Review

What We Know about Nasal Polyposis: The Clinician's Point of View

Philippe Eloy * and Gabriela Musat

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What We Know about Nasal Polyposis: The Clinician's Point of View

Philippe Eloy [1,*] and Musat Gabriela [2]

[1] ENT Department, CHU UCL Namur, Ave.Therasse,5530, Yvoir, Belgium
[2] ENT Department "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
* Correspondence: philippe.eloy@chuuclnamur.uclouvain.be

Abstract: Nasal polyposis is defined by a Th2-driven chronic inflammation of the nose and sinus with polyps visible in the nasal fossae. It is a prevalent disease with a significant impact on the HRQL. Allergy, allergic rhinitis, asthma, and aspirin intolerance are frequently associated. The management is individual. The first line of treatment is a long-term treatment with intranasal corticosteroids. Oral corticosteroids should be used with caution. When the medical treatment fails the patient is eligible for sinus surgery. In case of symptomatic recurrence after both medical treatment and ethmoidectomy, biologics are nowadays a very promising treatment effective on all the respiratory tract. Dupilumab seems in the literature the molecule of choice. However, besides the international guidelines published by EPOS and Euforea, the molecule prescribed depends also on the availability of it in each country and the criteria edited by the health authorities to get reimbursement. Long treatment is mandatory. Traditional medical treatment is necessary as a complement to biologics.

Keywords:

Introduction

Sinonasal polyposis is a distinct form of chronic rhinosinusitis characterized by various phenotypes and endotypes[1,2].

Chronic rhinosinusitis (CRS) in adults is defined as a chronic inflammation of the nose and paranasal sinuses, characterized by two or more symptoms, one of which should be a nasal blockage or nasal discharge and/or facial pain or pressure and/or reduction or loss of smell. The diagnosis is confirmed by endoscopic signs (such as nasal polyps/mucopurulent discharge/edema of the middle meatus) or radiologic signs such as (mucosal changes in the sinuses/ostiomeatal complex on CT). In order to comply with the diagnosis of chronic rhinosinusitis the clinical manifestations should last without resolution longer than 12 weeks

CRS is classified in chronic rhinosinusitis with nasal polyps (CRSwNP) and chronic rhinosinusitis without nasal polyps (CRSsNP) [2]. Patients with nasal polyps account for 10 to 40% of all CRS patients [3–5].

The EPOS guidelines distinguish between primary nasal polyposis and secondary nasal polyposis, associated with cystic fibrosis, primary ciliary dyskinesia and immunodeficiency [1,2].

We will focus our topic on the primary nasal polyposis.

Epidemiology

CRS affects approximately 10-12% of the general population although there are significant geographical variations all over the world [4–8]. : Europe 10.9% [3,4],USA 12% [7], France 2% [8], Denmark 7.8% [9], China 8%[10], Korea 6.9% [11,12].

The exact prevalence of NP in the general population is also not clearly known as epidemiological studies are missing. However, in the literature we can find some percentages : an overall prevalence of 1% to 4% and also, great differences between countries ranging from 2.1% in France [8], 7% in Sweden [9], 4.3% in Finland, 1–4.2% in the USA [9], 1.1–2.2% in China [10].

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Nasal polyposis (NP) is more prevalent in men than in women, except in cases of aspirin intolerance. It predominantly affects adults after the age of 40, and its prevalence increases with age [5,13].

Special attention is needed in the case of polyposis with debut in childhood.

Etiology and Pathophysiology (Phenotypic and Endotypic Variants of Polyposis)

The pathophysiology of CRSwNP is considered multifactorial as there is not a single molecular pathway explaining the modifications of the mucosa leading to the formation of polyps [14]. The present conception is that CRS is a chronic inflammation generated by an imbalance of interactions between the host, the commensal flora, different pathogens, and exogen stresses [15]. In the last period, a superantigen theory has been proposed for the pathophysiology of CRSwNP hypothesizing that the colonization with staphylococcus aureus which secretes superantigenic enterotoxins increases an eosinophilic inflammation leading to the formation of the polyps [16].

The categorization of CRSwNP into phenotypes and endotypes helps in understanding the underlying mechanisms and treat accordingly [1,2].

From the phenotypic perspective, NP can be categorized into two variants: neutrophilic and eosinophilic polyposis.

