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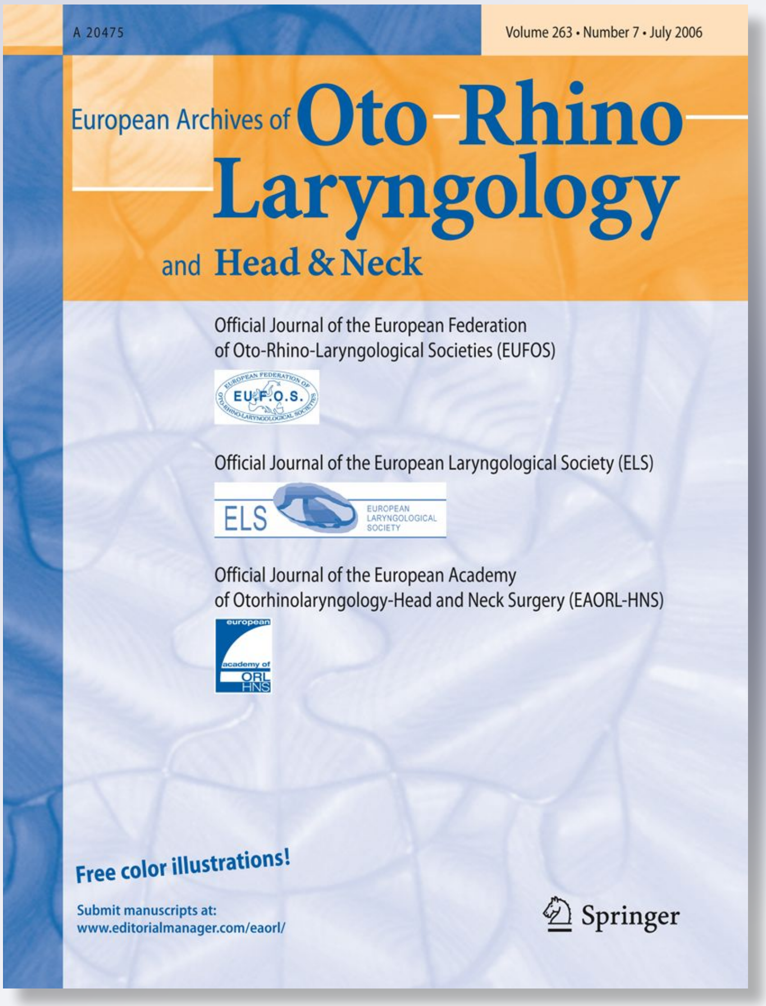
European Archives of Oto-Rhino-Laryngology
and Head & Neck

ISSN 0937-4477

Eur Arch Otorhinolaryngol
DOI 10.1007/s00405-012-2024-5



Springer

Eur Arch Otorhinolaryngol
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RHINOLOGY

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Received: 20 January 2012 / Accepted: 19 April 2012

Abstract The upper airway respiratory diseases (i.e. common cold, allergic rhinitis, nonallergic/vasomotor rhinitis, acute and chronic rhinosinusitis and nasal polyposis) in which nasal congestion is a common symptom are often undertreated due to the frequent inadequate efficacy and safety concern with current therapies. In scientific literature, few studies seem to support the hypothesis that nasal inhalatory treatment with thermal water promotes the improvement of nasal symptoms, even if the mechanisms by which the improvement from SPA therapy can be expected remain debated. A prospective comparative study with a pre–post design has been performed consecutively enrolling 33 (males 70 %) patients of both genders older than 12 years of age, affected by chronic sinonasal inflammation. All patients underwent a 14-days course of radioactive water warm vapour inhalations followed by nasal aerosol of the same thermal water 10 min each once/day at Merano Therme. At the beginning and end of the study, in all the subjects, nasal function evaluation by active anterior rhinomanometry, mucociliary transport time (MCTt) determination and nasal cytology were performed. After the inhalatory treatment, the mucociliary function was improved and the pathologic mucociliary transport times recorded at the beginning of the study being significantly reduced to physiologic ones. Besides, before treatment, the cytologic picture showed an inflammatory cell infiltration (eosinophils, neutrophils with/without bacteria, mast cells) in 37 % of patients; after therapy in 66 % of these patients, the rhinocytogram was normal. Our results suggest, according to the literature data, that SPA therapy with radioactive water could represent an alternative choice in chronic inflammatory diseases of the upper airways, nonresponsive to pharmacological therapy.

