



The value of Ems Mineral Salts in the treatment of rhinosinusitis in children

Prospective study on the efficacy of mineral salts versus xylometazoline in the topical nasal treatment of children

O. Michel^{a,*}, S. Essers^b, W.-J. Heppt^c, V. Johannsen^d,
W. Reuter^e, G. Hommel^f

^a *Klinik u. Poliklinik für HNO-Heilkunde, Klinikum der Universität zu Köln, Kerpenerstr. 62, 50924 Köln, Germany*

^b *Praxis für Hals-Nasen-Ohren-Heilkunde, Hoechberg, Germany*

^c *HNO-Klinik des Städtischen Klinikums Karlsruhe, Karlsruhe, Germany*

^d *Praxis für Hals-Nasen-Ohren-Heilkunde, Kiel, Germany*

^e *Praxis für Hals-Nasen-Ohren-Heilkunde, Lippstadt, Germany*

^f *Institut für Medizinische Statistik und Dokumentation, Gutenberg Universität Mainz, Germany*

Received 25 November 2004; accepted 3 April 2005

KEYWORDS

Rhinosinusitis;
Children;
Ems Mineral Salts
solution;
Xylometazoline;
Decongestants;
Therapy;
Controlled study

Summary The treatment of rhinosinusitis seen in the light of uncertain pathogenesis and variable symptoms is under discussion and ranges from the administration of antibiotics, decongestants and anti-allergic agents to no treatment. In this randomized, prospective, double-blind and controlled study the effect of a 14-day treatment (1–2 sprays into each nostril t.d.) with either isotonic Ems Mineral Salts (EMS) solution (Siemens & Co., Bad Ems, Germany) or xylometazoline solution (0.05%) was tested in children ($n = 66$) aged 2–6 years.

Main outcomes: the degree of mucosal inflammation, nasal patency, general state of health, condition of the middle ear, auditory function as well as an assessment of complaints by the parents.

With the exception of the hearing defects, all parameters showed a clear improvement in both treatment groups at the end of the observation period ($p > 0.001$). The hearing defects showed only a trend towards improvement. At the end of the study no differences between the treatment groups could be determined. However, at the intermediate examination after the first 7 days of treatment more favourable results were seen in the group treated with EMS.

* Corresponding author. Tel.: +49 221 47886635; fax: +49 221 47886636.
E-mail address: michel@uni-koeln.de (O. Michel).

No undesired medicinal effects were observed, although in 7 out of 34 cases the nasal spray was improperly used in the group treated with xylometazoline.

The results of the study show that there is no difference in efficacy between an exclusive treatment by EMS solution in children aged 2–6 years and a treatment with xylometazoline, but with the distinction that with EMS the length of use was not restricted, there were not the potential side effects of nasal decongestants, and there was no contraindication in the newborn and infants.

© 2005 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Rhinosinusitis is widespread in small children in the age group of between 2 and 6 years, with an average incidence of between 2 and 20 episodes per year. Symptoms are variable and sometimes unspecific. Nasal discharge, oral respiration, snoring, secretory otitis media, aversion to drinking, but also fever and an impaired general condition could be the clinical signs [1]. Rhinosinusitis typically initially occurs as a viral respiratory tract infection, but bacterial growth is demonstrated in 60% of patients with symptoms of an upper respiratory tract infection of at least 10 days duration [2]. Because the signs and symptoms of bacterial rhinosinusitis are similar to those of viral upper respiratory tract infections, the classification of rhinosinusitis and its different clinical forms have long been under discussion [3–5].

The foremost important role of antibiotics in the treatment of acute sinusitis is being viewed with increasing criticism: in a randomized, placebo-controlled trial in 188 patients neither amoxicillin nor amoxicillin-clavulanate offered any clinical benefit compared with placebo for children with clinically diagnosed acute sinusitis [6].

The question arises whether it could be sufficient to tackle the blocked nasal ventilation rather than to treat with antibiotics immediately [7]. To an increasing number of authors unrestricted nasal ventilation is viewed as the most important prerequisite for the resolution of infection.

