ORIGINAL ARTICLE

Efficacy of Isotonic Nasal Wash (Seawater) in the Treatment and Prevention of Rhinitis in Children

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Objective: To evaluate the potential of nasal isotonic saline application to prevent reappearance of cold and flu in children during the winter.

Design: Prospective, multicenter, parallel-group, open, and randomized comparison.

Setting: Eight pediatric outpatient clinics.

Patients: A total of 401 children (aged 6-10 years) with uncomplicated cold or flu.

Interventions: We randomly assigned patients to 2 treatment groups, one with just standard medication, the other with nasal wash with a modified seawater solution (Physiomer) plus standard medication, and observed them for 12 weeks.

Main Outcome Measures: The primary efficacy end points were nasal symptoms resolution during acute illness (visits 1 and 2). We also looked for reappearance of cold or flu, consumption of medication, complications, days off school, and reported days of illness during the following weeks when preventive potential was evaluated (visits 3 and 4).

Results: At visit 2, patients in the saline group achieved primary end points (measured on a 4-point numeric scale on which 1 indicated no symptoms and 4, severe symptoms) in the parameters nasal secretion and obstruction (mean scores vs nonsaline group, 1.79 vs 2.10 and 1.25 vs 1.58, respectively) ($P<.05$ for both). During the prevention phase (at visit 3, 8 weeks after study entry) patients in the saline group showed significantly lower scores in sore throat, cough, nasal obstruction, and secretion ($P<.05$ for all). By visit 3, significantly fewer children in the saline group were using antipyretics (9% vs 33%), nasal decongestants (5% vs 47%), mucolytics (10% vs 37%), and systemic antiinfectives (6% vs 21%) ($P<.05$ for all). During the same period children in the saline group also reported significantly fewer illness days (31% vs 75%), school absences (17% vs 35%), and complications (8% vs 32%) ($P<.05$ for all). Similar results were found at the final visit.

Conclusion: Children in the saline group showed faster resolution of some nasal symptoms during acute illness and less frequent reappearance of rhinitis subsequently.

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UPPER RESPIRATORY TRACT infections (URTI) and sinonasal symptoms are frequent complaints, especially in children.[1] The prevalence of sinusitis is as high as 32% in this age group.[2] Nasal irrigation with isotonic saline solutions seems effective in such health conditions and is often used in a variety of indications as an adjunctive treatment.[3] Although saline nasal wash is currently mentioned in several guidelines, scientific evidence of its efficacy is rather poor.[4,5]

A number of articles assessing from 20 to 200 patients with allergic rhinitis or chronic sinusitis have been published.[3] They compared solutions of different tonicity[6] or delivery devices[7] or assessed the potential of nasal wash to prevent or reduce allergy symptoms.[8] Although the results are controversial, nasal irrigation improves symptoms and often decreases the amount of prescribed medication.[9]

Less literature is available for URTI associated with common cold during the winter. Adam et al[10] evaluated the efficacy of hypertonic and normal saline spray in adults with cold or sinonasal symptoms and compared outcomes with an observation-only control group. Another recently published trial was performed to assess whether daily application of nasal saline could prevent common cold symptoms in healthy adults.[11]

We were not able to find any articles that assessed the use of adjunct nasal wash in children during a common cold or evaluated its preventive potential. We were interested in the 6- to 10-year-old age group because school children are at a higher risk of URTI and sinusitis than other groups.[12] We therefore carried out a prospective trial among children who came

Table 1. Chemical Composition of Isotonic Saline Solution[a]

Ion	Concentration
Elements, mg/L	
Sodium (Na^+)	2400
Chloride (Cl^-)	5850
Potassium (K^+)	51
Calcium (Ca^{2+})	360
Magnesium (Mg^{++})	1300
Sulfates (sulfur) (SO_4^{--})	2755
Iron (Fe^{++})	6
Trace Elements, µg/L	
Zinc (Zn^{++})	27.00
Selenium (Se^{++})	38.17
Copper (Cu^{++})	12.92

[a] (Physiomer; Goemar Laboratoire de la Mer, Saint Malo, France).

to pediatric outpatient clinics for treatment of acute cold or flu. The study was performed in 2 phases: initially we focused on symptom relief during acute illness, and we then assessed preventive potential in the same patient population.

The primary objectives of this trial were to (1) prove the efficacy and safety of nasal saline wash as adjunctive treatment during uncomplicated acute rhinitis for the resolution of nasal symptoms and (2) evaluate its potential to prevent the recurrence of cold and flu and complications. Secondary objectives included the evaluation of 2 different cleansing strengths (a medium jet and a fine spray) and 2 isotonic formulations with different ionic compositions (a nasal wash formula and a dual formula used for eye and nose wash).

