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Is the Effect and Safety of Single Daily Dose of Fluticasone Nasal Spray Better than Alternate Day Regimen in Allergic Rhinitis?

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Abstract

Introduction: The goal of corticosteroid therapy is to maximize efficacy, minimize potential systemic side effects, and improve patient adherence. Factors that will potentially improve adherence to treatment and differentiate the intranasal corticosteroids are dosing regimens, patient preference and cost effectiveness.

Aim and objective: To study and compare the efficacy and safety of daily versus alternate day regimen of fluticasone nasal spray.

Materials and methods: A prospective, randomized comparative study was done at a tertiary care hospital which included 80 patients of symptomatic allergic rhinitis with symptoms of at least one-year duration; divided into two groups; Group A patients received once daily fluticasone furoate nasal spray for 8 weeks along with levocetirizine for 7 days. Group B patients received alternate day fluticasone furoate nasal spray for 8 weeks along with levocetirizine for 7 days. Symptoms were assessed and compared using TNS (Total nasal symptom) score at 8 weeks and after 4 weeks of stopping treatment i.e., 12 weeks after initiation of the study.

Results: At 8 weeks, the mean TNS score was 0.85 ± 0.86 in Group A whereas in Group B the mean TNS score was 1.40 ± 1.08. This improvement, between both groups was statistically highly significant (p=0.007) indicating lower scores i.e., better outcome in Group A. After 4 weeks of stopping treatment i.e., 12 weeks after initiation of the study, the mean TNS score was 0.3 ± 0.42 in Group A whereas in Group B the mean TNS score was 0.45 ± 0.68. This improvement, between both groups was statistically significant (p=0.039) with marginally lower scores in Group A.

Conclusion: A good subjective as well as objective outcome in terms of symptom improvement can be obtained in patients with allergic rhinitis with once daily treatment as compared to those patients who received alternate day treatment with intranasal steroids spray.

Keywords: Allergic rhinitis (AR); Fluticasone furoate (FF); Intranasal corticosteroids (INSs); Corticosteroid therapy

Introduction

Allergic rhinitis is a significant health problem. Its prevalence has been estimated to be between 15-20%. It affects a large proportion of population at all stages of life including infancy. In the past 40 years, incidence of allergic rhinitis has increased due to industrialization and urbanization, which causes increase in exposure to allergen. Pollution and irritant as well as lifestyle changes, dietary modifications responsible for diminution of protective nutrients, decrease in infection leads to reduction in Th1-type immune response and stress [1-3].

There are several treatment options available for allergic rhinitis. Allergen avoidance is the first step for all severities. However, complete allergen avoidance is not always possible and therefore, is insufficient as a sole form of therapy in most cases. Pharmacological agents available for treatment of allergic rhinitis include decongestants, sedating and non-sedating antihistamines, leukotriene receptor antagonists, and intranasal steroids (INSs). Of these medications antihistamines and intranasal corticosteroids have been the cornerstone of therapy and are the most commonly prescribed medications for treating allergic rhinitis [4].

Intranasal corticosteroids are endorsed by guidelines as the recommended first line treatment for moderate to severe cases of SAR (seasonal allergic rhinitis) and PAR (perennial allergic rhinitis). They are recognized as the most effective medication for controlling the symptoms of allergic rhinitis. They can be administered orally, by intranasal spray, intramuscularly or by intranasal injection.

The goals of corticosteroid therapy are to maximize efficacy, minimize potential systemic side effects, and improve patient adherence. Factors that will potentially improve adherence to treatment and differentiate the intranasal corticosteroids are dosing regimens, patient preference and cost effectiveness.

