

3. Advances in the medical treatment of nasal polyps

Authors' affiliations:

N. Mygind, Associate Professor, Department of Respiratory Diseases, University Hospital of Aarhus, Aarhus, Denmark

The objectives of the medical management of nasal polyposis are to eliminate or reduce the size of polyps, re-establish nasal breathing, reduce symptoms of rhinitis, restore the sense of smell and prevent the recurrence of nasal polyps. Corticosteroids have a proven therapeutic effect on the symptoms of nasal polyposis and may reduce one of the underlying causes of polyps, inflammation. The efficacy of topical corticosteroids such as beclomethasone dipropionate nasal spray and betamethasone nasal drops in reducing polyp size and rhinitis symptoms has been demonstrated in several randomized, placebo-controlled trials. Flunisolide and budesonide have also been shown to delay the recurrence of polyps after surgery. Topical corticosteroids can be used as long-term therapy either alone in mild cases, or combined with systemic corticosteroids and/or surgery in severe cases. Most patients will respond well to topical corticosteroid treatment of their nasal polyposis; consequently, the requirement for repetitive nasal surgery will be reduced.

Introduction

The cause of nasal polyposis is largely unknown. Microscopic observations have revealed several characteristics of polyp disorder, but have also generated some controversies. Surgery used to be the only medical intervention, but over the last 20 years, topical corticosteroids have become the mainstay of medical treatment for nasal polyposis.

Polyposis – a definition

Polyposis is a disease of the mucous membranes in the nose and the paranasal sinuses, with localized formation of

To cite this article:

Mygind Niels. 3. Advances in the medical treatment of nasal polyps. *Allergy* 1999, 54, 12–16.

Copyright © Munksgaard 1999

ISSN 0105-4538

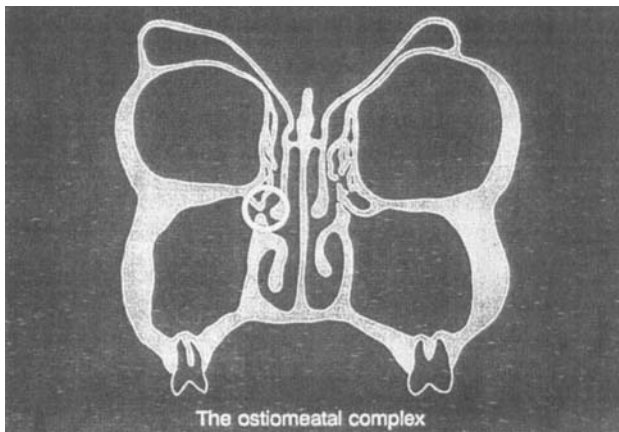


Figure 1. Diagram of ostiomeatal complex.

polyps. It can also be described as a type of self-perpetuating, eosinophil-dominated inflammation of unknown cause (1).

It is not fully understood how the disease involves almost the entire airway when polyp formation occurs in only a few square centimetres. The site of polyp formation is a particularly narrow area in the upper part of the nose, which is lateral to the middle turbinate, and around the openings of the ethmoid and maxillary sinuses (Fig. 1) (2). This is an area where the mucous membranes come into close contact, and it is a well-established fact that a mechanical stimulus of the mucous membrane epithelium can generate large amounts of cytokines and other inflammatory mediators (3, 4).

Histopathology

The polyp epithelium contains a high number of mast cells of the mucosal type (5). The polyp mast cells are heavily degranulated, even more so than in the adjacent mucous membrane or in allergy.

The histamine concentration in polyps is also remarkably high, exceeding levels of 4000 ng/ml (6). Such a histamine solution would produce a positive histamine reaction in a skin prick test and would cause itching if dripped into the eye. Although mast cells and histamine are actively present in nasal polyps, antihistamines appear to be ineffective in polyposis.

Polyps are characterized by massive tissue oedema, which results from a leakage of plasma through open endothelial junctions in the blood vessels (Fig. 2) (7).