Keywords URTI · SPA therapy · Sinunasal pathology

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Introduction

Nasal congestion, which may be described as a feeling of blockage or restricted airflow, often accompanied by aural fullness, is a common symptom in acute and chronic inflammatory processes of the nose and paranasal sinuses (i.e. common cold, allergic and nonallergic rhinitis, acute and chronic rhinosinusitis and nasal polyposis [1].

Nasal obstruction, besides limiting the quantity of air intended for pulmonary respiration and thus reducing the oxygen supply to the entire organism, impairs the normal aeration of the nasal sinuses and middle ear causing CO_2 accumulation. This in turn, stimulates sinus pH reduction and the production of mucus that cannot be drained due to the oedema constricting the sinus and tube ostia, promoting stasis of secretions, and thus providing fertile ground for proliferation of germs [2].

The airway epithelium is a complex physico-chemical and functional barrier against pathogens, allergens and

Published online: 16 May 2012

pollutants: it plays a central role to the defence of the respiratory tract, through the combined function of mechanical barrier, clearance through the mucociliary transport of ciliated and secretory cells and a variety of other innate and acquired immune defence mechanisms [3, 4].

When the epithelial barrier is damaged with cilia loss and excessive mucus formation, an inflammatory process is induced in an attempt to block antigens and allergens by releasing pro-inflammatory chemokines and cytokines [5].

The management of recurrent and chronic airway inflammation requires the integration of several different components: minimizing risk factors, educational programs, improving symptoms with a stepwise treatment approach and preventing recurrences. Although various pharmacotherapy options exist, no agent is universally efficacious, and there is a paucity of data supporting commonly used symptomatic therapies [1].

Inhalation of thermal water is traditionally used as part of the treatment of chronic sinonasal diseases and chronic bronchitis, but is not included among management options by the most recent guidelines, since uncertainty exists about indication; besides, the therapeutic mechanism of thermal water inhalation, its benefit and the underlying physiopathological mechanisms are not yet well clarified [6].

Mineral waters are classified according to their main physical and chemical characteristics (temperature, pressure, ionic concentration, radioactivity, and presence of specific ions or active chemical groups).

Besides the action of cleansing, massage, secretion dilution common to all, each thermal waters has typical therapeutical features and biological functions on the immune, cardiovascular and neuro-vegetative system [7].

The present study was conducted to evaluate the clinical effectiveness of warm vapour inhalation and nasal aerosol of radioactive (481 Bq/l Radon) hydrofluoric oligomineral water (Merano Therme) in patients with chronic nasal obstruction. Particularly, since objective methods are strongly recommended for use in the evaluation of pharmacologic agents that are expected to improve nasal airflow, endoscopic assessment was bilaterally performed and nasal obstruction was objectively assessed measuring nasal airflow resistance through active anterior rhinomanometry (AAR), and evaluating the mucociliary transport time (MCTt). Moreover, nasal cytology was also assessed.

Methods

Study design

A prospective comparative study with a pre–post design has been performed consecutively enrolling at the Merano Therme in Merano (BZ) Italy, 33 patients of both genders (males 70 %) older than 12 years of age, affected by chronic sinonasal inflammation. The main inclusion criterion was nasal obstruction evaluated by a 10 points Visual Analogue Scale (1 = nasal airways completely free; 10 = nasal airway completely blocked) higher than 7 in the previous 2 months. Clinically speaking, patients affected by chronic rhinosinusitis, persistent allergic rhinitis, and vasomotor rhinitis with inferior turbinate hypertrophy were included.

The comparative study was the one by Marullo and Abramo [8]: in this research, 37 adults subjects affected by chronic catarrhal inflammation of the nose and paranasal sinuses were treated by warm inhalation and aerosol with same thermal water; a control group of 20 subjects, selected according the same clinical characteristics were treated by warm inhalation and aerosol with natural water. The results of AAR, MCTt and nasal cytology before and after treatment were analysed.