Drainage of the anterior ethmoid, maxillary and (in older children) frontal sinuses converges at the ostiomeatal complex. Inflammation in this key area is observed in most cases of sinusitis. Patent nasal airways also guarantee the ventilation of the adjacent anatomically related areas such as the sinuses, the tracheobronchial system and the middle ear. Decreased mucociliary transport results in the disruption of mucociliary mucus clearance [8,9]. Elimination of the disease is accomplished when this clearance mechanism has been restored.

To achieve unrestricted air flow nasal decongestants such as sympathicomimetics were commonly used to reduce tissue oedema, to facilitate drainage, and to maintain ostial patency [10,11].

But their side-effects with systemic effects on the cardio-vascular system, the degenerative effect on the nasal mucosa by chronic hypoxia caused by the permanent vasoconstriction limit their use and dampen the motivation of the treating parents. Some of the decongestant sprays contain benzalkonium chloride, which has also been proved to have a negative effect on the ciliary movement and the clearance [12–14].

An alternative treatment consists of the use of salt solutions [7] – which according to Boek [15] may also have a negative effect on the ciliary beat – but controlled studies have, however, been lacking up to now [16,17].

This study was designed to determine the effectiveness of a topical treatment in children with acute rhinosinusitis according to the definition given by the American Academy of Pediatrics [16], whereby a natural mineral salts solution was to be compared with decongestive treatment using xylometazoline.

2. Material and methods

The study followed strictly the common national and international guidelines, good clinical practice and the Helsinki Declaration in its revised edition of 1996. The study was reviewed and accepted by the ethics committee responsible for the Medical Faculty of the University of Cologne and the General Medical Councils of Bavaria, Baden-Wuerttemberg, Westfalen-Lippe and Schleswig-Holstein. All parents of the patients gave written informed consent before participating in the clinical study.

The multicentric study was carried out as a randomized, prospective, double-blind and controlled study during a 6-month winter period from October to May. The effect of a 14-day treatment (1–2 sprays into each nostril t.d.) of either isotonic EMS solution (composition listed in Table 1; manufacturer: Siemens & Co., Bad Ems, Germany) or xylometazoline solution (0.05%) (XYL) was tested in children aged between 2 and 6 years. All children had an acute infection of the nose/upper airways with involvement of the middle ear (secretory otitis media).

Table 1 Composition of Ems minerals salts (EMS); ions in g/kg

Lithium	0.21
Sodium	290.9
Potassium	6.11
Magnesium	0.291
Calcium	0.016
Manganese	0.0001
Iron (II, III)	0.003
Fluoride	0.078
Chloride	188.4
Bromide	0.202
Iodide	0.005
Nitrate	0.355
Sulphate	9.24
Bicarbonate	474.4
Carbonate	14.0

Table 2 Exclusion criteria

Participation in another study during the past 30 days
Parents unable to understand the criteria of the study
Mental illness of any degree
Contraindication
Intolerance to Ems Mineral Salts solution
Bleeding disorder
Treated within the last 7 days with any kind of rhinological agent
Ancillary treatment with secretolytics, expectorants, antihypertensive agents, corticosteroids

The infection was judged on the clinical signs according to the common guidelines [16,17]. The excluding criteria are listed on Table 2.

All parents agreed to omit any additional treatment, e.g. antibiotics. All children included had not as yet received any previous treatment.

Following an initial examination a 14-day treatment period was commenced. After the first 7 days of treatment a control examination took place and then again a final evaluation was carried out on completion (day 14).

2.1. The grade of mucosal inflammation

The grade of mucosal inflammation was assessed and quantified through a sum score consisting of the following individual parameters: rubescence, swelling and discharge. The scale ranged from 0 score

points (worst value) to a maximum of 13 (best value).

