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Nasal Obstructive Disorders induce medical treatment failure in Pediatric Persistent Allergic Rhinitis (The NODPAR Study)

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ABSTRACT

Background. Allergic rhinitis (AR) is the most common chronic disease among children. To characterize the disease, a modified classification of severity (m-ARIA) has recently been validated in AR children. When medical treatment fails, surgery for nasal obstructive disorders (NOD) may be a therapeutic option. Our objective was to assess the prevalence of NOD and their influence in medical treatment response among children with persistent AR (PER). **Methods.** In a prospective, real-life study, 130 pediatric PER patients (13.1 ± 2.8 years, females 31.5%, severe rhinitis 49%) referred from Allergy to ENT department were assessed for their response (R, responders; NR, non-responders) to medical treatment (intranasal steroids and antihistamines or antileucotriens) by direct questioning and nasal symptoms VAS, the presence of NOD (septal deformity, turbinate enlargement and adenoidal hyperplasia), comorbidities, nasal symptoms, rhinitis severity (modified-ARIA criterion) and asthma control (International Consensus On Pediatric Asthma criterion). **Results.** After two months of treatment, the NR group presented a higher prevalence of obstructive septal deformity and severe inferior turbinate enlargement when compared with the R group. Higher septal deformity and turbinate enlargement scores were strongly associated with treatment refractoriness. The prevalence of severe PER was also higher for the NR group. Higher asthma control scores were associated with the probability of treatment-induced improvement. **Conclusions.** In pediatric PER patients, medical therapy refractoriness was associated with NOD, mainly septal deformity and turbinate enlargement. In those patients, ENT examination will facilitate an early NOD diagnosis in order to indicate potential corrective surgery.

Key words. Allergic rhinitis, nasal obstruction, nasal septum deformity, pediatrics, turbinate hyperplasia.

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INTRODUCTION

Allergic Rhinitis (AR) is the most common chronic condition in childhood (1). The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines developed a classification on the basis of the impairment of quality of life (mild and moderate/severe) (2). Recently, a modified criterion (m-ARIA) has been introduced, which discriminates moderate from severe patients in pediatric untreated patients (3).

The most frequent comorbidities in AR children are conjunctivitis, asthma and atopic dermatitis (4). Despite the importance of nasal obstruction as a relevant symptom in AR and that anatomical nasal obstructive disorders (NOD) may also be a significant comorbidity, few attention has been paid to nasal endoscopy and NOD in AR international consensus guidelines (2,5).

Septal deformity (SD), turbinate enlargement (TE), and adenoidal hyperplasia (AH), may cause nasal obstruction in children (5). Up to 48% of children present SD (6) but no study has investigated the prevalence of inferior TE in the pediatric general population. A relationship between nasal obstruction assessed by endoscopy and perception of nasal obstruction has been reported in children with AR (7). In addition, it has been suggested that TE might be a predictive sign for AR diagnosis in children (8).

To our knowledge there are no published studies describing the prevalence of NOD on pediatric AR patients nor its relationship with medical treatment failure.

In this real-life study, the main objective was to demonstrate the impact of NOD on failure of medical treatment in children and adolescents with persistent AR (PER), as well as their impact on disease severity.

METHODS

I. STUDY POPULATION AND DESIGN

A non-randomized, prospective, real-life study was performed from June 2013 to August 2015. Children and adolescents (n=130) diagnosed with moderate/severe PER according to ARIA guidelines criteria (nasal symptoms for more than 4 days a week and for more than 4 consecutive weeks) (2) referred from Allergy to ENT Department at Sant Joan de Déu Children's Hospital were included. All patients received treatment with daily oral intranasal steroids (fluticasone or mometasone) for at least 2 consecutive months at recommended doses. Non-asthmatic subjects added daily antihistamines (desloratadine). Asthmatic patients received daily leukotriene receptor antagonists (montelukast). Asthma pharmacotherapy (inhaled corticosteroids and beta-2 adrenergic agonists) was prescribed by pediatric allergists according to disease severity and level of control, with optimal maintenance doses sought on an individual basis. No patients had received systemic corticosteroids within 30 days prior to inclusion. PER severity was assessed by the m-ARIA items to classify patients on different levels: mild (no items affected), moderate (1-3 items affected) and severe (all of four items affected) (3).