METHODS

The study was approved by the ethics committee of the Motol Teaching Hospital in Prague and the ethics committee of the Teaching Hospital in Brno. All parents signed an informed consent form and obtained relevant information about the trial, which was designed as a multicenter, parallel group, open, and randomized comparison. Eight pediatric outpatient clinics participated in the study; every child was assessed by the same physician at each visit. Eligible patients were aged 6 to 10 years and were seeing the physician for a common cold or flu. Specific exclusion criteria were anatomic sinonasal disorders, known severe immune deficiency, and concomitant corticosteroid medication.

A total of 401 children met the inclusion criteria and were randomized to receive either standard treatment including antipyretics, nasal decongestants, mucolytics (those could be given based on patient status and parent discretion), and/or systemic antibiotics (n=101) without saline wash, or these same standard treatments with saline wash. The saline solution used was a commercially available product processed from Atlantic Ocean seawater (Physiomer; Goemar Laboratoire de la Mer, Saint Malo, France). As electrodialysis is used to establish isotonicity, the trace elements and minerals remain in concentrations similar to those found in seawater (**Table 1**). Patients randomized to the saline group were evaluated in 3 delivery strength subgroups: (1) medium jet flow (n=100); (2) fine spray (n=100); and (3) a dual formula for eye and nose wash with a fine spray (n=100). All researchers were blinded to saline solutions used.

Patients were observed for a total of 12 weeks, from January to April 2006, during which health status, symptoms, and medication use were assessed at 4 visits over the course of the trial. Acute illness was evaluated during the first 2 visits (up to 3 weeks), prevention during the following 2 visits (up to 12 weeks). The third visit, scheduled for week 8 after study entry, could be conducted over the telephone.

On study entry, children in the saline group and their parents were instructed about usage; the number of bottles provided was recorded in the protocol; and the patients were asked to return empty bottles, which were weighed to assess compliance. No restrictions were placed on the use of concomitant medication during acute illness, with the exception of systemic antihistamines, which are sometimes used to reduce mucosal swelling. Long-term use of systemic antihistamines for other indications (eg, allergy) initiated before trial entry was not an exclusion criteria.

Saline nasal wash was administered 6 times per day during acute illness and 3 times per day during the prevention phase. For the medium jet flow (saline group 1) 9 mL of saline was administered per application and per nostril; for both other sprays (saline groups 2 and 3), the volume was 3 mL per application and per nostril.

Randomization of patients was done by the physician. Patients were allocated to 1 of 4 groups (no wash or 1 of 3 types of nasal wash) based on the sequence of their appearance in the clinic.

PARAMETERS EVALUATED

At the first visit, we evaluated baseline parameters (sex, age, duration of illness, and concomitant diseases and medication) and overall health status (using a qualitative range from excellent to unsatisfactory). On entry and at all subsequent visits, nasal and several other parameters representing the status of the upper respiratory tract were assessed by the physician using a qualitative predefined range (1, no symptoms, through 4, severe symptoms). Some parameters had different scales, which are specified in **Tables 2**, **3**, **4**, and **5**. Concomitant medication use was also recorded at each visit, not by brand or molecule, but by group (eg, mucolytics). At all visits, parents were asked about days of sickness and absence from school. From the second visit, patients in the saline group were evaluated for their attitude concerning tolerability and sensations reported during and after application, using a qualitative range. Adverse events were recorded separately as was discontinuation. No laboratory testing was scheduled. Empty bottles returned were weighed to assess compliance. Patients with a compliance rate estimated at less than 75% were excluded from evaluation. For evaluation purposes, all the qualitative parameters were converted to a numeric scale.

Most of the parameters (clinical status) were evaluated by physicians during scheduled visits. Patients and/or parents assessed health status and parameters related to saline safety and tolerability.

STATISTICAL ANALYSIS

Statistical analysis was carried out using StatSoft Statistica software, version 7.1 (StatSoft Inc, Tulsa, Oklahoma). The level of statistical significance was set at .05 for each comparison.

Descriptive statistics are provided for quantitative parameters such as mean, standard deviation, and median. Qualitative data are presented as absolute frequencies and percentages.

Individual parameters were separately evaluated at each visit. For data measured on a Likert scale, the hypothesis of no difference in medians among 4 compared groups was evaluated using the Kruskal-Wallis 1-way analysis of variance based on ranks (corrected for ties). If this test showed significant differ-

Table 2. Selected Characteristics of 390 Patients[a]

