

Nasal Rinsing with Hypertonic Solution: An Adjunctive Treatment for Pediatric Seasonal Allergic Rhinoconjunctivitis

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Hipertonik Solüsyon ile Nazal yıkama: Pediatrik Mevsimsel Alerjik Rinokonjunktivitte Bir Tedavi Desteği

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Anahtar Kelimeler

Çocuk, polen, hipertonik solüsyon, nazal lavaj, rinokonjunktivit

Arka Plan: en son elde edilen sınırlı sayıda bulgular pediatrik alerjik rinitlelerde hipertonik tuzlu su lavajının ek bir tedavi modeli olarak işe yaradığını söylemektedir. Bu çalışmanın amacı mevsimsel polen rinokonjunktiviti olan çocuklara, hipertonik solüsyonlarla nazal irrigasyonun, rutin olarak önerilip önerilemeyeceğini açıklığa kavuşturur. **Yöntem:** Mevsimsel polen rinokonjunktiviti olan kırkdört çocuk seçildi. Yirmiiki hasta 7 hafta süren polen sezonu boyunca günde üç defa hipertonik tuzlu su ile nazal yıkama uygulanmak üzere randomize edildi. Yirmiiki hasta ise hiç nazal irrigasyon yapmadılar ve kontrol grubu olarak seçildiler. Her gruptan yirmişer hasta çalışmayı tamamladı. Kızarma ve kaşınma gibi oküler semptomların yanısıra nazal akıntının ve burun tıkanıklığının olup olmamasına dayanan bir ortalama günlük rinokonjunktivit skoru, polen sezonunun her haftası için hesaplandı. Gerekli olduğunda hastaların oral antihistaminik kullanmasına izin verildi ve hafta başına ortalama ne kadar ilaç aldıkları da ayrıca hesaplandı. **Bulgular:** Aktif grupta ortalama haftalık rinokonjunktivit skoru tüm polen sezonu boyunca azaldı. Bu fark çalışmanın 6. ve 7. ci haftalarında istatistiki olarak anlamlıydı. 7 haftanın 5'inde istatistiki olarak anlamlı olacak şekilde oral antihistaminik kullanımında azalma gözlemlendi. Aktif grupta hiçbir yan etki rapor edilmedi. **Sonuç:** Bu çalışma mevsimsel alerjik rinokonjunktiviti pediatrik hastalarda hipertonik tuzlu su kullanımını desteklemektedir. Bu tedavi yönteminin hasta uyumu yüksek, ucuz ve etkin olduğu kanıtlanmıştır.

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Key Words

Children · Grass pollen · Hypertonic solution · Nasal rinsing · Rhinoconjunctivitis

Abstract

Background: Recent but limited evidence suggests that nasal lavage with hypertonic saline may be useful as an adjunctive treatment modality in the management of pediatric allergic rhinitis. The aim of this study was to clarify whether nasal irrigation with hypertonic solution should be routinely recommended to children with seasonal grass pollen rhinoconjunctivitis. **Methods:** Forty-four children with seasonal grass pollen rhinoconjunctivitis were recruited. Twenty-two patients were randomized to receive three-times daily nasal rinsing with hypertonic saline during the pollen season, which lasted 7 weeks. Twenty-two patients were allocated to receive no nasal irrigation and were used as controls. Twenty patients per group completed the study. A mean daily rhinoconjunctivitis score based on the presence of nasal discharge and obstruction as well as ocular symptoms as reddening and itching were calculated for each week of the pollen season. Patients were allowed to use oral antihistamines when required and the mean number of drugs taken per week was also calculated. **Results:** The mean weekly rhinoconjunctivitis score in the active group was reduced during the whole pollen period. This

difference was statistically significant in week 6 and 7 of therapy. A markedly reduced intake of oral antihistamines was also observed in patients allocated to nasal rinsing, being statistically significant in 5 of the 7 weeks. No adverse effect was reported in the active group. **Conclusions:** This study supports the use of nasal rinsing with hypertonic saline in the pediatric patient with seasonal allergic rhinoconjunctivitis. This treatment proved to be tolerable, inexpensive and effective.

