

From the Medical Outpatients' Clinic, Division for Allergic Diseases, and the Otopathological Laboratory, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen, Denmark.

LOCAL EFFECT OF INTRANASAL BECLOMETHASONE DIPROPIONATE AEROSOL IN PERENNIAL RHINITIS

By

IB HANSEN & NIELS MYGIND

Intranasal steroids such as hydrocortisone, prednisone and dexamethasone have never been extensively used in the treatment of allergic rhinitis, partly because of lack of therapeutic response and partly because of reports indicating that such applications result in suppression of the adrenal cortex (4, 5, 7).

Recently intranasal beclomethasone dipropionate aerosol was found to have a remarkable effect on nasal symptoms in hay-fever, which made further therapy of nasal symptoms superfluous (6). It had only negligible effects on eye symptoms, and biochemical investigations showed no apparent influence on adrenal function, indicating a local effect.

In about half of the patients suffering from perennial rhinitis an allergy can be demonstrated (2). Therefore beclomethasone dipropionate used intranasally might be expected to have an effect on patients with perennial rhinitis; however, the degree of effect was unpredictable, as this disease is known to be more resistant to therapy than hay-fever because of multifactorial pathogenesis and chronic histological changes in the mucous membrane.

In order to measure the effect of beclomethasone dipropionate in perennial rhinitis, compared with seasonal rhinitis,

we present a trial, which was carried out in the same way as the study of the local effects of intranasal beclomethasone dipropionate aerosol in hay-fever.

MATERIAL AND METHODS

21 adult patients took part in the trial. They were suffering from moderate to severe perennial rhinitis (defined as a disease with at least two of the following symptoms: sneezing attacks, watery rhinorrhoea and nasal blocking due to swollen mucosa). They all attended the out-patient allergy clinic.

Besides being given an allergological investigation (intracutaneous skin tests) and blood tests, they were examined at the ENT-department, where nasal smears were taken. In 15 patients allergy was demonstrated. Eighteen patients had eosinophilia in the nasal smear, and 9 of these patients had blood-eosinophilia too (more than 400 eosinophils/ μ l). Ten patients were female, and 11 male. Their mean age was 29 years (range 15-65), and the average duration of the symptoms was 7 years (range 1-27).

The aerosol used was the same as is used for asthma (Becotide®), but it was equipped with a special nasal adaptor. It delivers 50 μ g per puff, and the dose was one puff into each nostril four times daily—i.e. a daily dose of 400 μ g. However, studies have shown that about 30 per cent of the delivered aerosol is retained in the canister and the adaptor, and thus the dose applied to the nasal mucosa is about 250-300 μ g a day.

Patients were allocated at random to two groups. The first group (8 patients) was given beclomethasone dipropionate aerosol for three weeks, followed by an identical-looking placebo aerosol for a further three weeks; the second group (13 patients) received the treatments in reverse order. Besides using the aerosol, patients were allowed to take antihistamine tablets if necessary. Every tablet taken was recorded, and the patients filled in diary cards daily, with the symptoms sneezing, secretion and nasal blocking being evaluated semi-quantitatively according to a scale from 0 to 3. In no case was the code revealed before the patient had reported his preference and the results had been evaluated. The investigation was carried out in October-November 1973.

RESULTS

15 patients preferred the active aerosol, 3 preferred the placebo aerosol, and 3 had no preference. The sum of all nasal scores per day in the two periods is shown in the graph. When the scores for the last two weeks of treatment in each period were compiled, the symptoms in the active period were reduced to 43 per cent of the symptoms in the placebo period.

TABLE 1

Patients' recording of symptoms during treatment with beclomethasone dipropionate aerosol and placebo

	Scores*—mean values		No. of patients	Wilcoxon†
	Beclomethasone dipropionate aerosol	Placebo		
Nasal blocking	6.3	13.8	21	$P < 0.01$
Nasal secretion	8.0	18.2	20	$P < 0.01$
Sneezing	6.0	14.6	21	$P < 0.01$
Antihistamine tablets	1.5	2.5	21	$P = 0.01$

* Values accumulated during last 2 weeks of each coded period.

† Matched pairs signed ranks test.

The reduction was due to a decrease in scores for all three symptoms; scores for sneezing, secretion and blocking were reduced to 40 per cent, 43 per cent and 46 per cent of the values in the placebo period (Table 1). In addition to this, the number of antihistamine tablets taken in the active period constituted 61 per cent of that in the placebo period.

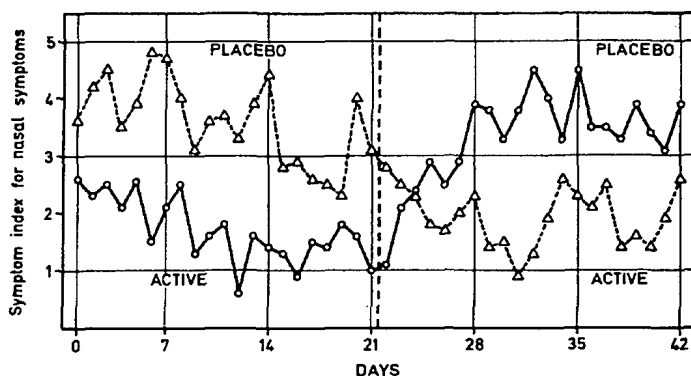


Fig. 1.

Average daily symptom scores for nasal symptoms in 21 patients with perennial rhinitis.

