine release. It has slower onset of action and the effect of tiotropium persists for 24 hours and the drug has once a day. Dry mouth is the only side effect reported frequently.

METHODS

The present clinical study was an open label randomized parallel group study conducted in patients with stable as well as exacerbated bronchial asthma in Andhra Pradesh Government RIMS General Hospital, Srikakulam (from March 2012 to June 2012). The study design was approved by institutional ethical committee.

2.1. Inclusion criteria

1. Patients in the age group of 20-55 years of either sex
2. Patients with a history of episodic wheezing, difficulty in breathing, chest tightness and cough with or without expectoration
3. Patients having nocturnal symptoms and family history of asthma
4. Patients with the history of seasonal and the diurnal variation.

2.2. Exclusion criteria:

1. Pregnant and lactating women,
2. Smokers and patients with symptoms related to occupation
3. Patients who were already on steroid treatment for bronchial asthma
4. Patients with history of pulmonary tuberculosis, chronic obstructive pulmonary disease, recurrent pulmonary emboli, carcinoid tumor, tropical eosinophilia.
5. Patients with history of diabetes mellitus, hypertension, chronic renal failure.
6. Patients with history of bronchogenic carcinoma and suspected malignancy anywhere in the body

After history was taken, a detailed clinical examination was done, these are, complete blood picture, Sputum examination, Random blood sugar, Serum creatinine, Chest X ray PA view, Electrocardiography. Pulmonary function tests with micro loop / micro lab spirometer with this, forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), forced expiratory ratio (FEV₁/FVC) are measured. A written informed consent was obtained from each patient

In total 80 patients of bronchial asthma cases, 50 patients are taken as test group and another 30 patients taken as control group. They were diagnosed based on the clinical findings and pulmonary function test. The study was conducted for a period of 12 weeks. The patients of bronchial asthma were randomized into two groups

Group-1 (Test): 50 patients of bronchial asthma treated with 18mcg of Tiotropium bromide metered dose inhaler (2 puffs /day).

Group-2 (Control): 30 patients of bronchial asthma treated with Salbutamol 100mcg by metered dose inhaler (2 puffs/t.i.d).

The respected group patients were advised to take Salbutamol (100mcg) and tiotropium bromide (18mcg) inhalation as needed. Metered dose inhaler with spacer was used for taking medication. Patients were shown inhalation technique with spacers. They were followed up once in every two weeks till a period of 12 weeks. At each visit, they were clinically assessed and pulmonary function tests were done. Scoring was done for cough, wheeze, breathlessness and severity of nocturnal symptoms.^{5,6}

0 - No symptoms

1 - Mild

2 - Moderate

3 - Severe.

Score for frequency of use of rescue medication⁷

0 - < 2 puffs/week

1 - < 2 puffs/day

2 - 2 to 4 puffs/day

3 - > 4 puffs/day

At each visit, patients were assessed for any adverse effects.

2.3. Statistical analysis

Data is presented in mean ± SEM and percentages as applicable. ANOVA was applied for comparison of the treatment groups. Unpaired Student's t-test was applied to test the level of significance.

RESULTS

Both the groups were identical, subjects in both groups comprise 80 cases out of which 50 (62%) patients were male and 30 patients were female (38 %). All the patients were followed up for 3 visits in the 1st week, 6th week and 12th week and under regular observation throughout the period, subjective clinical improvement was assessed, pulmonary function tests were done at each visit.

In cough Test group showed base line mean value was 1.68 (100%) which reduced to 0.46 (27.38%) at 12th week while in Control group the base line value was 1.321 (100%) which reduced to 0.950 (71.91%) at 12th week. In shortness of breath Test group showed base line mean value was 1.77 (100%) which reduced to 0.421 (23.78%) at 12th week while in Control group the base line value was 1.18 (100%) which reduced to 0.671 (56.86 %) at 12th week. In wheeze Test group showed base line mean

value was 1.84 (100%) which reduced to 0.36 (19.56%) at 12th week while in Control group the base line mean value was 1.08 (100%) which reduced to 0.705 (65.27%) at 12th week. In mucous secretion Test group showed base line mean value was 1.38 (100%) which reduced to 0.656 (47.53%) at 12th week while in Control group the base line mean value was 1.28 (100%) which reduced to 0.866 (67.65%) at 12th week.