Characteristic	Control (n=101)	Isotonic Saline Wash			
		Medium Jet (n=99)[b]	Fine Spray (n=95)[b]	Dual Formula (n=95)[b]	All Wash (n=289)[c]
Age, y	8.4 [1.5]	8.4 [1.5]	8.1 [1.4]	8.2 [1.5]	8.2 [1.5]
Male	58 (57.4)	53 (53.5)	47 (49.5)	51 (53.7)	151 (52.2)
Female	43 (42.6)	46 (46.5)	48 (50.5)	44 (46.3)	138 (47.8)
Study point duration, d					
Symptoms prior to study entry	6.3 [7.2]	6.2 [5.4]	6.8 [5.4]	5.9 [4.6]	6.3 [5.2]
From V1 to V2	10.7 [3.9]	11.2 [5.3]	10.4 [4.4]	10.1 [4.1]	10.5 [4.7]
From V2 to V3	36.9 [7.4]	36.8 [7.9]	37.4 [9.2]	37.6 [7.4]	37.3 [8.1]
From V3 to V4	38.4 [5.9]	38.4 [7.3]	38.3 [7.9]	38.5 [6.7]	38.4 [7.3]
Vaccinated for flu	9 (8.9)	11 (11.1)	13 (13.7)	11 (11.6)	35 (12.1)
Allergy	22 (21.8)	31 (31.3)	30 (31.6)	31 (32.6)	92 (31.8)
Long-term systemic AH use	11 (10.9)	18 (18.2)	12 (12.6)	10 (10.5)	40 (13.8)
Rhinologic symptom score[d]					
Sore throat	1.84 [0.81]	1.75 [0.81]	1.68 [0.73]	1.62 [0.75]	1.69 [0.77]
Dry cough	1.60 [0.76]	1.42 [0.67]	1.59 [0.77]	1.47 [0.79]	1.49 [0.74]
Productive cough	1.43 [0.74]	1.43 [0.73]	1.41 [0.77]	1.31 [0.65]	1.38 [0.72]
Nasal secretion	2.70 [0.61]	2.85 [0.63]	2.84 [0.61]	2.83 [0.58]	2.84 [0.60]
Sneezing	1.50 [0.67]	1.40 [0.57]	1.56 [0.68]	1.56 [0.75]	1.51 [0.67]
Itching	1.27 [0.55]	1.30 [0.56]	1.32 [0.55]	1.28 [0.54]	1.30 [0.55]
Loss of smell/taste	1.38 [0.84]	1.32 [0.62]	1.35 [0.67]	1.27 [0.54]	1.31 [0.61]
Nasal secretion type[e]	2.55 [0.64]	2.59 [0.62]	2.58 [0.61]	2.56 [0.61]	2.57 [0.61]
Nasal breathing score[f]	2.16 [0.67]	2.26 [0.69]	2.24 [0.74]	2.27 [0.78]	2.26 [0.74]
Medication used					
Antipyretics	24 (23.8)	26 (26.3)	22 (23.2)	20 (21.1)	68 (23.5)
Nasal decongestants	40 (39.6)	29 (29.3)	26 (27.4)	30 (31.6)	85 (29.4)
Mucolytics	20 (19.8)	15 (15.2)	13 (13.7)	17 (17.9)	45 (15.6)
Systemic antibiotics	5 (5.0)	6 (6.1)	1 (1.1)	2 (2.1)	9 (3.1)

Abbreviations: AH, antihistamines; V, visits during the trial.
[a] All data are reported as mean [SD] value or number (percentage) of patients.
[b] Multiple comparisons of treatments vs control if Kruskal-Wallis or logistic regression results were significant.
[c] Mann-Whitney or χ^2 tests.
[d] Rhinologic symptom scores: 1, no symptoms; 2, mild; 3, moderate; and 4, severe.
[e] Secretion types: 1, absent; 2, serosal; 3, seropurulent; and 4, purulent.
[f] Breathing scores: 1, without any difficulty; 2, minor difficulties; 3, difficult; and 4, impossible.

ence among the groups, we performed multiple comparisons between treatments (based on joint ranking).

For dichotomous data, we performed a logistic regression analysis, followed in case of significance by comparisons of "treated" groups vs control. Bonferroni correction for multiple comparisons was used for these contrasts.

In addition, we added a comparison of patients using nasal wash (treated) vs control (untreated), without differentiation of individually treated subgroups. Mann-Whitney and χ^2 tests were performed in this case.

Spontaneous complaints and local adverse events reported by the patients were listed by groups using nasal wash.

RESULTS

Of 401 patients, 390 were finally assessed; 1 patient was not available for visit 3 and was excluded from evaluation after the second visit. The remaining 10 patients either did not come to the second visit (n=4), did not comply with the entry criteria (n=2), or the parents decided not to continue (n=2); 1 patient was admitted to the hospital, and 1 was excluded because of low compliance. The average duration of the trial was 86 days. Baseline characteristics among groups were comparable as well as the average number of days between individual visits (Table 2).

ACUTE ILLNESS PHASE (VISIT 2)

Rhinologic score was used for efficacy assessment. Individual symptoms recorded in the protocol as predefined qualitative measures were converted to a numerical scale for evaluation purposes (score range, 1-4; 1, absence of symptoms, through 4, severe symptoms). The parameters assessed included nasal secretion and its type, nasal obstruction, sore throat, cough and expectoration including the nature of the expectorate, sneezing, itching, and loss of senses of smell and taste. Although the severity of symptoms was comparable at baseline, we saw faster clearing of some nasal symptoms in the saline groups. Symptom scores that differed significantly between groups were nasal secretion, type of nasal secretion, nasal obstruction, and sore throat (Table 3). Similar results were obtained if individual nasal wash subgroups and control were compared.

