

A comparison of triamcinolone acetonide nasal aerosol spray and fluticasone propionate aqueous solution spray in the treatment of spring allergic rhinitis

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Background: Many nasal corticosteroids with different potencies and formulations are available, but they have all been proven safe and effective. The clinical relevance, if any, of these differences is not yet completely established.

Objective: We sought to compare the efficacy, safety, and patients' acceptance of triamcinolone acetonide aerosol spray and fluticasone propionate aqueous solution in the treatment of spring allergic rhinitis.

Methods: After a drug-free baseline evaluation, patients with rhinitis were randomized to receive either a triamcinolone aerosol spray of 110 µg in each nostril once daily ($n = 117$) or a fluticasone solution spray of 100 µg in each nostril once daily ($n = 116$) in a single-blind, parallel-group study. The Rhinitis Index Score (sum of scores of symptoms on a scale from 0 to 3) was evaluated daily, in the morning before drug administration, for 21 days. The efficacy of each treatment was assessed by the mean reduction from baseline in the Rhinitis Index Score and in individual symptom scores. Patients' acceptance of the study drugs was also monitored by a daily questionnaire.

Results: Reductions of the Rhinitis Index Score (mean $\pm$ SEM) were 4.20 ± 0.21 and 4.60 ± 0.21 for triamcinolone and fluticasone, respectively ($p = 0.23$). There were no statistically significant differences between the drugs in the reduction of any of the individual symptoms. Patients expressed statistically significant differences between the drugs regarding acceptance; different properties of the aerosol and the solution were appreciated differently.

Conclusions: This study shows that triamcinolone acetonide aerosol and fluticasone propionate solution sprays are both

clinically equally effective, safe, and well tolerated for the treatment of spring pollen allergic rhinitis. (*J Allergy Clin Immunol* 1997;100:592-5.)

Key words: Triamcinolone acetonide, fluticasone propionate, aerosol, solution, rhinitis, seasonal, spring

Intranasal corticosteroid preparations are highly effective and safe drugs for the treatment of seasonal and perennial allergic rhinitis.¹ They relieve the symptoms of allergic rhinitis by their antiinflammatory actions, which include vasoconstriction, suppression of membrane permeability, and dampening of the immune response.²

There are at least five topical corticosteroids available for intranasal use. They do not all share the same potency or the same formulation, although they have all been proven clinically effective and safe. The rationale for choosing the potency and the formulation of a steroid is therefore not clear.

The triamcinolone acetonide metered-dose aerosol unit is a once-daily intranasal corticosteroid preparation for the treatment of seasonal and perennial allergic rhinitis.³ The most commonly encountered adverse events of this treatment are headache and upper respiratory tract infection.⁴ At therapeutic doses (440 µg/day) for 6 weeks, triamcinolone acetonide showed no measurable effect on hypothalamic-pituitary-adrenal axis function.⁵ A study has shown that 41% of patients allergic to ragweed had a clinically and statistically significant reduction in nasal congestion greater than that found in placebo-treated patients as early as 10 hours after the first dose of once-daily triamcinolone acetonide.⁶

Fluticasone propionate aqueous solution spray is also indicated for the once-daily treatment of seasonal and perennial allergic rhinitis. The most commonly reported side effects from clinical trials include nasal burning and epistaxis.⁷ No hypothalamic-pituitary-adrenal axis suppression was observed after doses of up to 1600 µg per day of intranasal fluticasone.⁸

The purpose of this study was to compare the safety,

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Abbreviation used

RIS: Rhinitis Index Score

efficacy, and patient acceptance of two different nasal steroids, triamcinolone acetonide aerosol and fluticasone propionate solution, as once-daily treatments for the relief of symptoms in patients with spring pollen allergic rhinitis.

