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Hay fever treatment with budesonide and beclomethasone dipropionate twice daily - A clinical comparison

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SUMMARY

Fifty-two patients with seasonal allergic rhinitis were admitted to a randomized clinical comparison between budesonide (Rhinocort®) and beclomethasone dipropionate (Becotide Nasal). All patients were sensitive to birch pollen, which was confirmed by a skin prick test. The drugs were administered intranasally 200 µg b.i.d. Symptoms were assessed over four weeks starting with a run-in period of one week. Daily pollen counts were recorded throughout the trial and showed a rather mild birch pollen season. The patients diary cards revealed a beneficial therapeutic effect of the two drugs. No statistically significant differences between the drugs were seen except with regard to sneezing symptoms, where the Rhinocort-treated patients showed less symptoms ($p < 0.05$). Side effects were few and transient with both drugs.

INTRODUCTION

Intranasal corticosteroids have formed a widely accepted treatment for nasal disorders such as allergic and vasomotor rhinitis as well as nasal polyposis (Mygind, 1978). A number of potent steroids with little systemic activity have been shown to provide effective and safe treatment. The first steroid with this properties to be introduced, beclomethasone dipropionate, (BDP) has been used till now, utilizing a four-times daily treatment regime. The more recent steroids, flunisolide and budesonide, were introduced with a more convenient twice-daily treatment (Pipkorn, Rundcrantz and Lindqvist, 1980; Turkeltraub, Norman and Crepea, 1976).

The aim of the present investigation was to compare the efficacy of the two steroids budesonide and BDP in the treatment of seasonal allergic rhinitis, using the same daily dose and the same twice-daily administration.

MATERIAL AND METHODS

Fifty-two patients were admitted to a randomized clinical study. Two parallel groups were compared during a three-week treatment period. All patients started their treatment on the same day. Pollen was counted simultaneously, and all

patients were seen before and after treatment by the same physician.

The study comprised 52 patients, 30 males and 22 females, their ages ranging from 16 to 49 years (mean age 29.6 years). All patients had at least a two-year history of hay fever with at least two of the following symptoms: blocked nose, running nose, nasal itching and sneezing. All patients had been referred to the allergy section of our ENT department and had been skin-prick tested. All of them had showed a positive reaction to birch pollen.

The trial had been approved by the Ethical Committee of the University of Göteborg, and all patients gave their informed consent to participate in the trial.

The trial was carried out as a blind comparison between budesonide and BDP spray in the following manner. The nasal sprays in the original devices were packed in identical numbered boxes randomized by the pharmaceutical company. The boxes were then handed out by a nurse.

Both drugs were given as pressurised freon-propelled aerosols delivering 50 µg of active substance per puff. Both preparations were administered by means of two puffs into each nostril morning and evening, providing the patient with a daily dose of 400 µg active substance. No other treatment was allowed. One patient did, however, develop unbearable eye symptoms which required treatment with Antasten-Privin® eye drops.

The trial started on May 1st with a base-line period of one week. On the 8th of May the treatment was begun, and the patients were followed for a three-week treatment period. All patients were provided with a diary card on which they should record the daily symptoms of blocked nose, running nose, nasal itching, sneezing, running eyes and itching eyes. The number of sneezing bouts were counted and then translated to the following scale: 0 bouts = 0, 1–5 bouts = 1, 6–10 = 2, > 10 = 3. The same scale was used with regard to the other symptoms as well, but in these cases 0 meant no symptoms, 1 = mild symptoms, 2 = moderate symptoms and 3 = severe symptoms.

Before the beginning and at the end of the trial, the patients were subjected to a complete physical ENT examination. One patient did not return to the follow-up visit, as he felt it to be unnecessary in view of the fact that he had not had any symptoms with the treatment. The diary card from him was not available for analysis.

POLLEN COUNT

A Burkhardt recording volumetric trap was mounted in a representative dwelling area in the town of Skövde. It was mounted 3 metres above the ground. Pollen was collected throughout the trial from May 1 to May 30. The daily pollen recordings were analyzed by the department of Taxonomy at the University of Göteborg. The pollen counts were expressed as the number of pollen per cubic metre of air.

