



## Rhino-bronchial syndrome in children: Pathogenic correlations and clinical-experimental aspects

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Asthma

### Summary

**Objective:** This study aims at defining the incidence of rhino-bronchial syndrome (RBS) in children in order both to verify the influence of nasal obstructions on the disease and to determine therapeutic strategies which may cure the syndrome effectively at its early stage.

**Methods:** The investigation includes 128 non-allergic children with obstructive disorders (adenoid hypertrophy, septal deviation, etc.) and rhino-sinus inflammations associated with bronchopulmonary diseases (asthma, chronic cough, bronchopulmonary infections). Medical and/or surgical treatment was chosen in consideration of the type and entity of the patients' main nasal pathology.

At least 1 year follow-up was provided for each case to establish the improvement in the disorders affecting both the lower and upper airways. The results were statistically assessed.

**Results:** Medical and mainly surgical treatment always cured the upper airways disorders in patients with chronic nasal obstruction and rhino-sinus inflammation. Improvement of bronchopulmonary disease was reported in about half of the patients (49.4%). Statistically significant results were obtained only in the group with recurrent bronchopulmonary infections (80.9%,  $p < 0.05$ ).

**Conclusions:** The study confirms that RBS may be quite frequent in childhood. This disorder has a multifactorial pathogenesis prevalently due to nasal obstruction and rhino-sinus infections.

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In the population studied, among the lower airways disorders, only infective bronchopulmonary inflammation showed a significant correlation in the assessment between lower and upper airways disorders. In order to prevent the progression of the syndrome to serious pathologic events of the lower airways, a prompt and effective treatment of children's nasal disorders is thus recommended.

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## 1. Introduction

Although rhino-bronchial syndrome (RBS) has not been fully recognized as a pathologic reality, many studies have dealt with the disease, explored its manifestation and suggested possible treatment. RBS can be defined as a nasological entity which occurs when either a hyperreactive, chronic or recurrent inflammatory process, however induced, or anatomical alterations of rhino-sinus district, facilitate the development of an inflammatory state of lower airways that could cause a function impairment [1]. The syndrome evolves from the primitive noxa localized in the upper respiratory tract to the bronco-pneumonic structure which is the disease target organ.

However, a pathologic condition in the two areas (nose and bronchi) has often been observed especially in immuno-allergic cases without there being any apparent concurrent association [2]. Such cases cannot therefore be included within RBS. In a recent paper 60% of the chronic rhino-sinusitis cases studied were shown to have associated lower airways involvement, without apparent real dependence relationship between the lower and upper airways [3]. A relationship between the diseases of the two areas has not yet been documented nonetheless the possibility of there being a link seems remote. Medical studies generally avoid considering the possible connection of the diseases in the two areas [4]. However, the recurrence/resistance of RBS has been supported through the *ex-adiuvantibus* criterion, i.e. the improvement of bronco-pneumonic disease after medical or surgical treatment of rhino-sinus disorders [5]. The results obtained after nose and paranasal sinus surgery can be significant especially if the operation is performed by modern endoscopic technique (Functional Endoscopic Sinus Surgery, FESS). This technique is particularly effective in asthmatic patients suffering from chronic rhino-sinusitis since it can actually improve their respiratory problems [6–9].

In the last few years, RBS has been the object of many studies aimed at defining its incidence, pathogenesis, clinical manifestations, and treatment.

With respect to RBS incidence, some epidemiological studies have found an evident correlation of the disease with the patients' age.

Whereas the occurrence of the disease has been found in only about 1/4 of adult patients suffering from disorders of the upper and lower airways [5], in childhood the disease seems to have a higher incidence. Studies carried out in Germany [10,11] reported a high correlation of RBS (53–65%) in asthmatic children. But these data were not confirmed by successive researches. Other studies carried out by Slavin [12] and by Rondelli et al. [13] have reported a scalar increase of the syndrome occurrence from infancy to adulthood. There seems to be a decrease in the older population (12% in the 2nd decade, 17% in the 3rd decade, 22% in the 4th decade, 32% in the 5th decade and 17% in the 6th decade).

RBS pathogenesis has not been well defined yet. Thus, its framing has been based on different and often contrasting hypotheses. The latter refers mainly to three nasal pathologies which can effect bronco-pneumonic structures, namely:

- nasal hyperreactivity;
- nasal sinus infections;
- nasal obstruction.

