Rhinology, 18, 171-175, 1980

Budesonide - a new nasal steroid

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SUMMARY

39 patients with seasonal rhinitis entered a double-blind study comparing nasal sprays of budesonide 400 µg/day and placebo. Symptoms were assessed over a treatment period of three weeks. There were statistically significant differences in favour of the active spray on all measures of assessment. Side effects were mild and the incidence was negligible.

INTRODUCTION

Local administration of corticosteroid has been shown effective in the treatment of allergic diseases in the respiratory pathways (Brown et al., 1972; Andersson, 1975). Efficacy in the treatment of allergic and vasomotor rhinitis as well as nasal polyps has been reported by a number of authors (Mygind, 1973; Gibson et al., 1974; Hansen and Mygind, 1974; Löfkvist and Svensson, 1975; Mygind et al., 1975). The possible side effect on the adrenal function has been studied by Harris et al., (1974). The drug predominantly used in Scandinavia is beclomethasone dipropionate (BDP). However, a number of cases have been reported, in whom BDP seems to have little or no effect. In the search for other steroids with potent local anti-inflammatory properties and low systemic activity a new steroid - Budesonide - has been synthetized.

Budesonide (16α, 17α, (22RS)-propyl-methylenedioxypregna-1,4-diene-11β, 21-diol-3,20-dione) has local anti-inflammatory properties comparable to those of fluocinolone acetonide. Its systemic glucocortiticoid activity was found to be 4-7 times lower than that of fluocinolone acetonide (Thalén and Brattsand, 1979).

AIM OF INVESTIGATION

The aim of the present investigation was to compare the clinical effect and side-effects of budesonide with those of placebo in patients with seasonal allergic rhinitis due to pollen.

MATERIAL AND METHODS

The study comprised 39 outpatients, 22 male and 17 female, and their ages ranged from 17 to 56 years (mean age 29.5 years). All patients had a history of hay fever with two or more of the symptoms blocked nose, running nose, and sneezing for at least two years. All patients had been referred to the allergy section of our

ENT department, and had been tested by skin-prick test (35) or by RAST (4). Patients younger than 16 years and pregnant women were excluded from the study.

The trial was a double-blind comparison between budesonide spray and an identical placebo spray. It was conducted over a three week period in the pollen season May–June 1979. All patients were randomly allocated to two groups, one receiving placebo and the other budesonide. The patients were instructed to begin their therapy as soon as nasal symptoms appeared. The test preparations were given twice-daily as a pressurized aerosol with one puff into each nostril morning and afternoon. The active spray provided a total daily dose of 400 µg. Before taking their first spray, the patients recorded the degree of symptoms according to a 4-graded scale (see below).

All patients were allowed to take Lunerin® mite tablets (containing 6 mg brompheniramine and 25 mg phenylpropanolamine) when the symptoms experienced were severe. Other medication for the rhinitis was withdrawn.

The patients' record included daily symptoms, consumption of Lunerin tablets and side-effects. The nasal symptoms for blockage, discharge, and sneezing bouts were judged according to the following scale.

No = 0, Mild = 1, Moderate = 2, Severe = 3

The patients were seen by the investigator before and after the treatment period when a general ENT examination was performed.

Three patients did not complete the treatment period. In no case was the reason side-effects.

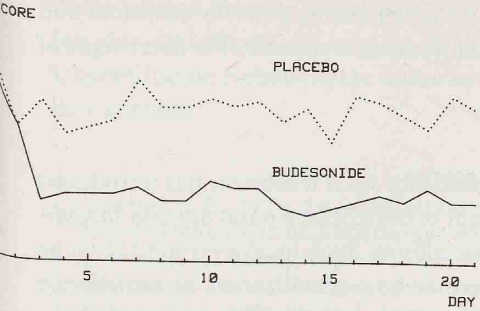
Before the code was broken the investigator made an overall assessment of each patient, classifying him/her as a responder or a non-responder to the treatment.

STATISTICAL METHODS

The data obtained from the diary cards were analysed by two-sided Student's t-test. Subjective assessments of overall symptoms were analysed by x^2-test with Yates' correction.

RESULTS

18 patients were treated with budesonide and 18 with placebo. The mean symptom score of the three-week period shows a statistically significant difference between placebo and budesonide in all of the nasal symptoms during the treatment period, favouring budesonide. There was no significant difference between the pre-values of the two groups (Table 1, Figure 1–4)). In the overall assessment there was a statistically significant difference between patients treated with placebo and budesonide respectively, favouring budesonide (Table 2). The consumption of Lunerin® tablets was 1 tablet in the budesonide group and 77 tablets by 9 patients in the placebo group.



e 1. Nasal discharge – daily mean values, 18 nts in each group. Max possible score is 3.