After treatment adherence was corroborated by direct questioning (forgetfulness of using intranasal steroids less than 8 times in 2 months), patients were asked "*Have your symptoms of allergic rhinitis improved with the treatment? (yes or no)*". Patients who reported lack of symptom's improvement (n=86) were included in the non-responders (NR) group while patients with successful improvement after medical treatment (n=44) were included in the responders (R) group.

Demographic data (age and gender), the use and duration of specific immunotherapy and the presence of comorbidities were evaluated. According to age, patients were stratified in children (6-11 years) and adolescents (12-17 years).

Exclusion criteria were: upper respiratory tract infection in the last two weeks, previous nasal/adenoidal surgery, or the presence of a serious concomitant illness. The Ethics Committee of our institution approved the study and signed informed consent was obtained from patient's legal guardians.

II. NASAL OUTCOMES

1. Nasal symptoms. A visual analog scale score (VASs) ranging from 0 (not at all bothersome) to 100 mm (extremely bothersome) was used to assess the severity for each individual symptom: nasal obstruction, smell loss, anterior and posterior rhinorrhea, facial pain, itching, sneezing, and epistaxis. Children under 12 years old were additionally guided by a faces rating scale (FRS) located above the VASs line. FRS is a picture projection technique in which six faces similar to “emoticon” are shown to a child. The first picture is a very happy smiling face and the last is sad and crying (7).

2. Nasal obstructive disorders (NOD). Nasal examination was carried out with a 2.4 mm flexible endoscope.

Septal deformity was scored (0-2) as: 0, no deformity; 1, non-obstructive with a partial nasal pathway obstruction; and 2, obstructive with the septum contacting the lateral nasal wall.

Turbinate size was classified in 4 grades (0-3) according to Friedmann’s classification (9): grade 0, normal; grade 1, mild enlargement; grade 2, moderate enlargement with no obvious obstruction; grade 3, severe enlargement with complete occlusion of the nasal cavity.

Adenoid size was scored in 4 grades (1-4) according to Parikh’s endoscopic classification (10): grade 1, adenoids without contact with other anatomic structures; in grades 2, 3, and 4 adenoids are in contact with torus tubarius, vomer, or soft plate (at rest), respectively. Thus, grades 3 and 4 cause bilateral choanal obstruction.

Nasal Endoscopy Scoring (Table 1). An endoscopic grading system (0-2) was created for analysis: 0, no nasal obstruction; 1, partial obstruction; and 2, total obstruction. This grading system was used to obtain the septal and turbinate score for each individual nasal cavity. The sum of left and right septum and turbinate scores defined the *Septal Deformity Score (SDS)*, and the *Turbinates Enlargement Score (TES)*, respectively. As adenoids affect both nasal cavities, the scores used were 0, 2 and 4, to obtain the *Adenoidal Hyperplasia Score (AHS)*. The *Total Nasal Disorders Score (TNDS)* was obtained with the sum of SDS, TES and AHS (0-12).

IV. TONSILAR HYPERPLASIA.

Tonsil size was graded according to Brodsky grading scale (0 to 4): grade 0, tonsils within the tonsillar fossa; in grades 2, 3, and 4 tonsils occupy $\leq 25\%$, 26-50%, 51-75% and $>75\%$ of the oropharyngeal width, respectively (11).

III. DIAGNOSIS OF ALLERGIC RHINITIS AND ASTHMA

Skin prick tests were performed using extracts against house dust mites (*Dermatophagoides pteronyssinus* and *farinae*); pollens (*parietaria judaica*, graminees, *plantagos*, *artemisia*, *salsola*, *chenopodium*, olive-tree, *cupressaceae*, *platanus*); animal dander; and *alternaria*. The level of asthma control was quantified (0 to 3) according to the International Consensus On (ICON) Pediatric Asthma (12): 0, no control, 1, partial control; 2, good control; and 3, complete control.

