

Budesonide – A New Steroid for Intranasal Use

A Double-Blind Clinical Comparison between Budesonide and Placebo in Patients with Seasonal Allergic Rhinitis.

A. WARLAND, P. MØLLER and N. LINDQVIST

Dept. of Otorhinolaryngology, University of Bergen, Norway, and Medical Department, AB Draco*, Lund, Sweden

Twenty-nine patients with seasonal rhinitis completed a double-blind study comparing budesonide nasal spray 200 µg b.i.d. with placebo. The patients were randomly assigned into two parallel groups. Symptoms were assessed over a treatment period of 3 weeks.

There were statistically significant differences in favour of budesonide on all measurements. Side effects were mild and the incidence was low.

Key words: budesonide; nasal spray; seasonal allergy.

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Hydrocortisone, prednisolone and dexamethasone were the first intranasally applied corticosteroids that showed efficacy in the treatment of hay fever (3, 5, 9). Of the mentioned corticosteroids only dexamethasone has been more frequently used. Other studies with this drug, however, also demonstrated that the symptomatic improvement was accompanied by adrenal suppression in several patients (1, 7, 10). Later, other corticosteroids such as betamethasone-17 valerate, beclomethasone dipropionate and flunisolide have been synthesized, and proved to be effective and safe when administered intranasally in patients suffering from allergic rhinitis (4, 8, 12, 13).

Recently, a new non-halogenated glucocorticosteroid with high local activity, budesonide (manufactured by AB Draco, subsidiary of AB Astra, Sweden), has been synthesized (Fig. 1). The substance, which is scarcely water-soluble, is rapidly biotransformed by the liver (2). While the anti-inflammatory effect of budesonide corresponds to that of the halogenated steroids of

16,17-acetonide type, the systemic glucocorticoid activity is 4–7 times lower than these (11). The most plausible explanation is the more rapid systemic biotransformation of budesonide.

In human vasoconstriction tests, according to the technique described by McKenzie, budesonide was found to be 2–3 times more potent than beclomethasone dipropionate. The same difference was not found regarding systemic activity where beclomethasone dipropionate was more active than budesonide (6). These properties indicate that budesonide should be of value for local treatment of rhinitis.

The aim of this study was to investigate the efficacy and possible side effects of budesonide in comparison with placebo in the treatment of patients suffering from hay fever.

MATERIAL AND METHOD

Thirty-one patients suffering from hay fever were included in the trial (Table 1). Before

* Subsidiary of AB Astra, Sweden.

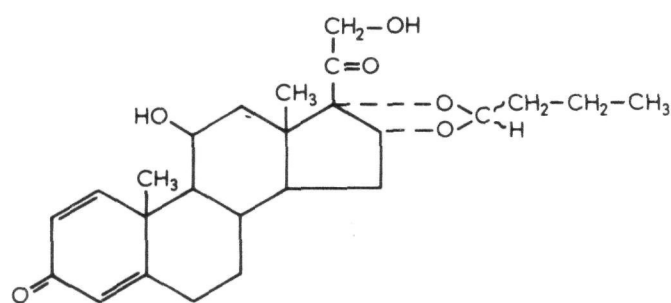


Fig. 1. The structural formula of budesonide.

Table 1
Patient characteristics.

Age	Mean	25 years
	Range	12–47 years
Sex	Male	14
	Female	17
Prick-test		
Positive to grass pollen		
tree pollen		
tree and grass pollen		
Positive nasal provocation to actual allergen		31
RAST positive (3 or 4)		18
RAST not examined		13

entrance to the study, the patients went through a routine ear, nose and throat examination.

Pregnant women, and patients younger than 12 years of age were excluded from the trial.

Budesonide was given as pressurized aerosols with two puffs into each nostril morning and evening, e.g. 8 a.m. and 8 p.m. Each puff delivered 50 µg budesonide. Similar aerosols containing the vehicle only (sorbitan trioleate, freon propellants 11, 12 and 114) were provided for the placebo group. The trial was a double-blind comparison between budesonide spray and placebo spray, being used over a period of 3 weeks. The patients were randomly assigned into two groups, one receiving placebo, and the other budesonide. The patients started the therapy the day after the nasal symptoms had appeared. If the patients did not notice any effect after 1 week, they were allowed to take Lunerin® mite tablets containing 6 mg brompheniramine and 25 mg phenylpropanolamine. All other medication for the rhinitis was withdrawn.

The day before taking the first spray, and then daily onwards, the patients recorded their symptoms scores for nasal blockage, nasal discharge, and sneezing bouts according to the following scale: no symptoms = 0, mild symptoms = 1, moderate symptoms = 2 and severe symptoms = 3.

In addition, the consumption of Lunerin mite tablets, and side effects, if any, were recorded daily. The patients saw the investigator before and after the treatment period, when a general ENT examination was carried out. At the end of the study, the investigator made an overall assessment of each patient, classifying him/her as a responder or a non-responder to the treatment. The investigator also asked the patients if they had experienced any side effects in addition to the answers on the performed questionnaires.

Wilcoxon's rank sum test with a two-sided alternative was used for the statistical analysis. Subjective assessment of overall symptoms was analysed by chi-square test with Yates' correction.

RESULTS

There were two drop-outs. One patient did not turn up after the trial, and the other misunderstood the given instructions. Of the remaining patients, 14 were treated with budesonide and 15 with placebo. The symptom scores differed in the two groups the day before the start of the treatment (Table 2, Fig. 2) being higher in the placebo group, but the difference was not statistically significant.

