

LITERATURE REVIEW

Difficulties in treating chronic rhinitis

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ABSTRACT

Rhinitis is a worldwide spread inflammatory disease, being defined by the presence of two or more of the following symptoms: nasal obstruction, rhinorrhea, sneezing or nasal itching. There are different factors which can lead to the inflammation of nasal mucosa: allergies, infections, medications, hormones or irritant substances. Classically, chronic rhinitis can be allergic or non-allergic. Due to the existing different types of chronic rhinitis, with indistinguishable specific symptoms, a correct and complete evaluation of patients is mandatory. The management of chronic allergic or non-allergic rhinitis should be individualized taking into consideration the etiology, symptoms' spectrum, duration and severity, physical exam findings, allergy work-up, co-morbidities, patient's age, patient's preferences.

KEYWORDS: chronic rhinitis, allergic rhinitis, non-allergic rhinitis, allergen-specific immunotherapy, turbino-plasty

INTRODUCTION

Rhinitis is a worldwide spread inflammatory disease, being defined by the presence of two or more of the following symptoms: nasal obstruction, rhinorrhea, sneezing or nasal itching^{1,2}. Chronic rhinitis is one of the most common chronic conditions in rhinology and affects almost 20 to 25% of the general population³.

There are different factors which can lead to the inflammation of nasal mucosa: allergies, infections, medications, hormones or irritant substances. So, according to all these possible causative factors, there are different types of chronic rhinitis. Classically, chronic rhinitis can be allergic (perennial and seasonal) or non-allergic. Non-allergic rhinitis (NAR) can be classified into several types, like: vasomotor rhinitis, hormonal-induced rhinitis, rhinitis medicamentosa, gustatory rhinitis, drug-induced rhinitis, etc.

PATHOPHYSIOLOGY OF CHRONIC RHINITIS

The identification of the pathophysiology of chronic rhinitis, allergic or non-allergic, has been a subject of clinical and scientific interest for the last decades⁴.

It is well known that, in case of allergic rhinitis (AR), the nasal congestion is an IgE-mediated reaction. The exposure to an allergen, known as the allergic sensitization, triggers the release of IgE directed against the allergen. Secondary to this reaction, the IgE will activate and get attached to the mast cells,

leading to the release of different immune mediators responsible for the nasal mucosa inflammation^{5,6}. The same reaction can be the cause of nasal congestion in case of occupational rhinitis.

In case of NAR, a non-IgE-mediated mechanism is present and it is important to identify the real cause of rhinitis and to make the difference between all pathological entities, including the less common ones – non-allergic rhinitis with eosinophils (NARES), NAR with mast cells (NARMA) or NAR with eosinophils and mast cells (NARESMA)^{7,8}.

In healthy individuals, the nasal mucosa does not include eosinophils, mast cells, bacteria or IgE. So, when all these entities are detected, a possible pathology has to be taken into account⁹.

EPIDEMIOLOGY

Chronic rhinitis affects a large part of the general population, being a significant cause of morbidity worldwide^{10,11}.

There are multiple studies in the literature analysing the incidence and prevalence of AR and NAR^{6,12,13}. Bauchau and Durban estimated that at least one of five adults from Western Europe is diagnosed with AR¹². Most authors classified the disease in allergic and non-allergic rhinitis, but there have also been described a significant number of patients with coexisting AR and NAR, the so-called mixed rhinitis¹⁴. According to this theory, the National Rhinitis Classification Task Force conducted a retrospective study on

975 patients, which concluded that 43% of patients had AR, 23% NAR and 34% mixed rhinitis^{14,15}.

Generally, it is estimated that 1 of 4 patients with chronic rhinitis is non-allergic.

Regarding the incidence, allergic rhinitis seems to be more frequent under 20 years of age and NAR in adult life^{16,17}. In both types of chronic rhinitis females are more affected^{15,17-19}.

CLINICAL CHARACTERISTICS

Due to the existing different types of chronic rhinitis, with indistinguishable specific symptoms, a correct and complete evaluation of patients is mandatory.

The diagnostic protocol should begin with a careful and detailed history of the symptoms onset, duration, triggers and associated pathologies. The gained information has to be correlated with the ENT examination findings – nasal endoscopic examination, rhinomanometry, cultures from nasal secretions for identifying bacteria or fungi, nasal mucosa cytology.