METHODS

This was a single-blind, randomized, two-parallel-group, multicenter study approved by local Ethics Review Boards. Male and female patients (age, 12 to 70 years) who had a diagnosis of spring pollen allergic rhinitis for at least 2 years but were otherwise healthy; who had a positive skin prick test response to one or more spring pollen allergens; and who were first seen with at least two nasal symptoms including rhinorrhea, congestion, sneezing, and itching at baseline were included after they had signed an informed consent form.

Women who were pregnant or of childbearing potential and not practicing an approved method of birth control were excluded from the study. In addition, patients meeting at least one of the following criteria were not allowed to participate: a clinically significant renal, hepatic, cardiac, respiratory (including asthma), neurologic, collagen-vascular, or psychiatric disease; cancer; untreated fungal, bacterial, or viral infections; nasal septal ulcers or perforation; nasal surgery or trauma; physical nasal obstruction greater than 50%; a history of habitual abuse of nasal decongestants; use of any systemic, nasal, or inhaled corticosteroid within 30 days of the screening visit; use of nasal sodium cromoglycate, anticholinergics, vasoconstrictors, or antihistamines (except astemizole) within 7 days of the screening visit; use of astemizole within 60 days of the screening visit; use of topical, oral, or both types of decongestants more than three times per week for the previous 3 months (90 days); use of cardiovascular drugs, hormones, neuroleptics, or any other drugs that can cause, suppress, or exacerbate the symptoms of allergic rhinitis; immunotherapy unless on a maintenance regimen at the time of screening; history of hypersensitivity or nonresponse to corticosteroids; and participation in another investigational study within 30 days of the screening visit.

Four visits were scheduled. At the screening visit (days -14 to -5), potential candidates were evaluated by the investigator according to the inclusion and exclusion criteria. From this visit on, the patients were drug-free and recorded their rhinitis symptoms daily in the morning. They used the following rating system: 0 = none, symptoms absent; 1 = mild, symptoms present but not annoying; 2 = moderate, symptoms present and annoying but do not interfere with sleep or daily living; 3 = severe, symptoms interfere with or patient is unable to carry out activities of daily living or is unable to sleep. To qualify for randomization, each patient had to have a Rhinitis Index Score (RIS) (sum of rhinorrhea, nasal congestion, sneezing, and itching) of at least 24 points (out of a possible maximum of 48) for the four highest scores of the last 5 mornings of the drug-free baseline evaluation period. This evaluation was defined as the baseline value for the RIS and individual symptoms score. Any patient who failed to reach the inclusion limit of 24 points within 14 days after the beginning of the drug-free

baseline evaluation was discontinued from the study. The patients were not aware of this inclusion threshold value.

Patients also completed, throughout the study, a daily questionnaire on 10 aspects of acceptance of the medication on a scale from 0 (not bothersome) to 4 (extremely bothersome). The daily total score was computed for each parameter by adding all scores given by the patients, and the mean over the 21 days of active treatment was estimated.

When patients met the score of 24 or more, they came to the site for the baseline visit (day 1). They were randomized to receive either triamcinolone acetonide nasal aerosol sprays (Nasacort nasal aerosol; Rhône-Poulenc Rorer Inc., Canada) of 110 µg (2 actuations of 55 µg each) in each nostril once daily in the morning or a fluticasone propionate spray (Flonase, Glaxo-Wellcome, Canada) of 100 µg (2 actuations of 50 µg each) in each nostril once daily in the morning. The drugs were dispensed by an independent collaborator, and the assessing investigators were not aware of the type of medication received by the patients. The patients continued to record their symptoms each morning before the use of the study drugs.

Patients also came to the site for two more visits after 1 week and 3 weeks of treatment, respectively. The patients' and the investigators' opinions on the global evaluation of treatment efficacy were recorded at each of these visits. Each global evaluation assessed treatment effectiveness relative to the highest 4 of 5 symptomatic days of the drug-free baseline period. Both the physicians and the patients recorded their perceptions according to the following rating scale: 0 = no effect of the medication on allergic rhinitis symptoms or impairment of symptoms; 1 = some allergic rhinitis symptoms have been improved but the overall discomfort has remained unchanged; 2 = allergic rhinitis symptoms and the overall discomfort have been reduced; and 3 = allergic rhinitis symptoms and the overall discomfort have been greatly reduced.

