

# The effect of intranasal beclomethasone dipropionate on the nasal mucosa

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## SUMMARY

*In a double blind study the effect of intranasal beclomethasone dipropionate aerosol (BDA) on the morphology of the mucosa of the middle nasal turbinate was examined. Histological specimens were taken from 22 patients receiving BDA and from 15 patients who had received a placebo. Specimens were taken before therapy and after one year of treatment. Polypectomy and ethmoidectomy had been performed on all patients prior to the beginning of treatment. The histological changes of allergic rhinitis were diminished to a greater extent in patients receiving BDA than in the patients in the placebo group. BDA therapy did not cause atrophic rhinitis nor other detrimental changes that could be demonstrated histologically.*

## INTRODUCTION

Intranasally administered beclomethasone dipropionate aerosol (BDA) has been used successfully in the treatment of seasonal and perennial allergic and vasomotor rhinitis, as well as in the treatment of nasal polyps. In 1976 there was an editorial in the British Medical Journal dealing with the use of BDA in the above mentioned diseases. In the editorial a suspicion that the use of BDA might cause secondary atrophic rhinitis, diffuse nosebleeding or diminishing of resistance to infection was expressed. Later studies, however, have shown that the use of BDA can be carried out without detrimental morphological changes in the nasal mucosa (Sørensen et al., 1976; Brown, 1977; Chatterjee et al., 1977; Mygind, 1977; and Poynter, 1977). Because a very effective anti-inflammatory drug (the effect of which is as much as 5000 fold that of cortisone) is under consideration, we wanted in this study to examine by means of a double blind method what kind of morphological changes in the middle turbinate mucosa of polyp patients are brought about by therapy with BDA.

## MATERIAL AND METHODS

The material is that which has been described for a double blind study in

the preceding article in this journal (Virolainen and Puhakka). Immediately before the initiation of the treatment radical ethmoidectomy was performed on the patients. A biopsy specimen of the posterior right mucosa of the middle turbinate was taken prior to the surgery and after one year a second biopsy was taken from the same side, but somewhat more anteriorly. Satisfactory pairs of specimens were obtained from a total of 43 patients, of which 22 had been treated with BDA and 15 with the placebo. Six asthma patients who received BDA treatment were also included. The histological specimens were fixed immediately in formalin, transferred to paraffin and the sections were stained with the van Gieson and Hematoxylin-Eosin (HE) method for light microscopy. The specimens were studied without knowledge of which patients had received BDA treatment and which had not. The quality of the epithelium, the thickness of the basal membrane, edema of the lamina propria, fibrosis, mucous glands and the type and number of inflammatory cells found in the mucosa were evaluated.

## RESULTS

### *Lamina propria*

Edema of the lamina propria and eosinophilia are typical of histological sections of allergic rhinitis (Fig. 1). In addition varying degrees of thickening of the basal membrane and signs of unspecific inflammation, such as plasma cells, lymphocytes, polymorphonuclear leucocytes and hyperplasia of mucous glands were demonstrated. The cases were divided into three groups on the basis of the severity of the aforementioned changes at the beginning of the study: 18 mild, 17 moderate and 8 severe cases of allergic rhinitis (Table 1).

Table 1. The intensity of allergic rhinitis among the patients before the first, second, third and fourth ethmoidectomy.

Type of operation	Number of patients	Allergic rhinitis		
		Mild	Moderate	Severe
First ethmoidectomy	25	14	8	3
Second	11	2	6	3
Third	5	2	1	2
Fourth	2	0	2	0
Total	43	18	17	8

Eosinophilia of the lamina propria was diminished more clearly in the cases receiving BDA treatment (55%) than in the placebo group (27%) or the asthma group (17%). The corresponding figures for the decrease in edema

Table 2. The change of tissue eosinophilia and edema in the mucosa of the middle turbinate after one year treatment with BDA or placebo.