When comparing the consumption of pharmaceuticals, we noted significantly lower consumption of nasal decongestants and mucolytics in the treatment groups than in controls. Other medication evaluated did not differ significantly (Table 3).

At visit 2, physicians were asked to assess the change in health status compared with the entry visit. A qualitative

Table 3. Efficacy Parameters at Visit 2 (Acute Phase)[a]

Characteristic	Control (n=101)	Isotonic Saline Wash			
		Medium Jet (n=99)[b]	Fine Spray (n=95)[b]	Dual Formula (n=95)[b]	All Wash (n=289)[c]
Rhinologic score[d]					
Sore throat	1.23 [0.47]	1.08 [0.27]	1.07 [0.26]	1.11 [0.43]	1.09 [0.33][e]
Dry cough	1.14 [0.38]	1.09 [0.35]	1.14 [0.43]	1.12 [0.35]	1.11 [0.38]
Productive cough	1.38 [0.63]	1.21 [0.54]	1.22 [0.49]	1.25 [0.62]	1.23 [0.55]
Nasal secretion	2.10 [0.74]	1.76 [0.67][e]	1.86 [0.79]	1.74 [0.67][e]	1.79 [0.71][e]
Sneezing	1.06 [0.24]	1.01 [0.10]	1.06 [0.29]	1.06 [0.25]	1.04 [0.22]
Itching	1.06 [0.24]	1.01 [0.10]	1.03 [0.23]	1.04 [0.20]	1.03 [0.18]
Loss of smell/taste	1.09 [0.35]	1.01 [1.01]	1.00 [0.00]	1.00 [0.00]	1.00 [0.06]
Nasal secretion type[f]	2.06 [0.69]	1.74 [0.65][e]	1.74 [0.62][e]	1.69 [0.65][e]	1.72 [0.64][e]
Nasal breathing score[g]	1.58 [0.68]	1.27 [0.51][e]	1.27 [0.56][e]	1.20 [0.50][e]	1.25 [0.52][e]
Medication					
Antipyretics	13 (12.9)	5 (5.1)	7 (7.4)	10 (10.5)	22 (7.6)
Nasal decongestants	36 (35.6)	15 (15.2)[e]	13 (13.7)[e]	18 (18.9)[e]	46 (15.9)[e]
Mucolytics	32 (31.7)	15 (15.2)[e]	14 (14.7)[e]	21 (22.1)	50 (17.3)[e]
Systemic antibiotics	9 (8.9)	7 (7.1)	6 (6.3)	3 (3.2)	16 (5.5)
Health status score[h]					
Entry during cold	2.60 [1.02]	1.88 [0.88][e]	1.93 [0.79][e]	1.80 [0.84][e]	1.87 [0.84][e]
Entry during flu	2.00 [0.91]	1.63 [0.75]	1.58 [0.79]	1.57 [0.68]	1.59 [0.74][e]

[a] All data are reported as mean [SD] score or number (percentage) of patients.
[b] Multiple comparisons of treatments vs control if Kruskal-Wallis or logistic regression results were significant.
[c] Mann-Whitney or χ^2 tests.
[d] Rhinologic symptom scores: 1, no symptoms; 2, mild; 3, moderate; and 4, severe.
[e] $P<.05$.
[f] Secretion types: 1, absent; 2, serosal; 3, seropurulent; and 4, purulent.
[g] Breathing scores: 1, without any difficulty; 2, minor difficulties; 3, difficult; and 4, impossible.
[h] Health status scores: 1, cured; 2, significant improvement; 3, partial improvement; and 4, no change.

Table 4. Efficacy Parameters at Visit 3 (Preventive Phase)[a]

