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Short- and long-term oral steroid therapy in patients with asthma exacerbation

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Abstract

Steroids are frequently used for symptom control in cases of asthma exacerbation. The aim of this study was to compare the effect of short-term and long-term oral steroid therapy on symptom control in patients with asthma exacerbation. Patients that received short-term (<10 d) and long-term (≥10 d) oral steroid therapy during asthma exacerbation were compared retrospectively. A visual analog scale (VAS) for symptom severity was administered, and the asthma control test (ACT) and pulmonary function tests were performed before and after treatment. The study included 69 patients and the overall mean duration of steroid treatment was 9.57±3.58 d (range: 5-25 d). Mean duration of short-term and long-term steroid treatment was 6.54±0.99 d and 11.63±3.21 d, respectively. Serious side-effects were not observed following oral steroid therapy. Post the short- and long-term oral steroid therapy there were not any significant differences between the 2 groups in terms of ACT, FEV_1 (forced expiratory volume 1), or VAS symptom scores. The findings show that in patients with mild asthma exacerbation short-term oral steroid therapy is as effective as long-term steroid therapy and can be safely used for symptom control during periods of mild asthma exacerbation.

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Introduction

Corticosteroids have anti-inflammatory, anti-allergic, and immunosuppressive effects, and are frequently used for the treatment of such conditions as asthma, nephrotic syndrome, vasculitis, autoimmune diseases, rheumatic diseases, neurological diseases, dermatological diseases, chronic urticaria and angioedema, allergic and non-allergic rhinitis, chronic rhinosinusitis, and anaphylactic shock. Corticosteroids can be administered locally, topically, intra-articularly, nasally, systemically, and via inhalation; however, long-term use of systemic corticosteroids can cause various undesirable side effects, including osteoporosis, growth suppression, iatrogenic Cushing syndrome, myopathy, peptic ulcer, diabetes, cataracts, glaucoma, increased risk of infection, adrenal insufficiency, and psychiatric problems [1-4].

Systemic steroids are frequently used in allergy practice to provide symptom control in cases of asthma exacerbation. In such patients the optimal duration of treatment that provides symptom control is variable. In some patients, symptom control is achieved with short-term systemic corticosteroid therapy, whereas in others long-term treatment is required. There is a lack of consensus regarding the optimal treatment duration; therefore, the present study aimed to compare the effects of short- and long-term oral steroid therapy on symptom control in patients with mild asthma exacerbation.

Materials and Methods

Study design and setting, and data collection

This retrospective study was conducted between June 2018 and June 2020. Data were obtained from patient medical records. Patients diagnosed as asthma that presented to the allergy clinic with exacerbation and received oral steroid therapy were evaluated. At our clinic oral steroid therapy is routinely initiated at a dose of 0.5 $mg \cdot kg^{-1} \cdot d^{-1}$ (maximum: 40 mg), and then the dose is reduced by 50% every 3 d. Oral steroid therapy is discontinued at the end of the planned treatment period. It is routine practice at our clinic that a pulmonary function test, asthma control test (ACT) [5], and visual analog scale (VAS) for symptom severity (from 1 to 10) are administered to all patients before and after oral steroid therapy. In total, 69 patients that received short-term (<10 d) and long-term (≥10 d) oral steroid (methylprednisolone) therapy were compared in terms of VAS symptom scores and disease control. While receiving oral steroid therapy for asthma exacerbation all the patients continued with their regular treatment. Side-effects were noted at the end of steroid therapy.

Asthma was diagnosed based on the Global Initiative for Asthma (GINA) guidelines [6]. An asthma exacerbation was defined as progressive shortness of breath, cough, wheezing, or chest tightness accompanied by decreased PEF (peak expiratory flow) and FEV_1 (forced expiratory volume 1) [6]. Patient demographic data, comorbid diseases, regular medications, and laboratory parameters (total IgE and eosinophil count) were obtained from hospital medical records.

Inclusion and exclusion criteria

Only patients with mild asthma exacerbation were included in the study. Exclusion criteria were age <18 years, pregnancy, lactation, use of systemic steroids at the time of presentation, chronic obstructive and restrictive pulmonary diseases other than asthma, any conditions for which systemic steroid use is contraindicated (such as active infection, active peptic ulcer, uncontrolled neuropsychiatric or ocular disease, and uncontrolled diabetes), severe asthma exacerbation (orthopneic, respiratory rate >30 min^{-1}, heart rate >120 bpm, and oxygen saturation <90%).

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows v.20 (IBM Corp., Armonk, NY, USA). Descriptive statistics are shown as mean ±SD and range for numerical data, and as frequency (n) and percentage (%) for categorical variables. Student's *t*-test was used to compare the means of 2 independent and dependent groups. The marginal homogeneity test was used to compare the proportions of 2 dependent groups. The chi-square test, Fisher's exact test, and the Mantel-Haenszel chi-square test were used to compare the proportions of 2 independent groups. The level of statistical significance was set at $p<0.05$.

Ethics statement

The study protocol was approved by Ethics Committee (no. GO 18/520-04). The study was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the nature of the study and provided written informed consent.

