

# Comparison of the Effect of Short Course of Oral Prednisone in Patients with Acute Asthma

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## Abstract

**Background:** Although corticosteroids are considered essential treatment for acute asthma and widely prescribed, we studied the value of oral corticosteroids in moderate persistent asthma (MPA) and severe persistent asthma (SPA), and comparison of those effects.

### Methods:

One hundred-one patients with acute asthma (48 with MPA, 53 with SPA) were studied to determine the efficacy of oral corticosteroids. All patients received other bronchodilator treatment. The patients were divided into two groups depending on initial FEV1 (less than 60% predicted as SPA and FEV1 between 60 to 80% predicted as MPA), and treated with oral prednisone 40 mg daily for 7 days. Spirometric variable and percentage of change to baseline FVC, FEV1 and FEF 25-75% after treatment was calculated.

### Results:

After 7 days of treatment, the increase in FVC, FEV1 and FEF 25-75% predicted values in both group of patients with MPA and SPA was significant ( $P < 0.001$ ).

The percentage of FVC, FEV1 and FEF 25-75% improvement in patients with MPA and SPA was  $19.3 \pm 11.2\%$  vs  $61.6 \pm 45.5\%$ ;  $29.5 \pm 14.2\%$  vs  $85.3 \pm 93.2\%$  and  $53 \pm 36.4\%$  vs  $128.7 \pm 108\%$  respectively.

### Conclusion:

Short course of oral prednisone administered in moderate and severe persistent asthma induces in spirometric measurements, that these changes together with percentage improvement of FVC, FEV1, and FEF 25-75% in SPA was higher than those with MPA.

## INTRODUCTION

The use of steroids in combination with bronchodilators in asthma is an accepted form of treatment<sup>1,2,3</sup>. The basis for this steroid treatment is derived from the concept that asthma has an important inflammatory component in its pathogenesis<sup>4,5</sup>.

Steroids are usually given for several days in large doses, either in an emergency room setting<sup>6,7</sup>, ambulatory care setting<sup>8,9</sup>, or during hospitalization. Acute exacerbation of asthma is a common reason for patients to seek treatment in the emergency department. Most patients are successfully treated and discharged with continued treatment at home. The guidelines for the Diagnosis and Management of Asthma, published by the National Institutes of Health,

recommends the steroids be considered in all patients after emergency for acute exacerbations<sup>12</sup>.

For the management of asthma in ambulatory patients, oral corticosteroids are clearly effective<sup>13</sup>. Recent studies in adults<sup>14</sup> and children<sup>15</sup> seen in an emergency room demonstrated a significant improvement in the clinical course of acute asthmatic episodes when early corticosteroid therapy was instituted. It would appear reasonable, then, to administer oral corticosteroids during the critical period following the management of asthma in the emergency room.

In the present study, we report the effect of oral prednisone, 40 mg/day for 7 days, in-patients treated for moderate and severe persistent of asthma. We also analyzed spirometric

changes in both groups and compared with them.

## MATERIALS AND METHODS

Patients were eligible for the study if they were 16 years of age or older had asthma as defined by American Thoracic Society (ATS) criteria<sup>16</sup>. The study group included 101 subjects who presented with acute asthma manifested as dyspnea, cough, or wheezing and a 1- second initial forced expiratory volume (FEV1) less than 60% of predicted normal value as severe persistent asthma, and FEV1 between 60 to 80% predicted considered as persistent moderate asthma, according to International Global Initiative of Asthma (GIBA) guidelines<sup>17</sup>. Patients were enrolled from March 2000 to June 2001 while being treated with oral prednisone 40 mg daily for seven days. Other inclusion criteria required to entrance study were: to be free of complicating medical illness, to have taken no oral or parenteral corticosteroids in the preceding four weeks, to be free of known contraindications to the administration of systemic corticosteroids, and for premenopausal women, to be nor breast feeding. Patients were also excluded if they were current smoker, or unable to perform spirometry. The subjects included in the study were also treated with conventional bronchodilators as deemed necessary. No subjects were using long –acting B2- agonists, Leukotriene antagonists, or antihistamines. Outpatients asthma treatment regimens were similar for both groups. The dose of 40-mg/day prednisone was chosen because it is a common outpatients regimen and, in adults, yields a moderate pharmacologic dose of about 5 mg/kg<sup>18</sup>. Spirometric measurements were made by using Fukuda spirometer (ST-95, Japan); variable were recorded from the best of three maximal forced expiratory maneuvers as determined by American Thoracic Society criteria, with a printout of graphic and numerical data retained for subsequent analyses