Characteristic	Control (n=101)	Isotonic Saline Wash			
		Medium Jet (n=99)[b]	Fine Spray (n=95)[b]	Dual Formula (n=94)[b]	All Wash (n=288)[c]
Rhinologic score[d]					
Sore throat	1.32 [0.65]	1.09 [0.35][e]	1.07 [0.30][e]	1.03 [0.18][e]	1.07 [0.29][e]
Dry cough	1.40 [0.68]	1.10 [0.36][e]	1.17 [0.50]	1.05 [0.27][e]	1.11 [0.39][e]
Productive cough	NA	NA	NA	NA	NA
Nasal secretion	1.86 [0.87]	1.24 [0.52][e]	1.33 [0.64][e]	1.30 [0.65][e]	1.29 [0.61][e]
Sneezing	1.21 [0.50]	1.07 [0.26]	1.05 [0.22]	1.05 [0.27]	1.06 [0.25]
Itching	1.08 [0.27]	1.00 [0.00]	1.03 [0.23]	1.02 [0.15]	1.02 [0.16]
Loss of smell/taste	1.19 [0.46]	1.02 [0.14]	1.02 [0.14]	1.04 [0.25]	1.03 [0.19]
Nasal secretion type[f]	NA	NA	NA	NA	NA
Nasal breathing score[g]	1.64 [0.73]	1.16 [0.42][e]	1.24 [0.58][e]	1.21 [0.51][e]	1.20 [0.50][e]
Medication					
Antipyretics	33 (32.7)	9 (9.1)[e]	8 (8.4)[e]	10 (10.6)[e]	27 (9.4)[e]
Nasal decongestants	47 (46.5)	6 (6.1)[e]	6 (6.3)[e]	3 (3.2)[e]	15 (5.2)[e]
Mucolytics	37 (36.6)	9 (9.1)[e]	9 (9.5)[e]	10 (10.6)[e]	28 (9.7)[e]
Systemic antibiotics	21 (20.8)	4 (4.0)[e]	5 (5.3)[e]	7 (7.4)[e]	16 (5.6)[e]
Illness and complications					
Reported illness	76 (75.2)	27 (27.3)[e]	33 (34.7)[e]	29 (30.9)[e]	89 (30.9)[e]
Reported school absence	35 (34.7)	16 (16.2)[e]	13 (13.7)[e]	20 (21.3)[e]	49 (17.0)[e]
Complications	32 (31.7)	8 (8.1)[e]	7 (7.4)[e]	9 (9.6)[e]	24 (8.3)[e]

Abbreviation: NA, not applicable.
[a] All data are reported as mean [SD] score or number (percentage) of patients.
[b] Multiple comparisons of treatments vs control if Kruskal-Wallis or logistic regression results were significant.
[c] Mann-Whitney or χ^2 tests.
[d] Rhinologic symptom scores: 1, no symptoms; 2, mild; 3, moderate; and 4, severe.
[e] $P<.05$.
[f] Secretion types: 1, absent; 2, serosal; 3, seropurulent; and 4, purulent.
[g] Breathing scores: 1, without any difficulty; 2, minor difficulties; 3, difficult; and 4, impossible.

Table 5. Efficacy Parameters at Visit 4 (Preventive Phase)[a]

Characteristic	Control (n=101)	Isotonic Saline Wash			
		Medium Jet (n=99)[b]	Fine Spray (n=95)[b]	Dual Formula (n=94)[b]	All Wash (n=288)[c]
Rhinologic score[d]					
Sore throat	1.12 [0.41]	1.06 [0.24]	1.04 [0.25]	1.03 [0.23]	1.05 [0.24]
Dry cough	1.04 [0.24]	1.02 [0.14]	1.04 [0.20]	1.03 [0.23]	1.03 [0.19]
Productive cough	1.13 [0.46]	1.02 [0.20]	1.03 [0.23]	1.02 [0.15]	1.02 [0.19]
Nasal secretion	1.55 [0.78]	1.20 [0.55][e]	1.24 [0.50]	1.23 [0.50]	1.23 [0.52][e]
Sneezing	1.10 [0.30]	1.04 [0.20]	1.05 [0.22]	1.10 [0.36]	1.06 [0.27]
Itching	1.11 [0.31]	1.04 [0.24]	1.05 [0.27]	1.04 [0.25]	1.05 [0.25]
Loss of smell/taste	1.11 [0.37]	1.00 [0.10]	1.02 [0.14]	1.01 [0.10]	1.01 [0.10]
Nasal secretion type[f]	1.53 [0.81]	1.16 [0.51][e]	1.23 [0.52]	1.23 [0.54]	1.21 [0.52][e]
Nasal breathing score[g]	1.39 [0.60]	1.10 [0.36][e]	1.12 [0.32]	1.17 [0.43]	1.13 [0.37][e]
Medication					
Antipyretics	20 (19.8)	8 (8.1)[e]	5 (5.3)[e]	6 (6.4)[e]	19 (6.6)[e]
Nasal decongestants	43 (42.6)	4 (4.0)[e]	7 (7.4)[e]	0 (0.0)[e]	11 (3.8)[e]
Mucolytics	24 (23.8)	4 (4.0)[e]	4 (4.2)[e]	6 (6.4)[e]	14 (4.9)[e]
Systemic antibiotics	9 (8.9)	6 (6.1)	3 (3.2)	3 (3.2)	12 (4.2)
Illness and complications					
Reported illness	53 (52.5)	22 (22.2)[e]	21 (22.1)[e]	21 (22.3)[e]	64 (22.2)[e]
Reported school absence	25 (24.8)	7 (7.1)[e]	8 (8.4)[e]	10 (10.6)[e]	25 (8.7)[e]
Complications	14 (13.9)	6 (6.1)	3 (3.2)[e]	3 (3.2)[e]	12 (4.2)[e]