There are a few newly formed glands which are abnormal because they have no innervation and do not show a regular production of secretion, but show a cystic degeneration. The number of goblet cells in the polyp is significantly reduced

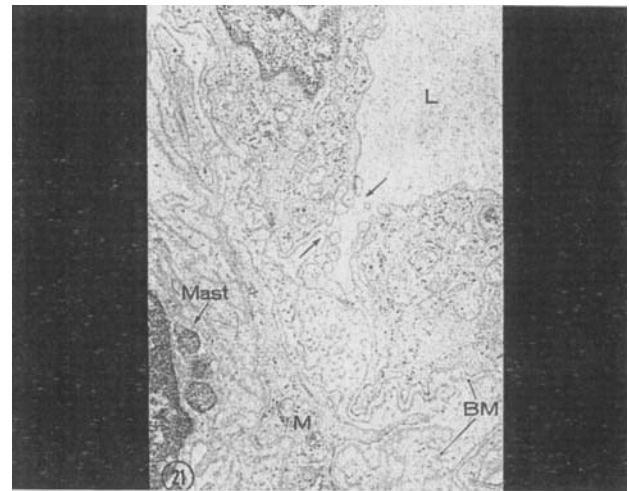


Figure 2. Electron microscopy of endothelial cells.

compared with the mucous membrane in the nose (8, 9). However, microscopic observation of single slides of polyp tissue may give the impression of an increased number of goblet cells; this is merely a result of the uneven distribution of these cells.

Eosinophils and inflammation

Polyposis is also characterized by eosinophilia. The eosinophils are activated and account for 20% of all cells (10). It is hypothesized that corticosteroids are effective in eosinophil-dominated inflammation, but have only marginal efficacy in non-eosinophil-dominated inflammation.

Intranasal flunisolide had only a marginal effect on nasal obstruction, owing to turbinate swelling in patients with sinusitis (11). Similarly, corticosteroids have demonstrated limited efficacy in conditions such as the common cold, which has neutrophil-dominated inflammation (12, 13).

The relationship between corticosteroids and eosinophil-dominated inflammation requires further investigation. Eosinophil markers such as the eosinophil cationic protein (ECP) or eosinophil peroxidase (EPO) may represent a useful tool to predict corticosteroid responsiveness in inflammatory conditions.

Eosinophilia and cystic fibrosis

There have been conflicting results regarding the extent of eosinophilia in patients with nasal polyposis associated with cystic fibrosis (CF) (14, 15). In 1977, Danish researchers studied the comparative polyp histology of 15 children with CF and 15 non-CF adult patients. The non-CF to CF eosinophil ratio was 22:1. The extent of eosinophilia was

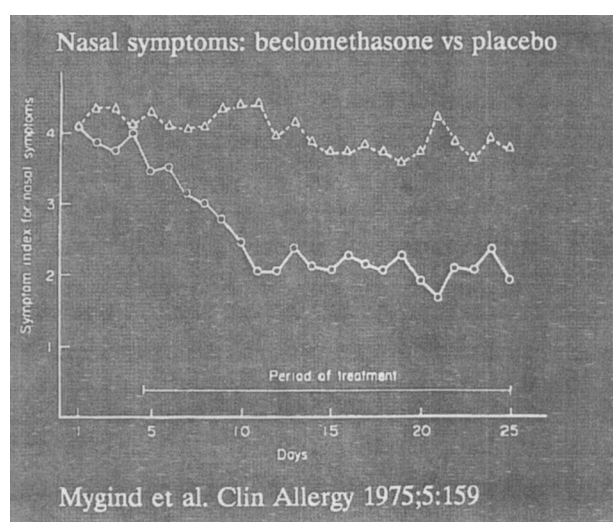


Figure 3. Graph of beclomethasone dipropionate effects on nasal symptoms – 25 days. Mygind et al., 1975.

concluded to be the distinguishing factor between CF and non-CF polyps [14].

