

Steroid therapy for nasal polyp: compliance due to cost and phobia in developing countries

Abstract

Nasal polyps are among the common conditions encountered by an otolaryngologist in routine clinical practice. It is a benign lesion, but can be troublesome due to variety of clinical symptoms. A condition, which can be diagnosed easily by clinical examination supported by CT scan of the paranasal sinuses, poses a challenge in the treatment. While surgical clearance with the aid of endoscopic sinus surgery can provide quick relief from nasal obstruction, it is frequently followed by recurrence. Medical treatment with systemic and intranasal steroid is increasingly used with success as reported by many authors around the world. Steroid has been used as a single modality of therapy or as an adjuvant to surgical therapy before and after the surgery. Considering the long duration of treatment required with intranasal steroids, a large proportion of patients discontinue the treatment after certain period of usage, due to number factors which include the cost of therapy and phobia of steroids. This is a review about the steroid usage in nasal polyp, with emphasis on the compliance.

Keywords: nasal polyp, steroid; phobia, cost, compliance

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Introduction

Nasal polyps are benign lesions arising from the mucosa of the nasal cavity or the paranasal sinuses. It is a clinical manifestation of some of the mechanisms that is present in few people. The prevalence of nasal polyposis ranged from 1% to 4.3%.¹ Presentations of nasal polyps is usually after the age of 20 years. It is very rare in children. Common symptoms of nasal polyps are nasal obstruction, increased nasal secretion, hyposmia or anosmia, postnasal drip with resultant cough and sleep disturbance. When the polyps become larger, they obstruct the sinus ostium, causing secondary sinusitis. Some patients present with a visible mass in the nasal cavity with a fear of having a tumour, after ignoring initial symptoms of nasal obstruction and discharge. Epistaxis is a rare symptom in nasal polyp, but can occur due to secondary rhino sinusitis, when the polyp is longstanding. Even though a simple disease, this can significantly affect the quality of life of the affected person.

Etiology of nasal polyp

Exact etiology of nasal polyp is unknown; however it is associated with many other conditions. Factors considered in the pathogenesis of nasal polyp are chronic rhino sinusitis, family history and genetic predisposition, atopy and allergy to inhalant and food allergens and aerodynamic factors.²

Allergy is the most common association of nasal polyp. Elevated IgE levels in these patients, and the response to steroid therapy, supports this theory. Asthma is associated with 25% to 32.6% of patients with nasal polyps.¹ Asthmatic patient have a twofold higher risk for having nasal polyps than individuals without asthma; however, polyps are more common in patients with nonallergic asthma compared with those with allergic asthma suggesting that bronchial asthma rather than allergy may be a predisposing factor.¹ Nasal polyps are present in both atopic and nonatopic Individuals.

Chronic rhino sinusitis is another cause for nasal polyposis. Antrochoanal polyps have been associated with bacterial rhino

sinusitis, whereas allergic fungal sinusitis causes multiple bilateral nasal polyps. Katzenstein et al.³ described the case histories of seven patients with asthma, nasal polyposis, sinusitis and allergic mucin within sinuses. This allergic mucin contained laminated mucin, eosinophils, Charcot-Leyden crystals, and fungal hyphae. They called this condition as "allergic aspergillus sinusitis".³ Later, de Shazo et al proposed diagnosed criteria for allergic fungal sinusitis.⁴

Cystic fibrosis, Aspirin (ASA) intolerance, Young's syndrome, Churg strauss disease, primary ciliary dyskinesia are few uncommon associations of nasal polyps. Samter's triad or ASA triad is the syndrome of nasal polyposis, asthma and ASA intolerance. This triad has been found in 8-39% of patients with nasal polyps.⁵ As many as 10% of children with cystic fibrosis may have concomitant nasal polyps.⁵

Diagnosis

Most of the cases of nasal polyp can be easily diagnosed with clinical examination alone. Anterior rhinoscopy will reveal multiple pale, oedematous mass which are generally bilateral (Figure 1). Nasal mucosa is hyperaemic with various stages of oedema. Sometimes posterior rhinoscopy or nasal endoscopy is needed to investigate the origin of the polyp. Smaller polyps limited to the middle meatus, ethmoidal bulla, frontal recess, and uncinate process are can be seen endoscopically. Mucus or purulent postnasal drip is often present in the pharynx.²



Figure 1 Specimen of nasal polyp.