Nasal hyperreactivity is commonly present in vasomotor mastocyte-dependent pathologies. It may origin either from abnormal nasal bronchial reflexes, by many considered the main factors of the syndrome [5,12–24], or from the release of chemotaxis mediators at nasal level, which are then absorbed by bronchial mucosa with consequent bronco-spastic phenomena [21,25].

*Nasal sinus infections* are due to post-nasal drip passage in the oro-pharynx and inhalation in the lower airways [4,5,12,26,27]. Moreover, the purulent inflammation may cause both a  $\beta$ -adrenergic blockage and a synthesis of inflammation mediators. Many authors consider both disorders important causal elements of RBS [12,28,29].

*Nasal obstruction* can undoubtedly be a fundamental pathogenetic factor since it limits or prevents important nasal functions, such as air conditioning and air filtering, with negative consequences in the lower airways.

RBS is thus a complex disorder and both the literature and our personal experience suggest that it can have different features in different ages with

respect to pathogenetic factors, clinical manifestations and consequent therapeutic implications.

The present study was carried out in collaboration with otolaryngologists and paediatricians in order to consider RBS in paediatric age, characterized by inflammatory, allergic and obstructive pathologies of the upper airways as well as by disorders of the tracheo-bronchial tract (asthma, asthmatic bronchitis, chronic cough, bronchopulmonary infections).

Our research was aimed firstly at establishing the incidence of RBS in children, secondly at defining its most important pathogenic factors and finally at identifying the most effective therapeutic strategies in order to cure the pathology as early as possible.

## 2. Materials and methods

One hundred and twenty-eight patients (4–10 years, mean age 7; 76 ♂, 52 ♀) with bronchopulmonary diseases associated to rhino-sinus obstructive and inflammatory pathologies, but without allergic disease, were investigated. The patients reported:

- Asthma—80 cases (62.5%).
- Chronic cough—25 cases (20%).
- Recurrent bronchopulmonary infections—23 cases (17.5%).

The lower airways involvement was diagnosed by the Pediatric Department of the University of Bari, following the investigation of the patients' clinical history, pulmonary function test, histamine bronchial provocation test and chest X-rays.

Mild or severe nasal obstruction was identified by otorhinolaryngologists in order to establish a correlation between the obstruction itself (and associated naso-sinus infections) and bronchopulmonary pathologies.

All patients were objectively examined by anterior rhinoscopy and fiberendoscopy of the nasal cavities. Anterior rhinoscopies were carried out by physicians on patient arrival. Nasal fiberendoscopy was always performed by the same otorhinolaryngologist and commented by the teaching equipe of the ENT Department of Bari University to ensure reliability of the examination. In collaborating patients (about 85%), nasal obstruction was later objectified through anterior active rhinomanometry. In other cases, a subjective evaluation of the obstruction was done considering the nasal resistance for each fossa. The obstruction extent was assessed both in pre-treatment conditions and after

performing the turbinate decongestion-test. The latter was carried out by instillation of a vasoconstrictor drug into each nasal fossa in order to identify the role of possible inflammatory component. The obstruction was considered mild when the total rhinomanometric resistances were 0.6–1 Pa/cm<sup>3</sup>/s at 150 Pa or when, in non-collaborating patients, a partial obstruction (adenoid hypertrophy of II–III degree according to Cassano scale [30] or light septal deviation with or without rhino-sinus inflammation) was noted by the physician. Severe obstructions had total resistances > 1 Pa/cm<sup>3</sup>/s at 150 Pa or an endoscopic picture of serious nasal alterations almost always associated with rhino-sinus pathology.

The therapy chosen for the patients with chronic obstructions was decided according to the obstruction characteristics:

- Surgery was carried out in cases of severe obstructions, where the anatomical and structural component prevailed.
- Medical therapy was administered (systemic antibiotics, antihistamines, topical corticosteroid, aerosol, nasal cleaning, etc.) according to pathology type and entity in patients without a very important anatomical and structural obstruction but with recurrent rhino-sinus infections (turbinate congestion and muco-purulent rhinorrhea).
- Disobstructive surgery was performed, in spite of medical therapy, when obstructive and inflammatory pathology of the nasal cavities persisted.

The results of medical and surgical treatment were evaluated both by otologists and by paediatricians in order to identify variations of rhino-sinus pathology and bronchopulmonary problems. Cases of bronchopulmonary disorders were attentively checked and variations of their condition were evaluated according to the following factors: improvement of symptoms (absence or reduction of asthmatic crisis and cough or bronchopulmonary infections), spirometric parameters and quantitative dose of medical therapy.

