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Efficacy Evaluation of Different Treatment Regimens with Fluticasone Propionate in Mild Persistent Asthma

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Abstract: Asthma is a chronic airway disorder and prevalence of asthma symptoms in children is about 1-30% and is increasing in many countries. Inhaled Corticosteroids (ICS) are one of the basic therapeutic agents for asthma and their daily frequency is one of the most important factors in the patient adherence to therapy. This study was designed to compare the effect of different frequencies of Fluticasone Propionate on the treatment of mild persistent asthma. This study is a randomized clinical trial on 100 patients with mild persistent asthma at the age of 2-14 years-old receiving Fluticasone Propionate 1 puff twice daily for first 3 months and then 2 puffs once daily for next 3 months are compared to 150 asthmatic patients with the same age range and severity of disease but receiving 1 puff twice daily for 6 months. There was no significant meaningful difference in therapeutic effects of Fluticasone Propionate between two studied groups but adherence to therapy was better in once-daily administered group. Considering the lack of significant difference between two groups and increased parental adherence in first group, the lower frequencies of spray administration after a partial improvement is suggested.

Key words: Asthma, fluticasone propionate spray, inhaled corticosteroid, dose frequency

INTRODUCTION

Asthma is a chronic condition involving the respiratory system; prevalence of asthma symptoms in children range from 1-30% of the population in different countries and There is good evidence that asthma prevalence has been increasing in some countries (GINA, 2006).

The cost of asthma care, vary in different contraries. In the united states, the costs of asthma have been estimated to be over $6 billion per annum,which accounts for 1% of the total united states expenditure on health and asthma costs are approximately 1% of the health budgets of most countries (Mclvor, 2001).

Inhaled corticosteroids (ICS) have been identified by both the National Asthma Education Prevention Program (NAEPP) and the Global Initiative for Asthma (GINA) as preferred component of controller therapy for patients of different ages and levels of severity of persistent asthma as well (GINA, 2006; NAEPP, 1997; Van Asperen *et al*., 2002).

Improved adherence to Inhaled Corticosteroids (ICS) is recognized as an important factor in reduced morbidity, mortality and consumption of health care resources and Poor adherence to ICS is recognized as a contributor to asthma treatment failure resulting in increased morbidity, mortality and increased consumption of health care resources (Stempel *et al*., 2005).

Ineffective asthma management resulting from a failure to adhere to the prescribed treatment regimen is a common problem, with noncompliance rates typically ranging from 30-70% among asthma patients. Consequently, a reduction in dose frequency to once-daily dosing is more frequently being considered as a treatment option in order to increase convenience and compliance (Nathan *et al*., 2000).

Fluticasone propionate (Flixotide®) is a trifluorinated corticosteroid with high Glucocorticoid activity. It is poorly absorbed from the gastrointestinal tract and undergoes extensive first pass metabolism. Oral bioavailability is reported to be only about 1%. Fluticasone propionate is stated to exert a topical effect on the lungs without systemic effects at usual doses. It is used by powder or aerosol inhalation for the prophylaxis of asthma (Sweetman *et al*., 2002).

This study is designed to evaluate the efficacy of different frequencies of Fluticasone propionate administrations as treatment of mild persistent asthma in children.

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MATERIALS AND METHODS

In a randomized controlled trial from Oct 2005 to April 2007, patients with mild persistent asthma at the age group of 2-14 years-old, who were receiving Fluticasone propionate 125 μg in different therapeutic course were studied.

The criteria for outcome assessment are symptom free nights and days, cough and wheezing free days and the days without necessity to relief therapy and Patients have been visiting monthly and we made contact with their families when needed. The patients were classified on the basis of GINA guidelines (2006) and the research agreements were signed by the patients before starting the trial and the patients divided in case and control groups randomly. Patients were instructed to complete a prepared chart to record exacerbation episodes of symptoms. Data were analyzed by the statistical software spss14 using paired T-test, exact fisher (F-test) and chi square (χ^2) test.

RESULTS

Two hundred and fifty patients were eligible for study but 10 patients were excluded and 240 patients were divided to case and control groups, finally 200 cases completed the trial.Baseline characteristics of patients are presented in Table 1.

Percentages of symptom free 24 h period (daytime and nighttime) are shown in Table 2.

Table 3 and 4 demonstrate comparison of two designed groups in wheezing and cough-free days and the days without necessity to relief therapy, respectively.

In addition, regular monthly visit and drug provision rate were 87.5% (105 patients) in case and 79% (95 patients) in control group, considering p-value (0.08%), the difference is not significant.