The radiologic evaluation (cranio-facial CT or MRI scan) can identify or exclude an inflammation of the paranasal sinuses mucosa.

To identify the atopic patients and to establish a diagnostic as allergic rhinitis, allergologic and immunologic profiles are mandatory.

So, we can say that the evaluation of patients with chronic rhinitis needs a multidisciplinary (ENTs and allergologists) approach.

Allergic rhinitis

An association between AR and some other conditions, such as asthma, sinusitis, sleep disturbances, nasal polyposis or conjunctivitis, has been observed. Although the link may be predominantly an allergic one, non-allergic factors may also be involved.

The classic symptoms of AR are represented by nasal obstruction due to the congestion of the nasal mucosa, sneezing, nasal itching, watery rhinorrhea, redness or swelling of the eyes (conjunctivitis). All these may be associated with cough, ear and facial pain, headache or sleep disturbances.

There are several studies evaluating the impact of AR symptoms upon patients' quality of life (QoL). A survey conducted in 2006 in America evaluated patients' perception of the symptoms of AR and the burden of AR on their daily activities²⁰. The telephone survey was performed on 2,500 adults, over 18 years of age, diagnosed with symptomatic AR, nasal allergies or hay fever. They had received medical treatment for their nasal allergies within the previous 12 months. All patients were asked about their condition and treatment. From the ten most common symptoms associated with allergic rhinitis, 61% of sufferers experienced

moderate to extreme bothersome postnasal drip during a nasal allergy attack, 62% moderate or extreme runny nose (anterior rhinorrhea) and 78% related moderate or extreme bothersome stuffed-up nose.

During the same year, a prospective, cross-sectional, international survey was performed in Europe. The survey assessed patients' and physicians' perception regarding the symptoms of allergic rhinitis and their impact on patients' QoL²¹. According to this survey (data recorded on 1,482 patients), in patients with seasonal allergic rhinitis, the most bothersome symptoms were represented by blocked nose (69%), itchy/red eyes (64%), watery eyes (68%) and sneezing (74%),

In a telephone and internet survey on 2,355 individuals with allergic rhinitis, Shedden found that nasal congestion was related as the most severe symptom of AR by 40% of participants, adults and children²². Also, it was the main reason for patients to seek medical advice. The author reported that one third of respondents had their nasal congestion recurred after taking medication.

Considering the complex pathophysiology of nasal congestion, this can contribute to patients' dissatisfaction with treatment.

Shedden, as well as other authors, showed that there can be an important impact of nasal obstruction upon sleep²²⁻²⁵. In healthy patients, with no nasal pathology, the nasal valve is the most important component of nasal resistance. At the nasal valve level, the cross-sectional area is of 30mm² and the velocity of the air-flow is of 12-18m/s, leading to collapse and increased resistance. On the other hand, when the air-flow reaches the nasal cavity its velocity decreases at 2-3m/s. In this area, the cross-sectional area is greater – 130mm²²⁶. Therefore the smaller the cross-sectional area, the more increases the velocity of the nasal airflow.

The same physiological pattern takes place in case of nasal mucosa congestion. The hypertrophy of the inferior turbinates mucosa due to inflammation and edema leads to a decrease in the cross-sectional area of the nasal cavity. The results are an increased air-flow velocity at this level, as well as an increased nasal resistance. This phenomena being influenced by body position, the nasal airway resistance becomes greater in horizontal position than upright²⁷.

Nasal congestion can predispose to sleep-related breathing disorders by switching to oronasal breathing and decreasing the pharyngeal patency.

Non-allergic rhinitis

Non-allergic rhinitis is a multifactorial disease and the identification of the onset factors is the clue for its treatment. Symptoms of NAR can be the same as in AR, but with negative allergy skin tests. Joint Task Force on Practice Parameters in Allergy and Asthma and Immunology showed that almost 50% of the patients presenting with rhinitis do not have allergic rhinitis²⁸.

Non-allergic rhinitis, as well as allergic rhinitis, represents a risk factor for asthma onset.

Vasomotor rhinitis, a subtype of NAR, is characterized by excessive, watery rhinorrhea often in response to odours, temperature or humidity changes, eating (gustatory rhinitis) or alcohol ingestion. The diagnosis of this entity is based on patient's history and exclusion of other diseases²⁹.