The results obtained and the correlations between the two groups were assessed statistically.

## 3. Results

### 3.1. Pre-treatment results

A chronic nasal obstruction was present in 81 subjects of the study group. This datum is statistically significant (63.2%,  $p < 0.05$ ). In this group of patients, 40 were suffering from asthma, 20 from chronic cough and 21 from recurrent bronchopul-

**Table 1** Grading of nasal obstruction in case group

	Cases no.	Chronic nasal obstruction		
		Mild	Severe	Total
Asthma	61	26	14	40 (65.5%)
Chronic cough	28	13	7	20 (71.4%)
Recurrent bronchopulmonary infections	39	9	12	21 (53.8%)
Total	128	48 (59.2%)	33 (40.8%)	81 (63.2%), ( $p < 0.05$ )

**Table 2** Rhino-sinusitis in patients with chronic nasal obstruction

	Chronic nasal obstruction	Rhino-sinusitis		
		Recurrent	Chronic	Total
Asthma	40	21 (52.5%)	8 (20%)	29 (72.5%)
Chronic cough	20	8 (40%)	2 (10%)	10 (50%)
Recurrent bronchopulmonary infections	21	13 (61.9%)	5 (23.81%)	18 (85.7%)
Total	81	42 (51.8%)	15 (18.5%)	57 (70.3%) ( $p < 0.05$ )

monary infections. Anterior rhinoscopy revealed naso-sinus disease only in 34% of cases, while nasal endoscopy confirmed the presence of pathology in all cases.

Cases of obstruction were further subdivided into two classes: mild (48 cases—59.2%) and severe form (33 cases—40.8%), respectively. Severe obstruction was identified mainly in patients with infective pulmonary conditions. (Table 1). These patients showed the following disorders, (a) adenoidal hypertrophy was prevailing or exclusive pathology in 14 cases; (b) important septum deviation form in 2 cases; and (c) sub-complete choanal diaphragms in 1 case. In the 16 remaining cases, anatomical and structural obstruction was partial but the malformation was aggravated by rhino-sinus inflammations associated to an important reduction of respiratory capacity. The percentage of rhino-sinus infections concomitant with obstruction was thus very high (57 cases—70.3%) with a good statistical significance ( $p < 0.05$ ); 42 children (51.8%) had recurrent and 15 (18.5%) had chronic form of the disease. A higher

percentage of rhino-sinus infections was identified in asthmatic (29 cases—72.5%) and infective bronchopulmonary pathologies (18 cases—85.7%) (Table 2).

Medical therapy was adopted in 48 (59.2%) children (26 asthmatics, 13 with chronic cough, and 9 with recurrent broncho-pulmonary infections). Of this group, 29 (35.8%) patients (20 asthmatics, 8 with chronic cough, and 1 with recurrent broncho-pulmonary infections), after medical therapy failure, underwent rhinopharyngeal or nasal surgery (adenoidectomy, septum correction, choanal diaphragm exportation). In 6 patients belonging to the medical therapy group, surgery was not carried out for different reasons (poor general conditions, surgery refusal, etc.). Surgery was performed in 33 (40.7%) children (14 asthmatics, 7 with chronic cough, and 12 with bronco-pneumonic infections) with predominance of anatomic and structural obstructive problems.

Totally, surgery was thus performed in 62 patients (76.5%) (Table 3).

**Table 3** Nasal obstruction treatment

Treatment type	Medical	Surgical (after medical treatment)	Surgical
Asthma	26	20	14
Chronic cough	13	8	7
Recurrent bronchopulmonary infections	9	1	12
Total	48 (59.3%)	29(35.8%)	33(40.7%)
62(76.5%)			

**Table 4** Post-treatment results

Improvement of bronchopulmonary pathologies after rhinopathy treatment			
	Medical	Surgical (after medical treatment)	Surgical
Asthma	3/26	6/20	5/14
Chronic cough	2/13	4/8	3/7
Recurrent bronchopulmonary infections	8/9	–/1	9/12
Total	13/48 (27%)	10/29(34.5%)*	17/33(51.5%)
		27/62(43.5%)	

\*Six cases did not undergo surgery.

### 3.2. Post-treatment results

The therapeutic plan resulted in either a solution of the problem or a satisfying improvement of the rhino-sinus pathologies in all the patients.