	Groups of patients		
	BDA (N = 22)	PLACEBO (N = 15)	ASTHMA (N = 6)
Tissue eosinophilia	= 7 (32 %)	6 (40 %)	1 (17 %)
	↓ 12 (55 %)	4 (27 %)	1 (17 %)
	↑ 3 (14 %)	5 (33 %)	4 (67 %)
Tissue edema	= 14 (64 %)	11 (73 %)	4 (67 %)
	8 (35 %)	2 (13 %)	1 (17 %)
	0 (0 %)	2 (13 %)	1 (17 %)

Symbols: = no changes during one year treatment, ↓ decreased and ↑ increased eosinophilia and oedema during one year treatment.

were 35%, 13% and 17% (Table 2). There were no unidirectional changes in the other parameters that were evaluated. The blood vessels of the nasal mucosa of all of the patients were dilated, but of regular structure, both at the beginning of the study and at the end of the study.

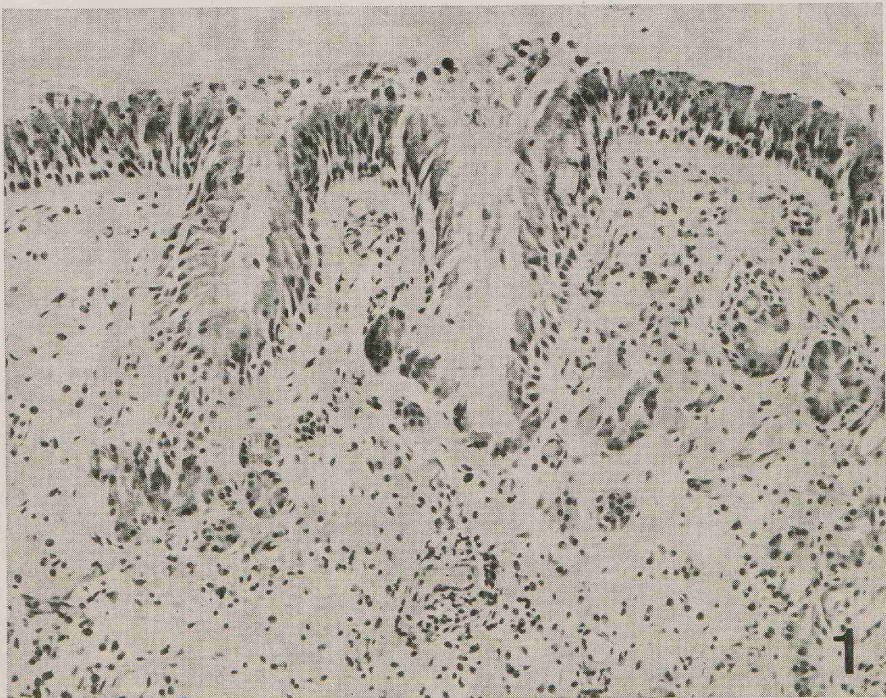


Fig. 1. A light micrograph of nasal mucosa of a patient with moderate allergic rhinitis. The mucosa is covered with normal respiratory epithelium but there are many eosinophils in the edematous lamina propria. Stained with HE. Magnification 340 x.

### Surface Epithelium

The nasal mucosa is normally covered with respiratory epithelium (Fig. 1). In nine mucosal specimens taken at the beginning of the study and in four mucosal specimens taken at the end, the epithelium had been destroyed (artefactual desquamation) such that only one or two layers of basal cells

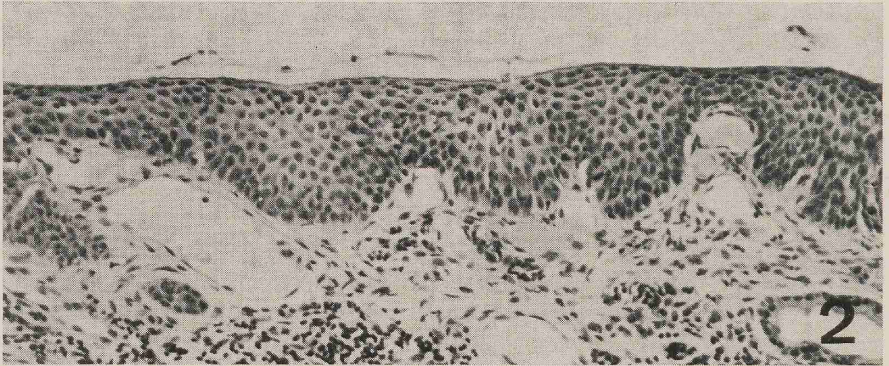


Fig. 2. A light micrograph of nasal mucosa covered with metaplastic squamous cell epithelium. Stained with HE. Magnification 340 x.