2.2. Nasal patency

Nasal patency was assessed by the physician at the times of examination, as well as by the parents through daily clinical observations of the child’s inspirations and expirations, and graded from 1 to 4 (worst to best), with grade 1 being totally blocked.

2.3. Middle ear and auditory function

Aeration of the middle ear was tested by otoscopy and tympanometry, aeration of the auditory function by audiometry. Evaluation was performed semi-quantitatively according to the following system: better (1), no change (0), worsened (–1) compared to the initial findings.

2.4. Statistical analysis

The effect of the treatment was determined for each group using Student’s *t*-test for paired groups.

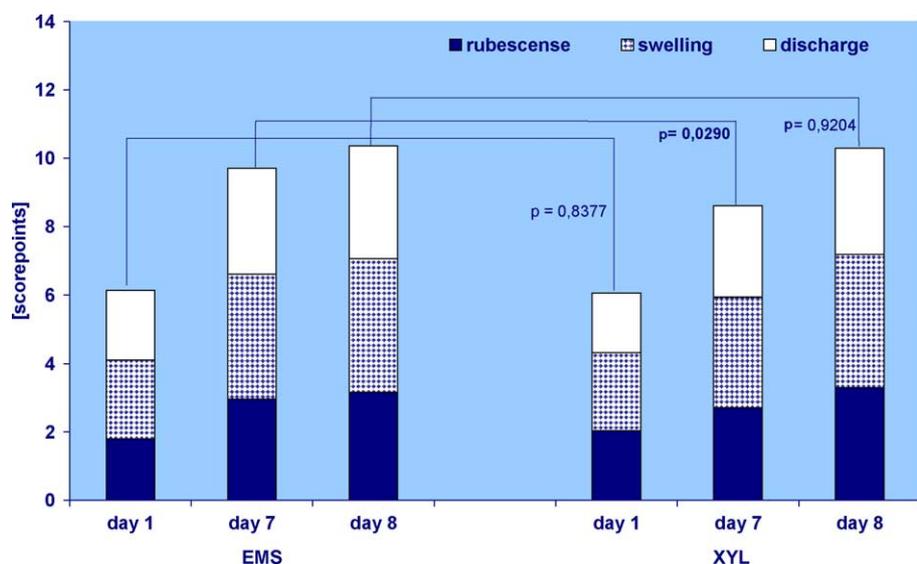


Fig. 1 Changing of inflammation score in number of points (mean).

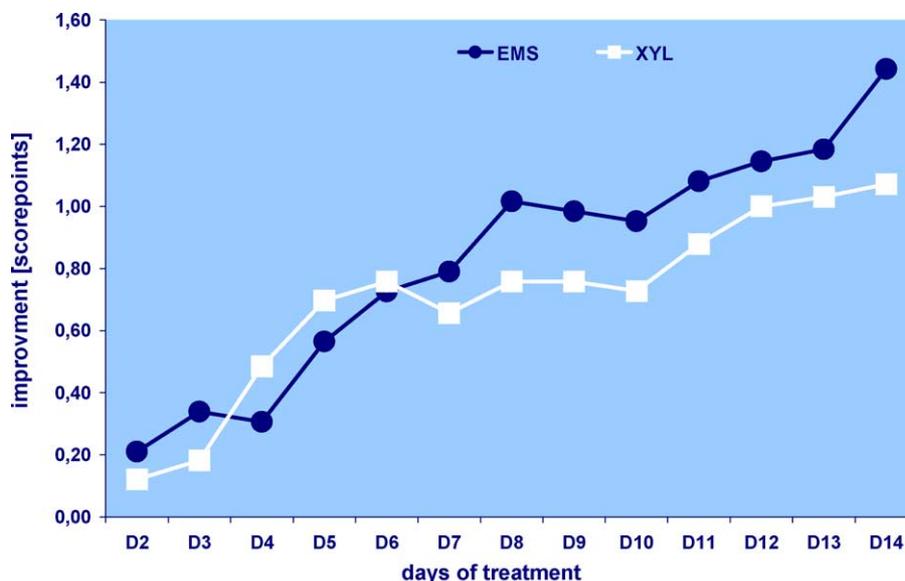


Fig. 2 Improvement of nasal patency in number of points (mean) ascertained by the parent's diary.

