Long-term Efficacy of Narivent® in the Treatment of Nasal Congestion

Valerio Damiani¹, Angelo Camaioni¹, Claudio Vitti¹, Giulia Schillani², Francesca Foltran³, Antonella Silvia Scirè⁴, Giada Morpurgo⁵, Dario Gregori³,*

¹ENT Department San Giovanni Addolorata Hospital, Rome, Italy
²Department of Life Sciences, University of Trieste, Italy
³Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiac, Thoracic and Vascular Sciences, University of Padova, Italy
⁴Zeta Research Srl, Trieste, Italy

Abstract: Rationale and aim: Nasal congestion is a common symptom in allergic and non-allergic rhinitis, rhinosinusitis and nasal polyposis. Although various pharmacotherapy options exist, no agent is universally efficacious. The aim of this study was to evaluate the clinical effectiveness efficacy of Narivent®, which is an osmotically acting medical device with anti-oedematous and anti-inflammatory effects, in a long-term (30 days) treatment.

Methods: A single-centre prospective study with a pre-post design was conducted with consecutive enrolment in an Italian Otolaryngology Department of 56 both genders patients with persistent nasal congestion.

Patients received 2 puffs of Narivent® into each nostril 2 times a day over the course of 4 weeks. The severity of symptoms was assessed subjectively as measured by a 0 to 10 visual analogue scale (VAS) and the presence/absence of symptoms and signs. Differences in subjective and objective severity measures before and after treatment were compared using Paired-Sample Wilcoxon Signed Rank Test.

Results: A significant improvement after treatment (p<0.001) has been recorded for the main subjective symptoms and objective signs (overall symptom burden, nasal congestion, cephalae, rhinorrhea, hyposmia, turbinate hypertrophy, mucosa status).

Conclusion: Study results confirm the efficacy of Narivent® in treating nasal congestion over a 4 weeks period.

Keywords: Persistent nasal congestion, Osmotically acting medical device, Anti-oedematous activity, Anti-inflammatory activity.

INTRODUCTION

Nasal congestion is a cardinal symptom of upper airway disorders, such as allergic and non allergic rhinitis, viral or bacterial rhinitis, rhinosinusitis and nasal polyposis [1-4]. It can be defined as an objective restriction of nasal cavity airflow and its characterization is an important part of the diagnosis, as well as the target of the treatment of these illnesses [5].

The pathophysiology of congestion involves neural, vascular, and inflammatory elements [6]. It is associated with the inflammation of the nasal epithelium which underlies many of the specific and interrelated factors that contribute to congestion and other symptoms of both allergic rhinitis and rhinosinusitis [7, 8]. A wide range of biologically active agents (e.g.: histamine, tumour necrosis factor-α, interleukins, cell adhesion molecules) and cell types contribute to inflammation, which can manifest as dilatation of nasal blood vessels, increased secretions and tissue swelling/oedema, ultimately leading to impaired airflow thorough nasal cavities [8].

Although congestion and obstruction are often used as synonymous, it is important to highlight that reversible nasal congestion is caused by mucosal inflammation and secretions, while obstruction refers to irreversible or constant blockage which may be due to mechanical factors, including occlusion (e.g.: nasal polyps), anatomical variation (e.g.: septal deformity, turbinate hypertrophy) or, rarely, tumors or granulomas [2, 9].

Common upper respiratory tract diseases are also described by other primary symptoms, including rhinorrhea, sneezing, nasal itching, reduction/loss of smell, facial pain or pressure and headache, even if patients generally identify nasal congestion as the most bothersome symptom [1-4].

The complaint of a blocked nose is therefore a complex clinical problem involving mucosal, structural, and even psychological factors. In clinical practice, it is frequently difficult to assess and quantify the subjective sensation of nasal airflow and to decide on the therapy most likely to be effective in restoring satisfactory nasal breathing [10].
Objective methods to assess the nasal airway include nasal endoscopy, rhinomanometry and rhinometry (which assess nasal airflow), exhaled nitric oxide (a marker of inflammation and/or nasal polyposis) and cytological evaluation (nasal smear, lavage and biopsy) [9, 11].

