# Use of Non steroidal Anti-inflammatory Drugs in Nasal Polyposis

For Partial fulfillment of Master Degree in
***Otorhinolaryngology (Review)***

***By***

**Amany Reda Shosha**

M.B.B.Ch.,Ain Shams University

***Under The Supervision Of***

**Prof. Dr. Mohamed Abdel Rauf**
Professor of otorhinolaryngology
Faculty of Medicine- Ain Shams University

**Prof. Dr. Waleed Farag**
Professor of otorhinolaryngology
Faculty of Medicine-Ain Shams University

*Faculty of Medicine*
*Ain Shams University*
*2014*

# Acknowledgement

I would like to express my deep thanks, gratitude and appreciation to Professor Dr. Mohamed Abdel Rauf Professor of otorhinolaryngology, for his extensive help, kind supervision and the continous encouragement throughout the course of this work.

Many great thanks and appreciation are also owed to Professor Dr. Waleed Farag Professor of otorhinolaryngology; for his great help, sincere cooperation and fruitful support during the conduction of this work.

Last but not the least I dedicate this work to my lovely family, my husband and my children Fares & Fayrouz (the apple of my eyes)

Thanks to all of you

With love…

**List of contents:**

# *List of abbreviation*

- ***AFS***

***Allergic fungal sinusitis***

- ***AI***

***Analgesic intolerance***

- ***AIA***

***Aspirin induced asthma***

- ***AR***

***Allergic rhinitis***

- ***ASA***

***Acetyl salicylic acid***

- ***CNS***

***Central nervous system***

- ***COX***

***Cyclo-oxygenase***

- ***CRS***

***Chronic rhinosinusitis***

- ***CT***

***Computerized tomography***

- ***EU***

***European union***

- ***FESS***

***Functional endoscopic sinus surgery***

- ***GIT***

***Gastrointestinal tract***

- ***IgE,G***

***Immunoglobulin E,G***

- ***IL8***

***Interleukin-8***

- ***NP***

***Nasal polyposis***

- ***NSAIDs***

***Non steroidal anti-inflammatory drugs***

- ***OA***

***Osteoarthritis***

- ***PGs***

***Prostaglandins***

- ***RA***

***Rheumatoid arthritis***

- ***RAST***

***Radioallergosorbent test***

- ***SAEs***

***Staphylococcus aureus exotoxins***

- ***TCR***

***T cell receptor***

- ***TH1,2***

***T helper cells 1,2***

- ***TNFα***

***Tumor necrosis factor α***

- ***US***

***United States***

- ***Vb***

***Variable b region***

- ***VCAM-1***

***Vascular Cell Adhesion Molecule-1***

# ***Introduction***

Nasal polyps (NP) are benign lesions arising from the mucosa of the nasal sinuses (commonly at the outflow tract of one or more of the sinuses) or from the mucosa of the nasal cavity. Having an uncertain etiology and a tendency to recur, they represent a challenging diagnosis for the physician to treat. **(Bateman et al.,2003)**

Management of polyposis involves a combination of medical therapy and surgery. There is good evidence for the use of corticosteroids (systemic and topical) both as primary treatment and as postoperative prophylaxis against recurrence. Surgical treatment has been refined significantly over the past twenty years with the advent of endoscopic sinus surgery and, in general, is reserved for cases refractory to medical treatment. Recurrence of the polyposis is common with severe disease recurring in up to ten percent of patients**. (Bachert et al.,2001)**

Recently it was found that when some patients with arthritis associated with nasal polyposis were treated by NSAIDS,the polyposis showed regression. **(Carol Eustice, 2009)**

# ***Aim of the work***

This study aims to review the available literature regarding the use of NSAIDS for patients with nasal polyposis, either for a concomitent condition or as a line of treatment for polyposis itself wiether they are useful or have no effect.

# *Review*

# *Chapter 1:*

## Epidemiology of nasal polyposis:

The earliest record of nasal polyposis is found in egyption literature of approximately 2,000 years BC. **(Yonge, 1906)**

Hippocrates (460-370 BC), the father of Medicine, had reffered to the "Nasal Growth" as "Polypus" due to their resemblance to the Sea-Polyp, and the name has persisted to this day. Hippocrates and other renowned physicians including Cladius Gallen , Paulus Aegineta and Fabricius Hildanus were known to have treated nasal polyposis in their time.**(Stevenson et al., 1949)**

Mounting evidence suggests that nasal polyposis (NP) is a clinical manifestation of multiple immunologic pathways, and because of that, the epidemiology is difficult to characterize. **( Gevaert et al., 2006)**

Phenotypically,chronic rhinosinusitis (CRS) can be classified as either CRS without NP or CRS with NP. CRS without NP, in general, reflects TH1- mediated inflammation **(Van Zele et al, 2006) .**

Idiopathic CRS with NP comprises the vast majority of cases of NP, and this term typically implies a clinical picture of diffuse sinonasal polyposis dominated by TH2-mediated (eosinophilic) responses, at least in western patients.

In rare cases, a distinct genetic, immunologic, or metabolic defect has been associated with the development of diffuse NP.