The polyposis with neutrophils is associated to a TH1 inflammatory profile. It is more common in Asian or Chinese adults or in children with conditions such as cystic fibrosis or primary ciliary dyskinesia.

The NP with eosinophils is mainly found in Caucasian patients, particularly in those with aspirin intolerance, allergic fungal sinusitis, or the Churg Strauss syndrome.

In the past these polyps were considered allergic polyps.

Endotypes are classified based on pathophysiologic mechanisms, and molecular and immunological profiles.

NP in Caucasians is mostly associated to a TH2 driven chronic inflammation. Type 2 immune response involves Th2 cells, eosinophils, ECP, and upregulation of IL4, IL5, and IL13. There is also a high level of total IgE in the serum and the nasal secretion [17,18].

Table 1 reminds the endotypîng of CRS, the different mediators and their localization. This is modified from Van Zele et al 2006.

Table 1. T. Van Zele *et al.*, "Differentiation of chronic sinus diseases by measurement of inflammatory mediators," *Allergy*, vol. 61, no. 11, pp. 1280–1289, Nov. 2006, doi: 10.1111/j.1398-9995.2006.01225.x. (19).

	Cells : eosino/neutron	**IgE (tot or specific**	**Pathogens Staphylo or other**	**Cytokines**	**Other mediators**
Blood	+	+		(+)	(+)
Culture Swab			+		
Nasal secretion		+	+	+	+
Nasal cytology	+				
Tissue	+		+	+	+
Nasal NO	(+)				

Type 1 (Th1) endotype is dominated by a type 1 immune response involving Th1 cells, macrophages, and cytokines like TNF α and IFN γ. These patients have persistent polyps with less eosinophilic infiltration and are resistant to corticosteroids.

Recognizing phenotypes and endotypes helps understanding the disease and ultimately improves patient management and outcomes.

Th2-driven inflammation responds well to corticosteroids and biologics.

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Nasal polyposis is frequently associated with other diseases or comorbidities such as allergy, allergic rhinitis, asthma, and aspirin intolerance.

Allergic rhinitis is a very prevalent disease in the general population. Its prevalence can be up to 30% in the Belgian population. It is therefore logical to suspect a causal etiologic link between allergic rhinitis and CRS with or without polyps [20].

A paper written by Wilson and published in 2014 tried to answer the question [21]. He searched the literature of articles examining the link between AR and CRS with NP. He found 18 articles. 10 of them found an association, 7 articles showed no association, and 1 article established a possible association. No articles examined the outcomes of CRSsNP or CRSwNP following allergy treatment. The conclusion was that the role of allergy in CRSwNP and CRSsNP continues to be controversial. Therefore and because of the high prevalence of allergic rhinitis in the general population, allergy testing and treatment remain a must in the diagnostic workup of CRSwNP.

In the past eosinophilic polyps were considered as allergic polyps, however studies did not demonstrate a higher incidence of allergic patients in the population of NP. Nasal polyposis is therefore no longer regarded as an allergic process but an inflammatory process that can involve the entire respiratory tract [22–24].

An interesting direction to be studied in the future would be the link between food allergy and nasal polyps signaled by some authors [25,26].

CRSwNP is frequently associated with asthma [27]. Nasal polyposis is associated with asthma in 40% of cases, thus indicating the fact that it is an inflammatory disease affecting the whole respiratory tract. A lung function testing must be done for a complete assessment of nasal polyposis to rule out asthma or bronchial hyperreactivity.

As a clinical presentation, NP can present as an isolated condition or can be associated with asthma with/or without aspirin intolerance. Aspirin intolerance is a condition that is associated with CRSwNP in 36-93%of cases [1,2]. The association between nasal polyps, aspirin intolerance, and asthma was known historically as Widal syndrome or Samter's triad is called nowadays aspirin-exacerbated respiratory disease (AERD) or NSAID exacerbated respiratory disease (N-ERD) [7]. Compared to the case of patients tolerant to aspirin, nasal polyps and asthma have generally a severe evolution in patients with aspirin sensitivity [28,29].

Clinical Manifestations and Diagnostic Methods

Subjective evaluation of CRSwNP is based on its symptoms: nasal obstruction, nasal discharge or postnasal drip, facial pain or pressure, and reduction/loss of smell.