IV. STATISTICAL ANALYSIS

Statistical analysis was performed using Epiinfo for Windows (Epiinfo TM 7.1.5; Atlanta, USA). Differences among group means were studied by an analysis of variance (ANOVA). The inter-group and intra-group analyses were performed with two-tailed tests with significance at the $p < 0.05$ level, and data were presented as mean $\pm$ standard deviation. Descriptive analysis was carried out for the demographic characteristics, and a comparative analysis between groups was performed using the χ^2 test. To determine the relationship between different comorbidities and medical response, logistic regression tests were performed with the binary outcome of lack of improvement as the dependent variable and comorbidities as independent variables. In order to validate the question for cataloging patients as responders or non-responders, a receiver operating characteristic (ROC) curve analysis was performed.

A recent clinical decision support system in AR (MACVIA) (13) has defined well-controlled AR as an overall VASs of 5 or less of 10cm. Using this cut-off criterion for the total-VASs (mean of nasal obstruction, itching, sneezing and anterior rhinorrhea), we performed a new logistic regression to retrospectively analyze the impact of NOD on treatment response.

RESULTS

1) Demographic characteristics.

A total of 130 patients were enrolled. Table 2 summarizes demographic and clinical data. The two groups (R and NR) were homogeneous in gender and age. According to m-ARIA classification, no mild patients were included in the study. Prevalence of severe rhinitis was higher in the NR group compared to the R group.

The most frequent comorbidities were asthma and conjunctivitis, without differences between NR and R groups.

2) Nasal Symptoms

All symptoms except epistaxis were significantly worse, displaying statistically significant higher VASs, in the NR group than in the R group (Fig 1). Nasal obstruction displayed the highest VASs in the NR group, while sneezing had the highest score reported for the R group. Moreover, a higher VASs in all nasal symptoms, except epistaxis, was associated with lack of improvement after medical treatment (Table 3). For hyposmia and facial pain, this association was maintained when eliminating chronic rhinosinusitis (CRS) as a potential confounding factor (OR=0.23 [0.1, 0.6]; $p=0.0005$ and OR=0.29 [0.1, 0.4]; $p=0.002$ respectively).

3) Nasal Endoscopic Disorders

Septal deformity and turbinate enlargement. The NR group presented higher SDS and TES (Fig 2A, 2C), prevalence of obstructive SD and TE (Fig 2B, 2D) when compared with the R group.

Adenoidal hyperplasia. Although we observed a tendency of higher frequency of obstructive AH and AHS in the NR group (Fig 2E, 2F), neither this difference nor the prevalence of AH reached statistical significance in these comparisons. However, there was a tendency of greater obstructive AH prevalence for younger children when compared to adolescents, nevertheless this difference was not statistically significant (table 4).

Combined nasal obstructive disorders. TNDS was also higher in the NR group (Fig 2G). Nearly half of the patients (45.5%) presented bilateral endoscopic nasal obstruction in the NR group whereas no cases were found in the R group (Fig 2H).

Medical treatment responsiveness (logistic regression). The presence of obstructive SD (OR=0.15 [0.05, 0.42]; $p=0.00003$), SDS, TES, and TNDS were inversely associated with improvement after medical treatment, based on odds ratios (Fig 3).

4) PER severity (m-ARIA)

Nasal obstruction ($61.5\pm23.8\text{mm}$ vs $46.6\pm29.4\text{mm}$, $p=0.003$), anterior (52.5 ± 30.3 vs $40.5\pm30\text{mm}$, $p=0.02$) and posterior (54.2 ± 33.4 vs $34.1\pm29\text{mm}$, $p=0.0007$) rhinorrhea, nasal itching ($52\pm33.5\text{mm}$ vs $32.2\pm30\text{mm}$, $p=0.0008$), sneezing ($57.9\pm32.5\text{mm}$ vs $4.75\pm31.8\text{mm}$, $p=0.02$), smell loss ($40.6\pm33\text{mm}$ vs $17.9\pm13\text{mm}$; $p=0.0002$), facial pain ($2.67\pm2.4\text{mm}$ vs $1.34\pm1.2\text{mm}$, $p=0.002$), and epistaxis ($12.5\pm12.3\text{mm}$ vs 3.9 ± 1.2 , $p=0.006$) were higher in severe than in moderate PER patients.

