Original Article

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Role of Low Dose Inhaled Corticosteroid in the Management of Bronchiectasis

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Abstract

Introduction: Bronchiectasis is a chronic inflammatory disease of the lungs with pulmonary function abnormality.

Materials and Methods: 23 non-smoker male bronchiectatic subjects were randomized into two arms. The study group consisting of 11 subjects was administered budesonide 400 mcg through spacer while the control group of 12 received placebo for a period of 3-week. The physician and the subjects were blinded. Spirometric indices of forced expiratory volume 1 (FEV1), forced vital capacity (FVC), FEV/FVC, peak expiratory flow, and reversibility of FEV1 to salbutamol 400 mcg administered through spacer were the outcome measures at 0, 7, 14, and 21 days. The data were analyzed by Student's *t*-test using SPSS 10.

Results: None of the indices showed significant differences between the two groups at different time points. The reversibility of FEV by 15% to salbutamol inhalation suggested a trend of improvement in the study group.

Conclusion: Low dose inhaled corticosteroid ICS does not improve spirometric indices in stable bronchiectatic subjects in the 3-week period. Reversibility of FEV shows a trend of improvement in the subjects. Long-term studies of combination inhalers of low dose ICS and long acting beta 2 agonists in bronchiectatic patients are required to assess the benefit.

Key words: Bronchiectasis, corticosteroid, spirometric indices

INTRODUCTION

Bronchiectasis is a chronic suppurative lung disease still widely prevalent in developing countries such as India. The condition is associated with permanent damage to airways and parenchyma due to inflammation.

A common cause for bronchiectasis is recurrent infection due to the colonization by bacteria. Tuberculosis, the common respiratory infection also results in widespread destruction, fibrosis, cavitation, and atelectasis.

The lung efficiency suffers due to the parenchymal and airway structural disorganization and functional impairment. Many studies documented a compromise in quality of life and pulmonary function parameters such as spirometry and diffusing capacity of the lung. Observations varied between restrictive, obstructive and mixed spirometric defects possibly due to factors such as the extent of the disease, type of bronchiectasis-cystic or tubular, and frequency and chronicity of infection. Airflow limitation reversible or irreversible and bronchial hyperreactivity are documented in bronchiectasis. In a series of cases, which underwent resectional surgery, prognosis, and recovery were better in patients without prior bronchial hyperreactivity.[1] Recently, the recognition of the overlap syndromes of chronic obstructive pulmonary disease (COPD), asthma, and bronchiectasis resulted in renewed interest in the disease phenotype of bronchiectasis and its response to various medications-bronchodilators, airway anti-inflammatory drugs, and antibiotics whether oral, injectable, or inhaled forms.[2]

Significant bronchodilator response in bronchiectatic subjects was well-documented by Murphy *et al.* in 1984.[3]

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The practice of long-term bronchodilator usage in bronchiectasis is common among family physicians and internists in India. Oral theophyllines and short acting beta 2 agonists are also widely prescribed. The benefit of inhaled corticosteroids in bronchiectasis has been justified by a few studies.

Recently, a randomized, double-blind, parallel group study in 40 bronchiectatic patients with formoterol-budesonide (18/640 mcg) combined inhaled therapy observed significant improvement in the quality of life and symptoms. The study, however, failed to show significant changes in spirometric parameters.[4]

Bronchial inflammation and symptoms improved in bronchiectatic patients treated with 1000 mcg of fluticasone dipropionate. The high dose was associated with side effects namely dysphonia, dry mouth, and local irritation.[5,6]

Low dose inhaled corticosteroids may have a role in the prognosis, frequency of exacerbations, long-term lung function of bronchiectatic patients. The present study was an attempt to examine the effect of low dose budesonide 400 mcg therapy in stable bronchiectatic patients on spirometric indices particularly bronchodilator reversibility which is an important indicator of the likely benefit of long-term treatment with inhaled steroids.

The role of inhaled steroids in bronchiectasis is controversial. None of the previous studies examined the effect of inhaled corticosteroids on post-bronchodilator reversibility in bronchiectatic patients. Effect of inhaled budesonide 400 mcg/day on ventilatory functions of 23 consecutive bronchiectatic patients was studied.

MATERIALS AND METHODS

The Institutional Ethical Committee permission was obtained, and the patient gave well-informed consent for the study after a careful explanation that the medicines were well-established and were in wide use for airway obstructive disease.

Bronchiectasis was diagnosed by clinical and imaging criteria. They were manually randomized into two groups. A total number of 31 subjects were eligible to be included in the study. Eight people did not consent to participate in view of the calendar time required for follow-up. The patients did not show any active bacterial or tuberculous infection at the time of inception into the study. Some of the patients gave a history of pneumonias or tuberculosis in the remote past. None of the patients was a smoker. Spirometry was performed using MicroLab 3300 (Mfd. MicroLab, Kent, UK). The instrument was auto calibrated. All the subjects underwent high-resolution computed tomography scan of the chest to confirm the diagnosis. Basic laboratory investigations to rule out diabetes, active infection, or immunocompromised state were performed. No attempt was made to diagnose cystic fibrosis since it is rare and not clinically suspected. Study group (n = 12) received inhaled budesonide 400 mcg/day through spacer while controls (n = 11) received placebo inhaler. Both groups received amoxicillin for a week before the study commenced and regular physiotherapy. Spirometry was performed at 7-day intervals at the same hour of the day. Forced expiratory volume 1 (FEV1), forced vital capacity (FVC), peak expiratory flow rate (PEFR), forced expiratory flow (FEF) 25-75, and "salbutamol reversibility" were tested as per the American Thoracic Society guidelines. Percent change in FEV1, FVC, PEFR, FEF 25-75%, and FEV1 reversibility at 0, 7, 14, and 21 days were analyzed by Student's t-test (SPSS 10).