Table 2 shows the severity of the symptoms, the radiologic signs, and the Polyp nasal score in the case of CRSsNP, CRS wNP, and cystic fibrosis.

Table 2. Ref. T. Van Zele *et al.*, "Differentiation of chronic sinus diseases by measurement of inflammatory mediators," *Allergy*, vol. 61, no. 11, pp. 1280–1289, Nov. 2006, doi: 10.1111/j.1398-9995.2006.01225. x. [19].

	Controls	**Chronic sinusitis**	**Nasal polyps**	**Cystic fibrosis: nasal polyps**	**One-way Anova Fisher test**
N	10	10	14	14	14
Ct score/ Lund & Mackay	0.75 (0-2)	6 (2-11)	16.3 (7-24)	14.5 (5-20)	<0.0001
Polyp score (Davos)	0	0	4.8 (2-6)	2.9 (0-6)	<0.0001
Total symptom score	4(3-5)	6.6 (4-10)	9.6 (3-14)	4.3 (0-9)	<0.0001
Nasal congestion	1.1 (0-3)	1.0 (0-3)	2.6 (0-3)	2.8 (2-3)	0.001
Sneezing	0	0.1 (0-1)	0.2 (0-2)	0.6 (0-2)	0.761
Rhinorea	0.3 (0-2)	1.6 (0-3)	1.6 (0-3)	1.0 (0-3)	0.19

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Loss of smell	0	0	2.3 (0-3)	1.0 (0-3)	<0.0001
Postnasal drip	0	1.4 (0-2)	1.3 (0-3)	0.6 (0-2)	0.001
Headache	0.9 (0-2)	2.5 (1-3)	1.6 (0-3)	1.2 (0-3)	0.003

Obviously, nasal obstruction is a typical symptom more severe in the case of NP while cephalalgia is less frequent in CRSwNP compared to CRSsNP, except for patients with a surgical history. Nasal obstruction can be evaluated using rhinomanometry, acoustic rhinometry, a simple PNIF test, or a visual analogic scale (VAS).

The smell disorders encountered in CRSwNP are more common than in CRSsNP. Olfactory dysfunction is frequent in patients with CRSwNP (90%) and does not depend on the degree of nasal obstruction. The smell dysfunctions can vary significantly among patients with nasal polyps. Assessing the smell with olfactometry is important because the patient has difficulty evaluating his smell; Nowadays, olfactometry can be easily conducted using either a sniffing test [30]or a UPSIT test [31].

Sleep apnea syndrome can be associated with nasal polyposis and is quite frequent [32]. Patients with CRSwNP with important polyposis should be assessed in order to detect sleep disturbances [32–34].

Anterior rhinoscopy is used to assess the patient with polyposis but the fiberoptic endoscopy is preferable because it allows a better visualization of the interior of the nasal fossae for the diagnoses of polyposis in the nasal meatus [35] . Figure 1 shows a grade IV at the anterior rhinoscopy

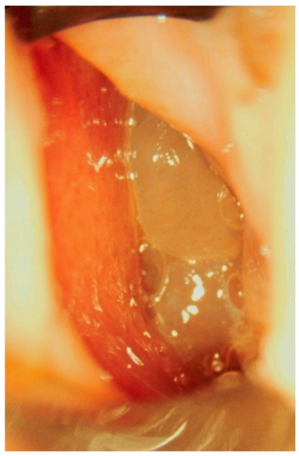

Figure 1. Nasal polyps, anterior rhinoscopy.

Figure 2 presents images of a nasal endoscopy showing nasal polyps in the middle and superior meatus on both sides.

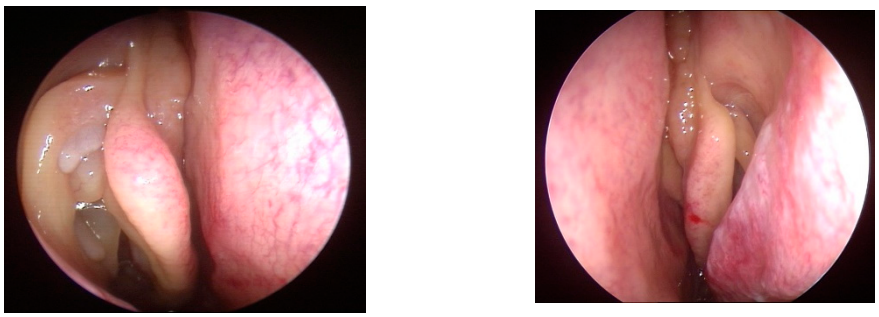

Figure 2. Nasal polyps, endoscopic view.

