

Comparative Trial of Flunisolide and Beclomethasone Dipropionate Nasal Sprays in Patients with Seasonal Allergic Rhinitis

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In order to evaluate the effects of flunisolide and beclomethasone dipropionate nasal sprays on seasonal allergic rhinitis, 45 patients were included in an open parallel comparative trial. The study design was open because of the different dosage schedules for the two preparations. Strict criteria were set up for patient selection, and all patients were carefully examined and assessed before and after the 4-week trial period. Throughout the whole treatment each patient kept a detailed daily record. A substantial or complete control of symptoms was achieved in 18 of the 21 patients on flunisolide and in 20 of the 22 on beclomethasone dipropionate. No serious side effects were observed. Thus it can be concluded that both test drugs are effective and well tolerated in the treatment of seasonal allergic rhinitis.

Key words: allergic rhinitis; nasal sprays; therapy.

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Treatment of seasonal allergic rhinitis with antihistamines and decongestants is often unsatisfactory. Antihistamines frequently cause somnolence, which is inconvenient for the patients. The use of decongestant nose drops may lead to rhinitis medicamentosa. Corticosteroids have long been known to be highly effective in allergic rhinitis. Even though allergic rhinitis is an unpleasant condition for the patient it is seldom disabling, and the severe systemic side effects of injected and oral corticosteroids therefore preclude any widespread use. When used topically, the corticosteroids may achieve the same therapeutic effect with small doses and therefore with a reduced risk of untoward systemic effects. The classical corticosteroids, however, still seem to be sufficiently absorbed from the mucosa and the gastrointestinal tract to give rise to dose-dependent pituitary-adrenal suppression (4).

It has been demonstrated that beclomethasone dipropionate applied intranasally has a

marked effect on the nasal symptoms of seasonal allergic rhinitis (3, 7). It has a powerful anti-inflammatory effect (6) and its action is considered to be local.

Like beclomethasone dipropionate, flunisolide is rapidly metabolized, presumably in its first passage through the liver, and has a relatively short half-life (8). In earlier studies (1, 9, 10, 11, 12) flunisolide has been shown to control nasal symptoms in both perennial and seasonal rhinitis significantly better than placebo and more efficiently than disodium cromoglycate in seasonal rhinitis (2).

In contrast to beclomethasone dipropionate, which is propelled by freons, flunisolide is formulated as a mildly viscous, aqueous solution and is administered by means of a pump spray device.

The purpose of this study was to assess the efficacy and tolerance of flunisolide in patients with seasonal rhinitis as compared with beclomethasone dipropionate.

MATERIAL AND METHODS

A total of 45 patients were entered into the trial, 22 on flunisolide and 23 on beclomethasone dipropionate. Two patients stopped the treatment prematurely, one because of headaches (flunisolide group) and one because of pharyngeal infection (beclomethasone dipropionate group). The patients were allocated to treatment groups according to a computer-generated randomization list. The remaining patient material comprised 43 patients, 17 women and 26 men. The mean age of the flunisolide group was 22.7 (SD 7.0) years and that of the beclomethasone dipropionate group 22.3 (SD 8.9) years. The flunisolide group had a mean disease duration of 10.0 (SD 7.2) years and the beclomethasone dipropionate group 11.1 (SD 9.6) years. Neither the distribution of age, sex and disease duration nor the incidence of other allergic diseases or allergy in the family indicated any significant differences between the two treatment groups. The two groups were also well matched for severity of eye and throat symptoms, sneezing, stuffiness and runny nose during the season prior to the study, and also in regard to eosinophils, mast cells and goblet cells in nasal smear at baseline.

To be enrolled into the trial, the patients had to meet the following criteria: 1) manifest al-

lergic rhinitis verified by a positive skin test and/or provocation test (allergens: timothy, alopecurus, Kentucky Blue, Meadow Fescue, which are the most troublesome allergens during July, 2) seasonal symptoms for at least 2 years, 3) no systemic disease, respiratory infections, nasal polyps, septum deviations or previous nasal or sinus surgery.

A run-in week was started on June 24, 1979. Medication was started on July 1 and ended on July 28. The grass pollen counts in Oulu for this period are presented in Fig. 1. The maximum grass pollen counts were observed during July 9–19. Each patient kept a detailed daily record of the symptoms and of the medication used. Every day during the trial, the following symptoms were recorded: runny nose, stuffiness, sneezing, and allergic eye symptoms. The severity of the symptoms was evaluated as follows: 0 = absent, 1 = mild, 2 = moderate, 3 = severe. The overall symptoms were compared with those of the previous season.

