

The effect of intranasal beclomethasone dipropionate on the recurrence of nasal polyps after ethmoidectomy

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SUMMARY

The purpose of this work was to examine in a double blind study the ability of beclomethasone dipropionate to prevent recurrence of nasal polyps in patients in whom radical ethmoidectomy had been performed immediately before. It analyzes the results in terms of the patients subjective symptoms, clinical status and rhinomanometry. After the follow-up period of one year 86% of the patients in the beclomethasone group and 60% in the placebo group had no subjective nasal symptoms. In clinical examination polyps were absent in 54% in the beclomethasone group and in 13% in the placebo group. Rhinomanometrically there was normal nasal patency in 68% in the beclomethasone and in 33% in the placebo group.

INTRODUCTION

The results of many studies show that good therapeutic results have been achieved with the use of beclomethasone in the treatment of seasonal allergic rhinitis (Mygind, 1973; Vilsvik, 1974; Prahl et al., 1976; Löfkvist and Svensson, 1975; Holopainen et al., 1977) and in the treatment of perennial rhinitis (Gibson et al., 1974; Hansen and Mygind, 1974). Beclomethasone has also been used successfully in the treatment of vasomotor rhinitis (Löfkvist and Svensson, 1976).

Beclomethasone has also shown to relieve symptoms of patients with nasal polyps. Sneezing, nasal secretions and stuffiness also decreased while the drug was in use (Mygind et al., 1975). Deuschl and Drettner (1977) observed that nasal resistance as measured by rhinomanometry was significantly decreased in nasal polyp patients using beclomethasone. The polyps shrunk, but did not disappear. For this reason they recommend beclomethasone as a supportive measure in conjunction with other treatment.

The etiological factors in the formation of nasal polyps are not entirely

known. Both infection and allergy contribute to the formation of polyps. Traditionally nasal polyp patients have been grouped together with allergic patients. Although allergy is often difficult to demonstrate with the most common allergy tests, the histological picture of the inflammatory reaction in the nasal mucous membrane and polyps is edematous and eosinophilic, a characteristic of allergic reactions.

Because allergy and infection both contribute to the formation of nasal polyps, surgical procedures alone do not render satisfactory results. This fact is demonstrated by the need for repeated surgery, sometimes even yearly. Beclomethasone alone has also been found to be insufficient in the treatment of polyps. In a nose with polyps the drug is unable to penetrate to the ethmoidal area where polyps originate. In addition, chronic infection is typical in most patients in this area, which also decrease the efficacy of the drug. The purpose of this work was to examine in a double blind study the ability of beclomethasone to prevent reformation of polyps in patients in whom radical ethmoidectomy had been performed immediately prior to the initiation of drug therapy due to recurrent polyps and to analyze the results in terms of the patients' subjective symptoms, clinical status and rhinomanometry.

MATERIAL AND METHODS

The material consisted of 46 patients who had undergone radical ethmoidectomy during the year 1977 at the Ear Department of the Turku University Central Hospital (TYKS) for recurrent nasal polyps. The operation was performed for the fourth time on two patients, for the third time on five and for the second time on eleven patients. The operation was the first for 25 patients.

Polyps had been removed numerous times on an out-patient basis previously. In order to insure uniformity in the results of the surgery, the operation was performed by only two doctors, using the same technique. There were 14 women and 29 men in the series. Their age ranged from 28 years to 72 years and the average age was 49 years.

Preoperatively a sample of nasal secretion was taken for eosinophil determination and a biopsy of the middle concha was taken for histopathological study. A similar biopsy was taken from the same area after treatment as well. In addition skin tests (Prick tests) were performed to determine if allergies were present. The patients were also asked about a history of allergy either personally or in the family. The size and location of the polyps were determined by rhinoscopy in the upper, middle and lower meatus and the findings were grouped into four categories: no visible polyps (0), small polyps with

good patency on respiration and inspection (1), moderate polyps with some patency (2), and large obstructing polyps (3). The patients were allocated at random to one of two groups, the first of which received the active beclomethasone dipropionate (Becotide^R) and the other placebo. The insufflators were identical and thus it was impossible to know which insufflator contained the drug and which the placebo. The daily dose was one puff into each nostril four times daily, which means 50 µg beclomethasone per puff, or a daily dose of 400 µg. Six patients suffered from such severe asthma that they all received beclomethasone. The drug therapy was initiated on the second postoperative day and it was continued, uninterrupted, for a year. No other medication was used during the trial, with the exception of the asthma patients.