To document their compliance with the study medication, each patient recorded the total number of sprays used each day on a diary card. A compliance lower than 85%, or missing 3 consecutive days in a row of medication, was previously classified as a major violation, and these patients were excluded from the efficacy analysis.

All nonsteroidal medications required by the patient to manage acute or chronic illness unrelated to rhinitis were permitted, except for medications that would interfere with the assessment of the study drugs. Steroids were not permitted, except for oral contraceptives and estrogen replacement therapy.

Primary efficacy variables were the changes from baseline in the mean RIS and the changes from baseline in the mean scores of each of the four individual rhinitis symptoms. The mean RIS was determined by summing the daily scores for each individual symptom and then calculating the mean. Secondary efficacy variables were the physicians' and patients' global evaluations and the patients' acceptance of the study medications.

All comparisons of the treatment groups for efficacy were two-sided at the 0.05 level of significance and were done by analysis of variance for parallel groups including center, treatment, and center-by-treatment interaction effects. Comparisons for physicians' and patients' global evaluations made between treatments were performed with the chi-square test. All comparisons of the treatment groups for patients' acceptance were one-sided at the 0.05 level of significance and were done by analysis of variance as described above.

Safety was monitored by recording the adverse events spontaneously reported by the patients.

TABLE I. Characteristics at baseline

Parameters	Triamcinolone	Fluticasone
No. of patients evaluated for safety	117	116
Gender		
Women	57	64
Men	60	52
Mean $\pm$ SEM age (yr)	28.5 $\pm$ 1.1	28.7 $\pm$ 1.1
Mean $\pm$ SEM duration of allergy (mo)	164.1 $\pm$ 10.3	160.4 $\pm$ 10.0
No. of patients evaluated for efficacy	111	112
Mean $\pm$ SEM RIS*	7.66 $\pm$ 0.14	7.69 $\pm$ 0.14
Mean $\pm$ SEM congestion score†	2.16 $\pm$ 0.05	2.14 $\pm$ 0.06
Mean $\pm$ SEM rhinorrhea score†	1.88 $\pm$ 0.06	2.00 $\pm$ 0.06
Mean $\pm$ SEM sneezing score†	1.81 $\pm$ 0.07	1.78 $\pm$ 0.05
Mean $\pm$ SEM nasal itch score†	1.80 $\pm$ 0.06	1.76 $\pm$ 0.06

*Sum of individual symptoms.

†On a scale from 0 (absent) to 3 (severe).

TABLE II. Mean $\pm$ SEM (%) changes from baseline over the 3 weeks of treatment

Parameter	Triamcinolone (%)	Fluticasone (%)	p Value
Rhinitis index	-4.20 $\pm$ 0.21 (-55)	-4.60 $\pm$ 0.21 (-60)	0.23
Congestion	-1.06 $\pm$ 0.07 (-49)	-1.19 $\pm$ 0.07 (-56)	0.58
Rhinorrhea	-1.10 $\pm$ 0.07 (-59)	-1.24 $\pm$ 0.07 (-62)	0.08
Sneezing	-1.05 $\pm$ 0.08 (-58)	-1.09 $\pm$ 0.06 (-61)	0.51
Nasal itch	-0.99 $\pm$ 0.06 (-55)	-1.07 $\pm$ 0.06 (-61)	0.64