Patients affected by acute viral rhinitis or obstructive polyposis were excluded; patients with a history of nasal steroid and vasoconstrictive drug therapies or systemic NSAIDs (nonsteroidal anti-inflammatory drugs), oral steroids or mucolytic treatments in the previous 2 months were also excluded from the study.

At the study enrollment, patients older than 18 years and parents of patients younger than 18 were asked for their verbal and written informed consent.

All patients underwent a 14-days course of warm vapour inhalations (20 cm from patient's face), the device distributes thermal water at a temperature of 38 °C in 8–10 μm micelles laying down on the mucosa of upper airways. This treatment was followed by aerosol of the same thermal water (2–4 μm micelles reaching the lower airways), each treatment lasting 10 min/day.

The double administration of thermal water by inhalation and aerosol is aimed at curing both upper and lower airways: during the past decades in fact, our understanding of the coexistence of upper and lower airway diseases has evolved because of epidemiological studies [9], new physiopathological and immunological acquisitions on the respiratory tract [10], as well as studies on the effects of medical treatment of sinonasal district [11] and FESS on lower airway hyper reactivity [12].

The treatment was performed at the thermal station. The chemical analysis of the water is given in Table 1.

Anagraphic data, clinical history collection and ENT examination were performed before and after inhalatory treatment. Moreover, nasal airflow resistances were measured by active anterior rhinomanometry according to validated criteria [13, 14] and MCTt [15] was measured with an inert, coloured tracer (charcoal powder) mixed with 3 % saccharine. Finally, nasal cells harvested from the head of inferior and middle turbinates

Table 1 Essential chemical composition of Merano Thermal water (Merano, BZ, Italy)

Parameters	Results	Unit of measurement
Atmospheric pressure	981	mbar
Air temperature	22	°C
Temperature at source	23.4	°C
Colour	Colourless	
Odour	Odourless	
Savour	Normal	
Deposit	Absent	
Acidity (pH)	7.48	u.pH
Conductivity (at source)	77	µS/cm
Total hardness	3.2	°F
Alkalinity (as CO_3^-)	0	mg/L
Alkalinity (as HCO_3^-)	34	mg/L
Oxidability	<0.5	mg/L
Ammonium ion (NH_4^+)	<0.02	mg/L
Nitrites (NO_2^-)	<0.002	mg/L
Fluoride (F^-)	1.3	mg/L
Chloride (Cl^-)	<1.0	mg/L
Nitrate (NO_3^-)	0.6	mg/L
Sulphate (SO_4^-)	9	mg/L
Radon concentration	246	Bq/L

Test report 10LA07560, 15 September 2010

using a brushing technique were placed on a microscopic slide and fixed immediately for cytopathologic examination. A May–Grunwald's–Giemsa stain was performed. All specimens were examined under light microscopy, evaluation was carried out at ×1,000 magnification and 10 representative microscopic fields for each slide were examined. The quantitative score of inflammatory cells was rated according to a scale previously described by Meltzer [16]. Bacterial and fungal presence in nasal mucosa was also evaluated.

Sample size calculation and statistical analysis

The study has been designed as a pre–post study comparing MCT times variation before and after treatment.

Sample size has been computed with reference to an alpha value of 0.05 and a power of 0.80, to detect an average difference of at least 3.5 s in MCTt after treatments as compared to mean MCTt levels before it, assuming a standard deviation of 3.5 MCTt, which was based on previously conducted pilot studies. Continuous variables were always expressed as median and interquartile difference and categorical variables as percentages and absolute numbers. Differences between nasal patency measurements before and after treatment were compared using Paired-Sample Wilcoxon Signed Rank test and Chi-square test, as appropriate. Proportion of participants with adverse effects attributed to the treatment was also computed.