Plain X-rays of the paranasal sinuses are almost obsolete now. CT scan of nose and paranasal sinuses will show the extent of nasal polyp, changes in the sinuses and anatomical variations, which are important considerations if surgical treatment is planned. Coronal CT is the standard view, which provides the required information in most of the cases. Axial view may be required in some cases, especially those with complications. The most important advantage of CT scanning is the precise view of the sinuses and ostiomeatal complex.² Nasal polyposis will be seen as homogenous soft tissue opacity in the nasal cavity and involved paranasal sinuses (Figure 2). In case of allergic fungal sinusitis, there will be heterogenous soft tissue opacity within the sinuses (Figure 3). Several staging methods have been described for assessment of the degree of inflammatory changes in paranasal sinuses on CT scan, the most commonly used is the Lund-Mackay system.⁶

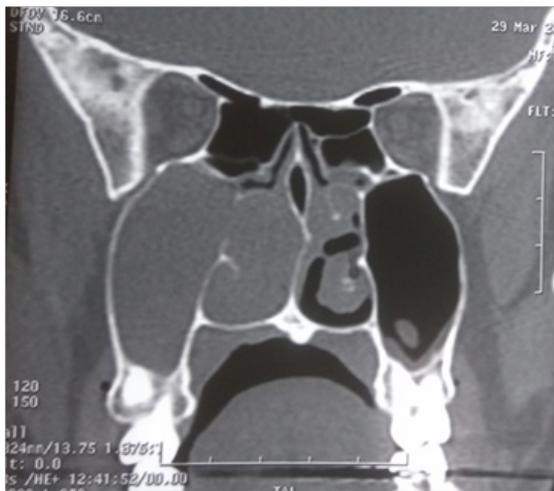


Figure 2 CT scan Nose and Paranasal sinus, showing an Antrochoanal polyp in right nasal cavity.

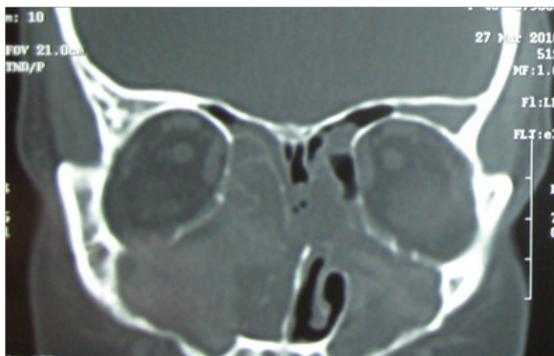


Figure 3 Heterogenous opacity seen in a case of allergic fungal sinusitis with bilateral nasal polyposis.

Pathology of nasal polyps

Nasal polyps are lined by a pseudostratified ciliated columnar epithelium, thickening of the epithelial basement membrane, scanty blood vessels and nerve endings, few glands and goblet cells. The stroma contains eosinophils, neutrophils, lymphocytes, monocytes, plasma cells, mast cells and macrophages. Mast cells occur about twice as frequently in nasal polyps as in the normal nasal respiratory mucosa and they were occasionally found within the surface epithelium and in the tunica media of larger veins. The mast cell granules of polyps are relatively small and they either lack the outer

lamellar element.⁷ Tissue eosinophilia is a general character of nasal polyps and is found in 80-90% of all cases.¹ Most nasal polyps are characterized by significant eosinophil accumulation compared with nasal mucosa from the same patients or from healthy individuals or patients with allergic rhinitis. However, antrochoanal polyps seem to have different cellular content, with a predominance of neutrophils and almost an absence of eosinophils. Polyps from both atopic and nonatopic patients have similar cellular profiles, with activated eosinophils, mast cells, and T cells, but they are different from polyps in patients with cystic fibrosis or antrochoanal polyposis.²

Treatment

Nasal polyposis can be a frustrating disease for the patient and for the treating physician. Management of nasal polyps comprises a combination of medical and surgical therapies. The recurrence of nasal polyposis constitutes a serious clinical problem. Recurrence rates up to 40-60% have been reported.⁸⁻¹⁰ These are used as either a primary treatment or following surgery, to prevent recurrence. Steroids have a multifactorial effect initiated by their binding to the cytoplasmic glucocorticoid receptor cell. The number of glucocorticoid receptors is reduced by glucocorticoid treatment.¹¹