Abbreviation: NA, not applicable.
[a] All data are reported as mean [SD] score or number (percentage) of patients.
[b] Multiple comparisons of treatments vs control if Kruskal-Wallis or logistic regression results were significant.
[c] Mann-Whitney or χ^2 tests.
[d] Rhinologic symptom scores: 1, no symptoms; 2, mild; 3, moderate; and 4, severe.
[e] $P < .05$.
[f] Secretion types: 1, absent; 2, serosal; 3, seropurulent; and 4, purulent.
[g] Breathing scores: 1, without any difficulty; 2, minor difficulties; 3, difficult; and 4, impossible.

range was used that was converted to a numerical scale for the purposes of evaluation (1, cured; 2, significant improvement; 3, partial improvement; and 4, no change). Health status improved significantly more in the groups using saline (Table 3).

PREVENTION PHASE (VISITS 3 AND 4)

For efficacy evaluation during the preventive period, similar measures were chosen to assess whether regular (3 times per day) nasal wash with isotonic saline can prevent the recurrence of URTIs. Besides rhinologic parameters and medication intake, days of reported illness, days of absence from school, and reported complications were recorded.

Rhinologic symptoms were scored the same as for acute illness and evaluated about 8 weeks after study entry. In several parameters, including dry cough, nasal secretion, and nasal breathing, saline groups had significantly lower occurrence or severity of symptoms (Table 4 and Table 5). Table 5 summarizes the results at the final visit (during week 12 after the study entry).

In terms of medication used, at visit 3, a significantly higher percentage of control patients than patients in the saline groups was using antipyretics, mucolytics, nasal decongestants, and systemic antibiotics (Table 4). The same results (with the exception of systemic antibiotics) were obtained at the final visit (Table 5).

Significantly fewer patients who used long-term saline wash reported days of illness (whether or not associated with absence from school), absence from school, and complications (Table 5). Most recorded events were otitis media, tonsillopharyngitis, bronchitis, and sinusitis.

OVERALL ASSESSMENT OF HEALTH STATUS

At trial entry and at the final visit, parents were asked to rate the child's health status on a 4-point qualitative scale, which was converted to a numeric scale for evaluation (1, excellent; 2, good; 3, satisfactory; and 4, unsatisfactory). At baseline, the mean score was identical for the control and saline groups (mean score, 2.45), which represented an average status of good to satisfactory. At visit 4, after 12 weeks in the study, the parents of children using saline rated the health status of their children as significantly better than did parents of children in the control group (1.51 vs 2.16) (**Table 6**). Similar results were obtained if individual nasal wash subgroups and control were compared.

SAFETY AND TOLERABILITY

To assess safety and tolerability, we evaluated only the saline subgroups. Starting from visit 2, children were asked about their sensations and feelings during and approximately 5 minutes after application of the nasal wash. Their qualitative assessment was converted to a 5-point numeric scale for further evaluation (1, very pleasant; 2, pleasant; 3, no complaints; 4, unpleasant; and 5, very unpleasant). Children using the fine spray

Table 6. Change in Health Status Reported by Parents by Study End[a]

Visit	Control	Isotonic Saline Wash			
		Medium Jet[b]	Fine Spray[b]	Dual Formula[b]	All Wash[c]
1	2.45 [0.59]	2.48 [0.58]	2.42 [0.56]	2.43 [0.58]	2.45 [0.57]
4	2.16 [0.64]	1.43 [0.52][d]	1.54 [0.67][d]	1.55 [0.58][d]	1.51 [0.59][d]

[a] All data are reported as mean [SD] scores. Health status scores: 1, cured; 2, significant improvement; 3, partial improvement; and 4, no change.
[b] Multiple comparisons of treatments vs control if Kruskal-Wallis or logistic regression results were significant.
[c] Mann-Whitney or χ^2 tests.
[d] $P < .05$.

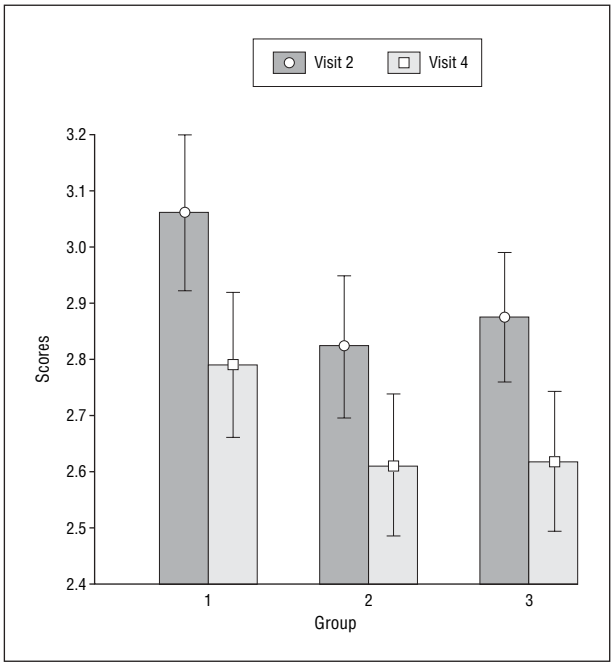

Figure 1. Sensations during application. Patients rated their sensations during isotonic saline wash application using a qualitative scale transformed into a quantitative range for evaluation (1, very pleasant; 2, pleasant; 3, no complaints; 4, unpleasant; and 5, very unpleasant).