Table 2 AAR and MCTt before–after measurements

	Before	After	*p*
Nasal respiratory flow			
Left ($N = 64$)	252/332/460	250/388/506	0.532
Right ($N = 64$)	267/346/499	222/408/522	0.586
Total ($N = 65$)	512/672/912	580/740/1,014	0.55
Nasal respiratory resistance			
Left ($N = 64$)	0.460/0.680/1.040	0.490/0.640/1.085	0.628
Right ($N = 63$)	0.485/0.615/1.012	0.430/0.690/0.975	0.839
Total ($N = 53$)	0.262/0.380/0.510	0.207/0.295/0.500	0.544
MCTt ($N = 65$)	12/14/16	11/12/14	0.039

Numbers are I quartile/median/III quartile. *p* value refers to a significantly different distribution of each given variables before and after treatment with thermal water. Nasal respiratory flow is expressed in cc × s, nasal resistance in Pa/cc × s; mucociliary transport time (MCTt) in minutes

N number of valid cases for each variable

Results

All subjects completed the treatment and no adverse effects were reported.

The Wilcoxon test did not disclose a significant difference between pre- and post-treatment for nasal respiratory flow and nasal resistances (Table 2). Nasal resistance values were however within normal range at the end of treatment.

On the contrary, MCTt was significantly reduced after inhalatory treatment (Table 2) ($p = 0.039$).

Out of 33 patients, before the treatment, nasal cytology was normal in 18 subjects, while inflammatory cells infiltrate was present in 14 patients with or without bacterial presence (6 and 8 patients, respectively); in one case, the cytologic examination was impossible due to insufficient sample. In 66 % (9 patients) of those having pathological findings at first evaluation, nasal cytology was normal after the treatment (Table 3).

The comparative study [8] showed an improvement of all the considered parameters in the study group, but not in the control group.

Discussion

Even if the frequency of upper airways inflammation/infection has caused nasal congestion to become a highly prevalent

Table 3 Nasal cytology, and bacterial and fungal presence before–after the inhalation therapy

	Before	After	*p*
Epithelial cells (*N* = 64)			
20–30	3 % (1)	3 % (1)	0.796
60–70	3 % (1)	0 % (0)	
70–80	25 % (8)	25 % (8)	
80–90	69 % (22)	72 % (23)	
Goblet cells (*N* = 64)			
05–10	12 % (4)	6 % (2)	0.16
10–20	12 % (4)	31 % (10)	
20–30	3 % (1)	0 % (0)	
30–40	72 % (23)	62 % (20)	
Neutrophils (*N* = 62)			
0	10 %(3)	16 %(5)	0.288
1+	61 % (19)	71 % (22)	
2+	0 % (0)	3 % (1)	
3+	26 % (**8**)	10 % (**3**)	
4+	3 % (**1**)	0 % (**0**)	
Eosinophils (*N* = 62)			
0	90 % (28)	94 % (29)	0.641
1+	10 % (**3**)	6 % (**2**)	
Basophils (*N* = 62)			
0	100 % (31)	100 % (31)	
Mast cells (*N* = 62)			
0	94 % (29)	97 % (30)	0.544
1+	6 % (**2**)	3 % (**1**)	
Macrophages (*N* = 62)			
0	100 % (31)	97 % (30)	0.313
1+	0 % (0)	3 % (1)	
Lymphocytes (*N* = 62)			
0	97 % (30)	97 % (30)	1
1+	3 % (1)	3 % (1)	
Plasma cells (*N* = 62)			
0	100 % (31)	100 % (31)	
Bacteria (*N* = 64)			
0	81 % (26)	91 % (29)	0.5
1+	3 % (**1**)	3 % (**1**)	
3+	16 % (**5**)	6 % (**2**)	
Mycetes (*N* = 64)			
0	100 % (32)	100 % (32)	

Absolute numbers of patients are reported in parenthesis. Number of patients with pathological inflammatory cells and bacteria before and after treatment are given in bold. *p* value refers to a significantly different distribution of each given variables before and after treatment with thermal water. The semiquantitative analysis and the inflammatory grading is made according to a scale previously described by Meltzer [16]

N number of valid cases for each variable

symptom, chronic rhinitis, rhinosinusitis are frequently undertreated due to the often inadequate efficacy or safety of current therapies [17, 18].

In the scientific literature, few studies seem to support the hypothesis that nasal inhalatory treatment with thermal water promotes the improvement of nasal symptoms even if the mechanisms by which the improvement can be expected remain debated.

