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Allergic perennial and non-allergic, vasomotor rhinitis treated with budesonide nasal spray

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SUMMARY

A recently synthetized, highly active, non-halogenated steroid, budesonide, in the form of a nasal spray was tested on 21 patients with an allergy demonstrated by means of cutaneous or RAST tests and 15 patients without allergy; these patients were further devided into two groups, 22 with nasal eosinophilia and 14 patients without.

There was a significant effect on both patients with vasomotor as well as allergic rhinitis, and in patients with nasal eosinophilia, while this was not the case in the group without eosinophilia.

Nasal eosinophilia must be considered an inexpensive and important diagnostic tool for the clarification of perennial rhinitis.

INTRODUCTION

Perennial vasomotor rhinitis is a common and frequently very uncomfortable condition (McAllen and Langmann, 1969; Hagy and Settipane, 1969). Further, it is observed frequently in childeren (Viner and Jackmann, 1976).

The disease is characterized by non-seasonal sneezing, nasal discharge and nasal congestion, as well as chronic inflammation of the nasal mucosa. It is normally termed allergic when a specific allergen is responsible for triggering the symptoms, and vasomotor in those cases where such an allergen cannot readily be identified with the normally employed allergologic diagnostics.

Promising results have been obtained in the treatment of perennial rhinitis with a recently synthetized, non-halogenated, topical, highly active steroid, budesonnide*, (Balle et al., in press; Thalen and Brattsand, 1979).

The object of the present investigations has been to study the occurence of RAST and cutaneous allergy in patients with perennial rhinitis, and, in addition, to evaluate the effect of treatment with budesonide nasal spray in patients with verified allergic perennial rhinitis as compared to patients without demonstrable allergy. Further, to study the difference in the efficacy of the treatment in patients with and without eosinophilic nasal secretion.

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MATERIAL AND METHODS

The materials comprises 39 consecutive out-patients from the Departments of Otorhinolaryngology and Lung Medicine, attending the allergy clinic, Aalborg Hospital, with perennial rhinitis, characterized by non-seasonal occurence of at least two of the symptoms: nasal discharge, nasal congestion and sneezing. There were 25 women and 14 men, between the ages of 18 and 52 years (mean 34 years). Pregnancy, diabetes mellitus, asthma requiring treatment, and chronic bronchitis as well as obstructing nasal conditions such as septum deviation and nasal polyps resulted in exclusion from the study. All the patients gave their informed consent to participate after both written and oral information regarding the study. A thorough case history was recorded prior to treatment, with particular attention to eventual provoking allergens in the environment of the patient. An ordinary E.N.T. examination was carried out, with sampling of the nasal secretion, for the determination of eosinophilic cells. All of those who had not previously been subjected to allergy testing were referred to the clinic. In all the patients where prick-testing for the allergy groups: tree and grass pollen, animal hair and dander, as well as house dust, mites, feathers, textiles, and moulds did not demonstrate a reaction (allergic reaction smaller than that of histamine), testing was continued employing the RAST test for the food groups: meat, fish and corn as well as eggs, milk, mould, house dust and mites.

All other medication for the perennial rhinitis was discontinued, however, in cases where the symptoms were unbearable, the patient was permitted the use of Clemastin (Tavegyl®) 1 mg. Serum cortisol levels were determined prior to and three times during the study, at the same time of day each time.

The participants were randomized to either placebo, 200 µg budesonide per day or 400 µg budesonide per day, given as one puff in each nostril morning and evening. The investigation was carried out using a double-blind, cross-over technique, and covered a total period of nine weeks. It was commenced with one week without any treatment followed by two weeks of spray treatment. This cycle was repeated three times in all, inasmuch as a wash-out period was introduced between each of the two week periods of treatment.

The patients were examined immediately after each spray period using rhinoscopy, and samples of the nasal secretion were taken for the determination of eosinophilic cells.

The eosinophilia of the nasal secretion was evaluated using a semiquantitatieve scale from zero to ++++, in accordance with the presence of eosinophilic granulocytes in the smear on a dry object glass (Aas, 1959). All the patients with more than + in the nasal secretion in one of the four samples were considered as positive for eosinophilia.