In pulmonary function test (FEV₁) Test group showed base line mean value was 1.421 (100%) which increased to 2.131 (149.96%) at 12th week while in Control group the base line mean value was 1.402 (100%) which increased to 1.895 (135.16%) at 12th week. In FVC Test group showed base line mean value was 2.148 (100%) which increased to 3.13 (145.71%) at 12th week while in Control group the base line mean value was 1.754 (100%) which increased to 2.146 (122.34%) at 12th week. In FEV₁/FVC%, Test group showed base line mean value was 59.286 (100%) which increased to 92.140 (155.41%) at 12th week while in Control group the base line mean value was 61.70 (100%) which increased to 65.10 (105.52%) at 12th week.

DISCUSSION

In the present study, the safety and efficacy of the tiotropium bromide was studied for its bronchodilatory

predominant action as an anticholinergic and long acting antimuscarinic agent in mild intermittent and mild persistent asthma patients. For efficacy of any drug, the mechanism of action, route of administration, frequency of administration, onset of action, duration of action, symptomatic improvement and side effect profile are all equally important to differentiate that drug from various bronchodilator medications in all the aspects tiotropium bromide fulfils all these qualities.

In this study mild intermittent and mild persistent bronchial asthma cases, tiotropium bromide treatment produced significantly greater improvement in lung function compared to the other bronchodilators or control drug. Patient's compliance was good. Tiotropium bromide is effective for severe asthma with non eosinophilic phenotype.⁸

As shown in Table 1 mean wheeze score in Test group (Tiotropium) was reduced from 1.32 (100%) at baseline to 0.46 (27%) at 12 week while in Control group (Salbutamol) the improvement was from 0.56 (100%) at baseline to 0.36 (52%) at 12 week, suggesting marked improvement in Test group compared to Control group.

Table 1: Comparison of tiotropium bromide 18mcg with salbutamol 100mcg MDI.

Disease symptoms	Control (Salbutamol)				Test (Tiotropium bromide)			
	Mean values in particular time				Mean values in particular time			
	Base line	1 st week	6 th week	12 th week	Base line	1 st week	6 th week	12 th week
Cough	1.321± 0.12	0.745± 0.06	0.612± 0.05	0.950 ± 0.07	1.68 ± 0.14	0.946 ± 0.07	0.628 ± 0.05	0.46± 0.03
Shortness of breath	1.18± 0.14	1.45± 0.09	0.462± 0.04	0.671± 0.05	1.77± 0.12	1.64± 0.17	0.521± 0.04	0.421± 0.01
Wheeze	1.08± 0.09	0.952± 0.07	0.843± 0.06	0.705± 0.03	1.84± 0.15	1.56± 0.10	1.06± 0.13	0.36± 0.02
Mucosa secretion	1.08± 0.09	1.28± 0.12	0.916± 0.07	0.866± 0.07	1.38± 0.09	1.26± 0.08	0.745± 0.07	0.656± 0.05
FEV ₁	1.402± 0.95	1.342± 0.82	1.62± 0.98	1.895± 0.99	1.421± 0.72	1.58± 0.78	1.742± 0.85	2.131± 0.96
FVC	1.754± 0.75	1.824± 0.80	1.98± 0.85	2.146± 0.92	2.148± 0.93	2.24± 0.94	2.64± 0.94	3.13± 0.99
FEV ₁ /FVC %	61.70± 3.03	62.42± 3.12	65.10± 3.50	64.342± 3.42	92.140± 4.50	62.14± 3.45	72.56± 3.81	59.286± 2.56