A complete and thorough examination using nasal endoscopy provides intense illumination and magnification of the nasal passages and is indicated especially for patients who experience chronic or recurrent acute rhinosinusitis symptoms, or those with suspected nasal polyposis [9]. In addition, the Lund–Mackay system of scoring nasal endoscopy findings is the only system regarding mucosal thickening (oedema) [12].

Inconsistency between subjective nasal obstruction and the appearance of the nasal cavities is not uncommon and there has always been controversy about the relationship between the subjective assessment of nasal obstruction and the objective measurement of nasal airway obstruction [13]. Even so, efforts are continuously being made to improve the ability to ‘objectively’ measure nasal patency [10].

However, available tools for the subjective evaluation, such as questionnaires, the Visual Analogue Scale (VAS) and various symptom scoring systems, are all capable of determining subjective changes in perceived congestion severity. Moreover, therapeutic intervention is always aimed at relieving subjective complaints and therefore subjective parameters are essential [12].

For this purpose, VAS offers a reproducible, quantifiable evaluation of patients’ symptoms, which may provide more subtle information than simply asking if the patient is better, the same or worse [14, 15].

Nasal congestion severely impacts upon quality of life (QoL) of patients suffering from chronic upper respiratory disorders and affects their ability to perform daily activities. Furthermore, when this symptom is poorly-controlled may contribute to sleep loss or disturbance and cause daytime somnolence, decreased alertness, increased accident rates and reduced work/school productivity [16].

Treatment strategies for relief nasal congestion may be considered as environmental control measures (e.g.: allergen avoidance in allergic rhinitis), pharmacologic therapy and surgical intervention. Standard conservative treatment for chronic conditions, such as chronic rhinosinusitis with or without nasal polyposis, is based on short or long-term antibiotics and topical steroids with the addition of decongestants - mostly in a short term regimen and for the acute attack itself [3].

Although various pharmacotherapy options exist, no agent is universally efficacious, and there is a paucity of data supporting commonly used symptomatic therapies [1].

The present study was conducted in order to evaluate the safety and the clinical effectiveness of Narivent® (a, an osmotically acting medical device with anti-oedematous and anti-inflammatory effects, in the treatment of nasal congestion associated with chronic upper airway disorders. Nasal obstruction was assessed both subjectively and objectively.

To understanding symptom severity from patient’s perspective a visual analogue scale (VAS), which is a well-established approach, was used [17]. The VAS allows patients to rate their symptoms on a linear scale, where 0 corresponds to symptoms that are not troublesome at all and 10 is the most troublesome imaginable [18].

**METHODS**

**Study Design**

A single-centre prospective study with a post-randomisation design was conducted in the ENT Department at the San Giovanni Addolorata Hospital, (Rome, Italy) with consecutive enrolment of 56 patients of both genders with persistent nasal congestion caused by allergic or non-allergic rhinitis, turbinate hypertrophy and sinus non-occlusive polyposis. Patients were excluded if they had: a diagnosis of cystic fibrosis; the presence of asthma episodes in the 30 days preceding the study; any acute upper respiratory infections; the presence of massive occlusive polyps in the sinus; used nasal or oral corticosteroids or decongestants during the four weeks preceding the study; or used antileukotrienes or antihistamines during the previous week.

At study enrolment, patients were asked for their verbal and written informed consent.

In accordance with the study protocol, patients received 2 puffs of Narivent® into each nostril 2 times a day over the course of 4 weeks. Patients were visited by the investigators twice during the study period, at the enrolment and after 1 month.

