



Original Research Article

Comparative Study of Oral versus Inhaled Steroid in the Treatment of Patients, Suffering From Moderate Asthma Attending in Tertiary Care Hospital at Muzaffarpur, Bihar

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Abstract

Objective: Present study was conducted to evaluate the effect of high doses of inhaled steroid fluticasone in comparison with oral steroid prednisone in adult patients suffering from moderate asthma exacerbations.

Materials and Methods: A total of 60 Patients of either sex, aged between 28 and 56 with moderate asthma exacerbations were included in the study. All the patients were randomized in two study Groups. Group A included 30 patients, Group B also contains 30 patients. Group A patients received fluticasone via a metered-dose inhaler and spacer 16 puffs (4,000 µg/day) and Patients in Group B receive one pill prednisone 30 mg/day. All the patients undergone Spirometry and CBC before treatment and after 2, 6 and 24 hour of treatment.

Result: Symptoms clearly improved in all the patients in both the study groups after 24 hours. There were no any differences recorded between the both study groups in peak expiratory flow or forced expiratory flow in one second, which improved progressively but then delayed slightly after 24 hours. Eosinophil counts were also improved. The patients improve faster with fluticasone treatment than with prednisone, but effect was same after 24 hours.

Conclusion: both treatments improved symptoms, airway obstruction and inflammation, and CBC at 24 hour. Prednisone and fluticasone reduced blood and sputum eosinophil counts, shows anti inflammatory effect of fluticasone are exerted locally.

Introduction

In acute asthma Systemic corticosteroids are now used because they prevent the progression of exacerbations, hospitalisation and reduce the morbidity of patients. Systemic corticosteroids play an important role in acute asthma, parenteral corticosteroids have no bronchodilator effect

within the first few hours of an acute asthma exacerbation but effect does occur within the first 6–8 h after administration and probably requires a number of hours to effectively improve airflow obstruction. Some study has questioned the efficacy of this treatment to control exacerbation during the first hours. The corticosteroid effect

may be slow because these drugs require ligand dependent activation of the corticosteroid receptor transcriptional factor.

In the other hand inhaled corticosteroids are recommended because they control the chronic asthma, reduce the chance of worsening after acute attacks of asthma and also reduce the need for oral prednisone. McFadden suggested that inhaled steroids would reduce edema and plasma exudation quicker than oral steroids.

However, a more complex mechanism cannot be discarded because early changes (within 2–3 h) in cellular and biochemical markers of bronchial inflammation have been described after systemic and inhaled corticosteroid treatment in uncontrolled asthmatics.

The aim of present randomized study was to compare the effect of high doses of inhaled fluticasone with oral prednisone in the patients suffering from asthma.

Materials and Methods

Present study was conducted in the Department of Pharmacology, S. K. Medical College, Muzaffarpur, with the help of Department of Medicine, and Microbiology during the period of October 2017 to March 2019. It was a prospective, randomized, open labeled study. A total of 60 Patients of either sex, aged between 28 and 56 with moderate asthma exacerbations were included in the study.

Inclusion criteria were Patients had acute asthma with no oral or i.v. steroid treatment in the last 4 weeks, All had been diagnosed with asthma from current or previous history of chest tightness, wheezing, dyspnoea or cough in association with variable airflow limitation, Variable airflow limitation was documented forced expiratory volume in one second ($FEV_1 < 8$) The exacerbation was considered moderate to severe, but not life threatening at baseline, strictly in accordance with the Global Initiative for Asthma criteria.

Exclusion criteria included smokers or previous smokers within the last year, and treatment with

oral or i.v. corticosteroids, cromoglycate, nedocromil, theophylline, allergen desensitization injections, and leukotriene antagonists at any time in the 4 weeks prior to the study. Long-acting β -agonists were permitted, but participants on this treatment were balanced between the two groups. Patients suffering with life-threatening exacerbations of asthma or any other serious medical conditions like heart disease, gastrointestinal, liver or renal disease and other chest disease were excluded from the study.

All the patients were randomized in two study Groups. Group A included 30 patients, Group B also contains 30 patients. Group A patients received fluticasone via a metered-dose inhaler and spacer 16 puffs (250 μ g) and Patients in Group B receive one pill prednisone 30 mg/day. All the patients undergone Spirometry and CBC before treatment and after 2, 6 and 24 hour of treatment.

Each treatment was given in a single dose under supervision at baseline and at 24 hour, as of which time patients were instructed to continue taking one tablet each morning and eight inhalations twice a day for 4 days. Measurements were made at baseline and at 2, 6 and 24 hour. At each proposed time, cough, wheeze, chest tightness and breathlessness were recorded.