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The results of pulmonary function testing were calculated as percentage of change relative to baseline FVC, FEV1 and FEF 25-75% by the following equation:

Percentage of change = [(observed – base) / base] × 100  
were observed is the post treatment values after 7 days, base is the baseline value on the day before treatment.

The Kolmogorov – Smirnov test was used to distribution of quantitative variables. Mean ± SD differences before and after a treatment between two groups of patients was calculated, and P values were compared by Student t-test for paired and unpaired data. Results were considered to

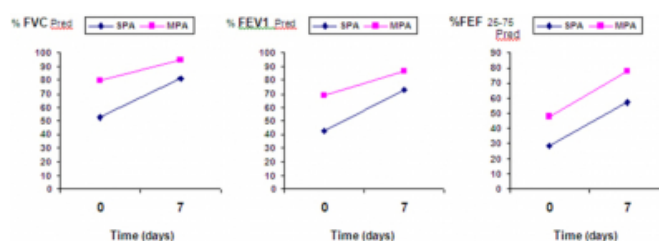
indicative significance at a P value of less than 0.05.

Statistical analysis was performed by means of a statistical software package (SPSS version 10.0 for windows).

**Results:** A total of 101 patients were enrolled, 48 (47.5%) in moderate persistent group (mean age 35.6 years, range 16-71), and 53 patients (52.5%) in severe persistent group (mean age 36.8 years, range 20-70). The characteristics of the patients in the two groups are shown in Table 1. Spirometric measures on arrival and after treatment are presented in Tables 2 and 3. There were no significant differences between the two study groups by age and sex (Table 1). FVC, FEV1 and FEF 25-75% predicted at presentation were 79.7±7.8%, 68.5±6.1%, 48.02±15.8% and 52.7±12.7%, 43.06±11.1%, 28.5±13.4% in moderate persistent and severe persistent asthma, respectively. After seven days of treatment values (% predicted) were 94.9 ± 10%, 87±9.5%, 78±24.8% and 81.2±12.2%, 72.9±13.5%, 57.3±20.8% respectively in patients with moderate persistent and severe persistent asthma (P<0.001). The level of improvement after treatment with prednisone in two groups of patients was significant (Table 3 and Fig. 1).

## Figure 1

Figure 1: The mean (SE) percentage predicted of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and forced expiratory flow 25-75 (FEF 25-75%) before and after therapy with Prednisone (MPA= moderate persistent asthma, SPA = severe persistent asthma).



The percentage of FVC, FEV1 and FEF 25-75% improvement in patients with moderate and severe persistent asthma was 19.3±11.2% Vs 61.6±45.5%, 29.5±14.2% Vs 85.3±93.2% and 53±36.4% Vs 128.7±108% respectively (Table 2). Patients with severe persistent asthma had a higher change in spirometric values than those who were in moderate persistent asthma (P<0.001).

Figure 2

Table 1: Characteristics of the patients in the study groups\*.