Rhinitis medicamentosa or rebound rhinitis is characterized by nasal congestion without rhinorrhea or sneezing and it is induced by the overuse of nasal decongestants. There is also described the drug-induced rhinitis due to oral contraceptives, antihypertensive drugs or psychotropic medications.

In the literature, the so-called "allergic-like" rhinitis – NARES and NARESMA – is described, in which eosinophils can be found in the nasal mucosa, but with negative nasal and serologic IgE. The nasal symptoms are similar to those of non-allergic rhinitis associated with nasal and ocular itching.

DIFFERENTIAL DIAGNOSIS OF CHRONIC RHINITIS

The differential diagnosis of chronic rhinitis should be made, first of all, between the two major types of rhinitis – allergic and non-allergic. In case of non-allergic rhinitis, we have to differentiate each subtype according to the etiologic factors.

Other pathologies with which the differential diagnostic has to be made, from the nasal obstruction point of view, are: nasal polyposis, deviated nasal septum, chronic rhinosinusitis.

We also have to pay attention to some of the minor symptoms of chronic rhinitis, like postnasal drip or cough. Postnasal drip is a symptom than can be found in the clinical picture of different disorders, such as common flu, allergies (the so-called allergic postnasal drip), rhinosinusitis, foreign bodies of the nasal cavities, pregnancy, certain medications (including birth control pills and blood pressure medications), food ingestion, changing weather temperature or gastroesophageal reflux disease (GERD).

According to Mladina et al.³⁰, two holes syndrome seems to be present in the majority of postnasal drip patients. They found posterior fontanel defects in more than half (57.3% of patients, N=723) of the patients with postnasal drip, the cause of this phenomena being the recirculation of mucus in the maxillary sinus.

Chronic cough can be found in the clinical context of different pulmonary and non-pulmonary disorders. From the ENT perspective, the non-pulmonary causes of chronic cough can be laryngopharyngeal reflux (GERD), neurogenic cough (post viral vagal neuropathy), asthma, rhinitis, allergy, rhinosinusitis, aspiration

due to glottis insufficiency, Zenker's diverticulum or angiotensin-converting-enzyme inhibitors.

TREATMENT

Nasal obstruction represents the most important symptom of chronic rhinitis^{31,32}. The major mechanism of nasal obstruction is inflammation and this can have a great impact upon patients' QoL. The treatment of nasal obstruction as symptom of chronic rhinitis has to be in accordance with its etiology.

Considering pharmacologic therapy, in case of *allergic rhinitis*, the treatment with intranasal corticosteroids represents the therapy of choice³³. The administration of intranasal corticosteroids (INCS) is recommended in practical guidelines as first-line pharmacotherapy in those cases with severe nasal congestion³⁴. Oral steroids should be considered the last line therapy, only for severe cases, due to their important adverse reactions (saline retention, hypertension, cardiac disorders, cushingoid status, peptic ulcer or femoral head osteonecrosis).

Several studies demonstrated the efficacy of INCS in relieving nasal blockage, nasal discharge and itch, postnasal drip^{35,36}. Even if there is an overall success of corticosteroid treatment, there is a low efficacy in case of AR, compared to patients diagnosed with NAR³⁷. In AR, maximum efficiency is gained by combining INCS with antihistamines³⁸.

Antihistamines represent one of the main therapeutic methods for allergic rhinitis treatment. This pharmacological agents are effective in symptoms like rhinorrhea, sneezing and nasal/ocular itching. Unfortunately, these substances also have adverse reactions. The first-generation antihistamines can produce nervous system depression, sedation, dizziness or impaired coordination³⁹.

Beside the anti-allergic effect, the second-line antihistamines have also an anti-inflammatory action, being useful in ameliorating nasal obstruction.

Oral and topical decongestants can also be used in treating AR. Oral formulas should be avoided in children, adults over 60 years old or patients with cardiac pathology. The risk in case of topic intranasal decongestants is the development of rhinitis medicamentosa. For this reason, the therapy is recommended for maximum 10 days^{1,39,40}.

Cromones, leukotriene, anticholinergic medication may be used to treat allergic rhinitis^{1,39-43}.