Cases of bronco-pulmonary disorders had varying results according to pneumologists' objective and functional evaluation (Table 4).

Of the 48 patients who underwent medical therapy, only 13 (27%) – and more precisely 3 asthmatics, 2 with chronic cough and 8 with infections – had satisfying improvements. In the group subjected to surgery as first treatment choice (33 patients), positive results were reported in 17 (51.5%) cases (5 asthmatics, 3 with chronic cough and 9 with infections).

Of all the 62 children who had been subjected to surgery to relieve the obstruction, an improvement of the pathology of the lower airways occurred in 27 cases (43.5%).

Medical and surgical treatment of the rhinopathies, globally evaluated, improved the bronchopulmonary pathologies in 40 patients (49.4%), a case percentage non-statistically significant ( $p > 0.05$ ).

The separate analysis of each group yielded more satisfactory results in 14 cases (36%,  $p > 0.05$ ) of asthma, in 9 cases (45%,  $p > 0.05$ ) of chronic cough and in 17 (80.9%,  $p < 0.05$ ) of infections (Table 5).

## 4. Discussion

This study was aimed at examining closely some aspects of RBS in pediatric age. In this age group

this disorder is often different compared to adult patients with respect to both epidemiological and pathogenic factors.

The study concerned children between 4 and 10 years old. The choice was made considering that children, younger than 4, are not always prone to collaborate while adolescents have often the same characteristics as adults.

In addition, RBS seems to be more frequent in the early childhood.

Nasal endoscopy was performed in all case because of its reliability in detecting obstruction sites and inflammatory pictures that anterior rhinoscopy often does not reveal (only 34% of the patients showed an alteration with the latter test).

The study focused on disorders of both the lower and the upper airways. The former included asthma and chronic cough, bronchial hyperreactivity recurrent infections of the bronchopulmonary tract. The latter comprised nasal obstruction, often secondary to adenoidal hypertrophy, and the related rhino-sinus cavities infective pathologies, due to a failure of nasal functions (air filtration, immunisation and conditioning).

In planning treatment of the obstructive pathologies, rhino-sinus inflammations were investigated and, when found to prevail over anatomic obstructions, a medical therapy was chosen on the basis of entity and the type of inflammation (hyper-secretive and infective, etc.).

An important nasal obstruction was identified in a significant percentage of asthmatic children (63.2%) who suffered either from chronic cough or from infective bronchopulmonary pathologies. A signifi-

**Table 5** Post-treatment results: improvement of bronchopulmonary pathologies after rhinopathy treatment with statistical assessment

	Cases no.	Nasal obstruction	Improvement	<i>p</i>
Asthma	61	40	14 (35%)	>0.05
Chronic cough	28	20	9 (45%)	>0.05
Recurrent bronchopulmonary infections	39	21	17 (80.9%)	<0.05
Total	128	81	40 (49.4%)	>0.05

cant number of concomitant rhino-sinusitis (70.3%) was observed in patients with recurrent or chronic RBS form, persistence of infective process for at least 4–6 months, muco-purulent secretions and hypertrophy of turbinates with consequent worsening of nasal obstruction.

Medical treatment was chosen for patients without a particular severe anatomical nasal obstruction and when the rhino-sinus pathology was prevalent.

Medical therapy gave rather modest results. Only in 40% of the patients, a satisfying control of the infection was obtained only in the upper airways whereas only 27% of the patients with bronchopulmonary pathologies obtained a satisfactory result. The therapy was beneficial in 8 out of 9 patients with lower and upper airways infections.

Surgical treatment yielded better results. In the present study, surgery was performed as a first choice treatment in cases of severe obstruction or after medical therapy failure. Surgical treatment resulted in improvement in all cases both with regard to the obstruction and to rhino-sinus inflammation. However, this approach did not yield satisfactory results in cases with bronco-pneumonic pathologies; an improvement was reported only in 43.5% of cases.

Medical and surgical treatment gave positive results in 49.4% of the cases. In this group upper and lower airways pathologies were present which could be considered expression of RBS. This result cannot be considered statistically significant ( $p > 0.05$ ). If the results are considered separately for the three groups with lower airways disorders (asthma, chronic cough and bronchopulmonary infections), a statistically significant datum can be observed in the group with infective pathologies. These findings support our claim about the advisability of including the intra-thoracic infective pathology in the syndrome characterization since this disorder can be influenced by rhino-sinus diseases.