Myers reported cases with intranasal injection of corticosteroids with complete regression of the polyp in few cases, and partial regression in large number of patients. He advocated the use of repeated injections of steroid into the polyp and concluded this method is very useful in patients where surgery need to be avoided.¹² Intranasal injections is not a routine practice now; instead steroid preparations are used most commonly as nasal spray or drops, and sometimes systemically. A short course of oral steroid followed by intranasal steroid spray can significantly reduce the nasal polyp, at times complete regression (Figure 4) & (Figure 5). Topical steroids have been investigated extensively. In all patients the addition of simple saline nasal douche for cleaning the nose prior to topical medications is beneficial, as these irrigations have been shown to improve nasal mucocilliary clearance.¹³

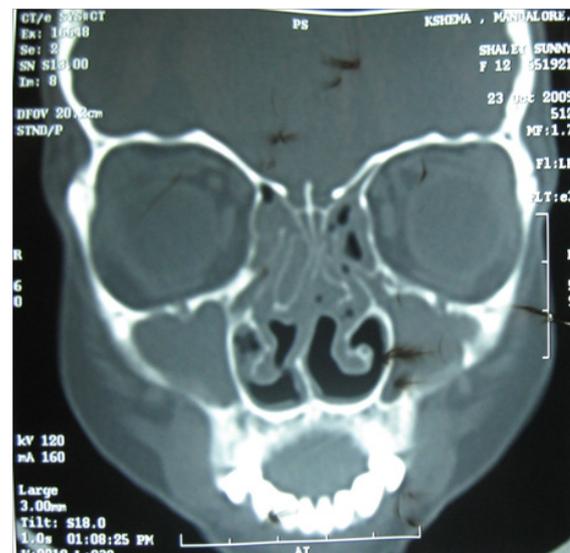


Figure 4 CT scan of a patient with bilateral nasal polyp (before treatment).

Van Camp C et al.,¹⁴ in their 25 patients treated with oral Prednisolone, observed 72% of the patients showing subjective improvement due to the involution of polyps in the nasal cavity. However, on CT of the paranasal sinuses only 52% showed a clear

improvement. Therapeutic efficacy seemed to be better in the group of ASA intolerant patients and worse in the allergic group.¹⁴



Figure 5 CT scan of patient in figure 4, after a short course of oral steroid and follow up intranasal steroid spray.

Bonfils P¹⁵ in a prospective study in 181 patients, treated with a standard regimen, combining short term oral Prednisolone and Beclomethasone nasal spray, observed that the treatment was successful in 68% of the patients given medical treatment alone. Mean symptom intensity declined by 35 to 80% at 6 months, but then remained unchanged for 2 years, during follow-up period. He concluded that medical treatment should be the first line therapy for nasal polyposis. Surgery should not be proposed until corticosteroid therapy has been found to be unsuccessful over a mean 6 months of a well-conducted treatment and good patient compliance.¹⁵

Rino K et al.,¹⁶ studied the effects of oral Prednisolone and Fluticasone nasal spray in the management of nasal polyp. Fluticasone propionate spray 200 mcg (two sprays twice daily) for 3 weeks along with oral Prednisolone 1 mg/kg in divided and tapering doses for 3 weeks was administered. They found 98.5% showing a reduction in nasal obstruction score after treatment, and 83.6% showing a reduction in nasal discharge symptom score. Sixty patients (89.6%) showed a reduction in hyposmia symptom score after treatment and 68.7% showed a reduction in facial pain symptom score after treatment. Nasal polyp size was found to be significantly reduced after treatment, and no patients developed any adverse effects during or following the treatment initiation except mild burning sensation with Fluticasone nasal spray in three patients, which subsided after a few days.¹⁶

Tuncer U et al.,¹⁷ observed polyp-free nasal cavity in 12%, clear involution of polyps in 76%, and no response to the therapy in 12% after local Fluticasone spray and oral methyl Prednisolone therapy and concluded that steroid therapy plays a major part in the treatment of the nasal polyposis, and steroids can delay the necessity for surgical intervention.¹⁷