Patients' education is also very important in case of allergic rhinitis. Patients' motivation is maybe the key of a successful therapy. The clinician has to explain the mechanism of the disease, its evolution and treatment options. At the same time, allergy avoidance can have a positive impact upon symptoms, even though it is not always possible.

The typical pharmacological treatment of allergic rhinitis has some limitations, such as polysensitization, failure in allergen eviction or adverse effects of the treatment. Polysensitization is common in patients with allergic rhinitis, the severity of symptoms tending to be more important in patients with sensitization to multiple allergens.

Allergen-specific immunotherapy has been proved to be extremely effective in patients with IgE-mediated symptoms triggers. The effects of this therapy can be sustained for years and it may prevent the development of new allergies. Immunotherapy decreases IgE concentration and reduces the production of eosinophils⁴⁴. There are two ways of administration – subcutaneous (SCIT) and sublingual (SLIT) immunotherapy.

SCIT was first used by Noon in 1911 and has demonstrated efficacy in the treatment of both allergic rhinitis and asthma^{45,46}. It can be used in children under 5 years and its effectiveness is preserved for a longer period of time after the treatment. For SLIT instead, its long-term effectiveness after the treatment has not been demonstrated yet⁴⁶.

Allergen-specific immunotherapy is indicated in severe cases, refractory to medical treatment, associated with different comorbidities and complications.

Like any other therapy, there are some disadvantages in what immunotherapy is concerned: long-time treatment (3-5 years) – the results are seen after 6-12 months of administration – requires cooperation from the patient and there are risks of anaphylaxis. Due to the long-term administration, patients can become noncompliant to treatment.

The pharmacological therapy of *non-allergic rhinitis* should be individualized according to the etiology and it should be chosen in accordance with patients' age, severity of the disease, associated pathology and patients' preferences.

As well as in case of allergic rhinitis, in non-allergic rhinitis, one of the first advices is to avoid the environmental triggers, such as cigarette smoke, strong odors (perfumes, soaps, etc.) or different medications.

First-generation antihistamines seem to have an important impact upon the symptoms of chronic rhinitis due to their anticholinergic activity, while oral second-generation antihistamines are not as effective in the treatment of NAR^{39,47}. On the other hand, topical nasal antihistamines are most effective when used on a regular basis and relieve symptoms like postnasal drip, nasal congestion or sneezing within minutes^{48,49}.

Intranasal corticosteroids have been found effective in treating NAR, especially vasomotor rhinitis, NARES and NARESMA^{39,50,51}. Their daily use may help relieve symptoms. Nevertheless, a better benefit is gained from using a combination of intranasal antihistamines and INCS.

Topic anticholinergic medication, such as ipratro-

pium bromide, is considered the best treatment for the watery nasal discharge in case of gustatory or vasomotor rhinitis^{52,53}.

Oral decongestants may help relieve nasal congestion and are recommended if intranasal antihistamines and INCS do not help. In case of decongestant nasal sprays, this should be considered only as an adjuvant therapy, their use being limited to only 2 or 3 days.

Nasal saline lavage has been proved to be helpful alone or in combination with INCS in patients with chronic rhinitis, in the long term.

In case of rhinitis medicamentosa, the first step is to withdraw the topical decongestant, and a short course of oral steroids and INCS may be found helpful.

Surgery has to be indicated only after three months of failed pharmacotherapy. There are also authors who invoke even a 6- or 12-month medical therapy before considering the surgical option^{1,39}. It is recommended in case of non-allergic rhinitis with turbinate hypertrophy and in those cases with associated nasal pathology (nasal septum deviation, nasal polyposis, etc.).

During the past years, many procedures have been described for reducing the inferior turbinates volume: lateroposition of the inferior turbinate, resection procedures (total or partial turbinectomy, submucosal turbinectomy, anterior turbinectomy, etc.), coagulating procedures (submucosal diathermia, electrocoagulation of the turbinate mucosa, cryotherapy, Argon plasma coagulation, radiofrequency turbinoplasty, laser diode or CO₂ turbinoplasty).

When considering surgery, the first question is if there is an involvement of the inferior turbinates mucosa or bone. The correct surgical intervention has to be chosen in accordance with the hypertrophy type of the rhinitis.