The therapeutic effects of mineral waters depend on their physical and chemical properties; particularly, previous studies on the therapeutic effects of sulphurous waters on airway chronic inflammatory processes demonstrated beneficial effects on mucus secretions; the sulphurous water acts in fact on the mucoproteins to open disulphide bonds and consequently lower the viscosity of the mucus [19, 20]. Moreover, because of the toxicity of sulphide, this water has antibacterial effects [6, 19]. Finally, the sulphurous water also has an immunomodulant activity: after treatment with water, higher serum and secretion concentrations of IgA and decreased serum concentration of IgE have been observed in previous clinical studies [21]; moreover, nasal cytology evaluation has found a post-treatment reduction of neutrophil count [6].

In the present study, we evaluated different parameters of the respiratory mucosa including nasal perviousness, mucociliary clearance and nasal cytology; we examined 33 patients before and after inhalatory treatment with radioactive hydrofluoric oligomineral water of Merano Therme.

Whereas no significant changes were noted for nasal resistance values, we observed a significant improvement of the mucociliary function due to water inhalations. The pathologic median MCTt (reference values used were 12.59 ± 3 min according to Passali and co-workers [22]) recorded at the beginning of the study being reduced to a physiological one after treatment.

Mucociliary transport is a physiological process that allows mucus to flow over an epithelial lamina of ciliated cells. It is an important defense mechanism against physical and biological insult in the nasal fossa, paranasal sinuses, and lower respiratory tracts. Inhaled foreign particles and microorganisms are caught by the mucus and transported towards the nasopharynx by means of nasal mucociliary activity. This process, which commonly prevents organic, inorganic, bacterial or viral particles from entering the organism, has a protective effect on the upper and lower respiratory system and is considered a first-line defense mechanism in humans.

The use of dye or radioactive tracers to measure MCTt has been available for nearly 30 years [22, 23]. It allows, if altered, one to recognize early alterations of rhinosinusal homeostasis. Although a crude measure, it has the advantage of considering the entire mucociliary system including cilia and periciliary mucous stratum.

More recent studies were performed with the aim of analysing the correlation between mucociliary clearance and rhinosinusal symptoms: Boatsman and co-workers [24] in a