Twenty years later, researchers in the UK conducted a similar study, but with better controls, improved quantification methods and a larger number of patients [15]. They found the non-CF to CF eosinophil ratio to be 4:1, with counts varying greatly from one polyp to the next. They concluded that eosinophils are present in varying degrees in patients with and without CF, and that the extent of eosinophilia is not a useful marker for distinguishing between these two polyp types.

The main difference between the two studies was that the UK study looked at adults with CF, whereas the Danish study looked at children with CF. It is possible that CF polyposis originates without the presence of eosinophils and that eosinophilia develops several years after the disease onset.

Intranasal corticosteroids – symptomatic efficacy

The symptomatic efficacy of intranasal corticosteroids in patients with nasal polyposis is well documented. They reduce nasal blockage, sneezing and rhinorrhoea by about 50%, and increase nasal airflow. This efficacy is maintained throughout the treatment course. After cessation of treatment, the recurrence of symptoms is slow in patients with mild polyposis and fast in patients more severely affected.

Many studies have investigated the symptomatic efficacy of intranasal corticosteroids such as beclomethasone dipropionate and budesonide in patients with nasal polyposis. A

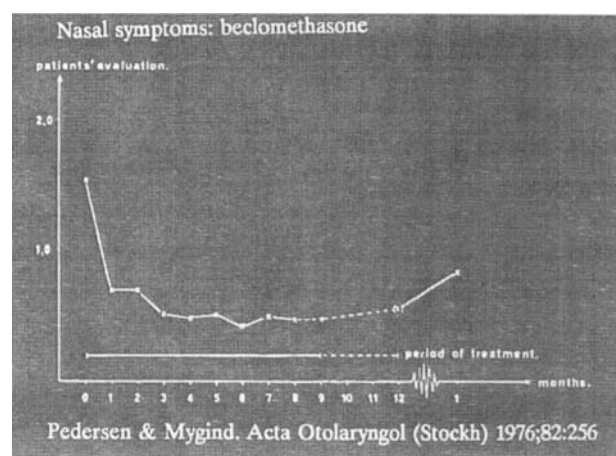


Figure 4. Graph of beclomethasone dipropionate effects on nasal symptoms – 1 year. Pedersen & Mygind, 1976.

Danish study conducted in 1975 demonstrated the efficacy of beclomethasone dipropionate, compared with placebo, in reducing the severity of nasal symptoms [16, 17] (Fig. 3). Fig. 4 shows the continued efficacy of beclomethasone dipropionate over a 1-year period and the slow recurrence of symptoms after treatment was discontinued. The efficacy of intranasal budesonide is illustrated in Fig. 5. Compared with placebo, budesonide significantly increased nasal peak flow over the 16-week study period [18].

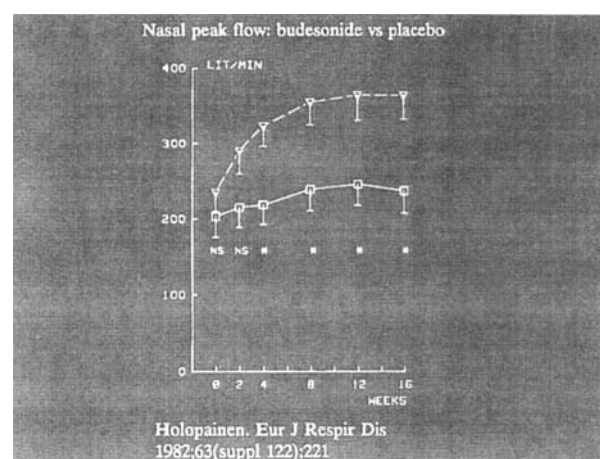


Figure 5. Graph of budesonide effects on nasal peak flow – 16 weeks. Holopainen, 1982.