The best methods of evaluating the aspect of inferior turbinates and nasal airway resistance are nasal endoscopic examination, imaging (CT scan) and rhinomanometry. From our point of view, in case of a patient with chronic non-allergic rhinitis, in whom the nasal endoscopy (Figure 1) and the cranio-facial CT scan reveals a hypertrophy of the inferior turbinates, with no signs of other associated pathologies (obstructive nasal septum deviation, rhinosinusitis, nasal polyposis, etc.) (Figure 2), we perform a rhinomanometry evaluation. This test helps us differentiate between the mucosal and the bone hypertrophy of the inferior turbinate.

If after the decongestion test we observe a significant improvement of the nasal airway resistance with normal volume air, like in Figure 3, we consider a hypertrophy of the mucosa of the inferior turbinates, and a laser or radiofrequency turbinoplasty can be recommended. On the other hand, if there is no improvement after decongestion, a hypertrophy of the bone is involved in the nasal obstruction (Figure 4) and a partial or total turbinectomy can be considered.

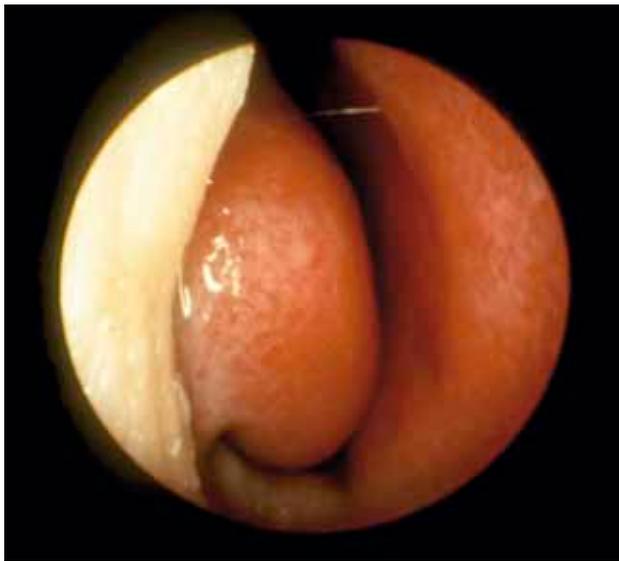


Figure 1 Nasal endoscopic examination – hypertrophy of the inferior turbinates



Figure 2 Cranio-facial CT scan, coronal slice, hypertrophy of the inferior turbinates with no other pathological signs