The symptoms, sneezing, nasal congestion and nasal discharge were recorded

daily on a specially designed patient card, employing a scale from zero to three in agreement with the severity of the symptoms.

RESULTS

Thirty-six of the 39 patients completed the treatment and filled in the cards correctly.

The distribution of the patients according to the various groups is shown in Figure 1. Many of the patients were allergic to more than one of the allergens, and thus appear in several of the columns. In 20 of the patients it was possible to identify one or more allergens by means of the prick test, while this was not the case in the remaining 16 patients. The RAST testing for the above mentioned allergen

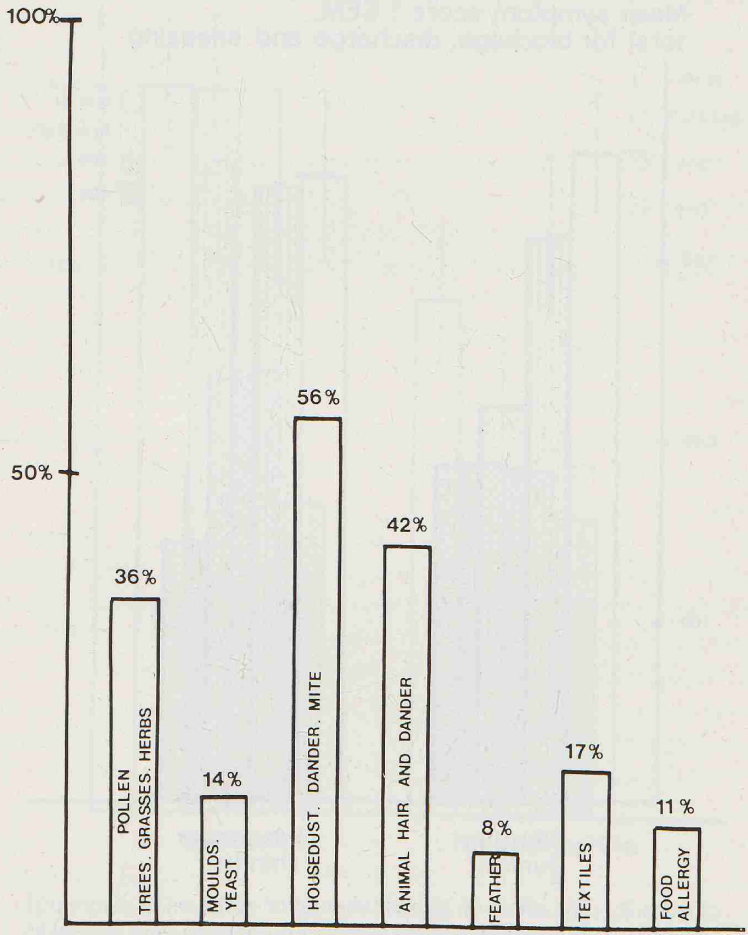

Figure 1. The distibution of the allergy findings following prick and RAST testing of 36 patients with symptoms of perennial rhinitis.

groups merely resulted in one of those with a negative cutaneous test showing a slightly positive reaction to milk and corn. House dust and mite allergy together occurred most frequently, followed by animal hair and dander.

Figure 2 shows the effect of 200 µg and 400 µg of budesonide per day, partly on 21 patients with allergy and partly on the 15 patients with vasomotor rhinitis, cases where the above mentioned allergy tests had been unable to demonstrate a responsible allergen. Compared to placebo there was a significantly better effect of 400µg of budesonide per day in both groups ($p<0.01$), while 200 µg of budesonide was able to give a significant improvement in the symptoms of the larger group with allergy ($p<0.05$).