Kowalski ML¹⁸ reported a randomized clinical trial by Vaidyanathan et al conducted in patients with bilateral moderate to large sized nasal polyps to assess whether initial therapy with oral steroids would lead to greater and sustained reduction in polyp size and greater improvement in symptoms, nasal airflow, and quality of life during the follow up treatment with topical steroids. Patients were randomly assigned to receive oral Prednisolone 25 mg/day or

placebo in identical tablets for 2 weeks. Then, patients in both groups received Fluticasone propionate nasal drops, 400µg twice daily, for 8 weeks, and then Fluticasone nasal spray, 200µg twice daily, for 18 weeks. Patients taking oral Prednisolone demonstrated a significant mean decrease in the polyp size in 2 weeks. The difference in polyp size between those in the oral corticosteroid group and those receiving placebo was maintained at 10 weeks. In the placebo group, sense of smell improved after administration of intranasal drop (at 10 weeks) but almost returned to baseline value after the completion of treatment with nasal spray. They noticed suppression of basal and dynamic adrenal function by oral Prednisolone at 2 weeks but returned to normal values after 10 weeks. They concluded that short course of oral corticosteroids could be recommended for most patients with nasal polyps as an initial therapy if subsequent treatment with topical steroids is planned.¹⁸

Cassano P¹⁹ evaluated the results of a medical treatment of nasal polyp with a combination of oral Deflazacort with a topical Beclomethasone dipropionate in the prevention of recurrence of nasal polyposis after surgery. In the follow up at 6, 12 and 24 months, the possible recurrence of polyposis, nasal blockage and the olfactory functions were evaluated. After six months the disease recurrence was observed in 33% of the cases, whereas after one year the percentage rose to 50%. At 24 months recurrence was observed in 57% of the patients. However most cases did not show any sign of further progression. Throughout the entire follow-up period under observation only 6 patients (20%) had recurrence severe enough to necessitate revision surgery. The comparison with a control group without receiving steroid therapy highlighted the significance of the results obtained. No important clinical side effects were observed during the study.¹⁹

Systemic steroid treatment is known to produce glucose intolerance due to increased hepatic production and decreased peripheral utilization of glucose. Deflazacort is proved to be significantly less diabetogenic than prednisone. Studies have been conducted to compare the efficacy and safety of Deflazacort and Prednisolone. It has been suggested that Deflazacort depresses the osteoblast less than Prednisolone, leading to a smaller decrease in serum osteocalcin levels with Deflazacort. Also, Deflazacort appears to have less negative impact on growth rate in children. Different studies show that a long-term treatment with Deflazacort has a smaller effect on glucose metabolism than other drugs of this class. The overall incidence of adverse events in Deflazacort recipients is lower than that recorded in patients treated with Prednisolone or Methylprednisolone.²⁰ Deflazacort is safer than other glucocorticoids because of its pharmacologic property of causing less calcium and hydroxyproline excretion, less metabolic effects on glucose balance and less neuronal degeneration compared with other glucocorticoids.²¹ Deflazacort produces less interference with glucose metabolism than Prednisolone in healthy subjects, prediabetic and insulin-treated diabetic patients. short-term glucocorticoid administration increased fasting plasma glucose levels after Prednisolone and Betamethasone, but not after Deflazacort.²²

Tae Wook Kang et al.,²³ studied the effectiveness of nasal irrigation with Budesonide after endoscopic surgery for recurrent nasal polyposis patients having asthma. They found that Budesonide irrigation reduced the nasal symptoms, prevented recurrence of polyp and improved the quality of life of these patients. The requirement of oral steroid was reduced in the study group. However, since the study sample was very small, the results of the study need to be supported by larger studies, before it is generalized.²³