Several patients stated that the active aerosol had an effect on sneezing and secretion after a few days of treatment. However, judging by the graph (Fig. 1), the effect on all symptoms was not maximal until the drug had been used for 2 weeks. After the treatment was discontinued, it took one week before the symptoms reached the same level as before treatment with the active aerosol. Absence of the usual sneezing attack early in the morning was a beneficial result of this sustained effect of the drug. Eight patients stated that use of the aerosol gave rise to some sneezing, especially in the placebo period. In 3 patients this symptom was rather inconvenient, but the treatment was never stopped because of side-effects. This was controlled by assessing the number of doses left in the aerosol. In no patient who received active treatment for several days was immediate irritation any problem. It can therefore be concluded that this form of administration of beclomethasone dipropionate was well tolerated.

Several patients felt dryness in the nose when they were on active treatment, but this was more a beneficial effect than an undesirable side-effect. After one week of treatment with the active aerosol, one patient complained of daily haemorrhagic secretion from the nose. This symptom ceased some days after the active treatment was stopped. Preliminary results of an uncontrolled open trial with long-term treatment of 50 patients seem to indicate the presence of this side-effect in about 5-10 per cent of patients. Rhinoscopy revealed the appearance of some haemorrhagic spots just around and on locus Kiselbachii. This indicated that the cause is not a mechanical effect of the nasal adaptor.

DISCUSSION

It has been demonstrated earlier that intranasal beclomethasone dipropionate aerosol in the given dose had only a local effect, on nasal symptoms (6). It is therefore very satisfactory that symptoms in patients with perennial rhinitis were reduced

to 43 per cent, and use of antihistamine tablets to 61 per cent of the pre-trial level. The corresponding percentage for hay-fever patients was 23 per cent and 12 per cent. Even though the effect in hay-fever was more pronounced than the effect in perennial rhinitis, the last mentioned was most impressive, as the results are very unsatisfactory when these patients are treated with other drugs; they need a new and effective treatment much more than the hay-fever patients.

Beclomethasone dipropionate aerosol was effective in patients with proven allergy as well as in other patients, indicating similarities in the inflammatory reactions in patients with perennial rhinitis. The most prominent feature of this reaction was eosinophilia, which was present in the secretions of nearly all patients. It is our impression that the drug is effective in patients with watery secretion with eosinophilia, but not in patients with purulent secretion containing neutrophils. This is in accordance with the experiences in treatment of asthma with corticosteroids (1). Even though the effect on all nasal symptoms was striking in most patients, they did not get complete relief of symptoms, unlike the hay-fever patients.

The dose used in this trial was unnecessarily high in many cases, and most patients spontaneously lowered the dose after the trial. However, a real dose-response study is lacking.

In order to avoid local side-effects it may be important to use the lowest possible dose of beclomethasone dipropionate. In the present study it is shown that use of this drug in a few patients causes daily bloody secretions from the nose. It is not yet known whether this is due to drying out of the mucosa or to direct effect of steroid on the blood-vessels, which is the case in the skin. Nor is it clear at the present moment to what extent this side-effect is correlated to the dose. The bronchi receive a much smaller dose per cm^2 , and this phenomenon is not described in the studies of asthma treatment with beclomethasone dipropionate (1, 3). It is possible to apply a relatively high dose of the drug per cm^2 to the nasal mucosa, which are easily inspected and biopted. Nasal studies are very suitable in helping to elucidate the local side-effects of beclo-

methasone dipropionate aerosol on the respiratory mucosa. Therefore, controlled long-term trials should be performed.

SUMMARY

In a dose, whose only effect was a local one on nasal symptoms, beclomethasone dipropionate aerosol was used intranasally in 21 patients with perennial rhinitis. The trial was a double-blind cross-over with three weeks in each period. 15 patients preferred beclomethasone dipropionate aerosol, three preferred placebo aerosol, and three had no preference. The drug had effect on sneezing, secretion and nasal blocking. Both the symptom index and the use of antihistamine tablets were reduced by about 50 per cent for the whole group. Beclomethasone dipropionate aerosol was well tolerated, but a few patients complained of daily occurrence of haemorrhagic secretion from the nose.

ACKNOWLEDGEMENT

We wish to thank Glaxo, Copenhagen for supplying the aerosols, and Mr. Osvald Nielsen, Rigshospitalet, for making the nasal adaptors used in this study.

REFERENCES

1. Brown, H. B., Storey, G. & George, W. H. S. (1972): Beclomethasone dipropionate: A new steroid aerosol for the treatment of allergic asthma. *Brit. med. J.* *1*, 585.
2. Bruun, E. (1955): Allergic examination and antiallergic treatment of vasomotor rhinitis. *Acta allergol. (Kbh.)* *8*, 256.
3. Bruun, E. & Hansen, I. (1973): Beclomethasone dipropionate aerosol (Becotide®) in severe bronchial asthma. *Acta allergol. (Kbh.)* *28*, 425.
4. Foulds, W. S., Greaves, D. P., Herxheimer, H. & Kingdom, L. G. (1955): Hydrocortisone in treatment of allergic conjunctivitis, allergic rhinitis, and bronchial asthma. *Lancet* *1*, 234.
5. Godfrey, M. P., Maunsell, K. & Bruce Pearson, R. S. (1957): Prednisolone snuff in hay-fever. *Lancet* *1*, 767.
6. Mygind, N. (1973): Local effect of intranasal beclomethasone dipropionate aerosol in hay fever. *Brit. med. J.* *4*, 464.

7. Normann, P. S., Winkenwerder, W. L., Agbayani, B. F. & Migeon, C. J. (1967): Adrenal function during the use of dexamethasone aerosols in the treatment of ragweed hay fever. *J. Allergy* 40, 57.

Address of author:

Ib Hansen, M.D.
Medical Department A
Rigshospitalet
Blegdamsvej 9
2100 Copenhagen
Denmark

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.