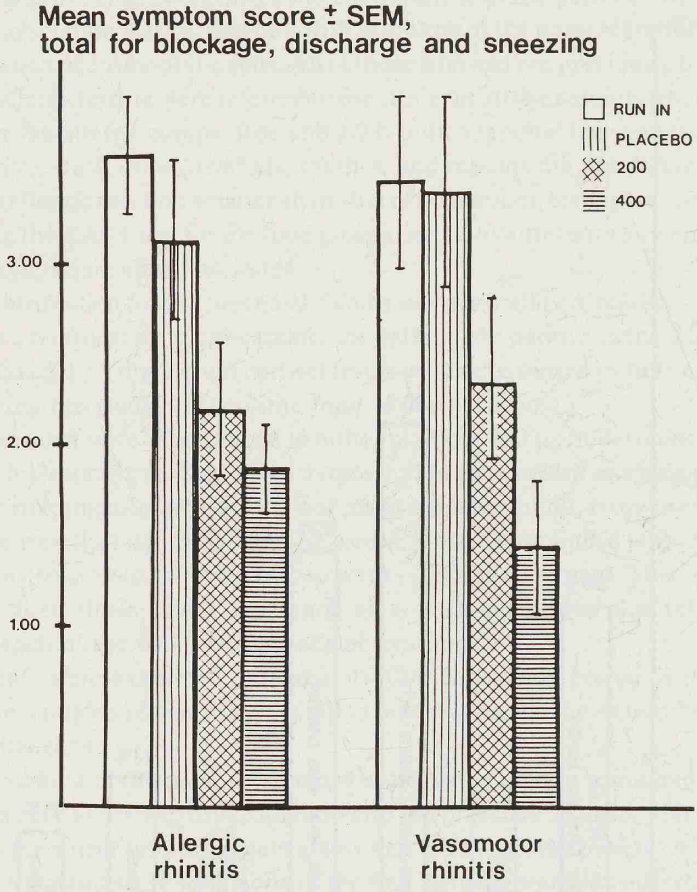

Figure 2. The effect of 200 and 400 µg of budesonide daily in 21 patients with cutaneous or RAST demonstrable allergy, and in 15 patients without demonstrable allergy, evaluated from the score cards completed during the last half of the treatment period.

Figure 3 shows the effect of 200 µg and 400 µg budesonide per day on 22 patients with eosinophilia of the nasal secretion and on 14 patients without. There was a significant improvement in the symptoms as compared to placebo ($p<0.001$) in patients with eosinophilia, where a dosage dependent effect could also be demonstrated ($p<0.05$). There was no siginificant improvement in the symptoms of the patients without eosinophilia, however, a considerable placebo effect could be observed here, the only time during the entire study. The side effects were trifling and the serum cortisol levels remained constant throughout the whole period of the investigation (Balle et al., in press).

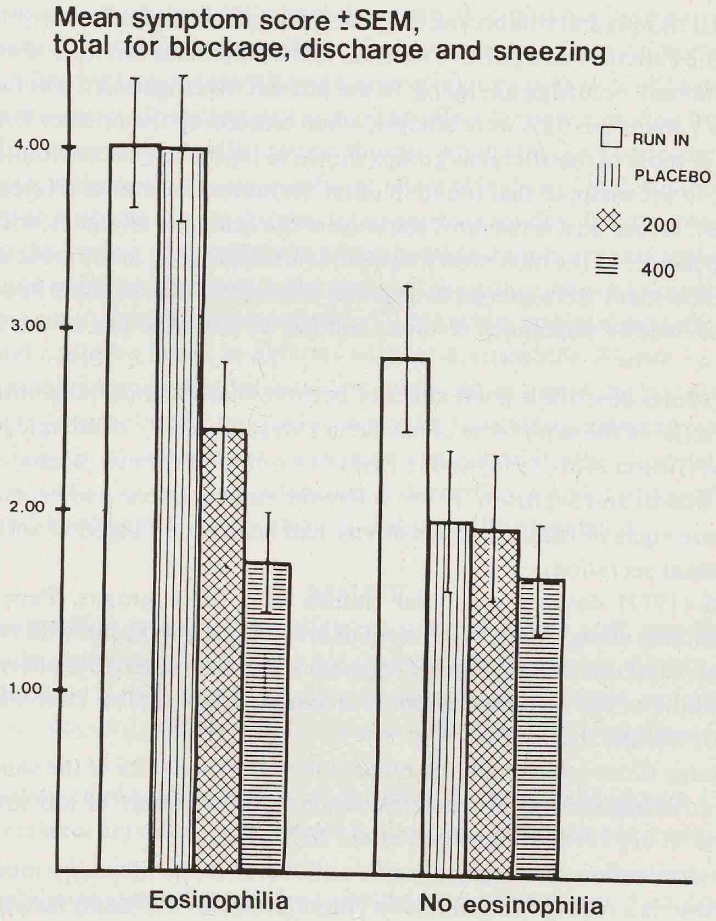

Figure 3. The effect of 200 and 400 µg of budesonide daily in 22 patients with eosinophilia of the nasal secretion and 14 patients without, evaluated from the score cards completed during the last half of the treatment period.

