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One-dose beclomethasone dipropionate aerosol in the treatment of seasonal allergic rhinitis. A preliminary report

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SUMMARY

Forty-one patients were treated during the birch pollen season for three weeks in a randomized, double-blind placebo controlled preliminary study. Ten patients were treated with beclomethasone dipropionate aerosol 400 µg once daily, 10 patients with placebo once daily, 10 patients with 400 µg beclomethasone dipropionate in the morning and placebo in the evening and 11 patients with 200 µg beclomethasone twice daily. The severity of the nasal symptoms was compared before the trial, during the pollen season without treatment, at the time of peak pollen counts and at the end of the treatment. Symptoms were equally controlled by beclomethasone dipropionate 400 µg once daily (two puffs of 100 µg per nostril), and 200 µg twice daily (two puffs of 50 µg per nostril twice). All active drug regimens were better than placebo. In conclusion, this study shows that one-dose beclomethasone dipropionate of 400 µg is effective in the treatment of seasonal allergic rhinitis.

INTRODUCTION

Beclomethasone dipropionate intranasal aerosol at a daily dose of 400 µg is widely used for the treatment of seasonal and perennial allergic rhinitis. In their open study in 1981 Munch et al. reported no differences in the efficacy of beclomethasone dipropionate when administered 100 µg four times or 200 µg twice daily in the treatment of hay fever. In the placebo controlled randomized study by Nuutinen et al. (1983) it was also confirmed that seasonal allergic rhinitis is treated as effectively by two-dose drug regimen than four-dose regimen. It is generally accepted that the fewer the drug administrations the fewer the irritative side-effects and the better the patient's compliance. We have compared a one-dose and a two-dose administration of intranasal beclomethasone dipropionate at

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a daily dosage of 400 µg in allergic rhinitis due to birch pollen in a placebo controlled randomized multicenter study.

MATERIALS AND METHODS

Patients

Forty-one adult patients (23 females and 18 males), who gave their informed consent, entered the study. The trial plan was accepted by the Ethical Committee of Kuopio University Central Hospital. The age of the patients ranged from 16 to 66 years with a mean age of 31.6 years. There were no statistically significant differences in the age, sex, height and weight between the treatment groups. All patients had had nasal symtoms requiring drug therapy at least for two pollen seasons but none of them had received immunotherapy during the last two years. All had a positive skin test to birch pollen. Patients with bronchial asthma, nasal polyposis, atrophic rhinitis, and chronic sinusitis were excluded. Patients did not use any antiallergic medication.

Design of the study

The rhinoscopic findings (mucosal swelling and nasal secretion) were recorded before the pollen season. The basic symptoms were recorded for five days before the pollen season and the records of the last two days were used for statistical analyses. Sneezing, nasal discharge, nasal blockage and nasal itching were recorded using a scale from 0 to 3 (0 = no symptoms; 1 = light symptoms; 2 = moderate symptoms; 3 = severe symptoms).

The patients were randomly divided into four groups; Group 1 (10 patients) = active drug 400 µg once daily (2 puffs of 100 µg per nostril at 7.00–9.00 a.m.); Group 2 (10 patients) = placebo once daily (two puffs of placebo aerosol per nostril at 7.00–9.00 a.m.); Group 3 (11 patients) = active drug 200 µg twice daily (two puffs of 50 µg per nostril at 7.00–9.00 a.m. and 7.00–9.00 p.m.); Group 4 (10 patients) = active drug 400 µg in the morning (two puffs of 100 µg per nostril at 7.00–9.00 a.m.) and placebo in the evening (two puffs of placebo aerosol at 7.00–9.00 p.m.). The patients were allowed to use antihistamine tablets (Phenylephrin. tannas 25 mg, Chlorpheniramin. tannas 6 mg, Mepyramin. tannas 37.5 mg) and the use of the tablets was recorded daily.

When the birch pollen concentration reached the amount of 10 grains/m^3, the symptoms were recorded for two days without medication (days 6–7), after which the treatment with intranasal aerosol was started. In the middle and at the end of the study (days 17 and 28) the patients were examined by the same doctor as before the pollen season. Nasal secretion and nasal mucosal swelling were evaluated using a scale from 0 to 2 (0 = nil, 1 = slight, 2 = pronounced). In the statistical analysis the Kruskal-Wallis one-way analysis of variance, the Mann-Whitney U test, Friedman two-way analysis of variance and Wilcoxon signed-rank test were used.