The medication consisted of either of the following:

Flunisolide. An aqueous 0.025% solution of flunisolide containing propylene glycol and polyethylene glycol was used in this study. The flunisolide solution was delivered to the nasal membrane by a metered pump spray device. After priming, this unit delivers approximately 25 µg flunisolide per spray. The treatment

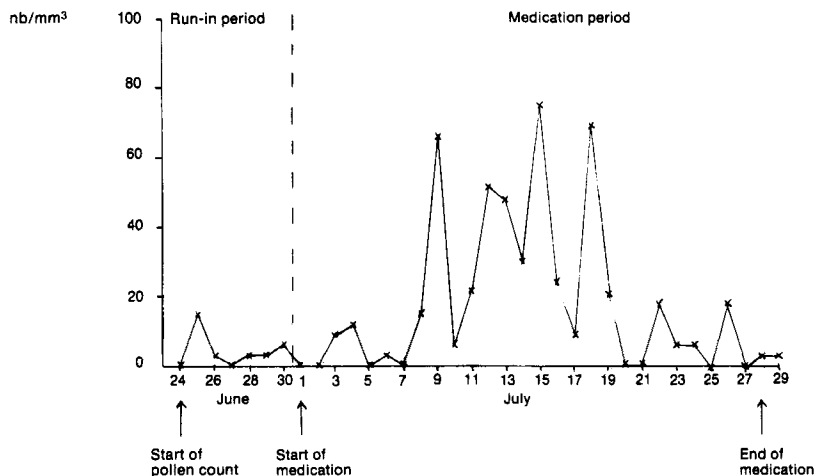


Fig. 1. Occurrence of grass pollen in Oulu during the study period.

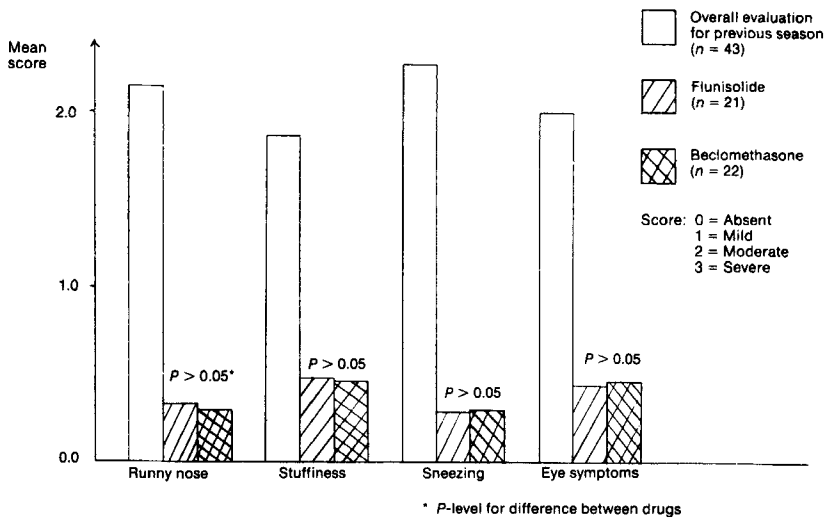


Fig. 2. Mean daily symptom score during 4 weeks of treatment.

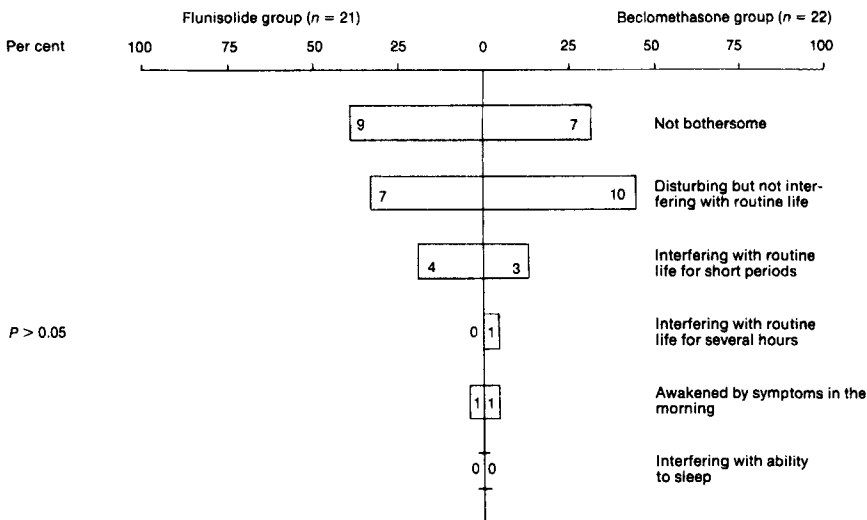


Fig. 3. Severity of nasal symptoms during treatment.

consisted of two sprays of the test drug into each nostril twice a day (a total of 8 sprays per day). This schedule provides approximately 200 µg flunisolide per day.