One month after the surgery rhinomanometry was performed on the patients. At six months after the operation in addition to rhinomanometry a clinical examination in which the location and size of possible polyps were determined as preoperatively was performed. Similar examinations were also performed after a year. The clinical examination was done by the operating doctor and at this time the patient himself evaluated the stuffiness of this nose according to the following categories: no symptoms, slight blockage, moderate blockage, severe blockage.

The rhinomanometry examinations were performed using the posterior technique and the results were expressed in accordance with the principles laid down by Fischer and Kortekangas (1969, 1977). The coefficient of nasal

breathing resistance is $W = \frac{\Delta P}{V^2} \cdot 10^3$.

The results were evaluated according to the following table.

1. < 10 unobstructed breathing
2. 11– 20 slight obstruction
3. 21– 50 clear obstruction
4. 51–100 marked obstruction
5. > 100 insufficient.

RESULTS

Beclomethasone was used by 22 patients and the placebo by 18. Six of the patients using beclomethasone were asthma patients. Three patients withdrew from the study, all belonging to the placebo group.

16 patients (37%) reported as history of some kind of allergic disease such as Besnier's prurigo, hayfever, allergic eczema or food allergy. Similar conditions were reported to be found in the families of 22 patients (50%). Eosinophils were demonstrated preoperatively in the nasal secretions of 26

patients (60%) and a positive result was present in Prick testing for common allergens in 14 patients (33%) (Table 1).

Table 1.

	Personal history of allergy	Family history of allergy	Eosinophils in nasal smears	Positive skin test
Group A	6	10	13	5
Group B	4	6	7	4
Group C	6	6	6	5
Total	16 (37 %)	22 (50 %)	26 (60 %)	14 (33 %)

A = Patients treated with beclomethasone dipropionate aerosol (N = 22).

B = Patients treated with placebo aerosol (N = 15).

C = Patients suffering also from bronchial asthma, treated with beclomethasone dipropionate aerosol (N = 6).

Of the patients who received beclomethasone, 10 described the blockage preoperatively as moderate and 12 as severe. In the placebo group the corresponding numbers were 6 and 9. Of the asthma patients one reported moderate blockage of nasal breathing and five reported severe blockage. Six months after the ethmoidectomy 18 patients from the beclomethasone group, 11 from the placebo group and 5 of the asthma patients reported their nasal breathing to be normal. A slight and moderate increase in resistance was found subjectively in 2 patients from the beclomethasone group and in one patient from the placebo group. Severe stuffiness was reported by 2 patients from the placebo group and by one of the asthmatic patients. One year after the operation 19 patients from the beclomethasone group, 9 from the placebo group and 3 from the asthma group reported nasal breathing to be normal. A slight increase in resistance was reported by one patient in each of the three groups. A moderate increase in breathing resistance was reported by 2 patients from both the beclomethasone and the placebo groups and one asthmatic patient. Severe stuffiness was reported by three patients from the placebo group and one asthma patient (Table 2).

Moderate polyps with some patency were found preoperatively upon rhinoscopy in 7 patients in the beclomethasone group, in 3 patients from the placebo group and in one of the patients in the asthma group. 15 patients from the beclomethasone group, 12 from the placebo group and 5 from the asthma group had large, obstructing polyps. Six months after surgery 10 patients from the beclomethasone group, 2 from both the placebo and asthma groups were found to be free of polyps. At this time small polyps were found in 9 of the beclomethasone patients, 5 patients from the placebo group and in 2 of the asthma patients (who were receiving beclomethasone).

Table 2. Intensity of nasal blockage

	Before operation			6 months after operation			1 year after operation		
	A	B	C	A	B	C	A	B	C
— no symptoms	—	—	—	18 (82 %)	11 (73 %)	5 (83 %)	19 (86 %)	9 (60 %)	3 (49 %)
— slight	—	—	—	2 (9 %)	1 (7 %)	—	1 (5 %)	1 (7 %)	1 (17 %)
— moderate	10	6	1	2 (9 %)	1 (7 %)	—	2 (9 %)	2 (13 %)	1 (17 %)
— severe	12	9	5	—	2 (13 %)	1 (17 %)	—	3 (20 %)	1 (17 %)

A = Patients treated with beclomethasone dipropionate aerosol (N = 22).

B = Patients treated with placebo aerosol (N = 15).

