ORIGINAL ARTICLE
Iran J Allergy Asthma Immunol
March 2006; 5(1): 17-22

A Comparative Efficacy of Oral Prednisone with Intramuscular Triamcinolone in Acute Exacerbation of Asthma

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Received: 8 September 2005; Received in revised form: 2 March 2006; Accepted: 5 March 2006

ABSTRACT

Corticosteroids are recommended for emergency management of an asthmatic attack. This study was designed to compare the effectiveness of oral and intramuscular steroid on spirometric results in acute asthma.

We performed a randomized trial involving 88 adults, aged 15-70 years, with acute exacerbation of asthma requiring treatment with steroids. All had been treated with standard bronchodilator regimens and then received oral prednisone, 40 mg/day for 7 days, or 40 mg/day intramuscular triamcinolone long acting (LA) for 3 days. Spirometric variable and percentage of change to baseline forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) after treatment were calculated.

Baseline characteristic were comparable in the oral prednisone group (n=44) and in the intramuscular triamcinolone LA groups (n=44). After 7 days of treatment, the mean (SD) FEV1 and FVC in both groups improved statistically over baseline values ($P<0.001$). The median percentage change improvement of FEV1 between two treatment groups was statistically significant: 68±45.3% vs. 53.4±46.5%, $P=0.04$) respectively, but for FVC although improvement with prednisone was better than intramuscular triamcinolone LA groups, it was not statistically significant (52.6±40.1% vs. 45.8±39.9%, $P=0.43$) respectively.

We conclude that in adults with acute asthma, oral prednisone is more effective than intramuscular triamcinolone LA in improvement of FEV1, but although efficacy of oral prednisone in improvement of FVC is more than intramuscular triamcinolone LA group, this effect is not significant.

Key words: Asthma; Prednisone; Triamcinolone

INTRODUCTION

Asthma is a disease that is characterized by airway inflammation and is manifested by pulmonary symptoms, reversible airway obstruction, and evidence of bronchial hyper-reactivity. It accounts for hundreds of thousands of emergency room visits yearly. Corticosteroid therapy is useful in managing the acutely ill asthmatic patient in the hospital.[1,2]

The Guidelines for the Diagnosis and Management of Asthma, published by the National Institutes of Health, recommended that steroids be considered in all

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patients as an emergency department(ED) treatment for acute exacerbations.[3] Earlier work had suggested a role for corticosteroids with a depo-repository release given via the IM route in asthmatic patients who had been discharged from the ED.[4-8]

Unfortunately, tapering doses of oral steroids are complicated, often involving numerous pills and frequent changes in dosage. Studies have shown that 12% to 22% of patients do not carry out their prescriptions after discharge from the emergency department.[9,10]

Hoffman and Fiel reported that intramuscular repository corticosteroids are at least as effective as oral corticosteroids in the management of the acute asthmatic patients.[5]

Since compliance with oral corticosteroids is a well-known problem, our study was undertaken to determine whether intramuscular triamcinolone acetate are as effective as oral prednisone therapy administered in the outpatient setting. We also analyzed whether spirometric results changed in the triamcinolone group compared with the prednisone group.

MATERIALS AND METHODS

Our study was conducted in the emergency room of Kashan Shahid Beheshti Hospital from March 2000 through June 2001. Patients were included in the study if they presented to the emergency room with acute asthma manifested as dyspnea, cough, or wheezing and a 1-second initial forced expiratory volume (FEV1) less than 70% of the predicted normal value. All patients between the ages of 15 and 70 were eligible for the study if they had a history of asthma and they were to be discharged home with instructions to continue treatment. Patients were excluded if they were pregnant, had diabetes mellitus, congestive heart failure, had clinical evidence of pneumonia or chronic obstructive pulmonary disease, had received steroids within 2 weeks of presentation, or were unable or unwilling to attend follow-up evaluation. The diagnosis was based on the American Thoracic Society Guidelines for the evaluation of impairment/disability in patients with asthma.[11]

The patients were approached for participation only after completion of their emergency therapy. The study was designed as randomized in two groups and the following treatment regimens were then compared after 7 days of therapy: (1) triamcinolone long acting (LA), 40 mg for intramuscular daily for 3 days, (2). In another group of patients, prednisone 40 mg per day for seven days was prescripted.