Table 1: Baseline characteristics of patients in case and control groups

Paprameter	Case group	Control group
Number of cases	105	95
Sex ratio	60/45	58/37
Age (month)	60±12	58±10
Family history of asthma	23%	20%
History of allergic rhinitis	15%	13%
Disease duration 1-12 months	38%	40%
Disease duration 12-24 months	33.5%	30.5%
Disease duration24-36 months	18%	20%
Disease duration >36 months	10.5%	9.5%
Number of previous attacks: 0	6%	8%
Number of previous attacks: 1-3	51%	49%
Number of previous attacks: 4-6	30%	32%
Number of previous attacks: 7-10	9%	7%
Number of previous attacks: >10	4%	4%
Number of previous hospitalizations: 0	70%	70%
Number of previous hospitalizations: 1	18%	17%
Number of previous hospitalizations: 2	10%	11%
Number of previous hospitalizations: >2	2%	2%

Table 2: Percentages of symptom-free daytime and nighttime in case and control groups

Groups	First 3 months	During 6 months
Case group	m = 69.86±2.2	m = 138.8±5.89
Control group	m = 70.18±4.48	m = 139.75±8.24
p-value	0.5	0.3

Table 3: Percentages of wheezing-free and cough-free days in case and control groups

Groups	First 3 months	During 6 months
Wheezing free days		
Case	m = 86.2±3.4	m = 173.3±2.6
Control	m = 85.4±3.5	m = 172.2±3.1
p-value	0.07	0.06
Cough free days		
Case	m = 75.5±4.3	m = 144.0±6.3
Control	m = 75.0±3.4	m = 145.0±5.2
p-value	0.3	0.17

Table 4: Percentages of the days without necessity to relief therapy in case and control groups

Groups	First 3 months	During 6 months
Case group	m = 79.86±2.2	m = 160.66±1.95
Control group	m = 79.87±4.12	m = 159.75±8.24
p-value	0.9	0.2

DISCUSSION

This study is designed to compare the efficacy of different frequencies of Fluticasone propionate sprays in the treatment of mild persistent asthma in children.

The results indicate that there is no significant difference between 2 groups and adherence to treatment is better in case group.

According to the study of Nathan *et al.* (2000), in the united states once-daily treatment with Fluticasone propionate resulted in an improving efficacy variables such as FEV1, morning and evening Peak Expiratory Flow (PEF), asthma symptom scores, nighttime awakening and albuterol use. A dose-related trend was observed for improvement in morning PEF and albuterol use.

Rand *et al.* (1992) showed that inhaled therapy for asthma involving administration three or four times daily has been associated with low levels of compliance.

In the study of Coutts *et al.* (1992), a reduction in dosing frequency is reported to increase compliance.

Hodges and Netherway (2005) reported that once-daily dosing with fluticasone propionate (100 μg) seemed to be clinically equivalent to twice-daily therapy for maintenance therapy of children with well controlled mild to moderate asthma.In clinical practice once-daily therapy improved patient compliance and this may be associated with improved control of asthma.

In the study of La Force *et al.* (2000), once-daily therapy with inhaled fluticasone propionate was found to have equivalent efficacy to twice-daily therapy in children with mild to moderate asthma and there were no statistical difference between the 2 treatment groups in either morning or evening PEF and diurnal variation was similar in both groups.

The results of our study and these 2 studies mentioned above may be explained by high lipophilicity and low hydrophilicity of fluticasone propionate that result in its delayed pulmonary diffusion and increased half life.

Boulet *et al.* (2000) showed that twice-daily dosing of fluticasone propionate was more effective than once-daily dosing so the twice-daily administration, can control the symptoms in most cases. The increases observed in FEV1 were not significantly different between the two groups but the incidence of exacerbations was more in once-daily therapy.

Mckenzie and Bush (2002) concluded that once-daily dosing is as effective as twice-daily in the treatment of asthma.

In the study of Li *et al.* (2006), a changing in the treatment protocol from twice-daily to once-daily fluticasone propionate maintaining total daily dose resulted in a significant improvement in Exhaled Nitric Oxide (ENO) and sputum eosinophils.

The results of our study are match with the previous comparisons of once-daily and twice-daily fluticasone propionate in children with asthma, in which no significant difference between the treatment groups was found and most of them state that lower frequencies of drug administration, result in better adherence o patients, cost effectiveness of therapy and lower mortality rate.

CONCLUSION

The lack of significant difference between the results of two groups in response to treatment and increased parental adherence and improved asthma control and minimized costs in the first group, suggest that once daily therapeutic regimen in the treatment of mild persistent asthma in children, could be better tolerated but this should be recommended after at least three months of twice daily regimen for better therapeutic and clinical results.

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