A physical examination was conducted at every visit through a complete ENT endoscopy. Data were collected as follows:

- Turbinates hypertrophy was classified according to the examiner’s personal experience as absent, good (turbinates obstructing 1/3 of nasal fossae), fair (turbinates obstructing 2/3 of nasal fossae) or poor (turbinates completely obstructing nasal fossae).
- Septal deviation was classified according to the examiner’s personal experience as absent, good (septum slightly deviated from baseline), fair (septum significantly deviated from baseline) or poor (obstructing septum).
- Nasal polyps were classified according to the Lund-Mackay scale [19, 20].
- Adenoid hypertrophy was classified as absent, good (slightly increased adenoids), fair (increased adenoids but not beyond tubal ostium) or poor (adenoids beyond tubal ostium) [21, 22].
- Nasal mucosa was classified by the examiner (only one possible answer) as: normal, hyperaemic, pallid/livid or atrophic.
- Nasal secretions were classified by the examiner (only one possible answer) as: absent, haemato-purulent, pallid/serous or mucous.

During each visit a VAS was used to quantify the subjective feeling of nasal obstruction, rhinorrhea, itching and dryness [23]. The subjective symptom score was obtained with a visual analogue scale modified from Eccles’
of the intranuclear protein HMGB1 (High-Mobility Group Box 1 protein), which may be considered as a cytokine and acts as a potent pro-inflammatory mediator when released in the extracellular environment [26, 27].

Sample Size Calculation and Statistical Analysis

The primary outcomes of the present study were symptom resolution (improvement in each symptom score from enrolment to week 4) and improvement in overall symptom burden (as measured by the overall VAS). Sample size was computed with reference to the following scenario: a type I error of 0.05 and a power of 0.80. At this error level, 51 subjects are required to detect as significant a change in VAS of 2 points (SD 4.5) after the administration of the treatment. Assuming a drop-out rate of 10%, 56 patients have been estimated as necessary for the conduct of the study. Continuous variables were always expressed as median and interquartile difference and categorical variables as percentages and absolute numbers. Differences between symptoms felt before and after treatment with Narivent® were compared using Paired-Sample Wilcoxon Signed Rank Test. Tests were performed using the R system [28].

RESULTS

Twenty-eight males and 28 females were enrolled. Median age was 48.5 years (1 quartile: 34.75; III quartile: 59). At the enrolment twenty-five per cent (14) of the patients reported rhinosinusitis, 4% (2) reactivation of rhinosinusitis, 4% (2) allergic rhinitis with positive clinical history for allergy and positive prick test results to Dermatophagoides pteronyssinus (Dpt), 18% (10) vasomotor rhinitis, 21% (12) polyposis and 29% (16) turbinate hypertrophy (Table 1).

Table 1. Study Population’s Characteristics. Numbers are 1 Quartile/Median/III Quartile

|                          | N     | Summary Statistics (N=56) |
|--------------------------|-------|---------------------------|
| Age                      | 56    | 34.75/48.50/59.00         |
| Gender                   |       |                           |
| M                        | 50%   | (28)                      |
| F                        | 50%   | (28)                      |
| Rhinosinusitis           | 56    |                           |
| Rhinosinusitis reacutization | 25%   | (14)                      |
| Allergic rhinitis        | 4%    | (2)                       |
| Vasomotor rhinitis       | 18%   | (10)                      |
| Turbinate hypertrophy    | 29%   | (16)                      |
| Polyposis                | 21%   | (12)                      |
| Septal deviation         |       |                           |
| Absent                   | 23%   | (13)                      |
| Good                     | 61%   | (34)                      |
| Fair                     | 14%   | (8)                       |
| Poor                     | 2%    | (1)                       |
| Nasal polyposis*         |       |                           |
| Absent                   | 77%   | (43)                      |
| I                        | 2%    | (1)                       |
| II                       | 7%    | (4)                       |
| III                      | 14%   | (8)                       |

*Classification according to the Lund-Mackay scale

model [24]. Patients rated the perceived degree of their obstruction on a scale of 0 (complete patency) to 10 (complete stenosis). Likewise, VAS was used for other symptoms. Adverse effect were also recorded. Study was conducted in compliance with the requirements of the local Institutional Review Board.