No differences between moderate and severe AR were found in terms of NOD prevalence. However, severe turbinate hyperplasia (OR=2.4 [1.1, 4.9], $p=0.01$), bilateral endoscopic nasal obstruction (OR=2.1 [1.1, 4.5], $p=0.02$), TES (OR=2.6 [1.1, 6.5]; $p=0.009$) and TNDS (OR=1.2 [1.1, 5.6]; $p=0.003$) were strongly associated with severe PER. Obstructive SD and SDS were not associated with PER severity.

5) Allergy study

Allergen sensitization details are described in table 2. Two thirds of patients (69.2%) had received specific immunotherapy with a mean duration of 2.91 years but no differences were observed between NR and R groups (63.9% vs 79.6%; $p=0.1$).

6) Comorbidities (asthma, conjunctivitis, CRS)

Although asthma prevalence, conjunctivitis, and CRS were not statistically different between NR and R groups, asthmatic patients in the R group had a better control of asthma (Table 2). The presence of asthma, conjunctivitis, or CRS did not increase the risk of medical failure, but a higher asthma control score increased the probability of improvement after medical

treatment. In addition, severe AR was inversely associated to medical treatment response (Fig 3).

7) Lack of improvement according to total-VASs

ROC analysis reported an area under the curve of 0.862, representing good accuracy for the question “*Have your symptoms of allergic rhinitis improved with the treatment? (yes or no)*”. Youden index displayed a cut-off point of <3.8cm in the total-VASs to define lack of improvement with a sensibility of 81% and a specificity of 76%. Using MACVIA (13) criterion (Total-VASs≤5cm), we observed an increased risk of lack of improvement for the presence of obstructive septal deviation [OR=4.4(1.8-10.7); p=0.008] and turbinate enlargement [OR=5.4(2.3-12.3); p=0.001], but not for obstructive adenoidal hyperplasia [OR=1.3(0.3-5.5); p=0.7].

DISCUSSION

The main findings of the present study are: i) VASs can be used as a simple quantitative method to evaluate nasal symptoms, disease severity and response to medical treatment in pediatric PER patients; ii) nasal obstruction is the main symptom associated with medical treatment failure; iii) there is a higher prevalence of NOD in PER pediatric patients refractory to medical treatment; iv) SD and TE are independent risk factors associated to the lack of improvement after medical treatment; v) in PER pediatric patients, a higher control of asthma is associated with AR improvement with medical treatment; vi) m-ARIA classification is a valid tool to discriminate severe from moderate PER pediatric patients, thus associating medical treatment refractoriness with a higher PER severity.

In real-life adult studies, the VAS has been used to assess effectiveness (14) and inadequacy (15) of treatments. Ciprandi et al. suggested that assessment of FRS and VAS may be used in clinical practice to quantify nasal obstruction in children but they did not investigate other AR symptoms (7). However, primary school children often underestimate their nasal obstruction (16).

In our study all nasal symptoms except epistaxis had significantly worse VASs in the NR group and were associated with medical treatment failure. Nasal obstruction was the most prevalent symptom in the NR group, which was linked to NOD. In the R group (with less NOD) however, we found that sneezing but not nasal obstruction was the predominant symptom. Although facial pain and smell loss are not considered classic AR symptoms, both of them had higher VASs and were related to medical treatment failure despite the elimination of CRS as a potential confounding factor.

It has been reported that PER induces hyposmia, probably linked to nasal obstruction and inflammation (17). However, the olfactory improvement with antihistamines seems to be more related to anti-inflammatory than to nasal patency changes (18), suggesting that NOD may contribute to the lack of smell improvement in treated patients.