(groups 2 and 3) reported higher comfort during and after application than the medium jet users (group 1) (**Figure 1** and **Figure 2**). By visit 4, the scores had improved, but they remained worse in group 1 (medium jet) than in the other groups. However, this difference was not statistically significant.

All the patients' complaints were recorded in the protocol during the course of the study. Overall, saline nasal wash was well tolerated; most complaints appeared in the medium jet group and were associated with the stronger flow of the wash. The number of complaints was too low for statistical analysis. At the second visit, only 25 patients recorded nasal wash complaints (8.7%), and at the final visit, this number had dropped to 7 (2.4%). The other reported complaints were burning and bitter taste. Three patients of 288 experienced nose bleeding.

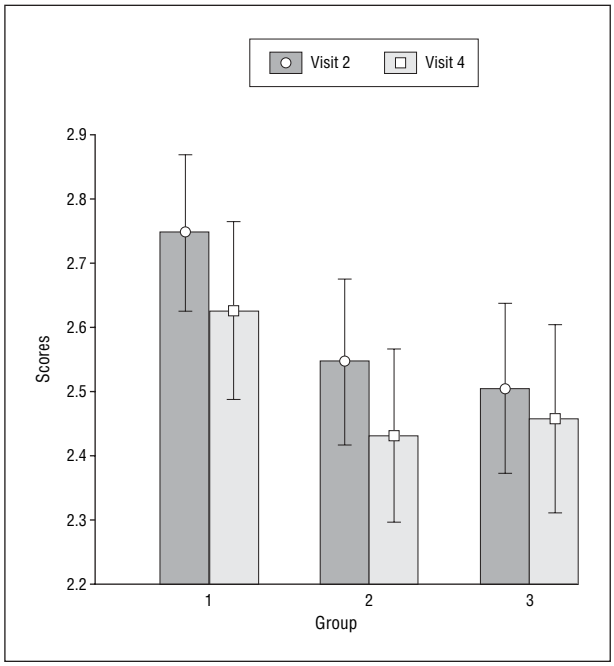

Figure 2. Sensations after application. Patients rated their sensations 5 minutes after isotonic saline wash application using a qualitative scale transformed into a quantitative range for evaluation (1, very pleasant; 2, pleasant; 3, no complaints; 4, unpleasant; and 5, very unpleasant).

COMMENT

The study results show that saline nasal wash significantly improved nasal symptoms in the common cold in children and shows potential to prevent the recurrence of URTI. Results were robust, consistent, and statistically significant in contrast to the few published articles that do not clearly show the benefits of nasal wash to treat the common cold.[3] Some literature describes the preventive potential of saline solution.[11]

Based on in vitro findings, saline has an anti-inflammatory activity because it reduces the production and release of interleukin 8 by the respiratory epithelium.[13] Among other mechanisms of action, a favorable environment for ciliary movement is assumed, especially in alkaline solutions.[14] However, another publication reported decreased ciliary activity in isotonic 0.9% saline solution.[15] These numerous conflicting results suggest that the exact mechanism of action is still unknown. It is not clear whether the effect is predominantly mechanical, based on clearing mucus, or whether salts and trace elements in seawater solutions play a significant role. Moreover a number of commercially available products differ in tonicity, dilution, application device, and other aspects. In our study, we used an undiluted product for which isotonicity was achieved by using electrodialysis. This manufacturing process preserves the concentrations of ions and trace elements to levels comparable with those of seawater.

Since we assessed the potential of seawater as an adjunctive treatment and evaluated it in prevention, we used nonblinded trials and observation to compare nasal wash with standard treatment. Physicians were aware which patients used nasal wash and their assignment to par-

ticular groups. However, physicians were not informed about the composition and device used in these groups; the nasal wash bottles were not labeled.

This largely nonblinded aspect is a weakness of the present study. However, the large number of participants, multicenter design, and consistence of results between individual parameters (assessed by physician, patient, and parent) lower the risk of bias. A blinded comparison of several presentations (eg, physiologic saline solution and diluted solution) could be a topic for future investigation.