C = Patients suffering also from bronchial asthma, treated with beclomethasone dipropionate aerosol (N = 6).

Table 3. Clinical findings of nasal polyps

Size of polyps	Before operation			6 months after operation			1 year after operation		
	A	B	C	A	B	C	A	B	C
— no visible polyps	—	—	—	10 (45 %)	2 (13 %)	2 (33 %)	12 (54 %)	2 (13 %)	2 (33 %)
— small polyps	—	—	—	9 (41 %)	5 (33 %)	2 (33 %)	5 (23 %)	4 (27 %)	2 (33 %)
— moderate polyps	7	3	1	3 (14 %)	7 (47 %)	1 (17 %)	5 (23 %)	8 (53 %)	1 (17 %)
— large obstructing polyps	15	12	5	—	1 (7 %)	1 (17 %)	—	1 (7 %)	1 (17 %)

A = Patients treated with beclomethasone dipropionate aerosol (N = 22).

B = Patients treated with placebo aerosol (N = 15).

C = Patients suffering also from bronchial asthma, treated with beclomethasone dipropionate aerosol (N = 6).

Table 4. Nasal patency one month, six months and one year after ethmoidectomy

	One month after operation			6 months after operation			One year after operation		
	A	B	C	A	B	C	A	B	C
Normal patency coefficient < 10	19 (86 %)	11 (73 %)	5 (83 %)	18 (82 %)	8 (53 %)	3 (50 %)	15 (68 %)	5 (33 %)	4 (67 %)
Some patency coefficient 11-20	3 (14 %)	4 (27 %)	1 (17 %)	4 (18 %)	6 (40 %)	3 (50 %)	5 (23 %)	7 (47 %)	2 (33 %)
Moderate patency coefficient 21-50	-	-	-	-	1 (7 %)	-	2 (9 %)	3 (20 %)	-

A = Patients treated with beclomethasone dipropionate aerosol (N = 22).

B = Patients treated with placebo aerosol (N = 15).

C = Patients suffering also from bronchial asthma, treated with beclomethasone dipropionate aerosol (N = 6).

Moderate polyps were found in 3 patients from the beclomethasone group, 7 from the placebo group and one of the asthma patients. Large obstructing polyps were found in one patient from the placebo group and in one asthma patient.

One year after surgery 12 of the patients using beclomethasone were free of polyps as well as two patients from the placebo group and 2 of the asthma patients. Small polyps were found in 5 patients from the beclomethasone group, in 4 from the placebo group and in 2 of the asthma patients. Moderate polyps were found correspondingly in 5 patients, 8 patients and one patient. One patient from the placebo group and one from the asthma group had large, obstructing polyps at one year after the surgery (Table 3). Upon rhinomanometry nasal breathing was found to be unblocked in 19 patients (86%) from the beclomethasone group one month after surgery. The corresponding figures for the placebo and asthma groups were 11 (73%) and 5 (83%). Slight blockage of nasal breathing was found in 3 patients from the beclomethasone group (14%), in 4 (27%) from the placebo group and in 1 (17%) from the asthma group.

Six months after the operation nasal breathing was still unblocked in 18 patients (82%) from the beclomethasone group, in 8 (53%) from the placebo group and in 3 (50%) of the asthma group. A slight increase in breathing resistance was found correspondingly in 4 (18%), 6 (40%) and in 3 (50%) patients. The nasal breathing of one of the patients from the placebo group was clearly blocked. At one year after surgery nasal breathing was normal in 15 patients (68%) from the beclomethasone group, in 5 patients (33%) from the placebo group and in 4 patients (67%) in the asthma group. Slight blockage of breathing was found correspondingly in 5 patients (23%), 7 patients (47%) and in 2 patients (33%). A clear rise in nasal breathing resistance was found in 2 patients (9%) from the beclomethasone group, and in 3 patients (20%) from the placebo group (Table 4).

DISCUSSION

Nasal stuffiness and increase in nasal secretions are the chief symptoms of nasal polyps. After several years the pressure atrophy caused by the polyps, may lead to shrinkage of the conchae and the clinical picture of atrophic rhinitis following the removal of the polyps. Nasal polyps have a strong tendency to recur, and for this reason surgical removal of the polyps alone does not achieve permanent recovery. Neither has beclomethasone alone been shown to be sufficient in the treatment of nasal polyps (Mygind et al., 1975; Deuschl and Drettner, 1977). Both the patients allergic tendency and frequently occurring hidden infection in the nose and sinuses contribute to

the rapid recurrence of polyps. In order to remove the contributory factor of infection, in this study radical ethmoidectomy and treatment of possible maxillary sinusitis were carried out on the patients in this study in addition to removal of the polyps before the double blind study was initiated.