Participants were followed in the respiratory day care setting for 6 hour and then discharged if symptoms improved and PEF increased by $\geq 30\%$ above baseline value. If the patients did not improve, they were kept in observation for 24 hours. During observation, it had been previously established that patients would be shifted to the other arm in case of worsening (decrease of PEF $> 20\%$ of baseline or clinical deterioration judged by the responsible physician). No other treatments were allowed other than nebulised salbutamol every 4 h and oxygen on demand.

Result

Symptoms clearly improved in all the patients in both the study groups after 24 hours. There were no any differences recorded between the both

study groups in peak expiratory flow or forced expiratory flow in one second, which improved progressively but then delayed slightly after 24 hours. Eosinophil counts were also improved. The patients improve faster with fluticasone treatment than with prednisone, but effect was same after 24 hours.

Discussion

In the treatment of moderate asthma attacks high doses of the inhaled fluticasone were as effective as oral prednisone. At 24 hour, both treatments improved symptoms, bronchoconstriction, eosinophilic bronchitis and plasma protein leakage. However, fluticasone had a tendency to act faster than prednisone and causing improvement on bronchoconstriction and reduces plasma protein leakage, although it's main effect was the reduction of sputum eosinophilia, which was significant as early as 2 hour after inhalation, reaching a maximum at 6 hours. Prednisone also reduced sputum eosinophilia, after 6 hour and they also showed a stronger and significant reduction in blood eosinophilia as compared with fluticasone.

The usefulness of inhaled steroids in the emergency room is unclear. The recent Cochrane review of this topic stated that inhaled steroids reduce readmission rates in patients with acute asthma. Nevertheless, it is unclear whether inhaled corticosteroids used in addition to systemic corticosteroids provide any benefit. The Cochrane review did not find sufficient evidence that inhaled corticosteroids provide clinically relevant changes in pulmonary function or clinical scores in acute asthma. Moreover, there is insufficient evidence that inhaled corticosteroids alone are as effective as systemic steroids. Further research was thus recommended to clarify this point. Some authors have suggested that inhaled steroids seem to act faster than oral steroids on symptoms and airway obstruction, although there is considerable controversy on this point in children.

In the present study, both prednisone and high doses of fluticasone after treatment clearly showed that they reduced airway inflammation and plasma protein exudation leads to reduced airway obstruction and improved symptoms, in a different way.

There is an increased plasma exudation in the airways. This correlates with bronchial hyperreactivity to histamine and decreases after corticosteroid therapy. A few other groups have investigated protein plasma leakage during asthma exacerbation and have shown that albumin leakage is highly increased as compared with that in stable asthmatics. Pizzichini et al. Showed that oral steroids in severe exacerbations of asthma decreased fibrinogen levels at day 7.

The reason for this discrepancy could lie in the different plasma proteins tested in each study, but whatever the case, the clinical relevance of this plasma leakage in the asthma exacerbation remains unknown. In a previous study, found that plasma leakage in acute asthma was weakly related to the degree of airway obstruction, suggesting that this effect may not account for the final severity of the exacerbation. Despite the fact that some relationship clearly exists, the importance of this finding should be further determined, since in the current study, a significant relationship between FEV₁ and albumin in the acute phase was found.

Many studies have shown a rapid, strong effect of inhaled steroids on bronchial eosinophilic inflammation, but such studies were generally performed on subjects with stable asthma or induced exacerbations. Very few data are available on naturally occurring exacerbations, probably because of the difficulty in obtaining bronchial secretions in the acute phase. The main outcome measure studied by many groups is, therefore, the improvement in airway obstruction, which is not a direct inflammatory marker. Data concerning the effect of inhaled steroids on sputum eosinophilia are not available in acute asthma.

However, exacerbations induced by stepping down the inhaled corticosteroid therapy confirm this evidence and it can be assumed that corticosteroids should reduce blood and sputum eosinophilia in acute asthma. At least three studies have reported that sputum eosinophilia improved after treatment with oral steroids. Pizzichini et al. described an improvement in sputum eosinophilia and eosinophil cationic protein levels at 24 hour. This was supported by the present authors' findings.

The main limitation of the present study is probably related to the high dose of fluticasone used, which is possibly not comparable with the doses used by others. In a very recent paper, Rodrigo used 3,000 µg/h during 3 hour with excellent results. However, the dose used in the study is twice the fluticasone dose accepted for self treatment of asthma attacks according to some guidelines. Differences in the dose used may be important, because published studies that obtained better results tended to use higher doses of inhaled steroids and lower oral steroid doses than those studies that found no benefits.