Another drawback of the present study is the missing link between statistical and clinical significance in the symptom score. We used a self-designed outcome scale without performing any additional analysis to establish a minimal clinically significant difference. This represents a limitation especially in the acute illness phase analysis, where differences are rather small. However, during the prevention phases, a reduced incidence of other relevant measures (eg, reported illness, school absence, occurrence of complications, and medication use) supports the validity of the clinical benefits of nasal wash. Even the difference of 0.98 in nasal secretion score and 0.97 in nasal breathing score seems to be clinically relevant (by judgment of physicians involved in the trial).

Children were asked to use nasal wash on a frequent basis especially during acute illness. We did not hear substantial complaints about compliance, and good compliance seemed to be confirmed by the weight of returned empty bottles. We excluded only 1 patient for poor compliance.

ACUTE ILLNESS

During acute illness, children using isotonic saline showed faster resolution of nasal secretion and obstruction as well as a reduction in the quantity of used medication; the difference in medication use was significant for nasal decongestants ($P < .001$) and mucolytics ($P = .002$). The reduced use of topical decongestants is important since they are appropriate only on a short-term basis. Long-term use of topical decongestants, which commonly occurs, especially in children, might lead to complications, including paranasal sinusitis and histologic changes in the mucosa. These complications were reported in experimental animals after long-term application of phenylephrine and oxymetazoline.[16] Furthermore, benzalkonium chloride, which is often used as a preserving agent in nasal decongestants or nasal corticosteroids, showed long-term adverse events on the nasal mucosa when used in combination with a vasoactive substance.[17]

In addition to faster symptom resolution, the saline nasal wash group in the present study showed a significantly higher improvement in health status, as assessed by physicians, than did the control group ($P = .02$).

Our outcomes were different from findings published by Adam et al[10] in 1998, who did not find differences between adults treated for common cold and rhinosinusitis with either isotonic or hypertonic nasal wash compared with an observation group. Different results could be explained by the different study population (children vs adults) and sample size (390 vs 119). In the discussion, the authors admit that the rather small sample size might have affected the results. Our study was conducted during a shorter period of time (from January to April 2006), with a limited recruitment period of 8 weeks to secure a comparable epidemiologic situation. The study by Adam et al[10] used a solution prepared from pickling salt and baking soda compared with the isotonic undiluted seawater solution used during our study. This raises again the question about the effect of seawater trace elements on efficacy.

PREVENTION OF UPPER RESPIRATORY INFECTIONS

At the third and fourth visits, children using saline nasal wash on a regular basis (3 times daily) showed fewer rhinologic symptoms. The recorded symptoms were consistent with the medication consumed; a higher percentage of children in the control group used antipyretics, mucolytics, nasal decongestants, and systemic antibiotics. Antibiotics are frequently used in children, and the resulting resistant strains of bacteria represent a threat all over Europe.[18] Saline nasal wash seems to be an appropriate means to achieve lower antibiotic consumption while reducing upper URTI infections and their complications. Moreover, other evaluated parameters also support preventive findings: a reduction in reported illness at visit 3 (untreated, 75% vs treated, 31%) and at visit 4 (untreated, 52% vs treated, 22%) compared with controls; a 51% improvement in school absences at the third visit (17% vs 35%) and a 64% reduction at the final visit (9% vs 25%), although both groups had similar absences from school during the period of acute illness (52% vs 50%). The same trends were noted for complication rates. All of these results are supported by higher parent satisfaction with the treatment.

An article by Tano and Tano[11] reported the preventive potential of saline nasal wash in young adults. Patients were randomly divided into 2 parallel groups. Each group recording symptoms used either physiologic saline spray or no nasal irrigation. After the first 10 weeks, both groups switched regimens and continued for another 10 weeks. The study found a significant reduction in the number of days when nasal symptoms occurred (secretion and/or blocked nose) and a reduction of URTI episodes during the nasal wash period. Although Tano and Tano[11] studied adults and evaluated parameters not identical to ours, both studies showed efficacy to prevent symptoms of rhinitis.

NASAL WASH SUBGROUPS

We did not find robust significant differences either during acute illness or in the prevention phase among individual nasal wash subgroups, although the groups differed in cleansing strengths (medium jet and fine spray) and saline ionic composition. In this age group, we did not find results supporting the hypothesis that stronger flow would be more effective than a fine spray. Furthermore, a reduction in concentration of sodium ions and higher potassium content was not less effective. These findings do not fully support the assumptions concern-

ing the importance of sodium chloride with respect to the efficacy of nasal wash.

In conclusion, the present trial has shown the efficacy of isotonic saline nasal wash processed from Atlantic Ocean seawater in faster symptom resolution, reduction of medical treatment, and improved health status in common cold and flu. During the weeks after acute illness when preventive potential was assessed, regular isotonic saline nasal wash proved to reduce episodes of URTIs compared with the control (observation only) group. Results showing reduction in URTIs were robust and consistent in a number of parameters, including rhinologic symptoms, medication consumption, reported illness, school absence, and complication rate. Children showed a higher acceptance for the milder cleansing strength (fine spray).

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