In our study almost half of the patients with uncontrolled PER had bilateral endoscopic nasal obstruction. In addition, obstructive SD and higher endoscopic scores were associated with medical treatment failure. PER may trigger the release of nasal and systemic proinflammatory mediators (19), leading to sub-epithelial inflammation and irreversible fibrosis of the inferior turbinate (20). Since turbinate congestion significantly diminishes drug delivery into the nasal cavity (21), this could partially explain why patients with NOD do not properly respond to medical therapy.

We found that all cases with obstructive AH belonged to the NR group, and observed a tendency of higher AHS for this group of patients. Additionally, almost 40% of PER patients with obstructive AH were children.

Several studies have observed an association between obstructive adenoids and chronic nasal obstruction in children (22,23). Moreover, AH have been associated with higher rhinitis severity and persistent duration (24). Persistent allergic inflammation can cause lymphoid hyperplasia of the adenoidal tissue (25), with a prominent eosinophilic inflammatory pattern (26). However, AR has been found less frequently in the age group of 7-10 years in which the AH incidence is the highest (27). These clinical observations suggest that AR is a persistent inflammatory process that can lead to AH, which may contribute and increase the resistance to medical treatment.

Additionally, here we report that all nasal symptoms were significantly worse in treated patients with severe than moderate PER, and that prevalence of severe AR is higher in the NR group. Thus, the fact that untreated children's moderate and severe PER are two different severity phenotypes (3), also applies for treated pediatric patients. Concerning nasal examination, the risk of having severe PER was found more than two-fold higher in patients with severe TE or bilateral endoscopic nasal obstruction whereas higher TES and TNDS, were associated with severe PER, suggesting that NOD may impair quality of life, contributing to AR severity.

In accordance with the Spanish AR pediatric population (4), there was a male preponderance in our cohort and the most frequent non-nasal comorbidities were asthma and conjunctivitis. Higher asthma control scores increased the probability of medical treatment improvement. It has been reported that AR has a major impact on asthma control (28). If AR and asthma are linked (29), it should not be surprising that treating AR would improve asthma symptoms.

MACVIA guidelines (13) proposes a new algorithm to optimize disease control, defining well-controlled AR as a VASs of 5 or less of 10 and recommending the use of combined INS+intranasal azelastine in non-controlled AR. Unfortunately, this drug was not yet available in our country by the time the study was initiated.

In conclusion, obstructive nasal SD and TE are strongly associated with a poor response to medical treatment in pediatric PER. Consequently nasal examination is necessary in these patients to differentially diagnose NOD, and to evaluate effective surgical procedures in order to improve nasal symptoms, disease severity, and patient's quality of life. Thus, nasal endoscopy, nasal symptom scores (VAS), and ARIA-m severity classification should be included in future pediatric AR management protocols and international guidelines. These are valuable tools to be used in daily real-life medical care, which may allow doctors to discriminate among different phenotypes of PER patients and better tailor AR treatment regimens to meet patient's needs, primarily in those showing resistance to medical treatment.

LIMITATIONS

- i) The main limitation is the absence of a clear and specific criterion to define medical responsiveness with the consequent low internal validity. However, results were corroborated by similar findings using the total-VASs cut-off point.

Moreover, the reliability of the question to define responsiveness was demonstrated by ROC analysis, significant higher symptoms VASs in the non-responders and association of higher VASs with lack of improvement in the logistic regression model; ii) there was a lack of immunologic parameters useful to better understand the pathophysiological meaning of the clinical data; iii) children sample size (n=38) was relatively low, maybe insufficient to compare NOD in age terms; iv) data analysis wasn't done blinded to reduce bias.

ii)

STRENGTHS

This real-life study is the first to demonstrate the impact of NOD on medical treatment failure and disease severity among pediatric PER patients. In daily medical practice, the decision of ENT specialists to indicate nasal surgery is very often based on a simple question of whether the patient have improved or not after conservative treatment (30). Our study mimics routine clinical practice conditions, providing high external validity. We have created a novel endoscopic scoring system which might predict clinical outcomes. Additionally, m-ARIA classification has proved the existence of 2 well defined phenotypes in treated moderate/severe PER children.