Statistical differences between the groups were determined by Student's *t*-test for unpaired groups, in the case of binominal parameters the exact Fisher's test was used. A *p*-level <0.05 was chosen to identify significant results.

3. Results

Seventy patients in four study centres could be included. Four drop-outs were registered: two of these did not reappear after the start of the treatment, and two developed severe infections during the treatment period and had to be excluded. 66 patients (female: 34, male: 32) with a mean age of 3.9 ± 1.1 years could be evaluated.

3.1. Inflammation

At the starting point all children who were included had acute infections of the upper airways, and the nasal mucosa showed moderate signs of inflammation. The averaged score for discharge, rubescence and swelling of the mucosa showed no statistical difference between the EMS group and the XYL group. The calculated score for inflammation (SI) was 6.14 ± 1.6 (EMS group) and 6.06 ± 1.7 (XYL group), respectively.

During the treatment period in both groups the calculated SI decreased at days 7 to 9.7 ± 1.5 EMS or 8.62 ± 2.3 Xyl ($p = 0.0290$), respectively. In particular, the parameter 'discharge' was significantly more greatly reduced ($p = 0.0163$) in the EMS group.

On day 14 (on completion) inflammation receded. The SI showed the following similar results: 10.36 ± 2.3 in the EMS group and 10.29 ± 3.0 in

the XYL group; no statistical significance was found ($p = 0.9204$) (Fig. 1).

3.2. Secondary parameters

3.2.1. Nasal ventilation

Nasal patency improved in both groups during the course of the study from mainly oral respiration to mainly nasal respiration: ($p < 0.0001$: EMS group: 2.15 ± 1.6 pts to 1.07 ± 0.7 pts; XYL group: 1.97 ± 1.7 pts to 1.04 ± 0.7 pts) no differences between the treatment groups could be determined, neither medically at the control examinations, nor from the parents' daily observations ($p > 0.4$). Fig. 2 shows the course of daily changes.

3.2.2. Otoscopy and tympanometry

At the beginning of treatment the following otoscopic findings were seen in the entire study group ($n = 66$): in approximately 10% a retracted tympanic membrane and in 90% signs of otitis media with effusion. In altogether, 14 out of 33 cases in the EMS group and 17 out of 34 cases in the XYL group a unilateral improvement was observed. In three cases from the XYL group a marked exacerbation was observed. Nevertheless, at the end of the observation period a secretory otitis was still observed in 35 patients. Only three patients in both groups were classified as normal. The tympanometry confirmed these results.

3.2.3. Auditory function

Audiograms could only be obtained in 30 of the 66 patients. One patient out of a third of each group showed an improved auditory function; in the other two thirds there was no change in the findings.