Medical Device Description

According to the Directive 93/42/EEC on medical devices and subsequent amendments, Narivent® belongs to class I medical devices based on the application of the rule 5 of annex IX.

Narivent® is a nasal spray which acts osmotically with anti-oedematous and anti-inflammatory effects and lubricant properties.

It is indicated to decrease nasal congestion caused by turbinate hypertrophy, vasomotor rhinopathies, and in the treatment of oedema associated with inflammatory conditions in rhino-sinus non-occlusive polyposis and adenoid pathology.

Narivent® is also indicated in the postoperative management of rhino-sinus diseases and in the treatment and prophylaxis of post operative recurrence of nasal polyps.

The anti-oedematous action of this medical device derives from the high concentration of mannitol, which is known in the medical field to carry out a wide osmotic activity [25], whereas the anti-inflammatory action is due particularly to the presence of glycyrrhizin, a glucosidic triterpene extracted from the roots of the liquorice plant. Glycyrrhizin is a natural anti-inflammatory and is the first direct inhibitor
Table 2. VAS Score Rating and Symptoms’ Subjective Evaluation before and after Treatment. Numbers are I Quartile/Median/III Quartile. P-Value Refers to a Significantly Different Distribution of each given Variables before and after Treatment with Narivent®.

|                           | N   | Pre (N=56) | Post (N=56) | Combined (N=112) | p-Value |
|---------------------------|-----|------------|-------------|------------------|---------|
| VAS                       | 55  | 6.080/7.080/8.050 | 2.000/3.010/3.545 | 3.015/6.010/7.085 | <0.001  |
| Nasal Congestion          | 55  | 0% (0)     | 13% (7)     | 6% (7)           | <0.001  |
| Absent                    |     |            |             |                  |         |
| Good                      |     | 0% (0)     | 67% (37)    | 33% (37)         |         |
| Fair                      |     | 29% (16)   | 15% (8)     | 22% (24)         |         |
| Poor                      |     | 71% (40)   | 5% (3)      | 39% (43)         |         |
| Cephalaea                 | 55  | 5% (3)     | 49% (27)    | 27% (30)         | <0.001  |
| Absent                    |     |            |             |                  |         |
| Good                      |     | 29% (16)   | 40% (22)    | 34% (38)         |         |
| Fair                      |     | 50% (28)   | 11% (6)     | 31% (34)         |         |
| Poor                      |     | 16% (9)    | 0% (0)      | 8% (9)           |         |
| Rhinorhea                 | 55  | 32% (18)   | 64% (35)    | 48% (53)         | <0.001  |
| Absent                    |     |            |             |                  |         |
| Good                      |     | 27% (15)   | 35% (19)    | 31% (34)         |         |
| Fair                      |     | 36% (20)   | 2% (1)      | 19% (21)         |         |
| Poor                      |     | 5% (3)     | 0% (0)      | 3% (3)           |         |
| Rhino-pharyngeal exudate  | 55  | 70% (39)   | 85% (47)    | 77% (86)         | 0.038   |
| Absent                    |     |            |             |                  |         |
| Good                      |     | 21% (12)   | 15% (8)     | 18% (20)         |         |
| Fair                      |     | 9% (5)     | 0% (0)      | 5% (5)           |         |
| Poor                      |     | 0% (0)     | 0% (0)      | 0% (0)           |         |
| Pain                      | 55  | 82% (46)   | 95% (52)    | 88% (98)         | 0.147   |
| Absent                    |     |            |             |                  |         |
| Good                      |     | 11% (6)    | 5% (3)      | 8% (9)           |         |
| Fair                      |     | 5% (3)     | 0% (0)      | 3% (3)           |         |
| Poor                      |     | 2% (1)     | 0% (0)      | 1% (1)           |         |
| Hyposmia                  | 55  | 4% (2)     | 33% (18)    | 18% (20)         | <0.001  |
| Absent                    |     |            |             |                  |         |
| Good                      |     | 32% (18)   | 56% (31)    | 44% (49)         |         |
| Fair                      |     | 50% (28)   | 9% (5)      | 30% (33)         |         |
| Poor                      |     | 14% (8)    | 2% (1)      | 8% (9)           |         |

One patient was lost to follow-up because of the presence of paradoxical nasal obstruction. Therefore, the statistical analysis was performed on 55 patients rather than 56.