STATISTICAL METHODS

Student's t-test was used for the statistical analysis of the symptom scores. x^2-test was used for the overall assessment.

RESULTS

51 patients completed the study. 26 of them received budesonide and 25 BDP. The average total daily nasal symptom scores are presented in Figure 1. The same figure shows the daily pollen count of birch pollen. As is clear from Figure 1, the birch pollen season in 1981 was a poor one. The maximum level of daily pollen reached 100/m^3, which should be compared with the previous season, when the maximum reached 1500/m^3.

The nasal symptom scores were very low in both treatment groups, and no statistically significant difference was recorded between the two, except with regard to the sneezing score which was significantly lower in the budesonide-treated group as compared to the BDP-treated group ($p < 0.05$) during the period May 10–17, when pollen counts reached the highest level.

Figure 2 shows the average daily eye scores. Since no eye medication was given,

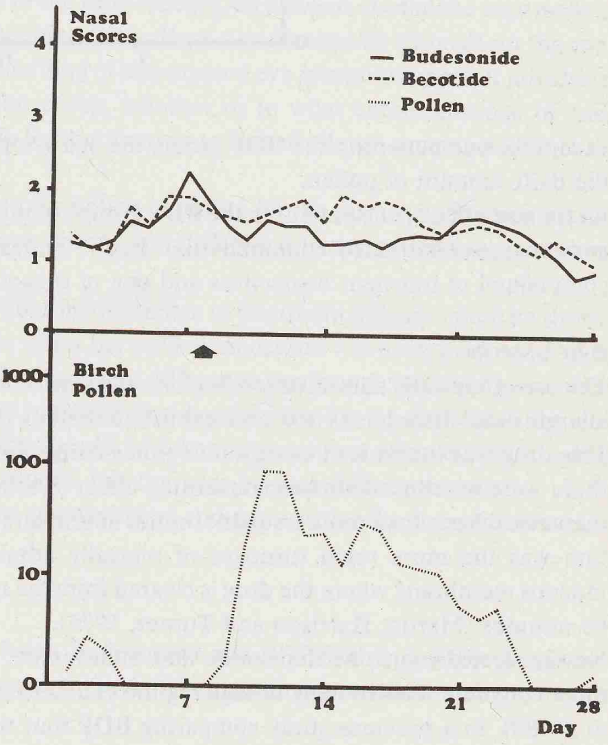

Figure 1.
Average total daily symptom score for nasal symptoms. Max. score is 12. Daily pollen count of birch pollen per cubic metre of air filtered.

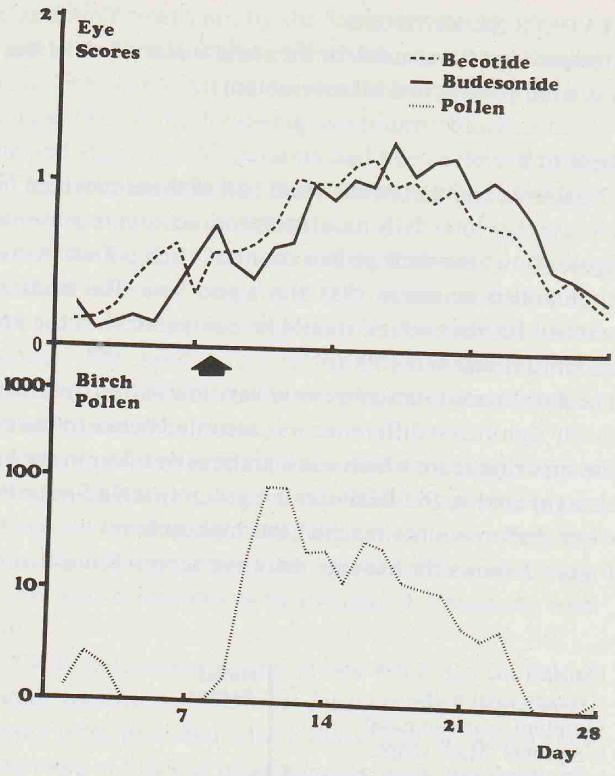

Figure 2.
Average total daily eye score. Max. score is 6. Daily pollen count of birch pollen per cubic metre of air filtered.

except for one patient in the BDP group, the eye symptoms presented followed the daily amount of pollen.