Results

The study included 69 patients that received oral steroid treatment. In total, 9 (13%) patients were male and 60 (87%) were female, and mean age was 43.41±13.63 years (range: 18-79 years). Based on skin prick testing and/or specific IgE measurement, 23 (33%) patients had atopy. The overall mean duration of oral steroid therapy was 9.57±3.58 d (range: 5-25 d). During the treatment period serious side-effects were not observed, although the most common side-effects were mild gastrointestinal complaints (18.8%), increased appetite (7.2%), and weight gain (5.6%). Patient demographic data and general characteristics are shown in Table 1.

Following oral steroid therapy there was a significant increase

Table 1. Patient demographic data and general characteristics.

	n=69
Age, years (mean±SD)	43.41±13.63
Gender, male (%)	9 (13%)
BMI (mean±SD)	27.5±4.72
Total IgE, $kU\ L^{-1}$ (mean)	131.92
Eosinophil, cells μL^{-1} (mean)	327.78
Treatment duration, d (mean±SD)	9.57±3.58
Smoker, n (%)	9 (13%)
Smoking, packs $year^{-1}$ (mean)	9.67
Comorbid disease	**n (%)**
Hypertension	11 (15.9%)
Diabetes mellitus	6 (8.7%)
Cardiovascular disease	6 (8.7%)
Cerebrovascular disease	4 (5.8%)
Gastroesophageal reflux	8 (11.6%)
Psychiatric disease	3 (4.3%)
Malignancy	1 (1.4%)
Thyroid disease	5 (7.2%)
Regular medications	
Inhaled steroid	67 (97.1%)
Long acting beta agonist	38 (55.1%)
Short acting beta agonist	34 (49.3%)
Long acting anticholinergic	4 (5.8%)
Leukotriene antagonist	56 (81.2%)
Omalizumab	9 (13%)
Mepolizumab	3 (4.3%)
Atopy (skin prick/sIgE+)	23 (33%)
Nasal polyp	14 (20.3%)
GINA	
Step 1	1 (1.4%)
Step 2	2 (2.9%)
Step 3	27 (39.1%)
Step 4	25 (36.2%)
Step 5	14 (20.3%)
Steroid side-effects	
Gastrointestinal complaint	3 (18.8%)
Increased appetite	15 (7.2%)
Weight gain	4 (5.8%)
Hyperglycemia	1 (1.4%)
Osteoporosis	1 (1.4%)

in ACT (p<0.001) and FEV_1 (%) values (p<0.001), and significant improvement in VAS symptom scores (p<0.001) (Table 2). Mean duration of short-term and long-term oral steroid treatment was 6.54±0.99 d and 11.63±3.21 d, respectively. Following treatment there were not any significant differences in ACT, FEV_1, or VAS symptom scores between the patients that received short-term and long-term oral steroid treatment (Table 3).

Discussion

This retrospective study investigated the effect of short- and long-term oral steroid therapy on symptom severity and disease control in patients with mild exacerbation of asthma. The findings show that short-term oral steroid therapy was as effective as long-

Table 2. VAS symptom scores, and ACT and FEV1 values before and after oral steroid therapy.

	Before oral steroid (mean±SD)	After oral steroid (mean±SD)	p-value
ACT	10.75±4.14	20.23±3.57	<0.001*
FEV_1 (%)	86.81±19.05	92.22±17.13	<0.001*
VAS symptom scores	**Before oral steroid (mean±SD)**	**After oral steroid (mean±SD)**	
Dyspnea	6.32±3.11	2.29±1.54	<0.001**
Cough	7.35±2.7	2.62±1.75	<0.001**
Sputum	4.59±3.12	1.75±1.27	<0.001**
Wheezing	5.80±3.03	2.19±1.43	<0.001**
Night waking	4.97±2.93	1.64±1.47	<0.001**

VAS symptom scores ranged from 1 to 10 (1: none, 10: very severe); *Student's *t*-test; **marginal homogeneity test.

Table 3. Comparison of the patients that received short-term (<10 d) and long-term (≥10 d) oral steroid therapy.