Therefore, it could be speculated that the dose of inhaled steroids needed to provide a benefit in acute asthma should be considerably higher than that used in stable asthma. The timing of the steroid administration may also be relevant. The present authors observed that the effect of both treatments was partially lost at 24 hour, suggesting that treatment should perhaps be administered twice daily to maintain efficacy.

Conclusion

High dose of inhaled fluticasone appears to have a faster and stronger effect in reducing symptoms in moderate exacerbations of asthma, airway inflammation and at least as effective as prednisone in reducing plasma exudation, bronchial obstruction. The early combination of inhaled steroid to oral prednisone could therefore be more effective than prednisone alone in acute asthma. Further studies are needed to investigate whether lower doses of inhaled fluticasone are as

effective as the higher dose, as well as the comparison of this association versus oral prednisone alone.

Reference

1. National Heart, Lung and Blood Institute/World Health Organization. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention. National Institutes of Health. Publication No. 02-3659. Bethesda, National Heart, Lung, and Blood Institute; 2002
2. Rodrigo G, Rodrigo C. Corticosteroids in the emergency department therapy of acute adult asthma: an evidence-based evaluation. *Chest* 1999;116:285–295.
3. Stein LM, Cole RP. Early administration of corticosteroids in emergency room treatment of acute asthma. *Thorax* 1992;47:588–591.
4. Barnes PJ, Pedersen S, Busse WW. Efficacy and safety of inhaled corticosteroids. New developments. *Am J Respir Crit Care Med* 1998;157: Suppl. 3 S1–S53.
5. Edmonds ML, Camargo CA Jr, Pollack CV Jr, et al. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. *Cochrane Database Syst Rev* 2003;3:CD002308
6. Rowe BH, Edmonds ML, Spooner CH, et al. Corticosteroid therapy for acute asthma. *Respir Med* 2004;98:275–284.
7. Harrison TW, Osborne J, Newton S, et al. Doubling the dose of inhaled corticosteroid to prevent asthma exacerbations: randomised controlled trial. *Lancet* 2004;363:271–275.
8. Edmonds ML, Camargo CA, Saunders LD, et al. Inhaled steroids in acute asthma following emergency department discharge. *Cochrane Database Syst Rev* 2000;3:CD002316

9. Rodrigo G, Rodrigo C. Inhaled flunisolide for acute severe asthma. *Am J Respir Crit Care Med* 1998;157:698–703.
10. Rodrigo GJ, Rodrigo C. Triple inhaled drug protocol for the treatment of acute severe asthma. *Chest* 2003;123:1908–1915.
11. Lee-Wong M, Dayrit FM, Kohli AR, et al. Comparison of high-dose inhaled flunisolide to systemic corticosteroids in severe adult asthma. *Chest* 2002;122:1208–1213.
12. Guttman A, Afilalo M, Colacone A, et al. The effects of combined intravenous and inhaled steroids (beclomethasone dipropionate) for the emergency treatment of acute asthma. The Asthma ED Study Group. *Acad Emerg Med* 1997;4:100–106.
13. Levy ML, Stevenson C, Maslen T. Comparison of short courses of oral prednisolone and fluticasone propionate in the treatment of adults with acute exacerbations of asthma in primary care. *Thorax* 1996;51:1087–1092.
14. Rodrigo GJ. Comparison of inhaled fluticasone with intravenous hydrocortisone in the treatment of adult acute asthma. *Am J Respir Crit Care Med* 2005;171:1231–1236.
15. McFadden ER Jr. Inhaled glucocorticoids and acute asthma: therapeutic breakthrough or nonspecific effect? *Am J Respir Crit Care Med* 1998;157:677–678.
16. Hill MR, Szeffler SJ, Ball BD, et al. Monitoring glucocorticoid therapy: a pharmacokinetic approach. *Clin Pharmacol Ther* 1990;48:390–398.
17. Laitinen LA, Laitinen A, Heino M, et al. Eosinophilic airway inflammation during exacerbation of asthma and its treatment with inhaled corticosteroid. *Am Rev Respir Dis* 1991;143:423–427.
18. Oh JW, Lee HB, Kim CR, et al. Analysis of induced sputum to examine the effects of inhaled corticosteroid on airway inflammation in children with asthma. *Ann Allergy Asthma Immunol* 1999;82:491–496.