It also enables scoring the size of the nasal polyps. Many scoring systems have been used over the years to quantify the dimensions of nasal polyps [35,36]. One of the most used scoring systems

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for grading nasal polyps is the Meltzer clinical scoring system [37]. This scoring categorizes polyps into four grades:

0= no polyps
1= polyps confined to the middle meatus
2=multiple polyps occupying the middle meatus
3=polyps extending beyond the middle meatus
4=polyps completely obstructing the nasal cavity

In 2023, Gevaert et al [38] proposed a new scoring system for the nasal polyps that also involves 4 grades as follows:

0=no polyps
1=small polyps in the middle meatus not reaching the inferior border of the middle meatus
2=nasal polyps reaching bellow the lower border of the middle meatus
3=large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle turbinate
4=large nasal polyps causing complete obstruction of the inferior nasal cavity

CT scans are the radiological investigation of choice for the diagnosis of CRSwNP [39]. The CT scans are useful in confirming the type of polyposis, either a diffuse type involving the ethmoidal sinuses allergic and the other paranasal cavities bilaterally or a central localization, called CCDA (central compartment atopic disease) [40]. The central compartment type is frequently associated with allergies.

As the concern for radiation exposure is increased worldwide, cone-beam technology might be an alternative to classic CT scans [41].

The classic radiologic staging used in rhinosinusal polyposis is the one proposed by Lund-Makay in 1993 [42]. When reading a CT scan of the paranasal sinuses, the reader assigns each sinus a score

- No abnormality = 0 points
- Partial opacification = 1 point
- Complete opacification = 2 points

For the ostiomeatal complex, the score is different:

- No opacification = 0 points
- Opacification = 2 points

The sinuses are grouped into frontal sinus, anterior ethmoidal sinus, posterior ethmoidal sinus, maxillary sinus, sphenoid sinus, and ostiomeatal complex. Each side is scored separately. A maximum of 24 points is possible. Despite its simplicity, it correlates well with the severity of the disease, the extent of surgery, treatment response, and complication rates [32,43].

Isolated areas of the scanner do not allow the differentiation between meatal polyposis and chronic sinusitis without polyps. The endoscopy remains the complementary examination of choice.

The MRI is not typically part of the assessment except for the patients in previously operated patients with the suspicion of mucocele, or neoplasia. MRI has a better capacity to describe soft tissue and does not have a radiation risk. By better defining soft tissue it can differentiate different masses of retained secretions.

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The analysis of the nasal secretions proposed by ST Vlaminck can be a valuable diagnostic tool in the diagnosis and monitoring of eosinophilic polyposis. The secretions can be collected by simple blowing or preferably by aspiration under endoscopic control. The collected material is then examined for eosinophils, Charcot Leyden chrystals, allergic mucin, and fungal hyphae [44–46].

Impact on the Quality of Life

CRS has a remarkable impact on health-related quality of life [47,48] and is associated with important healthcare costs [49–51]. The quality of life of the patient with nasal polyposis can be severely impaired and it should be assessed by questionnaires meant to analyze the impact of the pathology on daily life. SNOT 22 test is an effective tool for this purpose [52–55]. See Figure 3.

I.D.:_____ **SINO-NASAL OUTCOME TEST (SNOT-22)** DATE:_____

Below you will find a list of symptoms and social/emotional consequences of your rhinosinusitis. We would like to know more about these problems and would appreciate your answering the following questions to the best of your ability. There are no right or wrong answers, and only you can provide us with this information. Please rate your problems as they have been over the past two weeks. Thank you for your participation. Do not hesitate to ask for assistance if necessary.