RESULTS

All the subjects hailed from lower socioeconomic status from urban or semi urban areas in and around Hyderabad city. The city is located in semi-arid south central India with uniformly warm weather for the most part of the year with a short spell of monsoon and winter.

Only male subjects were taken into the study for convenience and feasibility of repeat visits or stay in the hospital for assessment.

Demographic characteristics

The study group consisted of 11 subjects with a mean age of 34.81 ± 11.65 years while the control group of 12 subjects had a mean age of 32.83 ± 14.91. None was a current smoker (Table 1).

No statistically significant change between study and control groups was observed. The study group revealed a higher mean of reversibility in FEV1 to 400 mcg of salbutamol by inhaler with a spacer on day 7 and 14 compared with the control group suggesting a trend of likely benefit from low dose budesonide inhalation on a regular basis (Table 2).

Table 1: Study group

Time	FEV1	FVC	FEV1 reversibility (%)
Day 0	1.58±0.67	1.94±0.97	8.18±7.3
Day 7	1.59±0.74	1.94±0.80	11.27±11.63
Day 14	1.61±0.8	2.07±0.93	11.79±15.48
Day 21	1.66±0.76	2.12±0.87	6.44±4.95

FEV1: Forced expiratory volume 1, FVC: Forced vital capacity

Table 2: Control group

Time	FEV1	FVC	FEV1 reversibility (%)
Day 0	1.28±0.48	1.45±0.65	5.92±8.93
Day 7	1.35±0.45	1.63±0.65	4.75±3.79
Day 14	1.38±0.5	1.72±0.72	4.82±5.90
Day 21	1.48±0.46	1.79±0.78	3.33±5.46

FEV1: Forced expiratory volume 1, FVC: Forced vital capacity

DISCUSSION

The present small study, though the results are not statistically significant, shows a trend of improved "reversibility" of FEV1 in the budesonide-treated bronchiectatic subjects. Spirometric indices, namely FEV1, FVC, FEF 25-75, FEV/FVC, did not show a significant difference at the weekly time-points between the control and study groups. The present study suffers from the limitation of not providing a study arm of combination inhaler of low dose corticosteroid- long-acting beta-agonists (LABA).

Margi Garcia *et al.* documented improvement in symptom score and quality of life on long-term administration of formoterol-budesonide inhaled therapy but failed to show improvement in lung function.[7] High dose fluticasone of 1000 mcg alone did not confer any benefit in spirometric indices though it had improved symptomatically in an earlier study. Long-term studies with low or medium dose corticosteroids and long acting beta agonists in bronchiectatic subjects are lacking. The above-mentioned studies predominantly included smokers. Inhaled fluticasone dipropionate 500 mcg daily was not found to be effective in improving the symptoms or pulmonary functions in another study.[8]

The common observation and practice of the Indian physicians to administer regular oral bronchodilator, theophylline lacks the support of pharmaco-dynamic data which are scanty in this area. Theophylline does not command merit in the global guidelines of asthma or COPD as an important primary drug for airway obstruction though it is accepted as an add-on drug for the suboptimal responders to steroid and LABA.[9] Its major advantage is the low price per dose. The combination inhalers of LABA and medium dose corticosteroids have become affordable, cheap, and widely available in India in the recent years. Many governmental and non-governmental health providers reimburse or dispense combination inhalers. Recently, a prescription audit study revealed that 78% of asthmatic patients used a combination of LABA and steroids as well as symptom relievers more than the controllers. Essential drug list of government hospitals did not include inhaled beta 2 agonists and corticosteroids. 60% of drugs were given by inhaled route.[10] The caveat, however, is the danger of irrational prescription without spirometric diagnosis and monitoring, and over the counter purchase by patients of these combination inhalers with a misconception that all "short-breath and wheezy syndromes" are similar.

Further well-designed studies of long-term corticosteroid inhalers and LABA and/or theophyllines in stable bronchiectatic patients will resolve the dilemma of choice of long-term therapy for bronchiectasis in the Indian context.

CONCLUSION

Our study concludes that the objective spirometric indices do not show significant improvement at weekly intervals in the low dose budesonide 400 mcg inhaler therapy group versus the control group of bronchiectatic subjects.

Reversibility of FEV to 400 mcg of salbutamol as an outcome measure shows a trend of likely benefit in the study group of bronchiectasis. The wider availability and reduced price of combination inhalers of LABA plus inhaled corticosteroid (ICS) have brought them to greater prescription by the family physicians on symptom-based assessment without spirometric evaluation of all the wheezy and short-breath patients. In addition, "over the counter" sales on self-prescription lead to the undesirable practice of over-use of these inhalers. Further studies with comparator arms of ICS plus LABA and ICS-theophylline are required to resolve the issue of appropriate treatment for stable bronchiectasis in India.

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