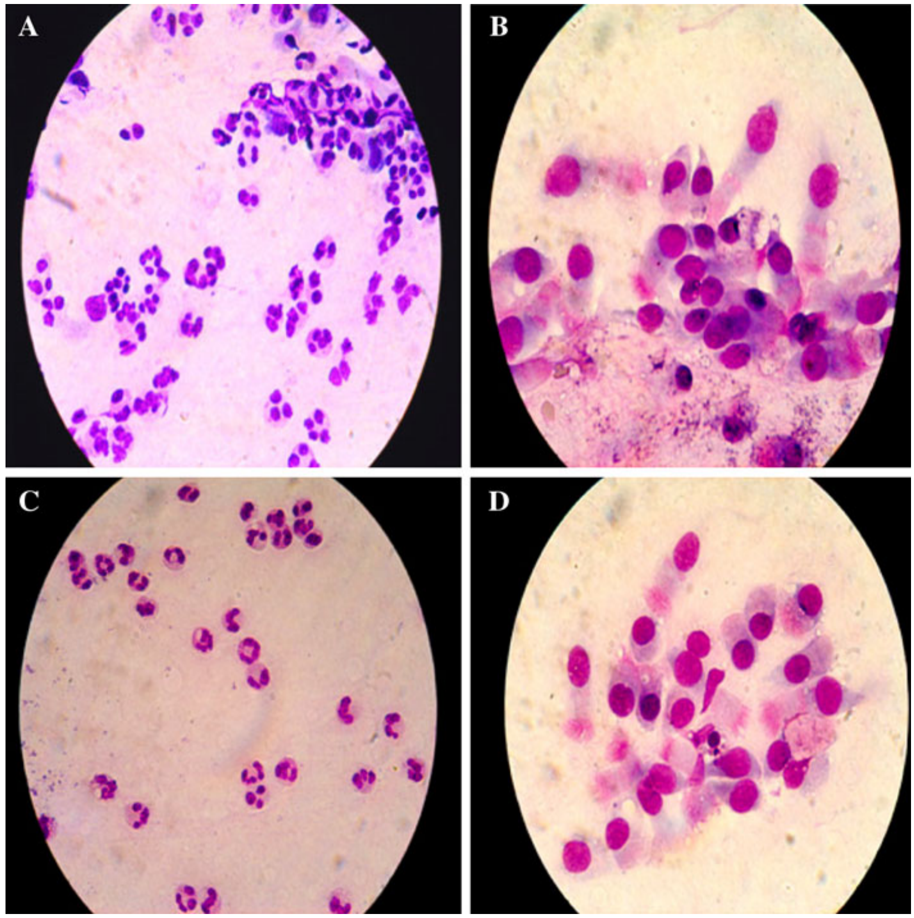

Fig. 1 Cytological picture in two patients before and after treatment by inhalation and aerosol with thermal water at Merano Thermal station. A neutrophilic infiltration is evident before the treatment (**a**, **c**), whereas a normal rhinocytogram can be observed after treatment (**b**, **d**). The prevalence of neutrophils is characteristics of all chronic inflammatory processes of the nose and paranasal sinuses

cross-sectional study on adult volunteers although stating that mucociliary clearance is important for the health of the sinusal cavities, could not find a clear correlation between rhinosinusitis symptoms severity as assessed by SNOT-20 scores and mucociliary transport times. On the contrary, Arnaoutakis and Collins [25], in children with symptoms of chronic rhinosinusitis, found a positive correlation between symptomatology and mucociliary transport times and velocity before and after adenoidectomy suggesting this test as a benchmark to demonstrate the specific symptomatic benefits from this surgical procedure.

In our previous experience, we demonstrated that in patients suffering from chronic sinonasal inflammation, the MCTt is delayed due to a reduction in the pericilia stratum and an increase in viscoelasticity of the mucus following the release of inflammation mediators [26].

The positive effect of the treatment with radioactive water was demonstrated also by the improvement of the rhinocytogram: in 66 % of the patients showing a pre-treatment inflammatory cells infiltration of the mucosa with abnormal number of neutrophils, eosinophils and mast cells with/without bacteria, the cytological picture was reduced to normal values after therapy.

Figure 1 reports the rhinocytogram before and after treatment in two different patients: the reduction of neutrophilic infiltration is evident.

As demonstrated in previous studies [8], the treatment with radioactive hydrofluoric oligominerals water has a positive effect in chronic aspecific inflammation of the upper respiratory tract: the impact on the mucociliary function and the cytological picture was evident, in some cases with a statistical significance in comparison with a control group treated with natural water: it could be supposed that besides the aspecific mechanical action of cleansing and drainage of secretions and inflammatory mediators, the radioactivity and the presence of fluorine ions characteristic of this water could have a denaturing and antiseptic effect on bacteria, viruses and allergens, thus decreasing the inflammatory load on the respiratory mucosa as confirmed also in the present study by the normalization of the cytological picture.

Due to the lack of side effects, thermal treatment could represent an alternative choice to pharmacological therapy in chronic, nonresponsive diseases of the upper respiratory airways.