Polyp patients are frequently classed as allergic, even though it is often difficult to demonstrate allergy. In our material 37% of patients had some kind of allergic disease and the family history was positive for allergy in 50%. Eosinophilic cells were present in the nasal secretions of 60% and in 33% the results of skin tests for the most common allergens were positive. Thus allergic symptoms and positive tests for allergy are common among polyp patients, supporting the local use of cortical steroid derivatives in treatment of these patients.

Nasal breathing was subjectively normal in 82% of patients using beclomethasone at six months and in 86% of such patients at one year after operation. In the placebo group the corresponding figures were 73% and 60%. The difference thus increases as the length of treatment increases. The patients receiving beclomethasone evaluated the treatment as being more beneficial than did the patients in the placebo group.

Six months after surgery 45% of the beclomethasone patients were found to be free of polyp upon clinical examination, compared to 13% in the placebo group. Moderate polyps were found in 14% of the beclomethasone group but in 47% of the placebo group. At one year after the operation 54% of the patients using beclomethasone were found to be free of polyps. In the placebo group only 13% were free of polyps. Moderate polyps were found in 23% of the patients in beclomethasone group and in 53% of the placebo group. The tendency for the recurrence of polyps after ethmoidectomy clearly decreases with the use of beclomethasone. The drug was unable to completely prevent the recurrence, but the fact that the length of the asymptomatic period increases is often a sufficient indication for treatment of the patient.

Normal breathing resistance upon rhinomanometry at one month following surgery was found in 86% of the beclomethasone group and in 73% of the patients in the placebo group. At six months after operation nasal breathing was normal in 82% of the beclomethasone group and in 53% of the placebo group. At one year after the operation the corresponding values were 68% and 33%. Thus nasal breathing resistance remained normal more often in the beclomethasone patients than in the placebo group. The decrease in nasal breathing resistance in patient using beclomethasone is caused not only by the absence of polyps but also by general shrinkage of the nasal mucosa. Clinically significant side effects were not found during the study. Other studies have shown that nasal insufflation of 400 µg beclomethasone per day

does not cause any systemic steroid effects (Mygind, 1973; Harris et al., 1974; Prahel et al., 1975).

Six patients complained of drying of the nose and crust formation on the nasal septum. Four of them belonged to the beclomethasone group and two to the placebo group. Perhaps this is a case of faulty application technique in which the gas is directed too much toward the septum and the rapid stream of gas on the same place causes drying (Mygind, 1978).

All of the asthma patients used beclomethasone after the ethmoidectomy. 83% of them had subjectively normal nasal breathing after six months and 50% after one year. The tendency for recurrence of polyps is known to be large in asthma patients. One third of the patients were free of polyps at one year, and the nasal breathing resistance was normal at the one year follow-up in 67%. Five of the six patients had been able to decrease the dosage of other asthma medication during the study. Because nasally administered beclomethasone only scantily reaches the bronchi, this aspect is not explained by beclomethasone's bronchial effect, rather by elimination of factors which provoke asthma, such as nasal stuffiness, excess nasal secretion and infection. There is not a danger of overdosage even though beclomethasone might initially be used both by inhalation for the treatment of asthma and nasally in the preventive treatment of nasal polyp (Harris et al., 1974).

ZUSAMMENFASSUNG

Durch eine Doppelblindversuch wurde die Fähigkeit des Beclomethasone Dipropionates untersucht den Neuwuchs der Nasenpolypen bei Patienten zu verhindern, an denen vor dem Anfang des Experiments eine radikale Ethmoidektomie vorgenommen war, und von denen die Polypen früher mehrmals entfernt worden waren. Nach einer Beobachtungszeit von einem Jahr waren 86% der Patienten, die Beclomethasone bekommen hatten, subjektiv symptomlos. Bei denen, die Placebo bekommen hatten, war die entsprechende Prozentzahl 60. In der klinischen Untersuchung konnte bei 54% in der Beclomethasone-Gruppe und bei 13% in der Placebo-Gruppe keine Neuwuchs der Polypen festgestellt werden. Rhinomanometrisch war der Atemungswiderstand bei 68% in der Beclomethasone-Gruppe und bei 33% in der Placebo-Gruppe normal.

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