Results mentioned as mean ± SEM

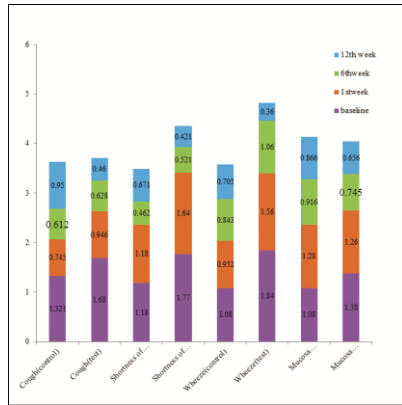


Figure 1: Comparison of tiotropium bromide 18mcg with salbutamol 100mcg MDI.

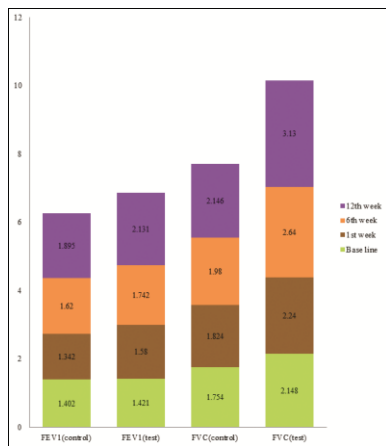


Figure 2: Comparison of tiotropium bromide 18mcg with salbutamol 100mcg MDI.

In the present trial, Tiotropium was superior in all respects and is very effective in bronchial asthma patients. The degree of bronchodilation in this trial is effective. There are very few trials available to prove the efficacy of tiotropium bromide in bronchial asthma patients. But in the present study, it is reported that tiotropium is also effective in mild intermittent and mild persistent asthma patients in both the aspects that is clinically as well as spirometric tests. Therefore, Tiotropium has the potential to provide superior bronchodilatation with once daily dosing. Present study supports the findings observed in the previous studies. No adverse effects were reported in any of the treatment groups, using tiotropium except in very few cases i.e. <10% dry mouth was seen. The dose used in the present study is well-tolerated and no adverse effects reported.

CONCLUSION

The present study proved tiotropium provide superior safety and efficacy relative to control drug in bronchial asthma patients in both clinical assessment score and spirometrically.⁹ Clinically, the mean score reports showed 60-70% improvement when compared to baseline.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Sharma HL, Sharma KK, principles of pharmacology, 1st edition 2007; 50: pp 658.
2. Harrison’s Principles of Internal Medicine, 17th edition 2010, p 02-08.
3. World Health Organization fact sheet No.307; Asthma 2009, Retrieved 2nd Sept.2010.
4. Subbarao P, Mandhane PJ, Sears MR. Asthma: Epidemiology, etiology and risk factors. CMAJ 2009; 181: E181-90.
5. Raphael GD, Lanier RQ, Baker J, Edwards L, Richard K, Lincourt WR. A comparison of multiple doses of fluticasone propionate and beclomethasone dipropionate in subjects with persistent asthma. J Allergy Clin Immunol. 1999; 103: 796-803.
6. Louis R, Lau LCK, Bron AO, Rodaan AC, Radermecker M, Djukanovic R. The relationship between airways inflammation and asthma severity. Am J Respir Crit Care Med. 2000; 161: 9-16.
7. Asthma Allergy & Airway Research Center [homepage on the Internet]. Information for Health Care Professionals. Asthma assessment [cited 2003 Mar 20]. Available from: <http://www.upmc.edu/AAARC/professionals.htm>.
8. H. Iwamoto, A.Yokayama, N. Shiota, H.Shoda, Y. Haruta, N. Hattori and N. Kohno. Tiotropium bromide is effective for severe Asthma with non eosinophilic phenotype. Eur.Resp.J., June 1,2008, 31 (6): 1379-80.
9. BJ O’Connor, LJ Towse, PJ Barnes. Clinical studies unit, Royal Brompton National Heart and Lung Hospital, American Journal of Respiratory and Critical care medicine London, UK Vol 154; No.4, Oct 1996 : 876-80.

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