During the 3 weeks of treatment the mean symptom scores in all of the nasal symptoms were statistically significantly lower in the budesonide group (Table 2, Figs. 2–4). The overall assessment of the effect also showed a statistically significant difference in favour of the budesonide group (Table 3). The difference in consumption of Lunerin mite tablets was also considerable; in the budesonide group, only six tablets were used by two patients, while 126 tablets were used by eight patients in the placebo group.

Table 2
Mean daily symptom scores ± SEM the day before and during the 3-week treatment.

Symptoms	Day before treatment		During 3 weeks' treatment		Difference	
	Budesonide	Placebo	Budesonide	Placebo	Budesonide – Placebo	
					Mean	t-value*
Nasal blockage	1.29±0.13	1.53±0.17	0.49±0.12	1.15±0.16	– 0.66	– 2.97**
Nasal discharge	1.43±0.20	1.93±0.20	0.72±0.11	1.41±0.13	– 0.69	– 3.41***
Sneezing bouts	1.07±0.22	1.67±0.23	0.66±0.12	1.32±0.16	– 0.66	– 2.99**

* Wilcoxon's rank sum test.
** = *P* < 0.01.
*** = *P* < 0.001.

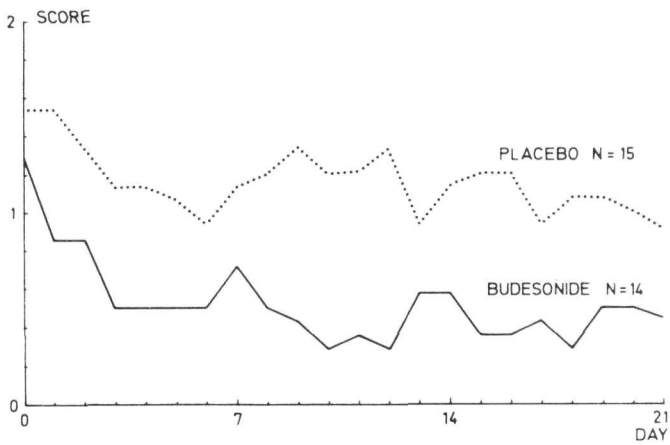


Fig. 2. Nasal obstruction – daily mean values. Max. possible score is 3.

Side effects were scarce and mild, and none of the patients had to discontinue the treatment due to side effects (Table 4).

DISCUSSION

The pollen season in the western part of Norway in 1979 was rather mild which is also seen from the rather low pre-test values. Due to ethical reasons, the patients were allowed to use Lunerlin mite tablets. Though the consumption of Lunerlin tablets was considerably higher in the placebo group, there were statistically significant differences in all of the nasal symptom scores between budesonide and placebo, favouring budesonide. The twice-a-day dosage was experienced as a great practical advantage by the patients who in earlier seasons had been

treated with beclomethasone dipropionate given 4 times daily.

The conclusion is that budesonide, administered 100 µg into each nostril twice daily, is an effective and safe drug in the treatment of hay fever.

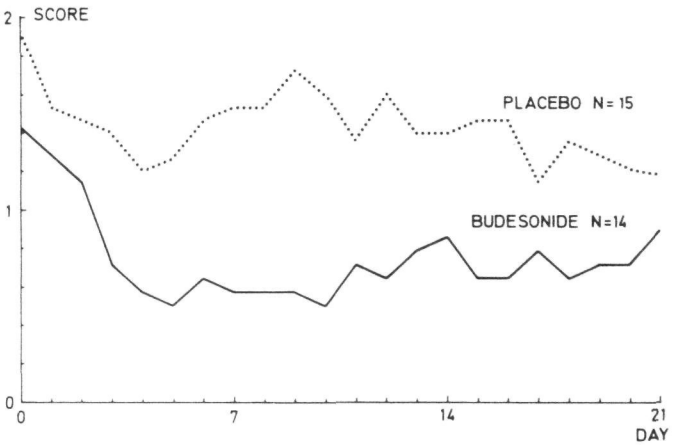


Fig. 3. Nasal discharge – daily mean values. Max. possible score is 3.

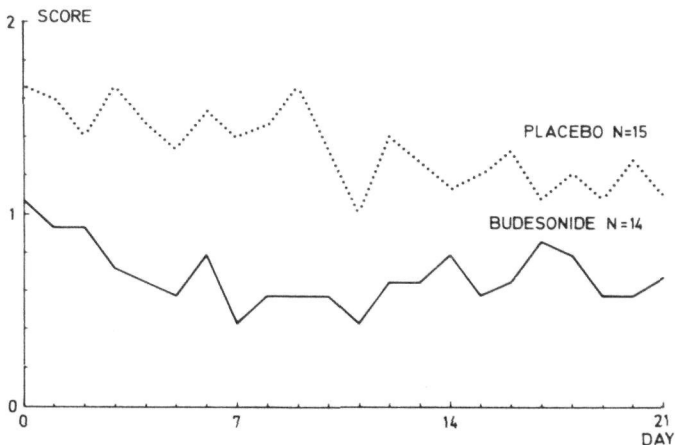


Fig. 4. Sneezing – daily mean values. Max. possible score is 3.

Table 3
Overall assessment of clinical efficacy

	Responders	Non-responders	Total
Budesonide	11	3	14
Placebo	3	12	15
Total	14	15	29

$\chi^2 = 7.8$. $P < 0.01$.
Responders – patients with effect of the spray.

Table 4
Side effects

Side effects	Budesonide	Placebo
Nose bleeding	0	1
Sore throat	1	1
Mild headache	0	1
Dry cough	1	1
Sneezing immediately after use of spray	1	1
Itching eyes	2	3
Nausea due to bad odour	1	0
Dry mucous membrane	1	0
Sex. function disorders	1	0

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Address:

A. Warland
Dept. of Otorhinolaryngology
University of Bergen
Norway

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