Table 2 shows the subjective evaluation of symptoms before and after treatment: nasal obstruction, cephalaea and rhinorhea significantly decrease (p<0.001) after the treatment and a significant improvement in reduced sense of smell was also observed (p<0.001). The overall symptom burden before and after is also reported.

At the physical examination (Table 3), a significant improvement in turbinate hypertrophy (p<0.001) and in the overall condition of the mucosa were observed (Fig. 1). A relevant decrease in secretion production was also recorded (Fig. 2).

Palatability of Narivent® was considered as Good by 73% (40) of the patients and as Fair by 27% (15) of them. No patients reported an unsatisfactory palatability judgement. Compliance was High in 75% (41) of the patients, Fair in 20% (11) and Poor in 5% (3). No adverse effects were reported by patients receiving the treatment.

**DISCUSSION**

Nasal congestion is a prevalent symptom of upper airway diseases and is one of the most common complaints dealt with in otorhinolaryngology. Among the pathologies responsible for general complete and continued or occasional nasal obstruction, specific and aspecific vasomotor rhinitis are the conditions with greater epidemiological impact [29]. The pervasiveness of allergic rhinitis and rhinosinusitis has caused congestion to become a highly prevalent problem; however, it is important to note that the perception of congestion in chronic rhinosinusitis can also be caused by polyps extruding into the nasal airway, producing a physical obstruction in the nostril [8].

Patients diagnosed with these upper respiratory conditions identify congestion as the most common and typically the most troublesome symptom. The negative effects of
Table 3. Physical Examination Results before and after Treatment. Numbers are I Quartile/Median/III Quartile. P-Value Refers to a Significantly Different Distribution of each Given Variables before and after Treatment with Narivent®.

|                                      | N  | Pre (N=56) | Post (N=56) | Combined (N=112) | p-Value |
|--------------------------------------|----|------------|-------------|------------------|---------|
| Turbinate hypertrophy                | 55 | 0% (0)     | 7% (4)      | 4% (4)           | <0.001  |
| Absent                               |    |            |             |                  |         |
| Good                                 |    | 9% (5)     | 71% (39)    | 40% (44)         |         |
| Fair                                 |    | 36% (20)   | 18% (10)    | 27% (30)         |         |
| Poor                                 |    | 55% (31)   | 4% (2)      | 30% (33)         |         |
| Adenoid hypertrophy                  | 55 | 0% (0)     | 2% (1)      | 1% (1)           | 0.319   |
| Mucosa status                        | 55 | 0% (0)     | 78% (43)    | 39% (43)         | <0.001  |
| Normal                               |    |            |             |                  |         |
| Hyperemic                            |    | 64% (36)   | 13% (7)     | 39% (43)         | <0.001  |
| Pallid/livid                         |    | 32% (18)   | 5% (3)      | 19% (21)         | <0.001  |
| Atrophyc                             |    | 4% (2)     | 4% (2)      | 4% (4)           | 0.985   |
| Type of secretion                    | 55 | 2% (1)     | 44% (24)    | 23% (25)         | <0.001  |
| Absent                               |    |            |             |                  |         |
| Haematic-purulent                    |    | 4% (2)     | 2% (1)      | 3% (3)           | 0.569   |
| Pallid-serum                         |    | 52% (29)   | 16% (9)     | 34% (38)         | <0.001  |
| Mucous                               |    | 43% (24)   | 38% (21)    | 41% (45)         | 0.616   |

Fig. (1). Nasal mucosa status before and after the treatment. Differences are statistically significant (p<0.05) for pre-post comparisons in normal, hyperemic and pallid/livid mucosa.