The correlation between nasal obstruction, rhino-sinus infections and bronco-pneumonic diseases seems to be more important in the child than in the adult [31]. In adulthood, nasal hyperreactivity seems to prevail.

Many studies consider RBS incidence in children lower than in adults. Our study seems to show that this conclusion may be based on apparent factors. The syndrome may be quite frequent in pediatric age when nasal obstruction and related infections are present: early interventions to remove the causes of obstructions and infections could solve nasal problems as well as prevent the installing of asthmatic or infective disorders.

## 5. Conclusions

A thorough analysis of the literature and of the results of the study suggest the following conclusions:

- RBS in children is an undeniable reality confirmed by many papers which have been published in the literature, notwithstanding the doubts expressed by some authors [4].
- RBS incidence is often overestimated due to the inclusion of the upper and lower airway pathologies in the syndrome evaluation without there being sufficient data to support relationship. The results of our study show that the pathology is rather frequent (about 50%) in paediatric age.
- Syndrome pathogenesis is multifactorial, but in the child the chain of events deriving firstly from nasal obstruction and, secondly, from nasal sinus infections appears to be the main cause of the syndrome.
- RBS in paediatric age has indeed pathogenetic features which are different from those of the adult, in whom nasal sinus hyperreactivity seems to play a pre-eminent role.
- Medical and surgical treatment of nasal disorders should be early and effective in order to have more chances of recovery of the lower airways pathologies. Delayed therapy could be ineffective because of the stabilization of severe pathologies in the upper and lower airways.

Pathologies which are often considered common, such as a recurrent cold, adenoid hypertrophy, allergic rhinitis should be better investigated, when important bronchopulmonary pathologies co-exist. A pathologic correlation between the two areas should never be excluded a priori.

## References

- [1] M. De Benedetto, L. Bellussi, P. Cassano, A. Cataldia, F. De Benedetto, E. De Campora, A. Foresi, D. Passali, Consensus report on the diagnosis of rhino-bronchial syndrome (RBS), *Acta Otorhinolaryngol. Ital.* 23 (5) (2003) 406–408.
- [2] N.J. Roberts, S.J. Lloyd-Owen, F. Rapado, I.S. Patel, T.M. Wilkinson, G.C. Donaldson, J.A. Wedzicha, Relationship between chronic nasal and respiratory symptoms in patients with COPD, *Respir. Med.* 97 (8) (2003) 909–914.
- [3] A. Ragab, P. Clement, W. Vincken, Objective assessment of lower airway involvement in chronic rhinosinusitis, *Am. J. Rhinol.* 18 (1) (2004) 15–21.
- [4] H. Lindemann, Does the rhino-sinu-bronchial syndrome exist? *Pneumologie* 46 (5) (1992) 173–178.
- [5] R.Z. Vinuya, Upper airway disorders and asthma: a syndrome of airway inflammation, *Ann. Allergy Asthma Immunol.* 88 (4 Suppl. 1) (2002) 8–15.