Beclomethasone dipropionate. A commercial preparation Becotide Nasal® (Glaxo) was used in this study. Each dose contains 50 µg beclomethasone dipropionate, oleic acid, trichloro-

fluoromethane and dichlorofluoromethane. The treatment consisted of one spray into each nostril four times a day (a total of 8 sprays per day). This schedule provides approximately 400 µg beclomethasone dipropionate per day.

As the assessment of the two drugs was based mainly on the patients' diary cards and as the patients were not aware of the efficacy of the

compared drug, a double-blind trial was considered to be unnecessary.

The patients were allowed to take antihistamine during the trial (Lunerin®, Draco). The number of tablets used was recorded.

The statistical analyses were carried out using analysis of variance, Student's *t*-test, the Mann-Whitney *U*-test, Wilcoxon's matched-pairs signed-ranks test and the Chi-square test.

RESULTS

The results in the two treatment groups were practically similar. The mean daily score was below 0.5 on a scale of 0–3 for all symptoms: runny nose, stuffiness, sneezing, and eye symptoms in the two treatment groups during the 4 weeks of treatment (Fig. 2). During the previous season the patients had estimated the intensity of their symptoms to be approximately 2 on an average, using the same scale.

An analysis of variance of the daily ratings of individual symptoms revealed no overall differences in symptom severity between the two treatment groups. However, the severity of sneezing, runny nose and eye symptoms varied over time. When this variance was partitioned by orthogonal contrasts, only sneezing showed a significant linear decrease. The nasal symptoms interfered with daily life during the test period in five patients in each of the two treatment groups, but no patient stated that the symptoms had interfered with his ability to sleep (Fig. 3).

A substantial or complete control of symptoms was achieved in 18 of the 21 patients on flunisolide and in 20 of the 22 on beclomethasone dipropionate. All but three patients in each of the treatment groups stated that their nasal symptoms had been less bothersome during the test period compared with the corresponding period in the previous season. In each of the treatment groups two cases were considered therapeutic failures by the investigator. Only three patients in the flunisolide group and one in the beclomethasone dipropionate group considered the nasal spray they had tried was not worth using the following season. Thus no significant difference was seen between the treat-

ment groups with regard to therapeutic outcome as evaluated by both the investigator and the patient.

Nasal smear was positive for mast cells in 24%, for eosinophils in 29% and for goblet cells in 95% of the patients after treatment. Compared with baseline the mean cell scores were reduced by between one fourth and one fifth. No significant difference was seen between the two groups.

During the trial the mean number of antihistamine tablets taken was 5.5 in the flunisolide group and 6.7 in the beclomethasone dipropionate group. The difference was not statistically significant.

Nasal side effects, mainly mild to moderate irritation of the nasal mucosa which was possibly related to the treatment with the test drugs, were observed in three patients in each treatment group. Sore throat also occurred in three patients receiving beclomethasone dipropionate treatment. Treatment was discontinued in one patient in the flunisolide group because of headache and in one patient in the beclomethasone dipropionate group because of pharyngeal infection.

DISCUSSION

All patients in this study had repeatedly manifested clinical symptoms of allergy, including rhinitis, during the grass pollen season. Allergy against grass pollen was also verified by skin tests and/or provocation tests. All patients had required medical treatment for their symptoms during the previous seasons.

The overall evaluation showed that the two treatments, beclomethasone dipropionate 400 µg/day and flunisolide 200 µg/day, had an equally good effect on the nasal symptoms. Only three patients in each group stated that their symptoms were much the same as during the previous season.

Good effect was noted in all nasal symptoms (runny nose, stuffiness and sneezing) and even eye symptoms. No differences were observed between the two groups concerning the control of these symptoms.

The side effects noted were slight, consisting, primarily, of local irritation. As it has also been shown that neither of these drugs affects the plasma cortisol level in the dosage used (5, 8), it can be concluded that both are effective and well tolerated in the treatment of seasonal rhinitis.

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