Subjects were treated for acute asthma in standard fashion. On initial presentation, spirometry was obtained, with the patient seated and wearing nose clips. Three forced vital capacities were obtained, with the highest FEV1 value for analysis. Follow-up was accomplished by a return visit 7 days after the patient's arrival, and was questioned about drug compliance. Physical examination and spirometry were again performed.

The Kolmogorov-smirnov test was used for distribution of quantitative variables. The mean±SD results for FVC and FEV1 before and after treatments between two groups of patients were calculated. Percentage of change was calculated as relative to baseline FVC and FEV1 by the following equation:

Percentage of Change= [(Observed-Base)/Base]×100

Where observed are the post-treatment values after 7 days, base is the baseline value on the day before treatment. Results were analyzed with Student's t-test for paired comparisons. P-value of less than 0.05 was considered significant. Statistical analysis was performed by means of statistical software package (SPSS version 10.0 for windows).

RESULTS

Eighty-eight patients were enrolled in the study including 44 (50%) in the prednisone group (mean age 42.3 years, range 15-70) and 44 (50%) patients in the triamcinolone LA group (mean age 41 years, range 15-70). The 46 male and 42 female patients had a mean age of 41.7 ± 16 years.

Table 1. Characteristic of patients in study groups (mean±SD).

Characteristics	Prednisone group (n=44)	Triamcinolone LA group (n=44)	P-Value
Sex (M/F)	22 / 22	20 / 24	0.67
Age (Yr)	42±16	41±16.6	0.7
Pretreatment FVC			
% predicted	62.59±14.74	62.25±12.73	0.9
Liters	2.18±0.84	2.11±0.71	0.6
Pretreatment FEV1			
% predicted	49.91 ±12.1	52.57±11.84	0.3
Liters	1.46± 0.56	1.52± 0.48	0.6

Table 2. Spirometric results in two groups of patients treated with prednisone and triamcinolone LA*

Characteristics	Prednisone groups (n = 44)		P. value‡	Triamcinolone groups (n = 44)		P. value‡
	Pre treatment	*Post treatment*		*Pre treatment*	*Post treatment*	
FVC, % Pred.	62.6 ±14.7	90.7± 12.9	<0.0001	62.3±12.7	83.7± 11.6	<0.0001
Liters	2.2± 0.8	30.1 ±1	<0.0001	2.1± 0.7	2.9± 0.9	<0.0001
FEV1, % Pred.	49.9 ±12.1	80.3± 12.9	<0.0001	52.6± 11.9	77.1± 12.9	<0.0001
Liters	1.5± 0.6	2.3 ±0.7	<0.0001	1.5± 0.5	2.2 ±0.6	<0.0001

* Values are expressed as mean±SD
‡ Student's t-test

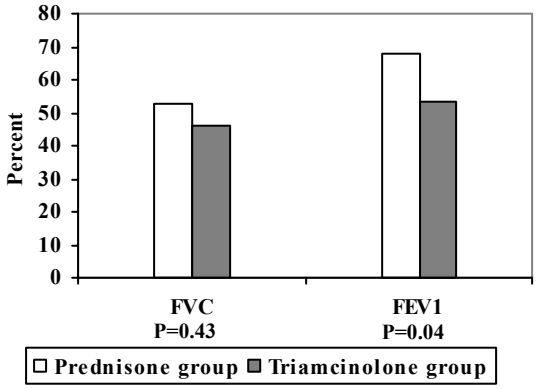

Figure 1. Comparison of the mean (SE) changes in FEV1 and FVC values after treatment (%) in both groups of patients treated with prednisone and traimcinolone LA.

Characteristics of the study patients are shown in Table 1. There were no significant differences between the two study groups by age, sex or spirometric findings. Spirometric results are shown in Table 2. Groups had comparable values at the time of arrival to treatment for FEV1 and FVC. FEV1 and FVC improved in both groups.

Mean values of FEV1 and FVC improvement in both groups after treatment were significant (Table 2).

Percentage change of improvement in FEV1 for both the prednisone and triamcinolone LA groups was 68±45.3% vs. 53.4±46.5% (P= 0.04); and for FVC was 52.64±40.1% vs. 45.8±39.9% (P= 0.43), respectively. Although there was greater improvement in all two parameters, in the prednisone group, the differences were significant for FEV1 (P= 0.04), however the change in improvement of FVC in both groups was not statistically significant (P=0.43), (Figure 1).