DISCUSSION

The rationel treatment of allergic perennial rhinitis would be the complete elimination of the responsible allergen. Many patients with symptoms of perennial rhinitis, however, do not demonstrate any reaction to the prick and RAST tests. The nasal provocation test, which presumeably provides the most exact picture of nasal hypersensitivity, still produces some disagreeable side-effects, it is time-consuming and often difficult to interprent, and for these reasons little used in clinical diagnosis (Holopainen et al., 1979). Thus it may often be difficult to identify the causative allergen.

Viner and Jackmann (1976) stated, in respect of 1271 patients suffering from perennial rhinitis and comprising the material of a multicentre investigation, that 64% of the patients had a positive reaction to the cutaneous test for one or more of the commonly occurring allergens. In the present investigation it was found that 21 of 36 patients, or 58% were allergic, when employing the prick or RAST tests for one or more of the allergens groups shown in Figure 1. The distribution corresponds, in the main, to that found in other Scandinavian studies (Holopainen et al., 1979). House dust is the most common of the causative allergens, with animal hair and dander as the next most frequent. It is remarkable, in the present investigation, how many were allergic to dogs and horses, this may possible be caused by the considerable popularity of these animals as pets (the use of the latter for riding).

Many reports describe a good effect of beclomethasone diprionate intranasally for the relief of the symptoms of hay fever (Mygand, 1973), of allergic perennial rhinitis (Gibson et al., 1974) and in cases of vasomotor rhinitis (Malm and Wihl, 1976; Lofkvist and Svensson, 1976), where the cutaneous test had been negative, but where signs of nasal hypersensitivity had been found together with eosinophilic nasal secretion.

Mygind (1977) devides perennial rhinitis into three groups. Patients with demonstrable allergy, patients without demonstrable allergy but with eosinophilia of the nasal secretion. In the third group there is no cutaneous allergy and no eosinophilia of the nasal secretion. It is assumed that topical steroids have no effect in the last instance.

The allergy is not reflected in the blood due to the small size of the shock organ. Blood eosinophilia and IgE determination are thus rarely of any great value (Mygind et al., 1978; Holopainen et al., 1979).

The determination of allergen specific antibodies in the blood, by means of the RAST test, is a reliable and simple in vitro method for the identification of allergens. The agreement between cutaneous and RAST tests is good with allergic rhinitis (Holopainen et al., 1974). In the present investigation, all the patients with a positive cutaneous test were also found to be allergic to house dust. The RAST testing of the cutaneous negative patients only demonstrated one case of a weakly

positive reaction to milk and corn; there were no additional house dust allergic patients. In relation to the expense RAST testing, in the present investigation, was found to be of little importance.

Kumar (1975) concluded in a study of 37 patients with allergic perennial rhinitis, that cutaneous allergy does not of necessity reflect nasal allergy. This is a possible explanation of the nine patients without eosinophilia in the four nasal secretion samples having a positive cutaneous test for one or more of the above mentioned allergen groups.

As other authors (Gibson et al., 1974; Malm and Wihl, 1976; Lofkvist and Svensson, 1976) who have observed a good effect of the topically active steroid beclomethasone dipropionate in patients with perennial rhinitis, we have also found in the present investigation a significant improvement in the symptoms of the patients following treatment with a new topical highly active steroid, budesonide. In our investigation, there was just as good an effect in those suffering from vasomotor rhinitis as in those with allergic rhinitis, when 400 µg of budesonide were given daily, while there was no significant effect of 200 µg of budesonide per day in the group with vasomotor rhinitis. If the patients are devided into two groups, based on the finding of eosinophilia of the nasal secretion, a significant effect of budesonide could be observed in the eosinophilia group, where a dosage dependent effect could also be demonstrated ($p<0.05$), while no significant effect of the compound could be found in patients without eosinophilia (Figure 3).