- [6] J.N. Palmer, D.B. Conley, R.G. Dong, A.M. Ditto, Pr Yarnold, R.C. Kern, Efficacy of endoscopic sinus surgery in the management of patients with asthma and chronic sinusitis, *Am. J. Rhinol.* 15 (1) (2001) 49–53.
- [7] T. Nonoyama, Y. Majima, S. Arima, K. Tekeuchi, Y. Sakakura, Study an endoscopic sinus surgery management of chronic sinusitis with nasal polyp, *Nippan. Sibriinkaka Gekkei Kaileo* 103 (9) (2000) 1001–1006.
- [8] H.J. Dhong, Y.S. Jung, S.K. Chung, D.C. Chai, Effect of endoscopic sinus surgery an asthmatic patients with chronic rhinosinusitis, *Otolaryngol. Head Neck Surg.* 124 (1) (2001) 99–104.
- [9] G. Dunlop, G.K. Scadding, V.J. Lund, The effect of endoscopic sinus surgery on asthma: management of patients with chronic rhinosinusitis, nasal polyposis, and asthma, *Am. J. Rhinol.* 13 (4) (1999) 261–265.
- [10] C. Viercow, M. Debeln, Mindheitsprodrome dei chronische unspezfishen atemwegsleiden, *Respiratory (Suppl.)* 27 (1970) 157–162.
- [11] G. Rachelefsky, M. Goldberg, R.M. Katz, G. Boris, M. Gyepes, M. Shapiro, M. Mickey, S. Finegold, S. Siegel, Sinusitis in children with respiratory allergy, *J. Allergy Clin. Immunol.* 61 (1978) 310–314.
- [12] R.G. Slavin, Sinusitis and bronchial asthma, *J. Allergy Clin. Immunol.* 66 (1980) 250–256.
- [13] R. Rondelli, M. Giorgi, A. Ferrara, La sindrome Rino-bronchiale in: *L'Ipersensibilità nasale-Ed VALEAS*, 1990.
- [14] L. Businco, L. Fiore, T. Frediani, A. Artuso, A. Di Fazio, P. Bellioni, Clinical and therapeutic aspects of sinusitis in children with bronchial asthma, *Int. J. Pediatr. Otol.* 3 (4) (1981) 287–294.
- [15] D. Nolte, D. Berger, On vagal bronchoconstriction in asthmatic patients by nasal irritation, *Eur. J. Respir. Dis.* 64 (Suppl. 128) (Part 1) (1983) pp. 110–115.
- [16] G.S. Rachelefsky, Chronic sinusitis in children with respiratory allergy: the role of antimicrobials, *J. Allergy Clin. Immunol.* 69 (1982) 332–338.
- [17] E.R. Mc Fadden Jr., Nasal-sinus-pulmonary reflexes and bronchial asthma, *J. Allergy Clin. Immunol.* 78 (1986) 1–10.
- [18] M.J. Schumacher, Pulmonary response to nasal-challenge testing of atopic subjects with stable asthma, *J. Allergy Clin. Immunol.* 78 (1986) 30–38.
- [19] R.G. Slavin, Sinusitis in adults and its relation to allergic rhinitis, asthma and nasal polyps, *J. Allergy Clin. Immunol.* 82 (5 Part 2) (1988) 950–956.
- [20] P.G. Bardin, B.B. Van Heerden, J.R. Joubert, Absence of pulmonary aspiration of sinus contents in patients with asthma and sinusitis, *J. Allergy Clin. Immunol.* 86 (1990) 82–88.
- [21] R.G. Slavin, Relationship of nasal disease and sinusitis to bronchial asthma, *J. Allergy Clin. Immunol.* 49 (2) (1982) 76–79.
- [22] C. Salomè, K. Yan, The response of the airways to nasal stimulation in asthmatic with rhinitis, *Eur. J. Respir. Dis.* 64 (Suppl. 128) (1983) 105–114.
- [23] P. Cassano, F. Latorre, A. Altamura, M. Colucci, L'effetto della provocazione nasale con metacolina sulla funzione polmonare in bambini asmatici, *Riv. ORL. Aud. Fon.* 4 (1991) 279–283.
- [24] G. Passalacqua, G.W. Canonica, Impact of rhinitis on airway inflammation: biological and therapeutic implications, *Respir. Res.* 2 (6) (2001) 320–323.
- [25] A.D. Adinoff, N.P. Cummings, Upper respiratory tract disease and asthma, *Semin. Respir. Med.* 8 (1987) 308–313.
- [26] S. Norn, P.S. Skov, C. Jensen, F. Espersen, J.O. Jarlov, C. Koch, Bacteria and their products release histamine and potentiate mediator release: new aspects in airway diseases, *Eur. J. Respir. Dis. Suppl.* 147 (1986) 230–234.
- [27] J. Corren, A.D. Adinoff, C.G. Irvin, Changes in bronchial responsiveness following nasal provocation with allergen, *J. Allergy Clin. Immunol.* 89 (1992) 611–618.
- [28] P.A. Eggleston, Upper airway inflammatory disease and bronchial hyperresponsiveness, *J. Allergy Clin. Immunol.* 81 (1988) 1036–1041.
- [29] R. Friedman, M. Ackerman, F. Wald, M. Casselbrant, G. Friday, P. Fireman, Asthma and bacterial sinusitis in children, *J. Allergy Clin. Immunol.* 74 (1984) 185–189.
- [30] P. Cassano, M. Gelardi, M. Cassano, M.L. Fiorella, R. Fiorella, Adenoid tissue rhinopharyngeal obstructions grading based on fiberoendoscopic findings: a novel approach to therapeutic management, *Int. L. Pediatr. ORL* 67 (2003) 1303–1309.
- [31] M. Bresciani, L. Paradis, A. Des Roches, H. Vernhet, I. Vachier, P. Godart, et al. Rhinosinusitis in severe asthma, *J. Allergy Clin. Immunol.* 107 (1) (2001) 73–80.

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