In this study we have used Fluticasone furoate (FF), which is the latest glucocorticoid officially approved for the treatment of allergic rhinitis. Fluticasone furoate demonstrates high lipophilicity with a remarkably fast association with the glucocorticoid receptor and a subsequently slow dissociation rate. These new pharmacologic characteristics provide the basis for its potent and prolonged anti-inflammatory activity at the target site. Fluticasone furoate presents an impressive pharmacodynamics profile compared to other new generation glucocorticoids due to which it has high affinity binding along with prolonged tissue retention and minimum systemic bioavailability. In this study the effect of the drug is being evaluated using Total Nasal Symptom Score (TNSS) to see improvement in symptoms in patients of allergic rhinitis [5].

Many patients are reluctant to use steroids on the daily basis for prolonged periods, due to concerns regarding prolonged steroid usage. In addition the cost of such medication is sometimes an issue. The aim of our study is, therefore, to explore alternate day topical steroid regimens in order to improve patient compliance and reduce overall cost of therapy [6].

Materials and Methods

Study population

Patients aged 18-60 years having clinical diagnosis on the basis of history and examination of allergic rhinitis with symptoms of at least one-year duration was included. Patients were excluded if they had nasal diseases (nasal polyps and/or deviated nasal septum) or an infectious disease (acute rhinitis, chronic rhinitis, congestive sinusitis, atrophic rhinitis, chronic rhinosinusitis, and flu-associated rhinitis) that would interfere with the evaluation of the efficacy of the drug. Subjects were also excluded if they had a systemic disease, including asthma, hypertension, and diabetes mellitus, or if they had undergone nasal surgery and immunotherapy for the purpose of treating AR. Female subjects who wanted to become pregnant or pregnant women or breast-feeding women were excluded. Subjects who were considered ineligible by the physician in charge were also excluded. The following medications were prohibited throughout the study period: steroid injections, oral steroids, or topical decongestants [7,8].

Study design and protocol

A Prospective, randomized comparative study was done at a tertiary care hospital. The study included 80 cases of symptomatic allergic rhinitis with symptoms of at least one-year duration; divided into two groups; Group A 40 patients received once daily fluticasone furoate nasal spray for 8 weeks along with levocetirizine for 7 days. Group B 40 patients received alternate day fluticasone furoate nasal spray for 8 weeks along with levocetirizine for 7 days. Symptoms were assessed using TNSS [6-8] at 8 weeks and after 4 week of stopping treatment i.e., 12 weeks after initiation of the study. Patients who completed all the visits including the follow-up are deemed to have completed the study. And the results were compared using chi square test. The study was approved by the institutional review board of our institution.

Results

At Pre-treatment time, the mean TNS score was 11.75 ± 0.84 in Group A whereas in Group B the mean TNS score was 11.23 ± 1.62. However, though the selection was randomized, there was slight difference in the scores between two group (p=0.037)

At four weeks, the mean TNS score was 6.23 ± 1.33 in Group A whereas in Group B the mean TNS score was 6.40 ± 1.58. This improvement, between both groups was statistically not significant (p= 0.297).

Condition improved further at 8 weeks. The mean TNS score was 0.85 ± 0.86 in Group A whereas in Group A the mean TNS score was 1.40 ± 1.08. This improvement, between both groups was statistically highly significant (p=0.007) indicating lower scores i.e., better outcome in Group A.

After 4 weeks of stopping treatment i.e., 12 weeks after initiation of the study; the mean TNS score was 0.3 ± 0.42 in Group A whereas in Group B the mean TNS score was 0.45 ± 0.68. This improvement, among both groups was statistically significant (p=0.039) with marginally lower scores in Group A.

Overall it is evident in Table 1 that mean score of 5 symptoms reduced within 4 weeks by nearly 50% (11.75 reduced to 6.23) followed by a further steep drop from 4 weeks to 8 weeks (6.23 reduced to 0.85). And even after 4 weeks of stopping the spray, there was further reduction in the scores (0.85 reduced to 0.23) indicating residual effect of spray.