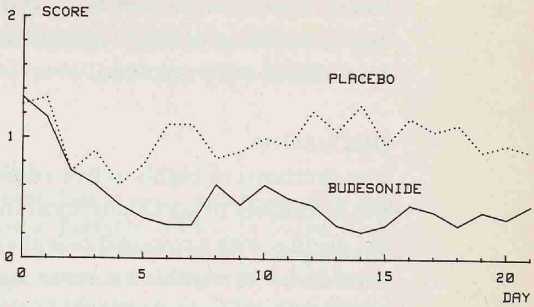
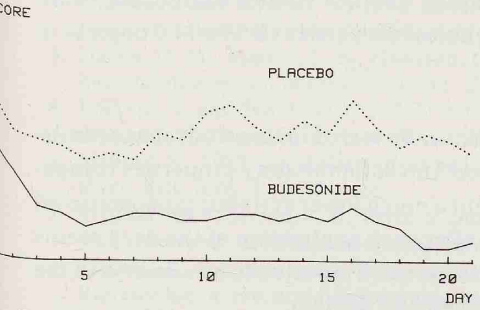


Figure 2. Sneezing – daily mean values, 18 patients in each group. Max possible score is 3.



e 3. Nasal obstruction – daily mean .values, 18 nts in each group. Max possible score is 3.

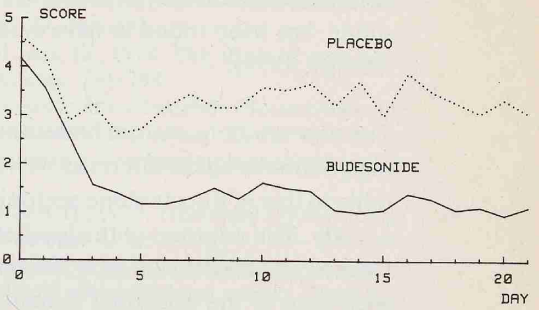


Figure 4. Total nasal symptoms – daily mean values, 18 patients in each group. Max possible score is 9.

Table 1. Mean daily symptom scores recorded in diary cards ± SEM.

	Before treatment		During 3 weeks of treatment			
					Diff. Budesonide-Placebo	
Symptom	Budesonide	Placebo	Budesonide	Placebo	mean	t-value
Nasal blockage	1,22±0,21	1,56±0,20	0,37±0,11	1,06±0,16	−0,69	−3,53**
Nasal discharge	1,61±0,18	1,78±0,19	0,60±0,10	1,26±0,15	−0,66	−3,67***
Sneezing bouts	1,33±0,18	1,28±0,14	0,45±0,08	0,99±0,17	−0,54	−2,90**
Total nasal symptoms	4,17±0,45	4,61±0,32	1,43±0,23	3,31±0,40	−0,79	−4,10***

** = $p<0.01$
*** = $p<0.001$

Table 2. Overall assessment.

	Responders	Non-responders	Total
Budesonide	17	1	18
Placebo	3	15	18
Total	20	16	36

$x^2 = 19,0$ $p<0,001$

Side-effects: One patient had a minor nose-bleed during placebo treatment and one complained of a sore throat during budesonide treatment. No other signs of side-effects were recorded.

DISCUSSION

The synthesis of highly active corticosteriods for local treatment has introduced the possibility of successful local treatment of the affected nasal mucosa in allergic rhinitis with a minimal risk of systemic effects. Such local treatment must be considered preferable in cases where either hyposensitization or antiallergic medication is not effective or causes side-effects. Although good results have been reported from the treatment of beclomethasone dipropionate, a number of cases do not respond to this drug. Recently, another steroid compound, flunisolide, has been found to have similar clinical properties (X World Congress of Allergy, 1979).

The new synthetic steroid budesonide, clinically tested in this study, has promising pharmacological effects as well as local anti-inflammatory properties comparable to that of fluocinolone acetonide, but a much lower systemic glucocorticoid activity. The duration of the local effect after each application of the drug seems to be longer than that of BDP. Budesonide has been reported to be effective in the treatment of the bronchial mucosa in bronchial asthma.

Our study was performed during the pollen season. The steroid was applied twice-daily using only the amount of the substance recommended for BDP. Although the pollen season 1979 was rather mild, the results are striking. All but one of the patients who received budesonide responded well to the treatment. The patient who failed to respond complained that she could not get her spray to function properly. None of the patients who received placebo was completely relieved from their symptoms although some were classified as responders. This patient discrepancy was also reflected in the intake of Lunerin® – one tablet only was taken by the budesonide group. The symptom scores demonstrate the same patient discrepancy.

CONCLUSION

Budesonide aerosol given twice-daily had good effect in the treatment of nasal symptoms in allergic rhinitis and negligible side-effects. Additional clinical studies have commenced in order to establish the clinical value of this new drug.

ZUSAMMENFASSUNG

In einer Doppelblindstudie bei Patienten mit allergischer Rhinitis wird Nasalatmung von Placebo bei Verabreichung mit 400 µg Budesonide während einer

dreiwöchigen Periode verglichen. Eine statistisch gesicherte Differenz zugunsten des aktiven Sprays wurde in allen studierten Variabeln nachgewiesen. Unerwünschte Nebeneffekte waren so unbedeutend, dass sie vernachlässigt werden konnten.

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