



Medical treatment of nasal polyps: a review

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ABSTRACT

Nasal polyp is macroscopic edematous mass and it is a most common nasal complaint of the patients. The exact etiology is still unknown and controversial, but the main causes are assumed to be the inflammatory conditions and allergy. Their clinical presentations are obstruction, rhinorrhea, postnasal drip. Nasal polyp is more common in allergic patients with asthma. Treatment of this complication is associated with both medical treatment and surgery. Corticosteroids (systemic and topical) are shown to be beneficial in reducing the size of nasal polyp. Corticosteroids are also used as a primary treatment and postoperative management for avoiding recurrence. The rate of leukotrienes is increased in polyps. It is reported that leukotriene receptor antagonists (antileukotriene) have a beneficial effect on nasal polyp treatment. Montelukast is an antileukotriene. It can be used to modify the symptoms of nasal polyp. There is no significant difference between corticosteroids and montelukast clinical efficacy.

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Introduction

Nasal polyps (NP) are macroscopic edematous masses characterized by yellow and soft tissue in nasal cavity (1). Nasal polyps are the most common nasal complaints of the patients. The mechanisms responsible for polyp formation and its recurrence have not been well clarified. During the past few years, there was an increasing interest in investigating the role of leukotrienes produced by eosinophils, mast cells, monocytes and basophiles.

Antileukotrienes are drugs that change the leukotriene pathway. The role of leukotrienes in asthma pathogenesis has been well established (2).

Nasal polyps are shown to have more leukotriene C4 (LTC4) and leukotriene B4 (LTB4) than the normal nasal tissue (3,4). Besides, the presence of LTC4 in nasal polyps may be a symptom of early polyp recurrence (5).

Cysteinyl-leukotrienes are the cause of bronchoconstriction, mucus production, mucosal

edema and inflammation. Antileukotrienes are the leukotriene receptor antagonists. Two main mechanisms can limit the leukotriene action, the first one is the inhibition of the leukotriene production by 5-lipoxygenase (zileuton), the second is by using cysteinyl leukotriene receptor 1(cysLt1 receptor) antagonists (montelukast, zafirlukast, panlukast) (6). Both procedures have been shown to have a significant effect on chronic stable asthma (7-9). FDA first approved montelukast in 2000 to prevent and treat the chronic asthma. It was then approved for the treatment of seasonal allergies and symptoms of asthma in 2003 and 2007 respectively (10). Although there are convincing evidences about the efficacy of montelukast on the diseases such as allergic rhinitis and asthma, its effects on NP has not been well-established. The aim of this study is to evaluate the effect of montelukast on polyp symptoms.

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Etiology

NP etiology still remains unknown (11). Several hypotheses have been made for this complication including autonomic nervous system failure, carbohydrates abnormal metabolism (12,13). But allergy and inflammation are known to be the main causes (14,15). Bateman et al. showed the possible conditions which can cause chronic inflammation in nose and nasal sinuses led to polyps (16), however, the basic reason of this disease is still unknown. Patients with allergy are at higher risk of NP, because both diseases have same symptoms like watery rhinorrhea, mucosal swelling, presence of eosinophils in nasal secretions (17). Settipane et al. in an epidemiological study on 6037 patients, demonstrated that such relation between NP and allergy can only be observed in 1%-2% of patients with positive skin prick tests (18). Several investigations have focused on the presence of eosinophilia mediators in NP tissue. Bachet et al. demonstrated that interleukine-5 (IL-5) is significantly higher in patients with NP compared to healthy controls (19). The correlation between polyposis and fungal cultures is clearly understood for many years (20). Millar et al. also demonstrated the relation between these findings and allergic bronchopulmonary aspergillosis (21).

Some diseases such as asthma, cystic fibrosis, and bronchiectasis are commonly associated by the presence of polyps (22). About 10% of those who suffer from NP have Samter's triad which includes polyposis, asthma, and aspirin hypersensitivity. Luxenburger et al. have shown the relation between HLA-A74 and NP (23) but our review of the literature failed to confirm these findings.

Epidemiology

Various studies have been performed to estimate the prevalence of nasal polyps which are briefly mentioned in Table 1. Hedman et al. in one epidemiological study with a population of 4300 individuals, reported a prevalence of 4% for NP (24).

Capline et al. in a study with 3000 atopic cases, showed that the prevalence of NP is 0.5% (25). An analysis on about 6000 patients performed by Settipane et al. showed the significant NP prevalence in the population of nonallergic asthmatic patients who were older than 40 (18). NP is more common in adults older than 20 years of age. Children younger than 10 years are not typically suffering from this condition and the presence of NP in these children may be the sign of cystic fibrosis. Males are more affected than females (2:1) (22). Symptoms of NP include nasal obstruction depending on the size of polyps, watery rhinorrhea and postnasal drip, anosmia, and hyposmia resulting in taste changes (26).