Furthermore, CRS with NP must be differentiated from antrochoanal polyps, which account for only 5% of polyp cases **(Larsen and Tos, 2002).**

Antrochoanal polyps are usually unilateral, solitary and most often arise from the maxillary sinus.This is a distinct disease process that often presents at a younger age compared to CRS with NP. In contrast to CRS with NP, antrochoanal polyps reveal lesser degrees of eosinophilia with a more normal appearing mucosal surface and basement membrane **(Ozcan et al., 2005).**

Allergic fungal rhinosinusitis is a known underlying pathophysiologic etiology in a subset of CRS patients and is strongly associated with NP. Ethnic and geographic variation has emerged as a potential modifier in NP pathophysiology.

The prevelance of nasal polyps (NP) in the population has been grossly estimated as 1-4%.

Large cohort studies have revealed a strong association between asthma and NP.

The incidence of NP increases with age and is likely the greatest between 40 and 60 years of age **(Bent et al, 1994).**

# ETIOLOGY AND PATHOPHYSIOLOGY:

The etiology of nasal polyps is multifactorial. It is widely accepted that there may be more than one cause. Some of the more commonly reported causes of nasal polyps include infection, allergy, immunologic factors, and hereditary diseases, such as cystic fibrosis and autonomic dysfunction. Kern and Shenck proposed a relationship between allergy and nasal polyps. **(Kern and Schenck, 1933).**

**Chronic infection:**

The most common pathogens are B-hemolytic streptococci, Staphylococcus aureus, Streptococcus pneumoniae, and Haemophilus influenza.

Polyps could be found in all sinusitis groups irrespective of an inducing agent and were not directly related to the presence of a certain microorganism.

Viruses have also been mentioned as a possible cause of nasal polyps ***(Weille and Gohd, 1957)***. However, a viral, etiology has not been shown, despite investigation for Adenovirus, Epstein-Barr virus, Herpes simplex virus, and Human papilloma virus ***[(Weille and Gohd, 1957) and ( Kozak et al., 1991)]***.

Also ***Larsen et al. (2001)*** reported in their search for human papilloma virus, using polymerase chain reaction, that the virus was not detected in nasal polyps.

**Staphylococcus infection:**

The presence of IgE antibodies to Staphylococcus aureus exotoxins (SAEs) has been reported to have a possible role in the severity of eosinophilic inflammation in nasal polyposis. **( Bachert C et al., 2002)**

**Allergy:**

At the beginning of the last century, an allergic aetiology of nasal polyps has been presumed, but never firmly demonstrated. The major features pointing to an allergic cause of nasal polyps include clinical symptoms similar to allergic rhinitis, the association with late-onset asthma and an elevated local IgE in polyp fluid as well as a pronounced tissue eosinophilia. However, polyps were found in only 0.5% of 3000 consecutive atopic patients examined by **Caplin et al, (1971).** Until today, an increased risk for allergic subjects to develop nasal polyps could not be demonstrated. In contrast, in a retrospective study by **Settipane and Chafee, (1977)** polyps were present in 2.8% of atopic patients, but in 5.2% of non-atopic subjects. In another study, there was a positive association between the blood eosinophil count and the presence of asthma with the number of polypectomies, but not with positive skin tests for different allergens.

Seasonal allergen exposure in patients with nasal polyps also did not enhance symptoms or markers of eosinophilic inflammation such as eosinophil percentage or eosinophil cationic protein concentration in nasal secretions **(Kieth at al, 1994).**

Although elevated total IgE was found in polyp fluid, there was no difference between polyps from allergic and non-allergic subjects.

However, it was noted that total IgE was higher in polyp fluid than the corresponding serum in both allergic and non-allergic polyp subjects. Local specific IgE production could also be demonstrated in nasal polyps associated with negative skin tests and serum RAST **.**

**Aspirin sensitivity:**

The pathogenesis of aspirin intolerance remains unclear. Nasal polyps are found in 35% to 96% of patients with aspirin sensitivity ***(Caplin et al., 1971)***

Samter's triad comprises patients with nasal polyps, asthma and aspirin sensitivity. Aspirin sensitivity is associated with asthma, anaphylactic chock, angioneuritic edema, and rhinorrhoea. These patients often represent the most severe cases of nasal polyps ***(Larsen and Tos, 2001)***.

***Albu et al. (2004)*** stated that patients presenting non steroidal anti inflammatory drugs (NSAID) intolerance or asthma are at risk for the development of recurrences after endonasal surgery for nasal polyposis.

**Cystic fibrosis:**

Nasal polyps have been reported in about 29% of patients with cystic fibrosis, most frequently in children aged between 4 and 12 years***[(Stammberger 1991) and ( Schramm and Effron 1980)]***.

The structure of polyps from cystic fibrosis patients does not differ from non-cystic fibrosis patients ***(Tos, 1985)***.

**Gene activation:**

Although information of the pathogenesis of polyposis is lacking, there are reports suggesting that a genetic predisposition underlies this disorder. These reports suggest that nasal polyposis involves deregulated cell growth, using gene activation in some ways similar to a neoplasm ***(Fritz et al., 2003)***.

**The role of environmental pollutants:**

Exposure to woodstoves, indoor tobacco smoke, pets and occupational exposure to noxious inhalant compounds have been reported to have a role in the pathogenesis of nasal polyposis. There is a strong association between the use of woodstoves as a principal source of heating and the development of nasal polypi ***(Pawankar, 2003)***.

Overall, the mechanism behind polyp formation is believed to be multifactorial. Recent evidence suggests an important role for proinflammatory cytokines, chimokines, and chemotactic factors in the pathogenesis of inflammatory polyps ***(Lane and Kennedy, 2003)***.