Fig. (2). Type of nasal secretion before and after the treatment. Differences are statistically significant (p<0.05) for pre-post comparisons in absent and pallid/serum secretion.
nasal congestion are far reaching and impact a person’s physical as well as emotional functioning. A persistent symptom of congestion, in fact, influences the quality of life (QoL) of patients, having negative impacts on daytime functioning and sleep. Persistent nasal congestion can cause sleep-disordered breathing and sleep fragmentation, reducing sleep time and quality as well as promoting daytime sleepiness and fatigue [2, 30, 31].

Taking into account the high prevalence, as well as the significant social and economic burden of nasal congestion, this symptom should be a key consideration in the treatment of patients with rhinologic disease [2].

The central pathophysiological mechanism of nasal congestion in common upper respiratory diseases is the inflammation of nasal mucosa, which can manifest as dilatation of nasal blood vessels, increased secretions and tissue swelling/oedema. That is why the development of pharmacologic therapies for congestion in these diseases aims at opposing vasodilatation, reducing nasal airway resistance and thus facilitating nasal breathing [8, 29].

A variety of pharmacologic therapies are available for the treatment of nasal congestion in common upper respiratory diseases and it is often a focus of treatment. The most extensively evaluated therapies include antihistamines, decongestants, leukotriene receptor antagonists, and intranasal corticosteroids [1].

Intranasal corticosteroids have potent and broad anti-inflammatory activities. They have proven to be more effective than other classes of agents for the relief of congestion in controlled clinical trials, but they do not reduce mean nasal congestion scores to normal levels, nor do they effectively reduce congestion in every patient [1]. Decongestants are sympathomimetic drugs, employed as systemic or topical products, which act by constricting capacitance vessels in the turbinates. They produce a decrease in subjective symptoms and nasal airway resistance, but side effects including systemic effects such as elevated blood pressure, tachycardia, palpitations, restlessness, insomnia, anxiety, tremors, and hypersensitivity reactions and topical effects such as burning, stinging, sneezing, or local irritation are frequently seen in patients with chronic nasal congestion treated [1, 7, 29, 32, 33].

The adverse event profile of topical and oral decongestants limits their usefulness in allergic rhinitis and the evidence supporting the utility of these drugs for relief of congestion associated with non-allergic/vasomotor rhinitis, rhinosinusitis, or nasal polyposis is very limited [1].

Many types of preparations have also been investigated to treat symptoms associated with these conditions, but substantial evidence for their benefit is poor. These medications include antral washings, isotonic/hypertonic saline as nasal douche, antihistamines (in allergic conditions), antihistamines, mucolytic agents/phytomedical preparations, immunomodulators/immunostimulants and bacterial lysate preparations [3].

Due to the many adverse effects related to standard therapies and long-term treatments and on account of the paucity of evidence for the efficacy of symptomatological therapy, there is a growing need for alternative or co-adjuvant treatments capable of relieving symptoms associated with these conditions and not involving major side effects.

Narivent® belongs to the medical devices category and it is a nasal lubricant which acts osmotically with anti- oedematous and anti-inflammatory action thanks to the presence of components such as eucalyptol, glycyrrhizin and mannitol. This pre-post study was conducted in order to verify if the treatment with Narivent® is effective in reducing nasal obstruction and other symptoms associated with chronic rhinosinusitis, allergic rhinitis, turbinate hypertrophy, sinus non-occlusive polyposis or vasomotor rhinopathies. Patients’ perception of nasal symptoms and objective testing of nasal obstruction were both assessed.

Our results showed a significant improvement in symptoms after treatment demonstrating that the action is not limited to a subjective sensation of increased nasal air flow, but corresponds to an objective reduction in nasal resistance.

In fact, a reduction in the main subjective symptoms, such as sensation of nasal congestion, cephalgia, rhinorrhea and an improvement in decreased sense of smell were found.