Total nasal symptom score		Pre treatment	4 weeks	8 weeks	12 weeks
Group A	Mean	11.75	6.23	0.85	0.23
	Standard deviation	0.84	1.33	0.86	0.42
	p-value (vs. Pre-treatment)	-	0	0	0
	p-value (8 week vs. 1 month)	-	-	-	0
Group B	Mean	11.23	6.4	1.4	0.45
	Standard deviation	1.62	1.58	1.08	0.68
	p-value (vs. Pre-treatment)	-	0	0	0
	p-value (8 week vs. 1 month)	-	-	-	0
p-value (Group A vs. Group B)		0.037	0.297	0.007	0.039

Table 1: Distribution of patients with Allergic rhinitis according to total nasal symptom score.

Discussion

In 2001, Allergic Rhinitis and its impact on Asthma (ARIA) guidelines were published in cooperation with the World Health Organization, suggesting that the treatment of allergic rhinitis makes use of a combination of patient education, allergen avoidance, pharmacotherapy, and immunotherapy.

Polypharmacy is common in allergic rhinitis. Comprehensive coverage of both nasal and ocular symptoms by fluticasone furoate nasal spray could potentially reduce the need for polypharmacy relative to agents that cover only nasal symptoms. The reduced need for polypharmacy would be expected to translate into a reduction in medical costs. This hypothesis was tested in a retrospective cohort analysis of pharmacy claims data from 793,349 patients with at least one claim for fluticasone furoate, budesonide, mometasone furoate, or

triamcinolone acetonide from 1 April to 31 July 2007 [9]. At index, 62.9% of patients were using mometasone furoate, 21.1% triamcinolone acetonide, 15.1% budesonide, and 1.0% fluticasone furoate (The low rate of use of fluticasone furoate is attributed to the fact that the study period occurred just after the drug's introduction in the US in 2007). Patients treated with fluticasone furoate compared with the other intranasal corticosteroids were 21% less likely to use concomitant prescription allergic rhinitis drugs (other than intranasal corticosteroids) and incurred significantly lower costs of concomitant allergic rhinitis drugs. The authors concluded that fluticasone furoate compared with the other intranasal corticosteroids in the study reduced the need for concomitant prescription allergic rhinitis medications and led to lower costs per patient with potentially significant savings for health plans [10].

In literature various studies have been done evaluating the efficacy of intranasal steroids as a long-term treatment regime for the treatment of allergic rhinitis. Many other studies are also done in past in which comparison of different intranasal steroid has been done. No similar study in the literature is found to our best of knowledge, which compares the once daily use of intranasal steroid with alternate day use in patients of allergic rhinitis.

In our study we noticed significant improvement in TNS scoring for all the five major symptoms i.e., recurrent sneezing, watery nasal discharge, nasal obstruction, nasal itching and watering of eyes, when compared with the pre-treatment values on 4 weeks, 8 weeks and 12 weeks follow-ups (Figure 1). However, on comparison between the two groups the once daily group had significantly better results when compared to alternate day group, but the improvement in the alternate day group was also significant when compared with the pre-treatment values.

In our study we also noticed significant improvement in ocular symptom (i.e., watery discharge from eyes). The mean score of watering of eyes was is 1.72 ± 0.6 in once daily group while 1.78 ± 0.7 in alternate day group at pre-treatment which reduced to 0.28 in once daily group and 0.28 in alternate day group at 8 weeks, whereas it further reduced to 0.08 in once daily group and 0.05 in alternate day group at 12 weeks. It is evident from scientific literature that intranasal steroid reduce ocular symptoms even though they cannot reach the eye anatomically (Figure 2).

Proper management of allergic rhinitis, as with any chronic disease is determined in part by patients acceptance and adherence to their treatment regimen, therefore patient's self-reported willingness to comply with nasal spray therapy is strongly affected by several factors, including efficacy, safety, ease of use, comfort during administration, and sensory attributes such as the smell, taste, and aftertaste of a nasal spray [8-11].