DISCUSSION

Our short term study indicates that the management of acute asthmatic outpatients, with oral prednisone in improvement of spirometric indexes (FEV1 and FVC) is more effective as compared with LA intramuscular triamcinolone. In this study the median percentage change improvement of FEV1 between two treatment groups was more than improvement in FVC.

Systemic corticosteroids should be a component of treatment of acute asthma in all patients. Systemic corticosteroids are also recommended for the treatment of impending episodes of severe asthma for which bronchodilator therapy has been inadequate. In the past, systemic corticosteroids were commonly withheld for many hours and even for days, while treating with bronchodilators and awaiting gradual spontaneous improvement in airway inflammation. In contrast, current guidelines encourage institution of systemic corticosteroids as soon as insufficient improvement with beta agonist bronchodilators is identified.[12]

One study examined the effect of high dose oral prednisone for one week early in the course of an acute exacerbation of asthma incompletely responsive to bronchodilators.[13] When compared to other drugs, steroids were more effective than ß-adrenergic agonists, theophylline, and cromolyn sodium in reducing airway hyperresponsiveness during maintenance therapy.[14-18]

Despite numerous clinical trials evaluating specific steroid preparations, doses, dosing frequencies and routes of administration, no single protocol or preparation has been found to be superior.

Although oral[19, 20] and intramuscular[4] steroid regimens are superior to placebo in reducing relapse rates after management acute asthmatic attack, comparison between oral and intramuscular regimens

are limited. Intramuscular injection of long-acting corticosteroid formulations appears to be as effective as oral therapy.[4,5,7,8,21] In a randomized trial of 190 adult patients with acute asthma, intramuscular injection of long-acting methylprednisolone (160 mg) resulted in a similar rate of relapse as oral methylprednisolone 20 mg PO QD for eight days.[21] This approach may be beneficial for patients unable to afford oral medication or those at high risk of medical noncompliance.

Ogirala et al. showed that the use of high-dose triamcinolone for 3 days along with oral prednisone significantly decreased emergency room visits and total oral steroid doses needed in patients with severe, steroid–dependent asthma.[22] Jonsson et al. found that oral administration of steroids was as effective as intravenous use in hospitalized patients with moderate exacerbation of airway obstruction.[23] Chapman et al. showed that a short course of oral prednisone reduced early relapsed rates after emergency room treatment of acute asthma.[19] Harris et al. reported that early intervention with oral prednisone appeared justified in preventing the need for a protracted course of treatment or emergency care.[13]

Because of potential problems with compliance in-patients sent home with prescriptions for tapering doses of oral prednisone, repository steroids might offer an advantage over oral steroids in preventing relapse of asthma after exacerbation. Hoffman and Fiel compared the use of oral steroids with a single injection of repository steroids on discharge from the emergency room and found intramuscular methyl prednisone to be as effective as oral methyl prednisone in preventing rehospitalization.[5] In another study that was performed in mild to moderate exacerbation of asthma, a single dose of 40-mg intramuscular triamcinolone produced a relapse rate similar to that of prednisone, 40 mg/day orally for 5 days.[7]

Green et al. found that 80 mg intramuscular methyl prednisone produced no difference in relapse rate, symptoms, or spirometry compared with oral prednisone after hospitalization for treatment of asthma.[24] Improvements in FEV1, FVC were much greater in repository group than in the oral group, but the differences did not achieve statistical significance.[24] In the present study, the improvement of FEV1 and FVC was calculated as relative to baseline FEV1 and FVC by this equation: percentage of change= [(observed – base)/base]× 100 was greater in oral steroids groups as compared with intramuscular triamcinolone LA groups. As shown in Fig.1 the median (SD) percentage change improvement of FEV1 between two treatment groups of asthmatic patients (oral prednisone and intramuscular triamcinolone LA) was statistically significant: (68±45.3% vs. 53.4±46.5%, P=0.04 respectively). However, in the current study the median (SD) percentage change improvement of FVC between two treatment groups although in patients that were treated with oral prednisone was better than another groups, the results were not statistically significant (52.6±40.1% vs. 45.8±39.9%, P=0.43) respectively. As results shown in Table 1, efficacy of prednisone in improvement of FEV1 and FVC before and after treatment is about 30.4% and 28.1%, but this difference in triamcinolone group is about 24.5% and 21.4% respectively. This difference has probably resulted from the method of prescription. In our study prednisone was prescripted 40 mg per day for seven days. However in Green et al. study a prescription for tapering doses of oral prednisone, from 40 mg to 0 mg, decreasing by 5 mg daily over 8 days was considered.[24]