1. Considering how severe the problem is when you experience it and how often it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale: →	No Problem	Very Mild Problem	Mild or slight Problem	Moderate Problem	Severe Problem	Problem as bad as it can be		5 Most Important Items
1. Need to blow nose	0	1	2	3	4	5		○
2. Nasal Blockage	0	1	2	3	4	5		○
3. Sneezing	0	1	2	3	4	5		○
4. Runny nose	0	1	2	3	4	5		○
5. Cough	0	1	2	3	4	5		○
6. Post-nasal discharge	0	1	2	3	4	5		○
7. Thick nasal discharge	0	1	2	3	4	5		○
8. Ear fullness	0	1	2	3	4	5		○
9. Dizziness	0	1	2	3	4	5		○
10. Ear pain	0	1	2	3	4	5		○
11. Facial pain/pressure	0	1	2	3	4	5		○
12. Decreased Sense of Smell/Taste	0	1	2	3	4	5		○
13. Difficulty falling asleep	0	1	2	3	4	5		○
14. Wake up at night	0	1	2	3	4	5		○
15. Lack of a good night's sleep	0	1	2	3	4	5		○
16. Wake up tired	0	1	2	3	4	5		○
17. Fatigue	0	1	2	3	4	5		○
18. Reduced productivity	0	1	2	3	4	5		○
19. Reduced concentration	0	1	2	3	4	5		○
20. Frustrated/restless/irritable	0	1	2	3	4	5		○
21. Sad	0	1	2	3	4	5		○
22. Embarrassed	0	1	2	3	4	5		○

2. Please mark the most important items affecting your health (maximum of 5 items)_____ ↑

Figure 3. SNOT test questionnaire.

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Sino-nasal Outcome Test (SNOT-22) has 22 questions with scores from 0-5 for each question. Studies have described the following stratifications: Mild: 8-20, Moderate: >20-50, Severe: >50.

The visual analogue scale is also another method to quantify the severity of the symptoms .

Management and Treatment Approaches

The management of nasal polyposis remains individual [56]. The classic treatment of rhinosinusitis with polyps is based on nasal lavages associated to long-term intranasal corticosteroids [57,58]. These corticosteroids reduce rhinitis symptoms, improve nasal breathing, reduce the size of polyps, and prevent, in part, their recurrence, but this treatment has minimal effect on the sense of smell [57]. The effect of corticosteroids is based on their ability to diminish eosinophilic infiltration by reducing their viability and activation. Intranasal corticosteroids can be administered via spray or in lavages and the literature regarding their use is quite rich and favoring nasal steroids. Topical corticosteroids usually used are fluticasone propionate, mometasone furoat, betamethasone, beclomethasone dipropionate. Budesonide in nasal rinses is commonly used, though it is off-label [59–61]. Side effects of nasal steroids are epistaxis, dry nose, local irritation but usually they are well tolerated.

Oral corticosteroids (OC) should be reserved for obvious polyps associated to severe symptoms. Despite their effectiveness, OC should be used for short term (less than 7 days and a maximum of 3 courses per year), given the important side-effects (osteoporosis, diabetes melitus, necrosis of the head of the hip, glaucoma). The anti-inflammatory effect cannot be separated from the metabolic effect. There is a need for special attention for patients with diabetes mellitus or severe glaucoma.

The mean annual cumulative dose of oral corticosteroids over the year should be monitored and should not exceed 1ooo mg of prednisolone [32].

Short term or long-term antibiotic treatments with macrolides or doxycycline are reported by some studies to have a moderately positive effect on the size of polyps, and patient symptoms [62,63]. Nevertheless, the danger of antimicrobial resistance should be considered.

Patients not responding after a trial of a maximum medical treatment (intranasal steroids for at least 8 weeks, at least 2 courses of OC over the year, and symptomatic recurrence) are eligible for surgery [2,32,64].

Surgical options include a primary surgery, a simple polypectomy, a polypectomy associated with a skeletonization of the different meatuses or a functional ethmoidectomy. In fact, there is no definitive consensus. Simple polypectomy improves the nasal blockage but is associated with early and high recurrence rate [65].

Therefore, most rhinologists recommend performing a complete ethmoidectomy with sparing of the sinus mucosa [66,67].

In the case of revision surgery for massive symptomatic recurrence of the polyposis the surgery is usually more extended, more aggressive and the attitude towards the mucosa is less conservative.

The surgical options are therefore a nasalization, a Draf procedure, or a reboot procedure with complete resection of the mucosa of all the paranasal sinus cavities [68,69] .