were visible. Inflammatory hyperplasia of the basal cells was found in the first specimen of five patients and after one year in the specimens of 21 patients. Squamous cell metaplasia was seen (Fig. 2) in the mucosa of the middle turbinate of 6 patients before initiation of therapy and after treatment in 16 patients. The distribution of the metaplasia between the various groups is seen in Table 3.

Table 3. The presence of squamous cell metaplasia on the mucosa of the middle turbinate of the patients before first, second, third and fourth ethmoidectomy and after one year treatment with BDA or placebo.

Type of operation	Number of patients	SQUAMOUS CELL METAPLASIA GROUPS OF PATIENTS			
		BDA (N = 22)	PLACEBO (N = 15)	ASTHMA (N = 6)	
First ethmoidectomy	25	Before treatment	1	1	1
		After 1 y. treatment	5	3	2
Second ethmoidectomy	11	Before treatment	0	0	0
		After 1 y. treatment	2	0	1
Third ethmoidectomy	5	Before treatment	1	1	0
		After 1 y. treatment	1	1	0
Fourth ethmoidectomy	2	Before treatment	0	1	0
		After 1 y. treatment	0	1	0
Total	43				

Four patients from the BDA group and two from the placebo group complained of dryness of the nose at the end of the study. There was squamous cell metaplasia as well as chronic moderate allergic rhinitis but not atrophy or fibrosis in the mucosa of the middle turbinate in 3 of these BAD patients and in one of these placebo patients.

#### DISCUSSION

Allergic rhinitis, as evaluated histologically, diminished more clearly in the patients receiving BDA therapy than in the patients receiving the placebo which is compatible with the findings of earlier studies (Mygind, 1977 and Poynter, 1977). In chronic rhinitis the basal cells of the respiratory epithelium proliferate or the respiratory epithelium may be totally replaced by squamous cell. Basal cell hyperplasia and squamous cell metaplasia were demonstrated simultaneously in the mucosa of the middle turbinate in many patients. This suggests that squamous cell metaplasia develops via hyperplasia of the basal cells. Squamous cell metaplasia was increased slightly more in the nasal mucosa of patients in the BDA group than in patients from the placebo group. All patients had been treated similarly and one factor which may be responsible for the squamous cell metaplasia may be surgery. Another significant factor is the means of administration of the drug, a point to which attention has also been previously directed (Mygind, 1977). If the drug stream comes too rapidly or is directed repeatedly at the same point the result may be the chronic irritation of the nasal mucosa and squamous cell metaplasia. For this reason the patient must be advised as to the proper method of application. Thirdly, the second specimen was taken more anteriorly and this mucosa is known to be more susceptible to irritating factors and more squamous cell metaplasia is also found normally from this area. Neither atrophic rhinitis nor nosebleed were found in any of the patients and thus in this respect the drug is safe, as has also previously been shown (Sørensen et al., 1976; Mygin, 1977 and Poynter, 1977).

#### ZUSAMMENFASSUNG

Durch einen Doppelblindversuch wurde die Einwirkung von intranasalen Beclomethasone Dipropionate Aerosol (BDA) auf die Morphologie der mittleren Nasenmuschelschleimhaut untersucht. Die histologischen Gewebeproben wurden von 22 mit BDA und von 15 mit Placebo behandelten Patienten genommen. Die Probeexzisionen wurden vor Beginn der Therapie und nach einem Jahr Therapiedauer genommen. Bei allen Patienten wurde vor Beginn der Therapie eine Polypectomie und eine Ethmoidectomy durchgeführt. Die histologischen Befunde der allergischen Rhinitis nahmen mehr ab mit BDA behandelten als bei denen mit Placebo behandelten Patienten. Die BDA

Behandlung verursachte keine atrophische Rhinitis oder eine andere histologisch wahrnehmbare schädliche Nebenwirkung.

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