Methylprednisolone and triamcinolone have been studied for the treatment of asthma. High-dose intramuscular triamcinolone seems to be more effective than low dose oral prednisone for patients with severe, life-threatening asthma[22, 25-27], and is more effective in asthmatics not responding to oral regimen.[27] In the long-term study triamcinolone seemed to have a significant advantage over prednisone in terms of FEV1 and FVC, but in short term study it showed only minor differences in therapeutic efficacy.[25]

Prescription was clearly a problem in asthma compliance with oral prednisone. In broader-based studies of compliance, non-compliance rates of 25% to 50% have been reported.[28] For this reason, triamcinolone or other depot corticosteroids may offer an advantage in management of the acutely ill asthmatic patient. It is necessary to remember that uncontrolled and self-administration of intramuscular triamcinolone LA may lead to occurrence of serious complications of steroids in asthmatic patients.

In this study the dose of 40 mg/day of prednisone was chosen because it was a common outpatient regimen and, in adults, yielded a moderate pharmacologic dose of about 5-mg/kg.[29] Triamcinolone acetate was chosen because of its anti-inflammatory and adrenal suppression similarities to prednisone.[29,30]

We conclude that in adults with acute asthma, oral prednisone is more effective than intramuscular triamcinolone LA in improvement of FEV1, but although efficacy of oral prednisone in improvement of FVC is more than intramuscular triamcinolone LA, this effect is not significant. Intramuscular triamcinolone LA may be an alternative to oral steroids especially in those patients that can not tolerate or comply with traditional dosing of oral steroids.

Larger studies would be useful to confirm our studies.