Surgery has its advantages but also its inconveniences and obvious risks. There are anesthetic risks, neurological, vascular, and orbital complications. There are also risks of late complications such as synechiae, mucoceles, and colonization with staphylococcus aureus. In Table 3 we compared the benefits and weaknesses of the surgical treatment versus the medical in the case of the CRSwNP.

Table 3. Comparison of the benefits and weaknesses of oral corticosteroids versus sinus surgery.

	Benefits	Weakness
Oral corticosteroids	Big improvement of the major symptoms Improvement of the HRQL:	Frequent and early recurrence of the symptoms Rebound effect

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	Improvement of the sleep quality, sense of smell, reduction of the facial pain, reduction of nasal blockage	Advers events: gain of weight, anxiety, nervosity, irritability Osteoporosis, diabetes melittus, necrosis of the head of the hip
Sinus surgery	Improvement of the HRQL Good outcome after a short and middle term	Frequent recurrence of the disease Iatrogenicity Need for a general anesthesia Possibility of minor and major intraoperative and postoperativecomplications

One important issue after surgery is recurrence of the nasal polyps. The percentage is highly variable. In EPOS they reported a percent of at least 40% of recurrence of nasal polyps at 3-5 years after FESS before the arrival of biologics [70,71].

Vlaminck S. found 40% recurrence rates 3 years after FESS and 62% recurrence rate after 10 years of follow up [44,46].

Calus et al found a 78.9% recurrence rate with a follow-up of 12 years. Among them, there was a 36.8% need for a revision surgery [72].

Biological Treatment and Ongoing Care

Based on these data it seems necessary to find new molecules as add-on treatments to intranasal steroids and surgery [73].

In recent years, biological therapies have been developed as an endotype-driven therapy. Indeed, they are monoclonal antibodies acting as antagonists to some specific mediators of the Th2 inflammatory cascade. Historically biologics have first demonstrated their efficacy for the treatment of moderate or severe asthma unresponsive to traditional therapies. Afterward, they have been used to treat uncontrolled nasal polyposis. Therefore, ENT specialists benefit from the experience of pulmonologists.

Specific criteria have been edited by EPoS and EUFOREA guidelines for the prescription of biologics by an ENT (1,2, 73-,75).

Biological treatment is indicated in the event of symptomatic recurrence of nasal polyposis after a well-conducted medical treatment, an complete ethmoidectomy, or in case of a contraindication for anesthesia.

According to EPOS, the indication of biological treatment in CRSwNP is

- Symptomatic uncontrolled nasal polyposis unresponsive to traditional medical treatment (medical therapy +/- surgery) with these additional criteria:
- Evidence of type 2 inflammation (tissue eos≥10/hpf, or blood eos≥250, or total IgE≥100)
- Need for systemic corticosteroids or contraindication for systemic corticosteroids (≥2 courses per year, or long term . 3 months low dose steroids)
- Significantly impaired quality of life (SNOT22≥40)
- Significant loss of smell (anosmic on smell test)
- Diagnosis of comorbid asthma (asthma needing regular inhaled corticosteroids)

In the absence of surgical history, four criteria are required. In case of a surgical history, three criteria are sufficient.

In 2023 they changed a little bit the criteria. The blood eosinophilia should be \150 instead of 250 in the initial report [76].

3 molecules are currently prescribed by the ENT and available in Belgium: omalizumab, mepolizumab and dupilumab.

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Omalizumab is an anti-IgE monoclonal antibody. It reduces the levels of the total IgE in a dose-dependent way. Very early after its administration a quick drop of the level of the serum IgE of 89 to 90% is observed.

Gevaert published 5 studies in 2013 (first study), 2021 (comparison of 2 cohorts of patients : polyp 1 and polyp 2), 2023, 2024 (long-term results) [77–81]. He demonstrated that compared to the placebo group, omlizumab reduced significantly the polyp nasal score, the symptomatology, the sense of smell and the opacity (Lund McKay score) on CT. The efficacy was similar in allergic and non-allergic patients. In patients with concomitant asthma lung function was also improved.

Mepolizumab is an anti-IL5 monoclonal antibody validated by the FDA. IL 5 is an interleukin that plays a major role in the multiplication, maturation and survival of the eosinophils, key cells in the TH2 inflammatory cascade [81,82].