RESULTS

No statistically significant differences were found in the symptoms or in the use of antihistamine tablets during the preseasonal pretreatment period. No statistically significant differences were found in the birch pollen concentrations between the treatment groups in the two centres. The symptoms and the use of antihistamine tablets were calculated for two days before the pollen season without medication (days 4–5), for the days 6–7 during the pollen season without medication, and for the days 15–18, 21–24 and 27–28 with medication. Maximum nasal symptoms appeared during the days 6–7 in all treatment groups. There were no statistically significant differences in the symptoms between the treatment groups during the days 6–7 (Table 1).

The mean of the nasal symptoms (nasal discharge, blockage, itching and sneezing) reduced significantly in the Groups 1 and 4 ($p < 0.05$ and $p < 0.01$, Friedman's test) during the treatment compared to the days 6–7 (Figure 1). The reduction of the symptoms compared to the seasonal pretreatment period was most

Table 1. Nasal symptom scores, mean ± SD.

symptom	day	active 400 µg x 1	placebo x 1	active 200 µg x 2	active 400 µg x 1 + placebo x 1
nasal discharge	4– 5	0.50 ± 0.58	0.45 ± 0.55	0.36 ± 0.67	0.40 ± 0.57
	6– 7	1.10 ± 0.77	0.80 ± 0.63	0.91 ± 0.66	0.95 ± 0.55
	15–18	0.52 ± 0.62*	0.48 ± 0.32	0.59 ± 0.60	0.65 ± 0.70
	21–24	0.67 ± 0.62	1.38 ± 1.15	0.64 ± 0.76	0.67 ± 0.59
	27–28	0.45 ± 0.55	0.85 ± 1.20	0.45 ± 0.47	0.39 ± 0.70
blockage	4– 5	0.50 ± 0.47	0.55 ± 0.50	0.91 ± 0.54	0.90 ± 0.57
	6– 7	1.25 ± 0.89	1.15 ± 0.67	1.09 ± 1.02	1.20 ± 0.75
	15–18	0.60 ± 0.52*	0.65 ± 0.67*	0.73 ± 0.43	0.75 ± 0.79
	21–24	0.58 ± 0.64*	1.10 ± 0.87	0.91 ± 0.63	0.65 ± 0.70
	27–28	0.65 ± 0.47	1.05 ± 0.96	0.50 ± 0.59	0.50 ± 0.79
itching	4– 5	0.15 ± 0.34	0.35 ± 0.41	0.59 ± 0.58	0.30 ± 0.35
	6– 7	1.10 ± 0.88	0.65 ± 0.63	0.77 ± 0.65	0.85 ± 0.53
	15–18	0.43 ± 0.62**	0.22 ± 0.42	0.30 ± 0.51	0.48 ± 0.46
	21–24	0.58 ± 0.72	0.73 ± 0.97	0.30 ± 0.53	0.45 ± 0.50
	27–28	0.35 ± 0.58*	0.70 ± 1.16	0.23 ± 0.52*	0.22 ± 0.44*
sneezing	4– 5	0.55 ± 0.50	0.70 ± 0.67	0.50 ± 0.74	0.40 ± 0.46
	6– 7	1.05 ± 0.86	1.20 ± 0.63	0.95 ± 0.76	0.90 ± 0.46
	15–18	0.48 ± 0.57	0.67 ± 0.61*	0.59 ± 0.59	0.40 ± 0.53
	21–24	0.58 ± 0.68	1.58 ± 0.96	0.64 ± 0.92	0.50 ± 0.42
	27–28	0.30 ± 0.42*	1.10 ± 1.13	0.50 ± 0.74	0.17 ± 0.35*

* $p < 0.05$, ** $p < 0.01$ compared with the 6–7th days' values (Wilcoxon's test)

pronounced in the 400 µg once daily group (Table 1). Studying individual symptoms, there was also a marked decrease during the treatment in the group treated with active drug twice daily. However, the difference was, apparently due to small number of patients, statistically significant ($p<0.05$) only in the relief of itching. The symptom scores during the treatment were compared to the pretreatment period within each treatment group. So, each numeric symptom score is not comparable between the treatment groups during the treatment. We are of the opinion, that this calculation should be done, at least in all non-crossover studies, to eliminate interpersonal variation in the nasal symptoms.