REFERENCES

1. Loren ML, Chai H, Leung P, Rohr C, Brenner AM. Corticosteroids in the treatment of acute exacerbations of asthma. Ann Allergy 1980; 45(2):67-71.
2. Fanta CH, Rossing TH, McFadden ER Jr. Glucocorticoids in acute asthma. A clinical controlled trial. Am J Med 1983; 74(5):845-51.
3. National Asthma Education Program, Executive Summary: Guidelines for the diagnosis and management of asthma. US Department of Health and Human Services Publication No. 91-3042 A. Bethesda, MD: National Institutes of Health, 1991.
4. McNamara RM, Rubin JM. Intramuscular methylprednisolone acetate for the prevention of relapse in acute asthma. Ann Emerg Med 1993; 22(12):1829-35.
5. Hoffman IB, Fiel SB. Oral vs repository corticosteroid therapy in acute asthma. Chest 1988; 93(1):11-3.
6. Lee CH, Lee CJ, Lan RS, Tsai YH, Chiang YC, Wang WJ, et al. Repository dexamethasone in the treatment of acute bronchial asthma. Chang Gung Med J 1993; 16(1):25-9.
7. Schuckman H, DeJulius DP, Blanda M, Gerson LW, DeJulius AJ, Rajaratnam M. Comparison of intramuscular triamcinolone and oral prednisone in the outpatient treatment of acute asthma: a randomized controlled trial. Ann Emerg Med 1998; 31(3):333-38.
8. Chan JS, Cowie RL, Lazarenko GC, Little C, Scott S, Ford GT. Comparison of intramuscular betamethasone and oral prednisone in the prevention of relapse of acute asthma. Can Respir J 2001; 8(3):147-52.
9. Saunders CE. Patients' compliance in filling prescription after discharge from the emergency department. Am J Emerg Med 1987; 5(4):283-6.
10. Thomas EJ, Burstin HR, O'Neil AC, Orav EJ, Brennan TA. Patient noncompliance with medical advice after the emergency department visit. Ann Emerg Med. 1996; 27(1):49-55.
11. American Thoracic Society. Guidelines for the evaluation of impairment/disability in patients with asthma: a statement of the American Thoracic Society. Am Rev Respir Dis 1993; 147(4):1056-61.
12. Williams SG, Schmidt DK, Redd SC, Storms W; National Asthma Education and Prevention Program. Key clinical activities for quality asthma care. Recommendations of the National Asthma Education and Prevention Program. MMWR Recomm Rep 2003; 52(RR6):1-8.
13. Harris JB, Weinberger MM, Nassif E, Smith G, Milavetz G, Stillerman A. Early intervention with short courses of prednisone to prevent progression of asthma in ambulatory patients incompletely responsive to bronchodilators. J Pediatr 1987; 110(4):627-33.
14. Cockcroft DW, Murdock KY. Comparative effects of inhaled salbutamol, sodium cromoglycate, and beclomethasone dipropionate on allergen-induced early asthmatic responses, late asthmatic responses, and increased bronchial responsiveness to histamine. J Allergy Clin Immunol 1987; 79(5):734-40.
15. Stempel DA, Busse WW, editors. Inhaled corticosteroids. First-line preventive therapy in asthma: Evidence from the current literature. J Allergy Clin Immunol 1998; 102:S1.
16. Kerrebijn KF, van Essen-Zandvliet EE, Neijens HJ. Effect of long-term treatment with inhaled corticosteroids and beta-agonists on the bronchial responsiveness in children with asthma. J Allergy Clin Immunol 1987; 79(4): 653-9.
17. Dutoit JI, Salome CM, Woolcock AJ. Inhaled corticosteroids reduce the severity of bronchial hyperresponsiveness in asthma but oral theophylline does not. Am Rev Respir Dis 1987; 136(5):1174-8.
18. Svendsen UG, Frolund L, Madsen F, Nielsen NH, Holstein-Rathlou NH, Weeke B. A comparison of the effects of sodium cromoglycate and beclomethasone dipropionate on pulmonary function and bronchial hyperreactivity in subjects with asthma. J Allergy Clin Immunol 1987; 80(1):68-74.
19. Chapman KR, Verbeek PR, White JG, Rebuck AS. Effect of a short course of prednisone in the prevention of early relapse after the emergency room treatment of acute asthma. N Eng J Med 1991; 324(12):788-94.
20. Fiel SB, Swartz MA, Glanz K, Francis ME. Efficacy of short-term corticosteroid therapy in outpatient treatment of acute bronchial asthma. Am J Med 1983; 75(2):259-62.
21. Lahn M, Bijur P, Gallagher EJ. Randomized clinical trial of intramuscular vs oral methylprednisolone in the treatment of asthma exacerbations following discharge

from an emergency department. Chest 2004; 126(2):362-8.

22. Ogirala RG, Aldrich TK, Prezant DJ, Sinnett MJ, Enden JB, Williams MH Jr. High-dose intramuscular triamcinolone in severe, chronic, life-threatening asthma. N Eng J Med 1991; 324(9):585-9.
23. Jonsson S, Kjartansson G, Gislason D, Helgason H. Comparison of the oral and intravenous routes for treating asthma with methylprednisolone and theophylline. Chest 1988; 94(4):723-6.
24. Green SS, Lamb GC, Schmitt S, Kaufman J. Oral versus repository corticosteroid therapy after hospitalization for treatment of asthma. J Allergy Clin Immunol 1995; 95(1 Pt 1):15-22.
25. Willey RF, Fergusson RJ, Godden DJ, Crompton GK, Grant IW. Comparison of oral prednisone and intramuscular depot triamcinolone in patients with severe chronic asthma. Thorax 1984; 39(5):340-4.
26. McLeod DT, Capewell SJ, Law J, MacLaren W, Seaton A. Intramuscular triamcinolone acetonide in chronic severe asthma. Thorax 1985; 40(11):840-5.
27. Peake MD, Cayton RM, Howard P. Triamcinolone in corticosteroid-resistant asthma. Br J Dis Chest 1979; 73(1):39-44.
28. Blackwell B. Drug therapy: patient compliance. N Eng J Med 1973; 289(5): 249-52.
29. American Hospital Formulary Service: Hormones and Synthetic substitutes: Adrenals 68:04:2094-2118. Bethesda, MD: American Society of Health-System Pharmacists, 1995.
30. Arnold HL Jr. Systemic steroid therapy with intramuscularly injected triamcinolone. South Med J 1978; 71(2):102-7.