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FIGURE LEGENDS

Figure 1. Nasal Symptom's severity (VAS) in pediatric PER patients. VAS data points of responders (grey columns) or non-responders (black columns) to medical treatment are plotted. Two-tailed Student's t-test was performed and difference between responders and non-responders groups were evaluated where, ***, $p<0.001$; **, $p<0.01$.

Figure 2. Nasal Obstructive Disorders (2A, -C, -E, -G) scores and (2B, -D, -F, -H) frequencies in pediatric PER patients depending on m-ARIA severity levels in responders (grey columns) or non-responders (black columns) to medical treatment. Two-tailed Student's t-test difference between responders and non-responders groups was performed where, ***, $p<0.001$; **, $p<0.01$.

Figure 3. Logistic regression model associations of comorbidities (independent variables) and Nasal Obstructive Disorders with the binary outcome of Medical Response (dependent variable) assessed by the direct question "*Have your symptoms of allergic rhinitis improved with the treatment? (yes or no)*". m-ARIA, modified Allergic Rhinitis and its Impact on Asthma. Probability of lack of improvement was evaluated where, black lines, $p<0.05$ association with lack of improvement; dark gray lines, $p<0.05$ association with improvement; light gray lines, $p>0.05$ no association with medical response.

Table 1. Endoscopic Scoring System

Septal Deformity	Score	Turbinate Enlargement	Score	Adenoids Hyperplasia	Score
No	0	No/Mild	0	No / Parikh Grade 1	0
Non-obstructive	1	Moderate	1	Parikh Grade 2	2
Obstructive	2	Severe (obstructive)	2	Parikh Grades 3 - 4	4
Total SDS (left + right)	0-4	Total TES (left + right)	0-4	Total AHS	0-4

SDS, Septal Deformity Score; AHS, Adenoidal Hyperplasia Score; TES, Turbinate Enlargement Score; TNDS, Total Nasal Disorders Score = SDS + TES + AHS.

Table 2. Demographic and Clinical Data

		Total	Non-responders Group			Responders Group			p**
			Males	Females	p*	Males	Females	p*	
Age	N (%)	130 (100)	59 (68.6)	27 (31.4)		30 (68.2)	14 (31.8)		NS
	Mean (SD)	13.1 (2.8)	13.42 (2.76)	13.22 (3.33)	0.76	12.73 (2.86)	13.14 (5.97)	0.64	NS
	6-11 years n (%)	49 (37.6)	23 (26.7)			15 (34.1)			NS
	12-18 years n (%)	81 (62.3)	63 (73.3)			29 (65.2)			
PER severity (m-ARIA)	Mild n (%)	0 (0)	0 (0)			0 (0)			0.00003
	Moderate n (%)	66 (50.7)	32 (37.2)			34 (77.3)			
	Severe n (%)	64 (49.2)	54 (62.8)			10 (22.7)			
Asthma	N (%)	75 (57.9)	46 (61.3)			29 (38.7)			NS
Asthma control (ICON)	Complete n (%)	27 (36)	11 (23.9)			16 (55.2)			0.03
	Good n (%)	30 (40)	21 (45.6)			9 (31)			
	Partial n (%)	14 (18.6)	10 (21.7)			4 (13.8)			
	None n (%)	4 (5.3)	4 (8.7)			0 (0)			
Conjunctivitis	N (%)	48 (36.9)	36 (41.9)			12 (27.3)			NS
CRS	N (%)	8 (6.1)	8 (9.3)			0 (0)			NS
Pure PER†	N (%)	31 (23.85)	18 (20.9)			13 (29.5)			NS
Medical treatment recieved	INS + antiH1 n (%)	55 (42.1)	40 (38.7)			15 (61.3)			NS
	INS + LRA n (%)	75 (57.9)	46 (61.3)			29 (38.7)			
Tonsils size (Brodsky)	Grade 0 n (%)	5 (4)	5 (4.3)			5 (2.2)			NS
	Grade 1 n (%)	74 (59.2)	43 (36.9)			31 (13.6)			
	Grade 2 n (%)	36 (28.8)	27 (23.2)			9 (3.9)			
	Grade 3 n (%)	10 (8)	8 (6.9)			2 (0.9)			
	Grade 4 n (%)	0 (0)	0 (0)			0 (0)			
Sensitization according to skin prick test	Monosensitization n (%)	46 (35.3)	14 (31.8)			32 (37.2)			NS
	HDM n (%)	118 (90.7)	77 (89.5)			41 (93.2)			NS
	Pollens n (%)	39 (30)	30 (34.9)			9 (20.4)			NS
	Animal dander n (%)	25 (19.2)	18 (20.9)			7 (15.91)			NS
	Alternaria n (%)	8 (6.1)	5 (5.81)			3 (6.8)			NS