Effects on polyp size

Polyp size is significantly reduced by intranasal corticosteroids compared with placebo [19], but it is difficult to determine whether intranasal corticosteroids act on the actual polyp or the mucous membrane. Moreover, nasal

sprays may not even reach the site of polyp formation. A nasal spray may not adequately deliver the corticosteroid to this area, but nasal drops administered in the "head downwards and forwards" position may be more effective (20, 21).

Postsurgical recurrence

Several studies have demonstrated a reduction in the recurrence of polyposis when an intranasal/systemic corticosteroid regimen is introduced after surgery. Intranasal budesonide reduced both the recurrence of symptoms and the need for further polypectomy over a 30-month period (22). Similar results were achieved in patients treated with corticosteroids after ethmoidectomy (23). Intranasal corticosteroids can therefore be used both in mild cases, to prevent the need for surgery, and in more severe cases after surgery, to prevent recurrence.

Effects on olfactory function

Intranasal corticosteroid sprays have a limited effect in reversing the reduced sense of smell in a patient with nasal polyposis. Although intranasal budesonide has shown some olfactory improvements compared with placebo, these differences have not been significant (24, 25). Similarly, intranasal beclomethasone dipropionate offered no olfactory advantages over placebo when it was administered after bilateral polypectomy (26).

Olfactory function can be restored during treatment with systemic corticosteroids, but this effect does not persist

once therapy is discontinued (27). Systemic corticosteroids can be useful in restoring the responsiveness to topical corticosteroids if the patient catches a cold and has a nose block. However, the adverse effects of long-term systemic corticosteroid therapy are well documented, and their use should be limited to short courses administered two or four times per year.

Effects on sinus disorder

Intranasal corticosteroids have a minimal effect on sinus disorder. Compared with placebo, intranasal beclomethasone dipropionate demonstrated no effect on sinus radiography over a 12-month period (28). This may be because intranasal sprays do not adequately deliver the corticosteroid to the region of the ostiomeatal complex which plays a key role in sinus disorder (29).

Conclusions

Intranasal corticosteroids improve rhinitis symptoms and nasal airway patency, and reduce both polyp size and their recurrence. Combined treatment with systemic corticosteroids and/or surgery is often needed in patients with more severe disease. Intranasal corticosteroid sprays do little to improve the olfactory system and sinus disorder. A nasal drop formulation may improve the efficacy of intranasal corticosteroids by allowing better drug distribution and penetration into the ostiomeatal region.

References

1. Mygind N, Lildholt T. *Nasal polyposis: an inflammatory disease and its treatment*. Copenhagen: Munksgaard, 1997.
2. Settipane GA, Lund VJ, Bernstein JM, Tos M. *Nasal polyps: epidemiology, pathogenesis and treatment*. New England and Regional Allergy Proceedings. Providence, RI: Oceanside Publications, 1997.
3. Hughes FJ. Cytokines and cell signalling in the periodontium. *Oral Dis* 1995;1:259-265.
4. Spadaro JA. Mechanical and electrical interactions in bone remodeling. *Eioelectromagnetics* 1997;18:193-202.
5. Drake-Lee A, Barker T, Thurley K. Nasal polyps. II. Fine structure of mast cells. *J Laryngol Otol* 1984;98:285-292.
6. Drake-Lee A, McLaughlan P. Clinical symptoms, free histamine and IgE in patients with nasal polyps. *Int Arch Allergy Appl Immunol* 1982;69:268-271.
7. Cauna N, Hinderer KH, Manzetti GW, Swansson EW. Fine structure of nasal polyps. *Ann Otol Rhinol Laryngol* 1972;81:41-58.
8. Larsen PL, Tos M. Nasal polyps: epithelium and goblet cell density. *Laryngoscope* 1989;99:1274-1280.
9. Tos M, Larsen PL, Moller K. Goblet cell density in nasal polyps. *Ann Otol Rhinol Laryngol* 1990;99:310-315.
10. Stiena PLE. Nasal polyps: relationship to infection and inflammation. *Allergy Asthma Proc* 1996;17:251-257.
11. Meltzer EO, Orgel HA, Backhaus JW, et al. Intranasal flunisolide spray as an adjunct to oral antibiotic therapy for sinusitis. *J Allergy Clin Immunol* 1993;92:812-823.
12. Johnston SL. Problems and prospects of developing effective therapy for common cold viruses. *Trends Microbiol* 1997;5:58-63.
13. Puhakka T, Makela MJ, Malrustrom K, et al. The common cold: effects of intranasal fluticasone propionate treatment. *J Allergy Clin Immunol* 1998;101:726-731.
14. Sorensen H, Mygind N, Tygstrup I, Flensborg EW. Histology of nasal polyps of different etiology. *Rhinology* 1977;15:121-128.