Compliance rates with fluticasone furoate nasal spray have not been systematically assessed in clinical practice, nor have compliance rates with fluticasone furoate nasal spray been directly compared with those of other intranasal corticosteroids. Future research comparing compliance with fluticasone furoate with that of other intranasal corticosteroids is warranted in light of the putative compliance-enhancing properties of fluticasone furoate.

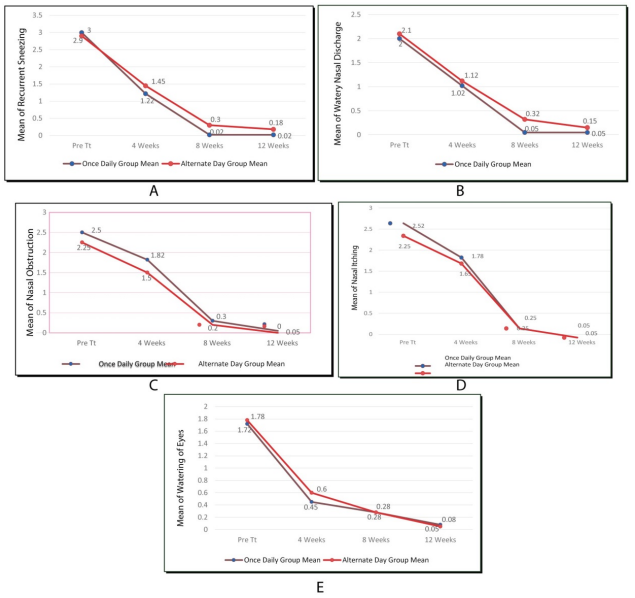

Figure 1: Comparison of outcomes of various symptoms between the two groups. A shows recurrent sneezing, B shows watery nasal discharge, C shows nasal obstruction, D shows nasal itching and E shows watering of eyes.

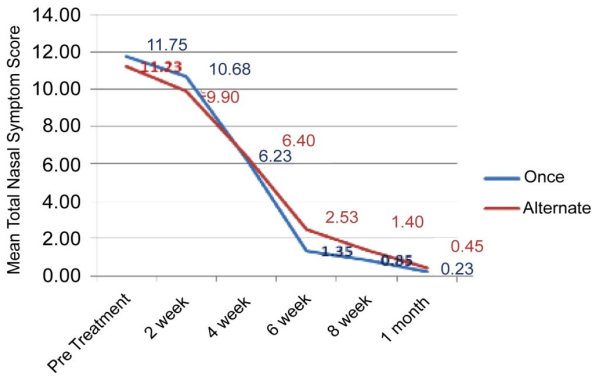

Figure 2: Mean change from baseline in TNS score (once daily vs. alternate day) in patients with allergic rhinitis according to total nasal symptom score.

The common adverse effects in our study were headache in 3 patients and epistaxis in 2 patients. No patient discontinued because of either adverse events or lack of efficacy. The adverse effects most commonly experienced with the use of intranasal corticosteroids are headache, throat irritation, epistaxis, stinging, burning, and nasal dryness. Although the use of intranasal corticosteroids has raised concern for potential systemic adverse effects, including the suppression of the hypothalamic-pituitary axis [12], the products currently available have not been shown to have such effects.

Lesser number of subjective and objective outcome measures and a short follow up period of three months were some limitations of our study. Other dosage schemes and different treatment periods with a

longer follow-up time have to be evaluated to further define the role of long term intranasal steroid in the treatment of allergic rhinitis.

Conclusions

Our observations suggest that a good subjective as well as objective outcome in terms of symptom improvement can be obtained in patients with allergic rhinitis with once daily treatment as compared to those patients who received alternate day treatment with intranasal steroids spray. We advocate that patients suffering from allergic rhinitis should be initially treated with once daily intranasal steroid spray therapy followed by alternate day intranasal steroid regime for maintenance. Further studies for evaluation of usefulness of intranasal steroids are recommended. Other dosage schemes and different treatment periods with a longer follow-up period have to be evaluated to further define the role of long term intranasal steroids in the treatment for allergic rhinitis.

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