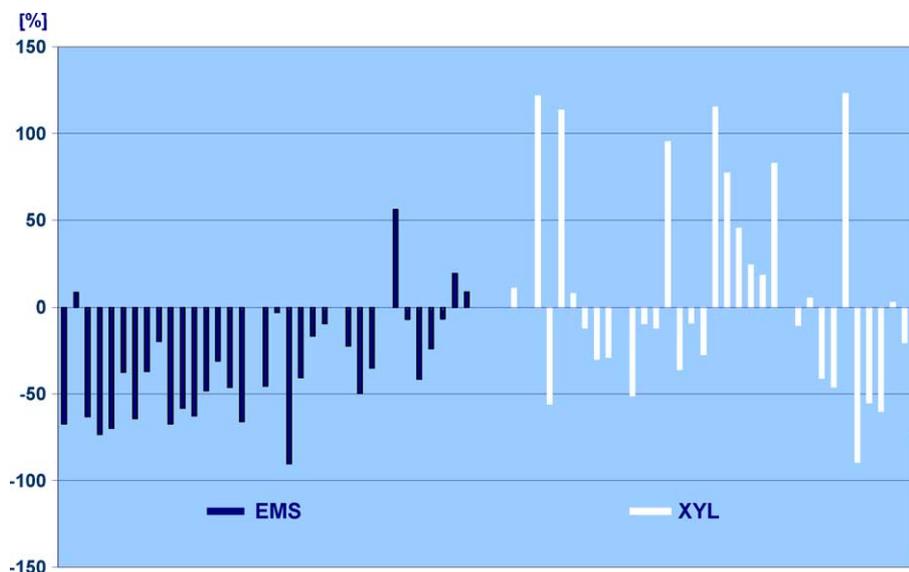


Fig. 3 Percentage deviation of drug usage from the calculated drug requirement of each individual patient.

In two patients out of each treatment group a deterioration took place within the period of observation. No differences between the treatment groups could be verified.

4. Adverse reactions

No adverse drug-induced reactions occurred in any of the cases. There were, however, seven patients in the XYL group who exceeded the total calculated dose by 70–120% (Fig. 3).

5. Discussion

Children aged between 2 and 6 years have a very high prevalence for rhinosinusitis with a concomitant high incidence of middle ear effusion with auditory impairment [5,10]. The majority has a viral or allergic cause, later becoming superinfected by bacteria such as *Streptococcus pneumoniae* (30–66% of episodes of acute bacterial rhinosinusitis in children), *Haemophilus influenzae* (20–30%) and *Moraxella catarrhalis* [4].

The general condition of the affected children shows various degrees of impairment, and symptoms of nasal discharge, blocked nose with oral respiration, secretory otitis media, as well as fever, go towards creating a general condition of impaired life quality both for the child and the parents.

Antibiotics, the treatment once considered to take first place, can no longer be considered dependable in this role, because more recent controlled studies have not proved them to have a higher beneficial effect than a placebo [6,18].

The role of unrestricted nasal patency is now increasingly seen as being crucial for promoting healing. This goal can be achieved by decongestive nose drops such as naphthazoline or xylometazoline (XYL), as recommended in guidelines issued by the Association of the Scientific Medical Societies (AWMF) in Germany or by the American Academy of Otolaryngology [1,5,16,17].

This concept is currently under discussion from another point of view, since these substances reduce ciliary activity [19], can trigger addiction because of the rebound effect and cause severe cardiovascular and pulmonary side effects in infants [21,22]. By inhibiting ciliary motion, topical decongestants may delay clearance of infected material. In addition, by decreasing the blood flow to the mucosa, topical decongestants may lower oxygen tension and impair the diffusion of antimicrobials into the sinuses.

As it appears at first sight to be harmless, saline solution has been propagated as an alternative. Nevertheless, in vitro studies have demonstrated that also a physiological saline solution reduces ciliary movement [15]. The use of hypertonic saline solution as a nasal wash was also included in the array of therapeutic weapons, but it is still controversial whether hypertonic saline solution decreases ciliary movement or not [23–25].

There has been no discussion yet concerning a natural product derived from a natural spring, Ems Mineral Salts solution, which has in several in vitro and in vivo studies been proved to enhance the ciliary activity of epithelial cells and to stimulate the regeneration of the nasal cell layer [26,27].

Prospective, placebo-controlled double-blind studies have shown the efficacy of Ems Mineral Salts compared to saline solution in the treatment of

chronic rhinosinusitis [26,28], as well as in postoperative care [29]. In both studies it became evident that the fibrinous coat, crusting and the inflammatory parameters receded significantly faster.

The results of our present study support those results obtained in adults. Under the clinical conditions described here concerning rhinosinusitis, no difference between treatment with a decongestant (xylometazoline) and the Ems Mineral Salts solution could be seen regarding the relief of symptoms. Both remedies led within the 14-day period to significant improvement. The data obtained on day 7 concerning the degree of inflammation as evaluated by swelling and nasal patency carried an even greater conviction because they reached with their statistical *p*-value a confirmative level compared to xylometazoline. In all other secondary parameters surveyed, Ems Mineral Salts solution reached exactly the same scores as the XYL group. Altogether, no statistical significance was seen between both of the tested groups.