References

1. Shedden A (2005) Impact of nasal congestion on quality of life and work productivity in allergic rhinitis: findings from a large online survey. Treat Respir Med 4:439–446
2. Kennedy DW (1995) International conference on sinus disease: terminology, staging and therapy. Ann Otol Rhinol Laryngol 104(S167):1–31
3. Diamond G, Legarda D, Ryan LK (2000) The innate immune response of the respiratory epithelium. Immunol Rev 173:27–38
4. Fokkens WJ, Scheeren RA (2000) Upper airway defence mechanisms. Paediatr Resp Rev 1:336–341
5. Vareille M, Kieninger E, Edwards MR, Regamey N (2011) The airway epithelium: soldier in the fight against respiratory viruses. Clin Microbiol Rev 24(1):210–229
6. Staffieri A, Abramo A (2007) Sulphurous-arsenical-ferruginous (thermal) water inhalations reduce nasal respiratory resistance and improve mucociliary clearance in patients with chronic sinonasal disease: preliminary outcomes. Acta Otolaryngol 127(6):613–617
7. Passali D, Bellussi L, De Benedetto M, Giordano C, Mira E, Paludetti G, Saglione F (2006) Crenotherapy and upper airways diseases. Acta Otorhinolaryngol Ital 26(4):5–54
8. Marullo T, Abramo A (2000) Effetti di un ciclo di crenoterapia inalatoria con oligominerali fluoridrati radioattivi. Acta Otorhinolaryngol Ital 20(63):1–13
9. Grossman J (1997) One airway, one disease. Chest 111:118–168
10. Corren J, Adinoff A, Irvin C (1992) Changes in bronchial responsiveness following nasal provocation with allergen. J Allergy Clin Immunol 89:611–618
11. Oliveira CAA, Sole D, Naspitz CK, Rachelefsky GS (1997) Improvement of bronchial hyper-responsiveness in asthmatic children treated for concomitant sinusitis. Ann Allergy Asthma Immunol 79:70–74
12. Dunlop G, Scadding GK, Lund VJ (1999) Effect of endoscopic sinus surgery on asthma management in patients with chronic rhinosinusitis, nasal polyposis and asthma. Am J Rhinol 13(4):261–265
13. Clement PAR, Gordon F (2005) Consensus report on acoustic rhinometry and rhinomanometry. Rhinology 43:169–179
14. Eccles EA (2011) Guide to practical aspects of measurement of human nasal airflow by rhinomanometry. Rhinology 49:2–10
15. Passàli D, Mezzedimi C, Passàli GC, Nuti D, Bellussi L (2000) The role of rhinomanometry, acoustic rhinometry, and mucociliary transport time in the assessment of nasal patency. Ear Nose Throat J 79(5):397–400
16. Meltzer EO, Jalowayski AA (1988) Nasal cytology in clinical practice. Am J Rhinology 2:47–54
17. Bousquet J, Van Cauwenberge P, Khaltaev N, Aria Workshop Group, World Health Organization (2001) Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 108(5 Suppl):S147–S334
18. van Cauwenberge P, Bachert C, Passalacqua G, Bousquet J, Canonica GW, Durham SR, Fokkens WJ, Howarth PH, Lund V, Malling HJ, Mygind N, Passali D, Scadding GK, Wang DY (2000) Consensus statement on the treatment of allergic rhinitis. European Academy of Allergology and Clinical Immunology. Allergy 55(2):116–134
19. Salami A, Dellepiane M, Crippa B, Mora F, Guastini L, Jankowska B, Mora R (2008) Sulphurous water inhalations in the prophylaxis of recurrent upper respiratory tract infections. Int J Pediatr Otorhinolaryngol 72(11):1717–1722
20. Costantino M, Lampa E, Nappi G (2006) Effectiveness of sulphur spa therapy with politzer in the treatment of rhinogenic deafness. Acta Otorhinolaryngol Ital 26:7–13
21. Salami A, Dellepiane M, Strinati F, Guastini L, Mora R (2010) Sulphurous thermal water inhalations in the treatment of chronic rhinosinusitis. Rhinology 48(1):71–76
22. Passali D, Bellussi L, Bianchini Ciampoli M, De Seta E (1984) Experiences in the determination of nasal mucociliary transport time. Acta Otolaryngol 97(3–4):319–323
23. Puchelle E, Aug F, Pham QT, Bertrand A (1981) Comparison of three methods for measuring nasal mucociliary clearance in man. Acta Otolaryngol 91(3–4):297–303
24. Boatsman JE, Calhoun KH, Ryan MW (2006) Relationship between rhinosinusitis symptoms and mucociliary clearance time. Otolaryngol Head Neck Surg 134(3):491–493
25. Arnaoutakis D, Collins WO (2011) Correlation of mucociliary clearance and symptomatology before and after adenoidectomy in children. Int J Pediatr Otorhinolaryngol 75(10):1318–1321
26. Passàli D, Ferri R, Becchini G, Passàli GC, Bellussi L (1999) Alterations of nasal mucociliary transport in patients with hypertrophy of the inferior turbinates, deviations of the nasal septum and chronic sinusitis. Eur Arch Otorhinolaryngol 256(7):335–337