As for side effects, one patient in the BDP group complained of cough and two of swollen eyes (untreated conjunctivitis). In the budesonide group one patient complained of transient hoarseness and one of sneezing after spray.

DISCUSSION

The use of topically administered Beclomethasone dipropionate for treatment of allergic nasal disorders is now an established therapy (Mygind and Clark, 1980). This drug was introduced using a four-times-daily application regime, although there were no clinical studies concerning effect as related to dosage interval. A theoretical basis for a more frequent topical administration than oral administration was the more rapid turnover of topically administered steroids on the mucous membrane where the drug is cleared from the mucous membrane within 60 minutes (Martin, Harrison and Turner, 1975).

Newer steroids, such as flunisolide and budesonide, were introduced using a more convenient twice-daily dosage regime (Turkeltraub et al., 1976; Pipkorn et al., 1980). In a previous study comparing BDP four times a day to budesonide

twice daily, using the same daily amount of active steroid (400 µg), budesonide was found to be more effective in relieving nasal symptoms in the treatment of hay fever (Pipkorn and Rundcrantz, 1982); the difference was statistically significant.

A recent report on dosage frequencies and on the effect of BDP in seasonal rhinitis found no difference between once, twice or four-times-a-day administration of BDP when the same daily amount of steroid was used (Munch et al., 1981). Although this suggested that the difference found between budesonide and BDP was due to drug efficacy and not to dosage-interval difference in the previous study, a clinical comparison between the two drugs, using the same dosage interval, seemed indicated.

Considering the differences between the actuation devices, the best way to make an objective comparison between the two drugs would have been to perform the study according to a double-blind, double dummy design. However, as this method requires another 8 actuations per day, this would be very inconvenient to the patient and thus involve a high risk of the patient's non-compliance.

The aim of the present investigation was to assess the effect on pollen-induced rhinitis due to birch pollen, one of the commoner allergenic varieties in Sweden, where the birch-pollen season is predictable and rather concentrated. To be able to make a fair evaluation of the drug efficacy, all patients started the treatment on the same day; we also recorded the pollens simultaneously throughout the trial. This together with the recording of non-treated eye symptoms made it possible to decide, without a placebo check, whether or to what extent absence of nasal symptoms was ascribable to treatment or to lack of allergy-causing pollen in the air.

Not only is there is a need for pollen-counting for the purpose of demonstrating the day-by-day differences. Noting the difference from year to year is perhaps even more essential.

Under the present conditions no difference in treatment efficacy could be shown. But when only those days when the pollen exposition was as its peak were taken into account, a statistically significant difference was found concerning one of the symptoms, sneezing. This indicates that not only the day-by-day variations with regard to pollen exposition should be taken into account when evaluating drug efficacy in hay fever treatment, but the year-by-year differences too.

Local side effects were few and never bad enough to cause the given treatment, to be abandoned.

CONCLUSION

In the treatment of hay fever, budesonide and BDP both constitute a safe and effective treatment of nasal symptoms when administered twice daily in a daily dose of 400 µg.

ZUSAMMENFASSUNG

Zweiundfünfzig Patienten mit Heuschnupfen, hervorgerufen durch Birkenpollen, nahmen an einer Versuchsreihe teil, in der ein Vergleich angestellt wurde, welche Wirkung Budesonide und Beclomethasone dipropionate (BDP) auf den Patienten hat. Beide Präparate wurden zwei Mal täglich während einer Zeit von drei Wochen zu je 200 µg lokal appliciert. Beobachtet wurden Augen- und Nasensymptome. Paralell dazu lief eine Registrierung von Birkenpollen in der Luft. Beide Behandlungsmethoden wiesen sich als klinisch effektiv. Es konnte kein Unterschied in dem Behandlungserfolg notiert werden, ausgenommen dem Effekt auf die Niesattacken, wo eine statistisch gesicherte Differenz zu Gunsten von Budesonide registriert wurde. Die Nebeneffekte, die beobachtet werden konnten, waren so gering, dass sie ausser Acht gelassen werden konnten.

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