Patients with perennial rhinitis should be subjected, as one of the first diagnostic procedures, to sampling of the nasal secretion for the determination of eosinophilia. This is both an inexpensive and simple procedure. Further investigation of the allergy naturally requires cutaneous and possibly RAST testing, while the role played by the nasal provocation is still not fully elucidated.

RÉSUMÉ

Les épreuves d'un steroide, nouvellement synthétisé, très actif, non-halogène, budesonide, employé comme spray nasal chez 21 malades avec allergie cutanée et malades avec RAST signalé, et chez 15 malades sans allergie, ont permis de diviser ces 36 cas en un groupe de 22 malades avec éosinophilie nasale et 14 malades.

On a constaté un résultat chez les vasomotteurs et chez les allergiques, ainsi que chez les malades avec éosinophilie nasale, alors que ce n'était pas le cas le group sans.

L'éosinophilie nasale est considérée comme peu onéreuse et d'un diagnostic important parmi les cas de rhinitis annuelle.

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REFERENCES

1. Aas, L., 1959: Eosinofili i sekret, T. norske Lægeforen. 79, 1237–1238.
2. Balle, V. H., Pedersen, U. and Engby, B., 1979: The treatment of perennial rhinitis with a new, non-halogenated, topical, aerosol packed steroid, budesonide, Acta oto-laryng., Stockh. (in press).
3. Gibson, G. J., Maberly, D. J., Lal, S., Ali, M. M. and Butler, A. G., 1974: Double-blind Cross-over Trial Comparing Intranasal Beclomethasone Dirpopionate and Placebo in Perennial Rhinitis, British Medical Journal, 4, 503–504.
4. Hagy, G. W. and Settipane, G. A., 1969: Bronchial astma, allergic rhinitis and allergy skin tests among college students, Journal of Allergy, 44, 323.
5. Holopainen, E., Salo, O., Backman, A. and Hannuksela, M., 1974: Undersokning och diagnos av alergisk snuva. Draco pro Medico, 4, 1–4.
6. Holopainen, E., Salo, O. P., Tarkiainen, E. and Malmeberg, H., 1979: Diagnostic procedures in chronic rhinitis, Acta Otolaryngol. suppl. 260, 13–15.
7. Holopainen, E., Salo, O. P., Tarkiainen, E. and Malmeberg, H., 1979: The most important allergens in allergic rhinitis, Acta Otolaryngol. Suppl. 360, 16–18.
8. Kumar, R., 1975: Evaluation of skin tests and desensitization in allergic rhinitis, The Journal of Laryngology and Otology, 195–805.
9. Lofkvist, T. and Svensson, G., 1076: Treatment of vasomotor rhinitis with intranasal Beclomethasone dipropionate (Becotide$^{(R)}$), Acta Allergologica, 31, 227–238.
10. Malm, L. and Wihl, J. A., 1976: Intra-nasal beclomethasone dipropionate in vasomotor rhinitis, Acta Allergologica 31, 245–253.
11. McAllen, M. K. and Langman, M. J. S., 1969: A controlled trial of Dexamethasone snuff in chronic perennial rhinitis, Lancet i, 968.
12. Mygind, N., 1973: Local effect of intra-nasal beclomethasone pipropionate aerosol in hay fever, British Medical Journal iv, 464.
13. Mygind, N., 1978: Nasal Allergy, Blackwell Scientific Publications, Oxford.
14. Mygind, N., Dirksen, A., Johnsen, N. J. and Weeke, B., 1978: Perennial rhinitis: an analysis of skin testing, serum IgE and blood and smear eosinophilia in 201 patients, Clinical Otolaryngology 3, 189–196.
15. Thalen, A. and Brattsand, R., 1979: Synthesis and anti-inflammatory properties of Budesonide, a new non-halogenated glucocorticoid with local activity, Arzneim.-Forsch./Rug Res. 29, 1687–1690.
16. Viner, A.S. and Jackman, N., 1976: Retrospective survey of 1271 patients diagnosed as perennial rhinitis, Clinical Allergy 6, 251–259.

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