TABLE III. Mean $\pm$ SEM sum of total daily scores for patients' acceptance*

Parameters	Triamcinolone	Fluticasone	p Value
Medication runs down throat	0.70 $\pm$ 0.18	6.77 $\pm$ 1.09	<0.01
Medication runs out of nose	1.19 $\pm$ 0.28	6.26 $\pm$ 0.88	<0.01
Medication tastes bad	2.84 $\pm$ 0.75	5.33 $\pm$ 1.10	NS
Medication causes sore throat	1.36 $\pm$ 0.50	0.77 $\pm$ 0.37	NS
Medication causes bleeding nose	0.37 $\pm$ 0.16	0.14 $\pm$ 0.09	NS
Medication causes dry nostril	4.88 $\pm$ 0.92	2.15 $\pm$ 0.055	<0.01
Medication causes bloody mucus	0.86 $\pm$ 0.29	0.65 $\pm$ 0.19	NS
Medication causes stuffed-up nose	10.67 $\pm$ 1.37	5.31 $\pm$ 0.83	<0.01

NS, Not significant.

*Evaluated on a scale from 0 (not bothersome) to 4 (extremely bothersome) by each patient.

RESULTS

A total of 233 patients were randomized to treatment, and each treatment was evaluated for safety. Ten were excluded from efficacy analysis for the following reasons: four for lack of minimum compliance with study drug intake, three for taking forbidden medication, one for faulty baseline evaluation, one for voluntary withdrawal, and one for an adverse event. Thus a total of 223 patients were able to be evaluated for efficacy. Table I presents the baseline characteristics of the patients. The two treatment groups were not statistically different for any of the parameters at baseline.

Mean changes from baseline in RIS and in individual symptoms over the 3 weeks of treatment are presented in Table II. Triamcinolone and fluticasone did not yield any statistically significant difference in the reduction of the RIS or of any individual symptoms scores. The

statistical powers to detect the observed differences, with an alpha value of 0.05, were calculated and found to be 0.915 for the RIS and greater than 0.99 for each individual symptom. There was no statistically significant difference between the two treatments in the physicians' and patients' overall evaluation.

The results of patients' acceptance of the study medication are presented in Table III, which shows differences between triamcinolone acetate aerosol sprays and fluticasone aqueous solution sprays for thixotropic properties, nostril dryness, and nose stuffiness.

Thirty-one (26%) of the patients receiving triamcinolone and 25 (22%) of the patients receiving fluticasone experienced a total of 44 and 40 adverse events, respectively, regardless of the relationship with the study medication. Adverse events considered drug-related and reported by more than 2% of patients were headache,

with an incidence of 5% and 9%, and epistaxis, with an incidence of 3% and 4%, in the triamcinolone and fluticasone groups, respectively.

Only one patient, receiving triamcinolone, was prematurely withdrawn from the study, after 7 days of treatment, because of a severe headache.

DISCUSSION

The only statistically significant differences between the two treatments were found in the patients' acceptance of the drugs, and these differences were anticipated in view of the different formulations used.

Actually, the thixotropic properties of the formulation of triamcinolone are made evident by the lower score given by the patients in relation to the medication running down the throat or out of the nose. On the other hand, the irritating properties of the aerosol spray on the mucosa may explain the higher score of triamcinolone on the parameters of dry nostrils and stuffed-up nose. The availability of an aqueous formulation of triamcinolone, sharing the same thixotropic properties as the aerosol spray, is likely to provide the advantages of the aerosol spray without the irritating effect on the mucosa. There may then be a place for both aqueous and aerosol formulations.

Regarding clinical efficacy, both drugs produced an appreciable reduction of the RIS and individual symptom scores without being statistically different. The biggest difference observed between the two drugs was a 7% difference in the individual symptom score for nasal congestion. A difference of this magnitude is not likely to be clinically significant. Although there is a trend for fluticasone to produce slightly greater reductions in

nasal congestion, the clinical significance of this finding is questionable, especially if sample sizes of more than 115 patients per group did not produce statistically significant differences with a power greater than 0.90.

In conclusion, this study shows that triamcinolone acetate and fluticasone propionate are equally effective and well-tolerated topical nasal corticosteroids for the treatment of spring pollen allergic rhinitis. The availability of a thixotropic aqueous preparation of triamcinolone acetate is likely to further improve the acceptability of this drug.

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