CHARACTERISTIC	Moderate persistent asthma (N=48)	Severe persistent asthma (N=53)
Age, (Yr.)		
Mean(SD)	35.58 (13)	36.77 (13.2)
Range	16 - 71	20 - 70
Sex, male/female	28 / 20	30 / 23
FEV1, % predicted		
Mean(SD)	68.46 (6.1)	43.06 (11.1)
Range	68 - 80	17 - 59
FEV1, (liters)		
Mean (SD)	2.25 (0.65)	1.38 (0.50)
Range	0.74 - 3.75	0.61 - 2.68
FVC, % Predicted		
Mean (SD)	79.7 (7.8)	52.74 (12.7)
Range	65 - 98	21 - 79
FVC, (liters)		
Mean (SD)	3.13 (0.87)	2.03 (0.73)
Range	1.34 - 5.62	0.78 - 3.87
FEF 25-75%, %predicted		
Mean (SD)	48.02 (18.8)	28.45 (13.4)
Range	20 - 96	7 - 66
FEF 25-75%, (lit/sec)		
Mean	1.98 (0.74)	1.16 (0.61)
Range	0.49 - 4.04	0.36 - 3.35

\* Percentages are given in parentheses

Figure 3

Table 2: Pulmonary Function in two Groups of Patients with Moderate and Severe Persistent of Asthma, Receiving Prednisone Before and After Treatment.

Variable	BEFORE TREATMENT		AFTER TREATMENT		PERCENT IMPROVEMENT	
	Moderate Persistent Asthma (N = 48)	Severe Persistent Asthma (N = 53)	Moderate Persistent Asthma (N = 48)	Severe Persistent Asthma (N = 53)	Moderate Persistent Asthma (N = 48)	Severe Persistent Asthma (N = 53)
FVC (liters)	3.13 ± 0.87	2.03 ± 0.73	3.71 ± 0.99	3.12 ± 0.92	19.3 ± 11.2	61.6 ± 45.5
FEV1 (liters)	2.25 ± 0.65	1.38 ± 0.50	2.85 ± 0.81	2.35 ± 0.7	29.5 ± 14.2	85.3 ± 93.2
FEF25-75% (liters/sec)	1.98 ± 0.74	1.16 ± 0.61	2.98 ± 1.15	2.32 ± 0.96	53 ± 36.4	128.7 ± 108.1

Expressed as a percentage of pretreatment results.

Figure 4

Table 3: Pulmonary Function in two Groups of Patients with Moderate and Severe Persistent of Asthma, Before and After Treatment with Prednisone. \*

Variable	Moderate Persistent Asthma (N = 48)		P Value **	Severe Persistent Asthma (N= 53)		P Value **
	Before Treatment	After Treatment		Before Treatment	After Treatment	
FVC, % pred (liters)	79.9±7.8	94.9±10	< 0.001	52.7±12.7	81.2±12.2	< 0.001
	3.13±0.87	3.7±1		2.03±0.73	3.12±0.92	
FEV1, %pred (liters)	68.5±6.1	87 ± 9.5	< 0.001	43.06±11.1	72.9±13.5	< 0.001
	2.3±0.7	2.85±0.81		1.38±0.50	2.35±0.7	
FEF 25-75%, %pred (lit/Sec)	48.02±15.8	78 ± 24.8	< 0.001	28.5±13.4	57.3±20.8	< 0.001
	1.98±0.74	2.98±1.15		1.16±0.61	2.32±0.96	

\* Values are expressed as means ± SD

\*\* Student's t-test

## DISCUSSION

Our results show that a short course of prednisone administered in moderate and severe persistent asthma in addition to conventional therapy induces improvement in spirometric measurements, that is significant in severe persistent asthma than moderate persistent asthma. Percent improvement of FVC, FEV1, and FEF 25-75% in patients with severe persistent asthma was higher than those with moderate persistent asthma (Fig. 1).

Glucocorticoids (GCs) represent a group of extremely potent antiinflammatory agents used both systemically and by inhalation in the management of persistent asthma <sup>20</sup>.