The only exception was seen in the observed side effects: our data prove the potential addiction to nasal decongestants by the fact that 20% of the children in the XYL group took up to 120% more drugs than prescribed. This was not seen in the Ems Mineral Salts solution group. Nevertheless, the excessive use of nasal spray in the XYL-group had neither on swelling nor on nasal ventilation any advantage over the normal use of EMS. The rebound swelling and the tendency to addiction has been described extensively in the literature [21,22,30] and the rashness of parents applying sprays in such a way is considerably alarming because of the risk of starting a career of rhinitis medicamentosa in early youth.

This permits the statement that an exclusive treatment by Ems Mineral Salts solution in children aged between 2 and 6 is better than the same treatment with xylometazoline, because it is without restrictions concerning the treatment period, without the potential side effects of nasal decongestants and without any contraindication in the newborn and infants.

References

- [1] P.A. Clement, C.D. Bluestone, F. Gordts, et al. Management of rhinosinusitis in children: consensus meeting, Brussels, Belgium, September 13, 1996, *Arch. Otolaryngol. Head Neck Surg.* 124 (1998) 31–34.
- [2] W.R. Bishai, Issues in the management of bacterial sinusitis, *Otolaryngol. Head Neck Surg.* 127 (2002) S3–S9.
- [3] Infectious rhinosinusitis in adults: classification, etiology and management, International Rhinosinusitis Advisory Board, *Ear Nose Throat J.* 76 (1997) 1–22.
- [4] J.B. Anon, Acute bacterial rhinosinusitis in pediatric medicine: current issues in diagnosis and management, *Paediatr. Drugs* 5 (Suppl. 1) (2003) 25–33.
- [5] P.A. Clement, C.D. Bluestone, F. Gordts, et al. Management of rhinosinusitis in children, *Int. J. Pediatr. Otorhinolaryngol.* 49 (Suppl. 1) (1999) S95–S100.
- [6] J.M. Garbutt, M. Goldstein, E. Gellman, W. Shannon, B. Littenberg, A. Randomized, Placebo-controlled trial of antimicrobial treatment for children with clinically diagnosed acute sinusitis, *Pediatrics* 107 (2001) 619–625.
- [7] U. Bollag, Why not saline nose drops? *Helv. Paediatr. Acta* 33 (1978) 91–94.
- [8] J.J. Homer, R.J. England, A.D. Wilde, G.R. Harwood, N.D. Stafford, The effect of pH of douching solutions on mucociliary clearance, *Clin. Otolaryngol.* 24 (1999) 312–315.
- [9] I. Braverman, E.D. Wright, C.G. Wang, D. Eidelman, S. Frenkiel, Human nasal ciliary-beat frequency in normal and chronic sinusitis subjects, *J. Otolaryngol.* 27 (1998) 145–152.
- [10] N.S. Jones, Current concepts in the management of paediatric rhinosinusitis, *J. Laryngol. Otol.* 113 (1999) 1–9.
- [11] P. Brihaye, M. Jorissen, P.A. Clement, Chronic rhinosinusitis in cystic fibrosis (mucoviscidosis), *Acta Otorhinolaryngol. Belg.* 51 (1997) 323–337.
- [12] C. McMahon, Y. Darby, R. Ryan, G. Scadding, Immediate and short-term effects of benzalkonium chloride on the human nasal mucosa in vivo, *Clin. Otolaryngol.* 22 (1997) 318–322.
- [13] W.M. Boek, S.G. Romeijn, K. Graamans, J.C. Verhoef, F.W. Merkus, E.H. Huizing, Validation of animal experiments on ciliary function in vitro. Part II. The influence of absorption enhancers, preservatives and physiologic saline, *Acta Otolaryngol.* 119 (1999) 98–101.
- [14] B. Marple, P. Roland, M. Benninger, Safety review of benzalkonium chloride used as a preservative in intranasal solutions: an overview of conflicting data and opinions, *Otolaryngol. Head Neck Surg.* 130 (2004) 131–141.
- [15] W.M. Boek, N. Keles, K. Graamans, E.H. Huizing, Physiologic and hypertonic saline solutions impair ciliary activity in vitro, *Laryngoscope* 109 (1999) 396–399.
- [16] Subcommittee on Management of Sinusitis and Committee on Quality Improvement, Clinical practice guideline: management of sinusitis, *Pediatrics* 108 (2001) 798–808.
- [17] J.M. Gwaltney, J.G. Jones, D.W. Kennedy, Medical management of sinusitis: educational goals and management guidelines. The International Conference on sinus Disease, *Ann. Otol. Rhinol. Laryngol. Suppl.* 167 (1995) 22–30.
- [18] A.W. Dohlman, M.P. Hemstreet, G.T. Odrezin, A.A. Bartolucci, Subacute sinusitis: are antimicrobials necessary? *J. Allergy Clin. Immunol.* 91 (1993) 1015–1023.
- [19] T. Deitmer, R. Scheffler, The effect of different preparations of nasal decongestants on ciliary beat frequency in vitro, *Rhinology* 31 (1993) 151–153.
- [20] F. Musshoff, A. Gerschlauser, B. Madea, Naphazoline intoxication in a child—a clinical and forensic toxicological case, *Forensic Sci. Int.* 134 (2003) 234–237.
- [21] P. Graf, K. Toll, J. Palm, H. Hallen, Effects of sustained-release oral phenylpropanolamine on the nasal mucosa of healthy subjects, *Acta Otolaryngol.* 119 (1999) 837–842.
- [22] W. Garavello, M. Romagnoli, L. Sordo, R.M. Gaini, C. Di Bernardino, A. Angrisano, Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: a randomized study, *Pediatr. Allergy Immunol.* 14 (2003) 140–143.
- [23] H. Degirmencioglu, A. Karadag, Z. Avci, H. Kurtaran, F. Catal, Is hypertonic saline better than normal saline for allergic rhinitis in children? *Pediatr. Allergy Immunol.* 15 (2004) 190.
- [24] D. Shoseyov, H. Bibi, P. Shai, N. Shoseyov, G. Shazberg, H. Hurvitz, Treatment with hypertonic saline versus normal saline nasal wash of pediatric chronic sinusitis, *J. Allergy Clin. Immunol.* 101 (1998) 602–605.