	Short-term (n=28)	Long-term (n=41)	p-value
Age, years (mean±SD)	46±14.35	41.63±12.99	0.194*
Gender, male (%)	1 (3.6%)	8 (19.5%)	0.073***
BMI (mean±SD)	28.13±4.51	27.07±4.88	0.364*
Total IgE, kU L^{-1} (mean)	77.86	162.20	0.318*
Eosinophil count, cells μL^{-1} (mean)	194.74	400	0.083*
Treatment duration, d(mean±SD)	6.54±0.99	11.63±3.21	<0.001*
Smoking duration, packs $year^{-1}$ (mean)	7.20	12.75	0.392*
Atopy, skin prick/sIgE+ (%)	8 (28.6%)	15 (36.6%)	0.079**
Nasal polyp (%)	4 (14.3%)	10 (24.4%)	0.305**
GINA			
Step 1	1 (3.6%)	-	0.054****
Step 2	1 (3.6%)	1 (2.4%)	
Step 3	13 (46.4%)	14 (34.1%)	
Step 4	10 (35.7%)	15 (36.6%)	
Step 5	3 (10.7%)	11 (26.8%)	
Before oral steroid	**Short term (n=28) (mean±SD)**	**Long term (n=41) (mean±SD)**	
ACT	11.11±4.23	10.51±4.12	0.563*
FEV_1 (%)	93.14±12.89	82.94±21.23	0.047*
Dyspnea (VAS score)	6.21±3.07	6.39±3.17	0.803**
Cough (VAS score)	7.25±2.90	7.41±2.58	0.771**
Sputum (VAS score)	4.50±2.79	4.66±3.36	0.449**
Wheezing (VAS score)	5.50±2.93	6.00±3.11	0.414**
Night waking (VAS score)	4.39±2.80	5.37±2.98	0.868**
After oral steroid	**Short term (n=28) (mean±SD)**	**Long term (n=41) (mean±SD)**	
ACT	19.75±3.64	20.56±3.53	0.359*
FEV_1 (%)	95.95±12.41	89.94±19.28	0.198*
Dyspnea (VAS score)	2.28±1.21	2.29±1.74	0.321**
Cough (VAS score)	2.60±1.39	2.63±1.97	0.164**
Sputum (VAS score)	1.79±1.03	1.73±1.43	0.076**
Wheezing (VAS score)	2.14±0.93	2.22±1.71	0.106**
Night waking (VAS score)	1.25±0.51	1.90±1.82	0.586**

ACT, asthma control test; VAS, visual analog scale (symptom scores ranged from 1 to 10 = 1: none, 10: very severe); *Student's t-test; **Chi-square test; ***Fisher's exact test; ****Mantel-Haenszel chi-square test.

term therapy for providing symptom control. Serious side effects were not observed, but the most common was mild gastrointestinal side-effects (n=13, 18.8%).

Asthma is characterized by chronic airway inflammation and non-specific bronchial hyperactivity, and is known to affect approximately 334 million people worldwide [7-10]. Since the 1950s, local and systemic corticosteroids have been widely used to treat various inflammatory diseases, especially asthma [11]. Oral steroids are used to relieve acute asthma attacks and as a means of controlling symptoms in patients with severe asthma [6,12,13]. Currently, the Global Initiative for Asthma (GINA) guideline recommends the use of biological agents in patients with severe asthma when indicated [6]. Low-dose maintenance oral steroid therapy is further recommended as the step 5 treatment to maintain disease control. The GINA guideline also recommends short-term oral steroid therapy for patients with loss of symptom control or exacerbation.

Although the GINA guideline recommends short-term oral steroid treatment for asthma exacerbation, there is a need for additional research to determine the optimal duration of treatment. The present findings show that VAS symptom scores are similar in asthma patients that receive short-term and long-term oral steroids. Although pre-treatment FEV_1 was slightly lower in the long-term therapy group, all the other clinical characteristics were similar. Short-term oral steroid therapy was observed to be effective and well tolerated in asthmatic patients with mild exacerbation that did not require hospitalization; however, the optimal duration of treatment for severe asthma exacerbation should be determined via further studies. A review by Bleecker *et al.* [14] of patients with varying degrees of asthma severity reported that short-term oral steroid treatment ranged from 3.6% to 62.0% and long-term oral steroid treatment ranged from 1.2% to 30.9%. A randomized study by Hasegawa *et al*. [15] observed that 1 week and 2 weeks of oral prednisolone (0.5 mg kg^{-1}) treatment were equally effective for treating asthma exacerbation. They reported that the increase in PEF after oral steroid therapy was similarly significant in the 1-week and 2-week treatment groups. In the present study there was a significant increase in FEV_1 after oral steroid therapy in both groups, although the increase in FEV_1 was greater in the long-term treatment group.

In the present study serious side effects were not observed in either group, although the most common were mild gastrointestinal complaints (18.8%), increased appetite (7.2%), and weight gain (5.6%), all of which were well tolerated by the patients. Transient hyperglycemia was observed in 1 patient and osteoporosis (that did not cause pathological fracture) was observed in 1 patient. Matsumoto *et al*. [16] observed that loss of bone mineral density was greater in asthmatic patients that received >2 short courses of systemic steroids per year. A retrospective cohort study conducted in the USA in 2017 reported that the risk of sepsis, venous thromboembolism, and fractures increased in patients that received short-course systemic steroids for respiratory diseases [17]. It was also reported that the risk of side effects increases with both short- and long-term systemic steroid use [18].

This present study has some limitations. Firstly, patients with severe asthma exacerbation were not included, which may limit the generalizability of the findings. Secondly, although the clinical characteristics of the patients in both groups were similar before steroid therapy, a small subgroup of patients might have benefited from a longer course of steroid therapy. Despite these limitations, this study is unique in terms of its evaluation of a patient population that is frequently encountered in allergy practice.

Conclusions

In patients with mild asthma exacerbation, short-term oral steroid therapy is as effective as long-term therapy and can be safely used for symptom control during period of asthma exacerbation.

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