Non compliance for steroid therapy

In spite of having researches which have proved the efficacy and safety of steroid usage in nasal polyp, a large proportion of patients will discontinue the treatment after a small duration of usage. Patient perceptions, beliefs and preferences, formulation characteristics and cost are the common barriers to the initiation of and adherence to steroid therapy.²⁴ The common fears with steroids were habituation, damage to mucous membranes, and adverse effects on other systems.²⁵ Safety concerns and the fear of loss of effectiveness if used for long period, was the other concerns which prevented people from using steroids.²⁶ Mahadevia PJ et al.,²⁷ studied the Patient preferences for sensory attributes of intranasal corticosteroids by measuring the strength of preferences for 6 sensory attributes; smell, taste, aftertaste, throat rundown, nose runout, and feel of spray in nose or throat. Preferences were measured for 3 intensity levels of each sensory attribute; no taste, weak taste, and strong taste. They noted that aftertaste was the most important attribute in 28% of patients, taste in 19%, throat rundown in 18%, nose runout in 12%, smell in 11%, and feel of spray in 7%. They noticed 77% of the patients accepting to adhere to a daily regimen for 3 months if the spray had the lowest level of each sensory attribute; only 4% of patients, if given a spray with moderate levels of the sensory attributes.²⁷ With large number of steroid preparations in market, and many of them being over the counter products, there is variable preference to a particular compound and its preparation among patients. Many patients preferred Fluticasone furoate over Mometasone furoate after treatment for 2 weeks, and Triamcinolone acetonide was preferred over Mometasone in several single dose studies.²⁸ Fluticasone furoate was preferred over Fluticasone propionate in terms of having fewer odours, causing less nose runout/throat rundown, and having fewer aftertastes.²⁹

Counselling regarding proper self-administration may improve adherence and facilitate better symptom control. Pharmacist has a major role in clarifying any potential misperceptions about intranasal steroids, which could be a barrier to their appropriate use when indicated. The benefit in intranasal steroids may not be immediate, some benefit may be achieved within 3–4 hours, but these medications provide optimal symptom control only when used continually for long periods. Moreover, patients should be instructed to continue using the spray to maintain symptom control and not simply resort to as and when required approach.

Compliance to prescribed medications has been evaluated less seriously, especially in developing countries. Inadequate and irregular treatment will cause prolonged duration of treatment, dissatisfaction of patients, low quality of life, and unnecessary financial burdens. Ocak E evaluated the adherence to steroid therapy in allergic rhinitis patients. They noticed few interesting findings in their study. Patients having more than two dependent children, patients who did not benefit initially from the medication, who experienced side effects or who travelled more than 5 days per month had poor adherence. Patients who benefited initially from the medication, those who were living with less than two dependent children, and those who had fewer side effects had better adherence to the therapy. Patients with higher education levels seemed to be more regular than the rest of the group. In order to avoid non-adherence, it is essential to re-examine the patient at regular intervals and to change the medicine if necessary.³⁰ Initial treatments with a short course of systemic steroid will encourage the patient to continue with the intranasal steroid therapy, as it gives better initial relief.

Prolonged use of topical nasal steroids has been shown to elevate intraocular pressure (IOP). This is true for the older generation

corticosteroids. The newer intranasal steroids are thought to have a minimal effect on IOP because of their low bioavailability. The first report about IOP and inhaled steroids was published in 1993 by Dreyer.³¹ Glaucoma was reported in three patients during treatment with inhaled Beclomethasone dipropionate. Simsek A et al investigated intraocular pressure (IOP) alterations in patients using Mometasone furoate and Fluticasone furoate nasal spray for six months. IOP was measured at the 3rd, 6th, 12th, and 24th weeks of treatment for each patient. They did not observe increase in IOP with this spray during 6-month follow-up period, and concluded that new generation intranasal steroids can be used safely used in normal healthy individuals.³²

Conclusion

Nasal polyp present as soft, painless, non neoplastic swelling due to hypertrophy and oedema of mucosa and submucosal tissue in the nasal cavity and paranasal sinuses. The goal of treatment of nasal polyposis is symptomatic relief with elimination of polyps from the nose and paranasal sinuses and minimizing recurrence. Surgery often alone fails to achieve the desired goals in nasal polyposis. Oral and topical corticosteroids are quiet effective in this regard, when used alone or as an adjuvant to surgical treatment. Deflazacort, a relatively new molecule of corticosteroid has bone sparing with less metabolic sequelae, less diabetogenic and appears to be a safer option than other systemic corticosteroids in patients with nasal polyposis. Counselling about the safety of the steroid is essential to alleviate misconceptions about steroid among the patients for achieving better compliance. Pharmacists, with updated knowledge, can play a key role in maintaining adherence to steroid therapy. Corticosteroids should be used with caution in 'at-risk' patients, particularly those with diabetes, uncontrolled hypertension, and peptic ulcer

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Conflict of interest

The author declares there is no conflict of interest.

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