Continued administration is also effective in reducing the immediate pulmonary response to an allergen challenge and can augment the sensitivity and number of beta adrenergic receptors <sup>21</sup>. Early intervention with oral prednisone appears justified in preventing the need for a protracted course of treatment or emergency care <sup>9</sup>.

The use of short courses of oral corticosteroids after discharge from the emergency room has been recommended previously. For example, Shapiro et al. reported that children with asthma improved more rapidly after emergency therapy when treated with oral steroids <sup>22</sup>. In adults, Fiel et al. reported a decrease in the relapse rate from 21 to 6 percent in patients given a tapering course of methylprednisolone <sup>6</sup>,

which included an intravenous bolus of the drug.

Wempe et al. attempted to evaluate the effects of GCs on bronchodilators or both airflow obstruction and bronchial hyperresponsiveness (BHR) in a randomized, double blind, cross – over study with budesonide, prednisone, and placebo. Both GCs were equipotent in increasing the prebronchodilator FEV1 (improvement in FEV1 of 13% over placebo treatment) and decreasing the degree of BHR at the conclusion of treatment <sup>23</sup>. In present study, the degree of improvement in FEV1 in patients with severe and moderate persistent asthma was 29.8% and 18.5% respectively (Table 3).

Bhagat and Grunstein evaluated the effect of either prednisone (60 mg/day) or placebo for 7 days in 10 patients with atopic asthma and found significant improvements in the mean baseline FEV1 and log PD20 – FEV1 after prednisone compared with baseline and placebo therapy. Of note, although all patients increased their PD20 values after prednisone, the greatest improvements came from those patients who had FEV1 values below 75% of predicted <sup>24</sup>. In our study the percent of improvement in FEV1, FVC and FEF 25-75% in patients with severe persistent was higher than those with moderate persistent asthma (Table 2) were. A recent study from Robinson et al. found similar results in a group of adults with moderate asthma <sup>25</sup>.

Despite of 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. Both oral <sup>6,8</sup> and intramuscular <sup>26</sup> steroid regimens are superior to placebo in reducing relapse rates after emergency department treatment.

For patients with asthma who have protracted exacerbations requiring prolonged courses of antiinflammatory therapy, high dose inhaled GCs may offer substantial risk-benefit advantages over the oral approach <sup>27</sup>, although we detected no serious side effects or toxicity from the short-term use of prednisone in present study.

Littenberg and Gluck evaluated the effect of a single parenteral GCs dose versus saline in the emergency room treatment of acute asthma <sup>14</sup>. They concluded that prompt use of GCs in the emergency room treatment of asthma could reduce the number of hospitalizations and affect substantial savings in health care costs.

A similar study by Stein and Cole failed to demonstrate any

difference in the subsequent hospitalization of those received methylprednisolone versus those who received saline <sup>7</sup>. It is difficult to determine why the results of the two studies differ in that both were double blind, placebo – controlled studies. Although FEV1 values were not measured in the study by Stein, these authors suggested that their patients may have had less airflow obstruction than those of Littenberg et al <sup>14</sup>.

The time course of the response is probably dependent on the clinical state of the patients with exacerbations of chronic asthma requiring more time to achieve a maximum response than the same patients during remission. This is supported by findings of a previous study, which showed the time course of the response to oral GCs treatment in patients with chronic airflow obstruction who were not experiencing an exacerbation <sup>28</sup>.

The results for the group showed a plateau occurring at eight days, and the average duration of response was 5.1 days <sup>28</sup>.

Previous investigators recognized that asthmatic patients have exhibited peak improvement in pulmonary function within 12 hours after a single oral prednisone dose <sup>13</sup>, and maximal improvement in pulmonary function has been observed 7 days after initiating twice – daily prednisone in acutely ill asthmatic patients <sup>9</sup>.

Our study confirms that short – term oral GCs therapy in acute asthmatic attack was effective, and response to treatment in severe persistent asthma was better than patient with moderate persistent asthma.

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