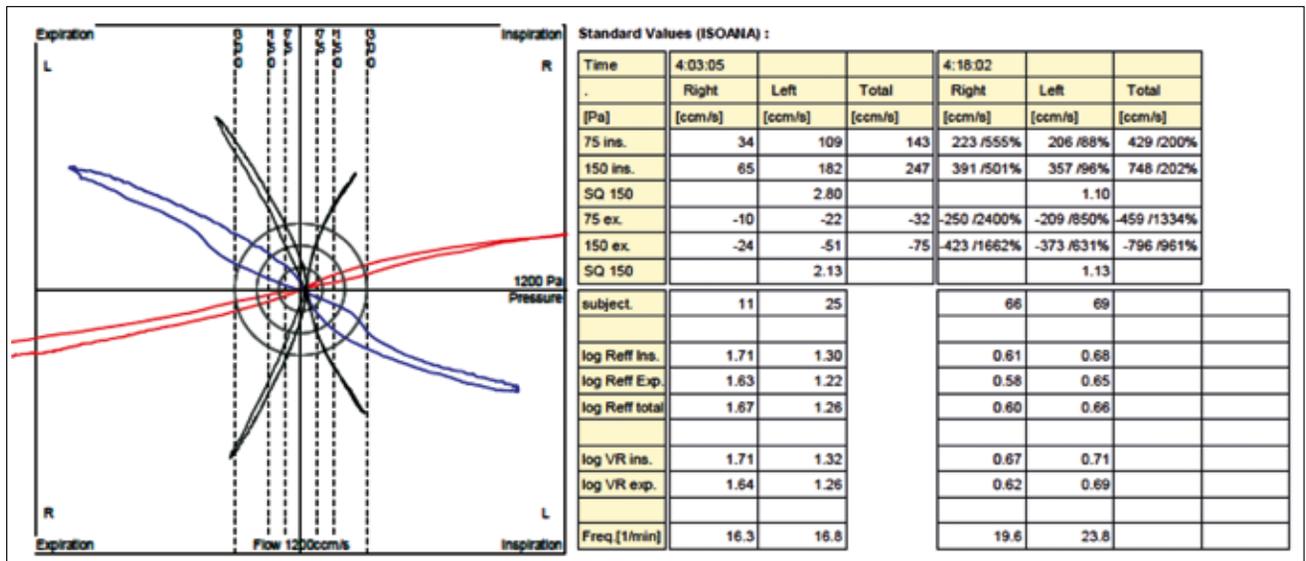


Figure 3 4-Phase Rhinomanometry result – severe nasal obstruction before decongestion (red curve – right nostril, blue curve – left nostril) and normal breathing parameters after decongestion (black curves)

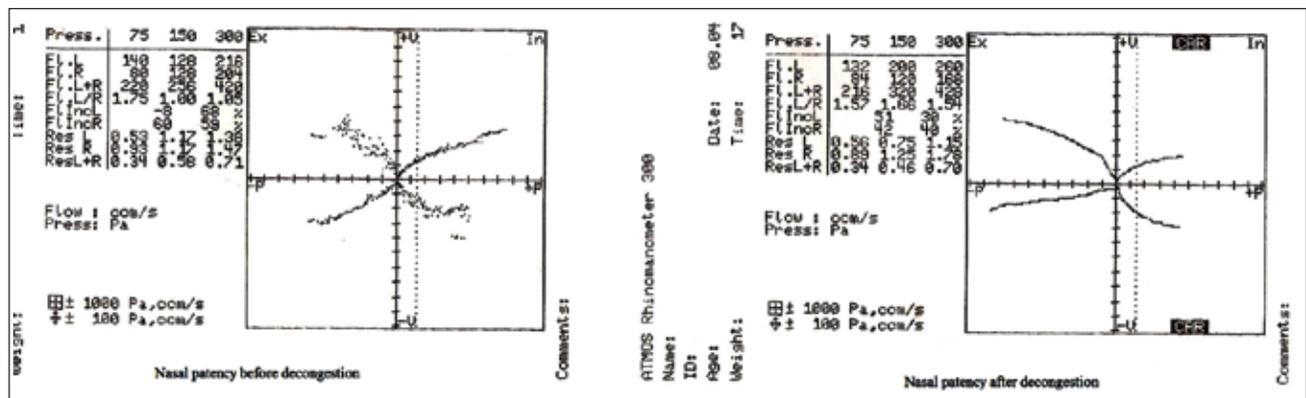


Figure 4 Rhinomanometry – severe nasal obstruction before and after decongestion

OUR EXPERIENCE

We performed a prospective study, between 2009 and 2011, on 726 patients (456 men and 270 women) diagnosed with chronic rhinitis.

Our evaluation protocol consisted in anterior rhinoscopy, nasal endoscopic examination performed before and after decongestion, rhinomanometry for an objective evaluation of the nasal airway resistance and a cranio-facial CT scan.

Analyzing the data, we encountered 167 patients with allergic rhinitis confirmed by the allergologists (23%) and 559 patients with non-allergic rhinitis (77%) (Chart 1). In NAR patients group (N=559), 30.95% (173 patients) were diagnosed with vasomotor rhinitis, 48.48% (271 patients) with rhinitis medicamentosa, 9.48% (53 patients) with NARES and 6.8% (38 patients) with hormonal rhinitis (Chart 2).

The AR patients group were followed-up by the allergologists and received proper pharmacological and immunological treatment.

All patients with NAR underwent the maximal time of medical treatment, three months, according to the etiology of rhinitis.

In the final survey we included those patients with vasomotor rhinitis and rhinitis medicamentosa (n=444). From all 444 patients, in 173 cases, the correctly conducted medical therapy (intranasal corticosteroids, antihistamines, ipratropium bromide) did not present any subjective or objective (rhinomanometry) success and the surgical therapy – radiofrequency turbinoplasty – was indicated.