There were no statistically significant differences in the use of antihistamine tablets between the active groups. In the placebo group the use of antihistamines increased significantly ($p<0.05$, Friedman's test) during the treatment. In the placebo group nasal blockage and sneezing decreased slightly ($p<0.05$,

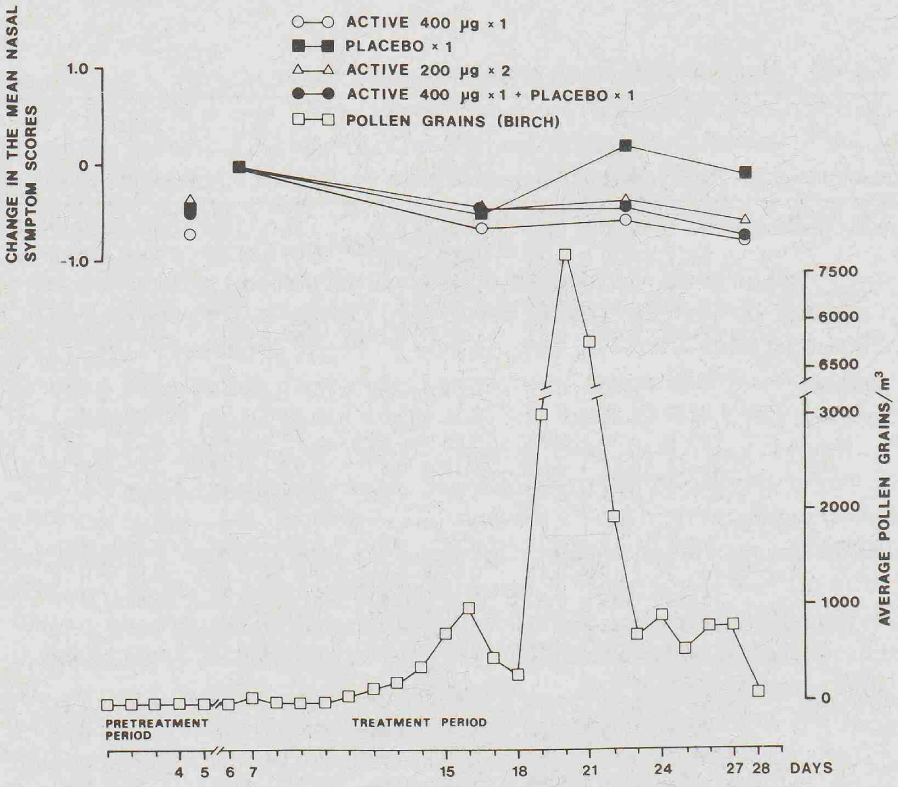

Figure 1. The mean of the nasal symptoms and the average of pollen grains during the study.

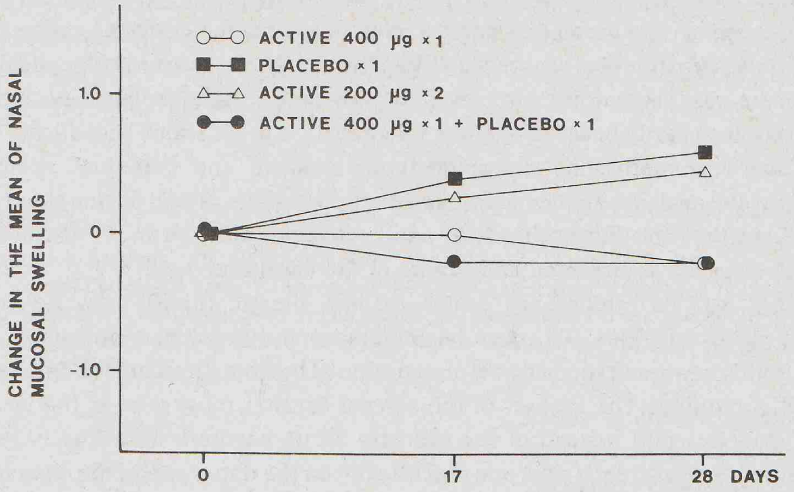

Figure 2. Change in the mean of nasal mucosal swelling evaluated in rhinoscopy.