15. Rowe-Jones JM, Shembekar M, Trendall-Smith N, MacKay IS. Polypoidal rhinosinusitis in cystic fibrosis: a clinical and histopathological study. *Clin Otolaryngol* 1997;22:167-171.
16. Mygind N, Pederson CB, Prytz S, Sorensen H. Treatment of nasal polyps with intranasal beclomethasone dipropionate aerosol. *Clin Allergy* 1975;5:159-164.
17. Pedersen CB, Mygind N. Long term treatment of nasal polyps with beclomethasone dipropionate aerosol. II. Clinical results. *Acta Otolaryngol* 1976;82:256-259.
18. Holopainen E, Grahne B, Malmberg H, Makinen J, Lindqvist N. Budesonide in the treatment of nasal polyposis. *Eur J Respir Dis* 1982;63 Suppl 122:221-228.
19. Johansen LV, Illum P, Kristensen S, Winther L, Petersen SV, Synnerstad B. The effect of budesonide (Rhinocort) in the treatment of small and medium-sized nasal polyps. *Clin Otolaryngol* 1993;18:524-527.
20. Mackay IS. Topical medical management of allergic conditions of the nose. II. Intranasal steroids. In: Mackay I, editor. *Rhinitis: mechanisms and management*. London: Royal Society of Medicine, 1989:183-198.
21. Penttila M, Holmstrom M, Poulsen P, Hollingworth K. The efficacy and tolerability of fluticasone propionate (FP) nasal drops 400 µg once daily and twice daily compared with placebo in the treatment of nasal polyposis. *Allergy* 1998;53 Suppl 43:109.
22. Karlsson G, Rundcrantz H. A randomised trial of intranasal beclomethasone dipropionate after polypectomy. *Rhinology* 1982;20:144-148.
23. Virolainen E, Puhakka H. The effect of intranasal beclomethasone dipropionate on the recurrence of nasal polyps after ethmoidectomy. *Rhinology* 1980;18:9-18.
24. Lildholdt T, Rundcrantz H, Lindqvist N. Efficacy of topical corticosteroid powder for nasal polyps: a double-blind, placebo-controlled study of budesonide. *Clin Otolaryngol* 1995;20:26-30.
25. el Naggar M, Kale S, Aldren C, Martin F. Effect of Beconase nasal spray on olfactory function in post-nasal polypectomy patients: a prospective controlled trial. *J Laryngol Otol* 1995;109:941-944.
26. Doty RL, Shaman P, Dann M. Development of the University of Pennsylvania Smell Identification Test: a standardised microencapsulated test of olfactory function. *Physiol Behav* 1984;32:489-502.
27. Mygind N, Lildholdt T. Nasal polyps treatment: medical management. *Allergy Asthma Proc* 1996;17:275-282.
28. Dingsor G, Kramer J, Olsholt R, Soderstrom T. Flunisolide nasal spray 0.025 % in the prophylactic treatment of nasal polyposis after polypectomy. *Rhinology* 1985;23:49-59.
29. Hardy JG, Lee SW, Wilson CG. Intranasal drug delivery by sprays and drops. *J Pharm Pharmacol* 1985;37:294-297.