Patients' survey was conducted using a standard 0 to 10 VAS (visual analogue scale), with 0 representing no symptoms and 10 the most severe ones. The symptoms assessed preoperatively and during each follow-up visit (at 6 and 12 months) included nasal obstruction, rhinorrhea, sneezing and nasal itching. At 12 months after surgery, patients filled out a Global Patient Assessment (GPA) questionnaire designed to monitor patients' satisfaction after the procedure. We wanted to know: 1). if the patients would choose to undergo the same procedure again, if needed (yes/not sure/no); 2). how would the patient rank his or her overall experience (on a scale of -5 to 5, with -5 being the worst outcome possible and 5 being the best outcome possible).

54 patients were lost during the follow-up or refused to complete the questionnaires.

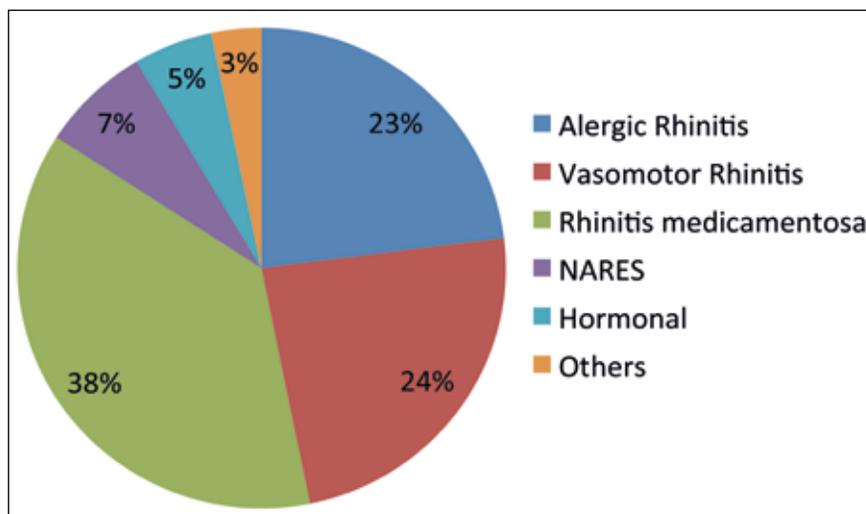


Chart 1 Classification of chronic rhinitis in the study group

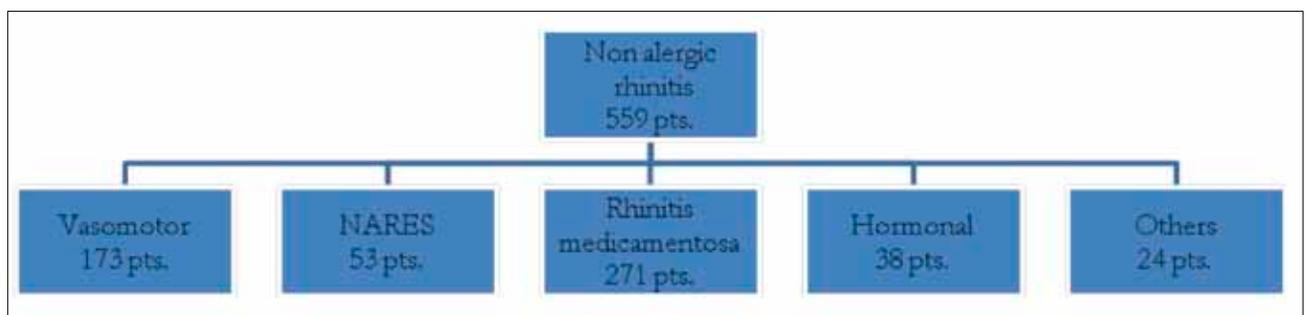


Chart 2 Classification of non-allergic rhinitis (pts. – patients)

We considered a “favourable response” from our patients the improvement of at least the nasal obstruction, without worsening of any other of the remaining symptoms, and patients’ satisfaction with the surgery results. The response rates were of 77.31% (92 of 119) at 6 months after surgery, respectively of 60.50% (72 of 119) after 12 months.

Analyzing the VAS results, we observed a statistically significant improvement in all assessed symptoms at 6 and 12 months postoperatively, compared with the pre-treatment evaluation (Table 1).

After 12 months from the surgery, 18 patients needed an additional nasal surgery – submucosal resection of the inferior turbinates.