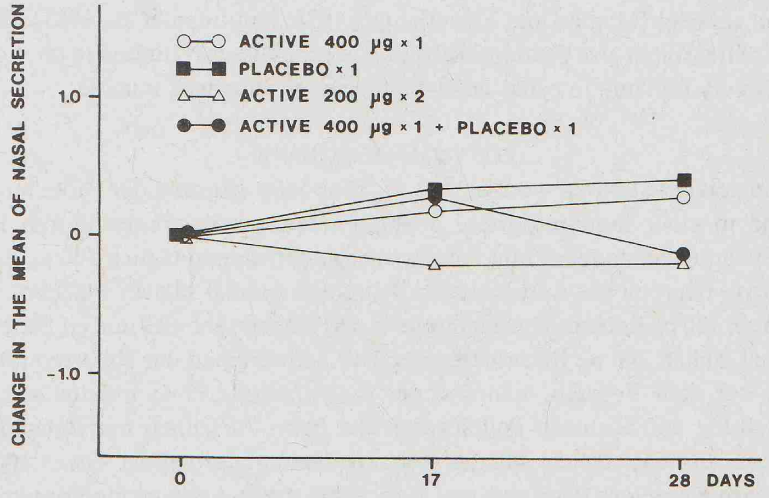

Figure 3. Change in the mean of nasal secretion evaluated in rhinoscopy.

Wilcoxon's test) between the days 6–7 and 15–18. However, the use of antihistamine tablets was most prominent in the placebo group during the days 15–18. Change from the preseasonal evaluation in nasal mucosal swelling and secretion, seen in rhinoscopy, showed no statistically significant differences between the treatment groups, although both the mucosal swelling and the secretion increased more in the placebo group (Figures 2 and 3).

DISCUSSION

During many years there has been a great demand for a simple, effective and harmless treatment of seasonal allergic rhinitis. In the treatment of moderate and severe nasal symptoms intranasal steroids have largely replaced systemic antihistamines partly because of fewer side-effects, e.g. sedation. The efficacy of intranasal beclomethasone dipropionate in seasonal and perennial allergic rhinitis at 400 µg daily, divided in four or later in two doses, is well documented. It is obvious that the fewer the drug administrations the fewer are the local side effects, such as irritation and drying of the nasal mucosa.

According to this preliminary study seasonal allergic rhinitis may be also treated effectively with 400 µg of beclomethasone dipropionate aerosol once daily. In this treatment mode a new preparation of beclomethasone dipropionate aerosol is required: the adapter of the aerosol canister must release 100 µg of active drug per puff instead of the ordinary 50 µg per puff. The drug is best distributed, when on each side, one puff is taken on the upper part of the nose and another on the lower part of the nose. This distribution of the drug was shown in a cadaver model by Mygind and Vesterhauge (1978). To get the best distribution of the drug in the nose the adapter should be at right angle to the aerosol canister (Mygind and Vesterhauge, 1978; Nuutinen et al., 1983). In this mode of treatment also the administration of propellants is limited to once daily. This is very unlikely to cause any side effects on the nasal mucosa.

ZUSAMMENFASSUNG

Einundvierzig Patienten wurden drei Wochen lang während der Birkenpollenperiode in einer randomisierten, doppelblinden, placebokontrollierten Pilotuntersuchung behandelt. Zehn Patienten erhielten einmal täglich 400 µg Beclomethazon-Dipropionat-Aerosol, zehn Patienten einmal täglich Placebo, zehn Patienten 400 µg Beclomethazon morgens und Placebo abends, und elf Patienten zweimal täglich 200 µg Beclomethazon. Der Schweregrad der Nasensymptome wurde vor dem Versuch, während der Pollenperiode ohne Behandlung, bei Feststellung der höchsten Pollenwerte und beim Abschluss der Behandlung beurteilt. Einmal täglich 400 µg Beclomethazon-Dipropionat (zwei 100-µg-Stösse pro Nasenloch) und zweimal täglich 200 µg Beclomethazon-Dipropionat (zweimal zwei 50-µg-Stösse pro Nasenloch) konnten die Symptome gleich wirksam kontrollieren. Alle aktiven Behandlungsschemata waren wirksamer als das Placebo. Die Untersuchung zeigt also, dass sich die periodisch auftretende allergische Rhinitis durch Beclomethazon-Dipropionat in einer Tagesdosis von 400 µg wirksam kontrollieren lässt.

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