P*, ANOVA comparison between males and females; P**, Chi square corrected (Yates) comparison between non-responders and responders groups; CRS, Chronic Rhinosinusitis; NS, Not significant; INS, intranasal steroids; antiH1, antihistamines; LRA, Leukotriene receptor antagonists; †, PER patients without asthma, conjunctivitis or CRS.

Table 3. Logistic regression model with increase in the nasal symptom VASs as a predictor variable for medical treatment refractoriness

One centimeter increase in symptom VAS	Risk of lack of improvement after medical treatment	
	Point Estimate OR (CI)	p
Nasal obstruction	2.47 (1.82-3.35)	0.00001
Sneezing	1.33 (1.16-1.53)	0.00001
Posterior rhinorrhea	1.45 (1.24-1.7)	0.00001
Anterior rhinorrhea	1.35 (1.16-1.57)	0.0001
Itching	1.2 (1.06-1.36)	0.002
Hyposmia	1.34 (1.13-1.59)	0.0005
Facial pain	1.52 (1.2-1.93)	0.0005
Epistaxis	1.11 (0.86-1.44)	0.4

Logistic regression with the binary outcome of lack of improvement as dependent variable and nasal symptoms VAS as independent variables (risk of medical refractoriness for every 1 cm increase in VASs), where, OR, Odds ratio; CI, 95% Confidence interval

Table 4. Prevalence of Nasal Obstructive Disorders According to Age.

	Children (6-11 y.o.)			Adolescents (12-18 y.o.)			P*
	Responders	Non-responders	Total	Responders	Non-responders	Total	
Obstructive Septal Deviation n (%)	2 (10)	11 (37.9)	13 (26.5)	3 (12.5)	28 (49.12)	31 (38.2)	NS
Obstructive Turbinate Enlargement n(%)	0 (0)	19 (65.5)	19 (38.7)	0 (0)	36 (63.1)	36 (44.4)	NS
Obstructive Adenoidal Hyperplasia n(%)	0 (0)	5 (17.2)	5 (10.2)	0 (0)	4 (7)	4 (4.9)	NS
Severe Rhinitis (ARIAm) n (%)	6 (30)	15 (51.7)	21 (42.9)	4 (16.7)	39 (68.4)	43 (53.1)	NS
Asthma n (%)	14 (70)	19 (65.5)	33 (67.3)	15 (62.5)	27 (47.4)	42 (51.8)	NS
CRS n (%)	0 (0)	3 (10.3)	3 (6.1)	0 (0)	5 (8.8)	5 (6.2)	NS
Conjunctivitis n (%)	6 (30)	7 (24.1)	13 (26.5)	6 (25)	29 (50.9)	35 (43.2)	NS

P**, Chi square corrected (Yates) comparison between children and adolescent groups; NS, Not significant