- [26] G. Bachmann, G. Hommel, O. Michel, Effect of irrigation of the nose with isotonic salt solution on adult patients with chronic paranasal sinus disease, *Eur. Arch. Otorhinolaryngol.* 257 (2000) 537–541.
- [27] G. Wolf, B. Koidl, B. Pelzmann, Zur Regeneration des Zilienschlages humaner Flimmerzellen, *Laryngorhinootologie* 70 (1991) 552–555.
- [28] H.M. Wendeler, J. Müller, R. Dieler, J. Helms, Nasenspülungen mit isoosmotischer Emser-Salz-Lösung bei chronischer Rhinosinusitis. Nasenspülungen mit isoosmotischer Emser-Salz-Lösung bei chronischer Rhinosinusitis, *Otorhinolaryngol. nova* 7 (1998) 254–258.
- [29] O. Michel, J. Charon, Postoperative Inhalationsbehandlung nach Nasennebenhohleneingriffen. Eine plazebokontrollierte, doppelblinde und randomisierte Studie, *HNO* 39 (1991) 433–438.
- [30] P. Graf, Long-term use of oxy- and xylometazoline nasal sprays induces rebound swelling, tolerance, and nasal hyperreactivity, *Rhinology* 34 (1996) 9–13.

Available online at www.sciencedirect.com