The overall subjective assessment of the sensation of nasal obstruction made by patients through the VAS also showed a relevant reduction after the treatment period.

A physical examination of patients treated with Narivent® showed an improvement of the general conditions, achieving the best results in mucous status, in turbinate hypertrophy and in secretion production.

No adverse effects were reported by patients over the treatment period and the compliance with the product was generally assessed as high.

Final Remarks

This study therefore provides evidence that, in patients with nasal turbinate hypertrophy and specific (allergic rhinitis) or non-specific vasomotor rhinitis, and in the treatment of oedema associated with chronic rhinosinus inflammatory conditions, Narivent® can improve nasal symptoms control over a long period of time.

ACKNOWLEDGEMENTS AND CONFLICT OF INTERESTS

The authors are deeply thankful to DMG Italia for providing Narivent® free of charge for the conduct of the study.

Authors Antonella Silvia Sciriè and Giada Morpurgo have ongoing contracts with DMG Italia for conducting clinical studies.

The other authors of the above manuscript declared no conflict of interest.

REFERENCES

[1] Meltzer EO, Caballero F, Fromer LM, Krouse JH, Scadding G. Treatment of congestion in upper respiratory diseases. Int J Gen Med 2010; 8(3): 69-91.

[2] Stewart M, Ferguson B, Fromer L. Epidemiology and burden of nasal congestion. Int J Gen Med 2010; 8(3): 37-45.

[3] Fokkens W, Lund V, Mullol J. European Position Paper on Rhinosinusitis and Nasal Polyps group. European position paper on
Long-term Efficacy of Narivent® in the Treatment of Nasal Congestion

The Open Medical Devices Journal, 2012, Volume 4    79

rhinosinusitis and nasal polyps 2007. Rhinology 2007; 20(Suppl): 1-136.

[4] Corey JP, Houser SM, Ng BA. Nasal congestion: a review of its etiology, evaluation, and treatment. Ear Nose Throat J 2000; 79(9): 690-8.

[5] van Sprosten E, Ingels KJ, Jansen AH, Graamans K, Fokkens WJ. Evidence-based recommendations regarding the differential diagnosis and assessment of nasal congestion: using the new GRADE system. Allergy 2008; 63(7): 820-33.

[6] Nathan RA. The pathophysiology, clinical impact, and management of nasal congestion in allergic rhinitis. Clin Ther 2008; 30(4): 573-86.

[7] Davis SS, Eccles R. Nasal congestion: mechanisms, measurement and medications. Core information for the clinician. Clin Otolaryngol 2004; 29: 659-66.

[8] Nacermo RM, Bachert C, Barami JN. Pathophysiology of nasal congestion. Int J Gen Med 2010; 8(3): 47-57.

[9] Krouse J, Lund V, Fokkens W, Meltzer EO. Diagnostic strategies in nasal congestion. Int J Gen Med 2010; 8(3): 59-67.

[10] André RF, Yuyk JD, Ahmed A, Graamans K, Noël Trent TJ. Correlation between subjective and objective evaluation of the nasal airway. A systematic review of the highest level of evidence. Clin Otolaryngol 2009; 34(6): 518-25.

[11] Turner PJ, Kemp AS. Allergic rhinitis in children. J Paediatr Child Health 2012; 48(4): 302-10.

[12] van Sprosten E, Ingels KJ, Jansen AH, Graamans K, Fokkens WJ. Evidence-based recommendations regarding the differential diagnosis and assessment of nasal congestion: using the new GRADE system. Allergy 2008; 63(7): 820-33.

[13] Thulesius HL, Cervin A, Jessen M. The importance of side difference in nasal obstruction and rhinomanometry: a retrospective correlation of symptoms and rhinomanometry in 1000 patients. Clin Otolaryngol 2012; 37(1): 17-22.

[14] Kim CS, Moon BK, Jung DH, Min YG. Correlation between nasal obstruction symptoms and objective parameters of acoustic rhinometry and rhinomanometry. Auris Nasus Larynx 1998; 25(1): 45-8.