Histology and immunology

The histology of nasal cavity is now completely clear. The inferior meatus is covered by stratified squamous or pseudostratified columnar ciliated epithelium. This space is covered by seromucinous glands in deep and superficial layers. Despite the presence of more inflammatory cells in middle meatus, other histological characteristics of inferior and middle meatuses are the same. Contrary to what we discussed about normal nasal tissue, nasal polyps are completely different and predominantly consist of edematous tissue with lesser glands. Joel et al. has categorized the histological features of nasal polyps in three main parts: (1) cysts of the glands are abnormally dilated, (2) seromucinous glands are virtually disappeared and (3) presence of inflammatory cells, mainly eosinophils (1). Generally, inferior and superior meatuses are consisting of IgG1, IgG2, and IgG3. The rate of IgG production is higher in nasal polyps than inferior and superior meatuses. Despite the normal tissue, macrophages are extremely high in nasal polypoid tissue. Polypoid tissue also has more B-lymphocytes in comparison with normal tissue. Consequently, nasal polyps consist of the higher antigen-presenting cells, immunocompetent cells, and inflammatory cells such as eosinophils and mast cells in comparison with inferior meatus.

Clinical features

Polypoid tissue usually appears in middle meatus and can be characterized by multiple pale, gray polypoid masses. Loose connective tissue, edema, and inflammatory cells are the histological features of polypoid tissue (17). NP surface is usually covered by pseudostratified respiratory epithelium. NP can be histochemically differentiated from rhinosinusitis by detecting IL-5 due to the presence of eosinophil (27). 85% of nasal polyps contain eosinophils while the rest have mostly neutrophils (28).

Treatment of NP

There are still arguments about the treatment of nasal polyps, either to use medical treatment or surgery. Few studies advocated the use of medical treatment alone. Treatment of NP varies individually in procedures which are observation, medical, and surgical treatments. NP therapy starts with medical treatment in order to reduce the NP size or to eliminate it, improve sinus drainage, restore olfaction and taste (17). Surgical treatment is not the purpose of this study and should be well clarified in more specific studies.

Efficacy of corticosteroids on NP

Corticosteroids usage in the NP treatment was

first established by Mygind et al. (29). Corticosteroid clinical effects on nasal polyps have shown by several placebo-controlled trials (30). Topically administered corticosteroids have shown to be effective in treating the upper (NP and rhinitis) and lower (asthma, chronic obstructive pulmonary disease) respiratory tracts (31). When administered, the protein synthesis pattern changes in affected cell due to modified gene transcription which leads to corticosteroid clinical features (30,32). These features are expressed in 3 ways as following:

T Cells and cytokines

Many evidences are considering T cells as a cause of inflammatory reaction in nasal polyposis (30). Corticosteroids significantly reduce these inflammatory reactions by reduction in the number of lymphocytes, their activation, and cytokine production (33).

Mast Cells

The influence of mast cells on nasal polyposis is not been well established but evidence showed that the reduction in mast cells numbers in asthma and rhinitis when using corticosteroids. These finding may suggest the importance of mast cells in nasal polyposis (30,34).

Eosinophils

Eosinophils penetration decreases in the presence of the topical corticosteroids. The presence of corticosteroids induces the eosinophil apoptosis in cell culture.

Despite these advantages, corticosteroids alone do not solve any problem in individuals with NP. Sorensen et al. demonstrated that patients became unresponsive to corticosteroids in the presence of underlying disease such as cystic fibrosis, primary dyskinesia, or other conditions characterized by neutrophilic penetration rather than eosinophilic penetration (35). Insufficient delivery of medications in grade 3 NP and pleural infections can temporary make the condition unresponsive as well. Bandia et al. alleged that the use of corticosteroids could be helpful in nasal blockage but less improvement was reported in olfaction (30).

Efficacy of montelukast on NP

Focus on the antileukotriene drugs has been increased since it has been demonstrated that the rate of leukotrienes was higher in polyps (36-39). Convincing evidences have also shown that the administration of antileukotrienes drugs lead to symptoms improvement and stabilization or reduction of sinonasal polyps. (36,37,39). Mostafa et al. compared the efficacy of montelukast and beclomethasone dipropionate spray in postoperative management of patients with NP. Both groups showed significant reduction in symptoms. It is also reported that montelukast has a better effect on itching, postnasal discharge, and headache. This

study also suggested the administration of antileukotrienes for patients with rhinorrhea, sneezing, itching, or headache (40). These findings are supported by other studies (6,41). Several investigations have demonstrated the efficacy of oral antileukotrienes in symptom recovery and improvement in nasal endoscopic findings (42-44). Furthermore, aspirin sensitive patients undergoing montelukast therapy have shown a reduction in recurrent nasal polyp rate after surgery (37,45). An investigation by Kieff and Busaba demonstrated that montelukast therapy had a better response in perennial allergic rhinitis than nonallergic patients (46). Wobst et al. in a blind, placebo-controlled trial with 24 NP patients proved that the administration of 10 mg/day of montelukast modified the nasal airflow and reduced polyp eosinophils (47). It is also suggested that montelukast is more effective in lower airways than upper airways (38).

Conclusion

The exact etiology of NP is still unknown. Generally, the conditions leading to inflammation cause the NP. Polypoid tissues contain eosinophils and neutrophils. NP is more common in adults older than 20 and it is less frequent in children younger than 10. The review of literature shows the efficacy of topical and systemic corticosteroids. Corticosteroids affect protein synthesis pattern in cells thus, they result in its clinical features. Moreover, corticosteroids result in cell apoptosis when using in cell culture. It seems that corticosteroids are useless in the presence of underlying disease characterized by neutrophilic penetration rather than eosinophilic. Our review shows that the antileukotrienes have beneficial effects on sinonasal polyps and they reduce the size of the polyps. We also found no significant difference between montelukast and corticosteroids in respect to the symptom modification.

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Conflict of Interest

The authors declare no conflict of interest.

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