JK Han published in 2021 a well known study called Synapse conducted during 52 weeks [84]. This is a phase 3 RCT double-blind study demonstrating the efficacy and safety of Mepolizumab for the management of severe bilateral refractory nasal polyposis refractory to conventional treatment and requiring multiple sinus surgeries. The study demonstrated a significant reduction of the level of blood eosinophilia, an improvement of the nasal polyp score, an Improvement of the SNOT 22 after 8 weeks, a reduction of the VAS for nasal blockage, a reduction of the rescue medication by oral steroids, a reduction and delayed for revision surgeries for 52%, which was significant compared to the placebo group [85]. The Safety profile was similar to that observed with the placebo. A significantly greater proportion of patients (30%) in the mepolizumab group compared with the placebo group (10%), no longer required surgery at Week 25.

Dupilumab is an anti-IL4 and IL13 monoclonal antibody also validated by the FDA.

A study called Liberty NP sinus 24 & Liberty NP sinus 52 was published by Bachert et al in 2019 in the Lancet [86]. This was a multicentric RCT double blind control study with 2 different timing: the first conducted during 24 weeks and the other during 52 weeks. During these periods, they observed a significant reduction of the nasal polyp score, and nasal congestion, statistically significant after 8 weeks of treatment, compared to placebo. The period of time before using OC or performing a revision surgery was longer in the group with dupilumab. The symptoms recurred if the medication was stopped after 24 weeks. However, it is still as effective in the group of treatment for 52 weeks.

The question to be answered for the clinicians : which is the best biologic to prescribe to treat severe uncontrolled nasal polyposis.

Based on some metaanalysis and recent real life studies, dupilumab seems to be the most effective biologic compared to mepolizumab or omalizumab [87–90] with a good safety profile.

However, dupilumab can be associated with a transitory hypereosinophilia whose meaning is unclear [90].

However, the prescription of one drug instead of another depends also on the availability, the costs, and the criteria elaborated in the specific country to obtain reimbursement.

These molecules must be used for a long period of time. In any case, the clinician should wait for a minimum 2 months of treatment to observe significant effect and there are rapid responders and slow responders. This was perfectly well demonstrated in the Synapse Study. Patients stopping their treatment after 24 week shave a recurrence of their symptoms and polyps; patients treated for 52 weeks without interruption remain improved during all the duration of the study [86].

An important factor for the future is the cost and the criteria edited by the authorities to give the reimbursement compared to the cost of the most classical management. The response is evaluated based on the history, the presence of polyps at the nasal endoscopy, or the scanner.

According to EPOS and EUFOREA a minimum of 6 months of treatment is required to evaluate the efficacy. The two international forums recommend the evaluation of the response to biological treatment in CRSwNP based on 5 criteria:

- Reduced nasal polyp size
- Reduced need for systemic oral corticosteroids
- Improved quality of life
- Improved sense of smell
- Reduced impact of comorbidities

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The response is evaluated at 6 months and 1 year.

If the treatment is effective, it should be continued for several years with regular checks every 6 months. In any case, the patient should not discontinue the intranasal corticoids or the bronchodilator. If there is no response to any of the criteria the treatment should be discontinued or a switch to another drug can be done. Now there is no deadline to stop the treatment. Real-life studies with long-term follow-up (5 or 10 years) are necessary to confirm all our expectations.

Conclusion

Nasal polyposis is defined by a Th2-driven chronic inflammation of the nose and sinus with polyps visible in the nasal fossae

It is a prevalent disease with a significant impact on the HRQL.

Allergy, allergic rhinitis, asthma, and aspirin intolerance are frequently associated.

The management is individual.

The first line of treatment is a long-term treatment with intranasal corticosteroids. Oral corticosteroids should be used with caution.

When the medical treatment fails the patient is eligible for sinus surgery.

In case of symptomatic recurrence after both medical treatment and ethmoidectomy, biologics are nowadays a very promising treatment effective on all the respiratory tract. Dupilumab seems in the literature the molecule of choice.

However, besides the international guidelines published by EPOS and Euforea, the molecule prescribed depends also on the availability of it in each country and the criteria edited by the health authorities to get reimbursement.

Long treatment is mandatory. Traditional medical treatment is necessary as a complement to biologics.

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