[15] Hilberg O, Grymer LF, Pedersen OF. Turbinate hypertrophy, evaluation of the nasal cavity by acoustic rhinometry. Arch Otolaryngol Head Neck Surg 1990; 116: 283-9.

[16] Anolik R. Desloratadine and pseudoephedrine combination therapy as a comprehensive treatment for allergic rhinitis and nasal congestion. Expert Opin Drug Metab Toxicol 2009; 5: 683-94.

[17] Krouse J, Lund V, Fokkens W, Meltzer EO. Diagnostic strategies in nasal congestion. Int J Gen Med 2010; 8(3): 59-67.

[18] Passali D, Ferri R, Becchini G, Passali GC, Bellussi L. Alterations of nasal mucociliary transport in patients with hypertrophy of the inferior turbinate, deviations of the nasal septum and chronic sinusitis. Eur Arch Otorhinolaryngol 1999; 256(7): 335-7.

[19] Lund VJ, Mackay IS. Staging in rhinosinusitis. Rhinology 1993; 31(4): 183-4.

[20] Lund VJ, Scadding GK. Objective assessment of endoscopic sinus surgery in the management of chronic rhinosinusitis: an update. J Laryngol Otol 1994; 108(9): 749-53.

[21] Saedi B, Sadeghi M, Mojtahed M, Mahboubi H. Diagnostic efficacy of different methods in the assessment of adenoid hypertrophy. Am J Otolaryngol 2011; 32(2): 147-51.

[22] Cassano P, Gelardi M, Cassano M, Fiorella ML, Fiorella R. Adenoid tissue rhinopharyngeal obstruction grading based on fibredendoscopic findings: a novel approach to therapeutic management. Int J Pediatr Otorhinolaryngol 2003; 67(12): 1303-9.

[23] Ciprandi G, Mora F, Cassano M, Gallina AM, Mora R. Visual analog scale (VAS) and nasal obstruction in persistent allergic rhinitis. Otolaryngol Head Neck Surg 2009; 141: 527-9.

[24] Eccles R. Nasal airflow resistance and nasal sensation of airflow. Rhinol Supp 1992; 14: 86-90.

[25] Sweetman SC. Martindale. The Extra Pharmacopoeia. 35th ed. London: Pharmaceutical Press 2007.

[26] Asl MN, Hosseiniazedeh H. Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds. Phytother Res 2008; 22(6): 709-24.

[27] Cavone L, Muzzi M, Mencucci R, et al. 18β-glycyrrhetinic acid inhibits immune activation triggered by HMGB1, a proinflammatory protein found in the tear fluid during conjunctivitis and blepharitis. Ocul Immunol Inflamm 2011; 19(3): 180-5.

[28] R Development Core Team R. A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing 2012.

[29] Passali D, Salerni L, Passali GC, Passali FM, Bellussi L. Nasal decongestants in the treatment of chronic nasal obstruction: efficacy and safety of use. Expert Opin Drug Saf 2006; 5: 783-90.

[30] Craig TJ, Sherkat A, Safaei S. Congestion and sleep impairment in allergic rhinitis: Curr Allergy Asthma Rep 2010; 10(2): 113-21.

[31] Sardana N, Craig TJ. Congestion and sleep impairment in allergic rhinitis. Asian Pac J Allergy Immunol 2011; 29(4): 297-306.

[32] van Cauwenberge P, Bachert C, Passalacqua G, Bousquet J, Canonica GW, Durham SR. Consensus statement on the treatment of allergic rhinitis. EAACT. Allergy 2000; 55: 116-34.

[33] Baena-Cagnani CE. Safety and tolerability of treatments for allergic rhinitis in children. Drug Saf 2004; 27: 883-98.

Received: August 08, 2012
Revised: August 15, 2012
Accepted: August 17, 2012

© Damiani et al.; Licensee Bentham Open.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.