Considering the GPA questionnaire results of the remaining patients (101 patients): 69.31%, meaning 70 patients, responded “yes” to having the same surgical procedure again if needed; 27.72%, 28 patients, responded “no” and 2.97%, 3 patients, responded “not sure”. The mean score of GPA questionnaire was 2.9, so patients had a significantly positive response regarding the effect of the nasal surgery upon their symptoms and quality of life.

The objective evaluation was performed with the help of rhinomanometry (Figure 5).

CONCLUSIONS

According to the international guidelines, as well as our own experience, the management of chronic allergic or non-allergic rhinitis should be individualized taking into consideration the following: symptoms’ spectrum, duration and severity, physical exam findings, allergy work-up, comorbidities, patient’s age, patient’s preferences.

Before choosing the therapeutic strategy (medical, surgical), we have to differentiate allergic and non-allergic rhinitis and establish the etiology of non-allergic rhinitis.

In addition, a treatment plan should use step-up and step-down approaches: step-up when therapy is inadequate and step-down after symptom relief is achieved or maximized.

Table 1
Preoperative and follow-ups VAS results

Symptom	Preoperatively	6 Months	12 months	P-value
Nasal obstruction	6.65(1.92)	2.74 (1.72)	4.45 (2.54)	<.001
Rhinorrhea	5.90(2.79)	2.84 (2.47)	3.79 (2.97)	<.001
Sneezing	5.15(2.77)	2.51 (2.12)	3.50 (2.77)	<.001
Nasal itching	3.67(3.03)	1.51 (1.87)	2.41 (2.30)	<.001

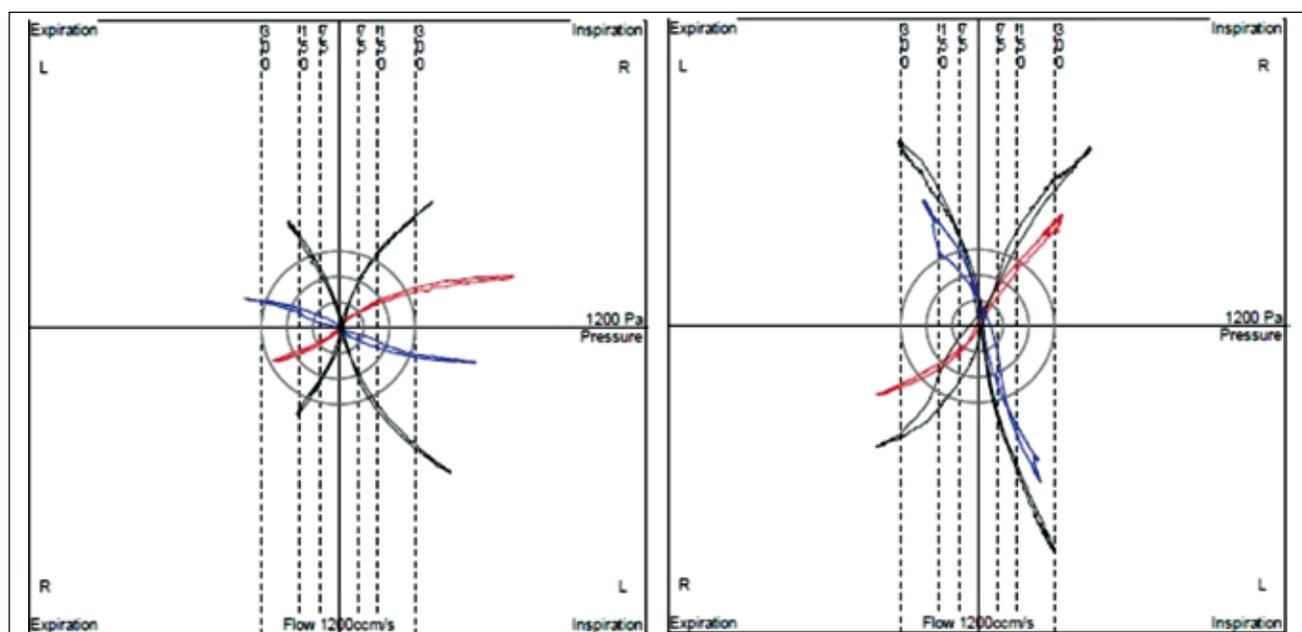


Figure 5 4-Phase Rhinomanometry before and 6 months after surgery; normal nasal airway resistance before and after decongestion at 6 months after surgery

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