Figure 1

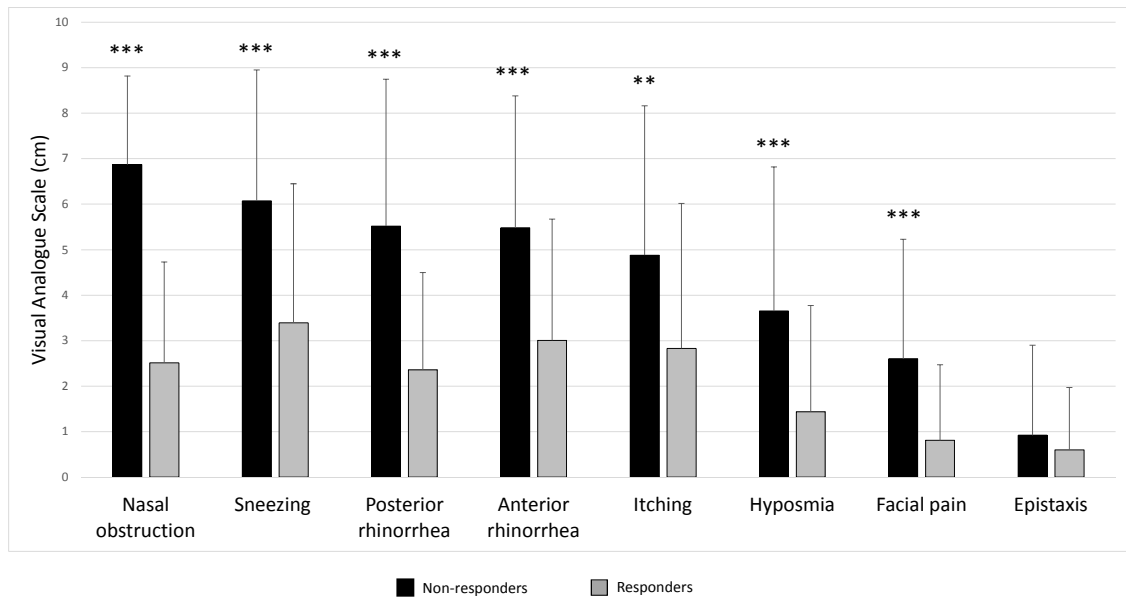


Figure 2

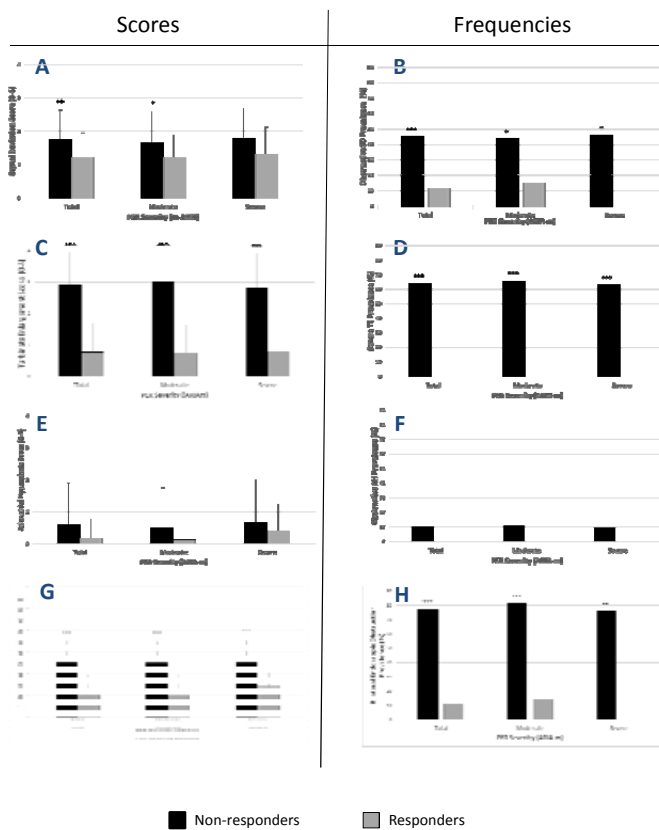


Figure 3