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Introduction

Nasal douching has initially gained popularity as a postoperative measure particularly after sinus surgery [1, 2]. Since then, it has become clear that this simple and economic adjunctive treatment may be of benefit in many other sinonasal diseases, e.g. rhinitis and rhinosinusitis. The main effect of nasal irrigation is to remove debris, mucus or mucopus, which may provide some symptomatic relief per se but may also help to prevent secondary infections and support mucosal healing [3–5]. Recently, it has been shown that the chemical properties of the douching solution are also important in order to provide an optimal environment for mucociliary function. Specifically, both studies in vitro and in vivo have demonstrated that nasal irrigation with hypertonic saline im-

proves mucociliary clearance while buffered normal saline had no such effect [6–8]. From a clinical perspective, the use of nasal douching with hypertonic saline has proven to be effective in chronic sinusitis both in children and adults [9, 10]. In this regard, however, clinical statistical evidence to justify a widespread clinical use of nasal irrigation with hypertonic saline also for other sinonasal indications is still poor.

In a previous small preliminary study, we have documented that nasal rinsing with hypertonic saline solution may be effective in the prevention of symptoms in pediatric patients with allergic rhinitis to *Parietaria* [11]. Results from this study were encouraging but the inclusion of children selectively affected by rhinitis allergy to *Parietaria* currently limit inferences to other forms of seasonal sinonasal allergies. To further investigate this issue, we have set up a randomized controlled clinical trial in order to clarify whether nasal irrigation with hypertonic solution should also be routinely recommended to children with seasonal grass pollen rhinoconjunctivitis.

Materials and Methods

Children aged less than 16 years and affected by grass pollen rhinoconjunctivitis for at least 1 year were invited to participate in this randomized study. Specifically, the following criteria for inclusion were adopted: (a) typical anamnesis for seasonal allergic rhinoconjunctivitis; (b) marked positivity of the skin prick tests (≥ 2 plus) to grass pollen extracts in a hydroglyceric solution titrated at 20,000 biological units (BU)/ml (SARM Allergeni, Rome, Italy), and assessed according to the already-known guidelines [12]. Patients were excluded because of: (a) coexistence of nasal polyposis and/or bronchial asthma; (b) sensitization to other allergens, and (c) previous specific immunotherapy. The use of nasal rinsing with hypertonic saline differed from our previous study [11] regarding the following points: (1) patients with rhinoconjunctivitis rather than those with rhinitis alone were included, and (2) children with allergy to grass pollen instead of those with allergy to *Parietaria* were enrolled. All patients were followed up by two of the authors (M.R. and C.D.). The study was approved by the local Institutional Review Board, and informed consent was obtained from the parents of the children before study entry.

The protocol of the study is described elsewhere and is herein only briefly reported [11]. Based on grass pollen count observed in 2001, a study period lasting 7 weeks (from April 29 to June 2, 2002) was chosen. Results from a volumetric pollen trap (Burkard Manufacturing, Rickmansworth, UK) located in our area confirmed that this study period was largely coincident with the pollen season. More specifically, levels of the grass pollen count were low during the 1st week of treatment and rapidly increased at the beginning of the 2nd week. The highest levels were observed between the 2nd and the 4th week.

Patients were recruited on March 31, 2002, and were randomly assigned to the active or control group according to randomiza-

Table 1. Basal characteristics of the patients completing the study

Characteristics	Nasal rinsing	Control
Patients	20	20
Age, years	9.3 \pm 2.4	9.0 \pm 2.6
Females	13 (65%)	12 (60%)
Males	7 (35%)	8 (40%)
Duration of disease, years	1.5 \pm 0.7	1.6 \pm 0.7

Age and duration of disease: means \pm SD.

tion tables. Patients randomized to the active group were instructed to perform intranasal rinsing three times daily using the hypertonic saline solution (NaCl 3%, 925 \pm 30 mosm/kg, pH 7.45 \pm 0.2) in a bottle fitted with an atomizer for pediatric use. Each rinsing consisted of three sprays per nostril (1 spray = 50 μ l) nebulized at a mass median aerodynamic diameter of about 18 μ m. No local therapy was prescribed to the control group. During the study period, patients and their parents were instructed to keep a daily record of four allergic symptoms. The degree of severity of nasal symptoms as discharge and obstruction, as well as of ocular symptoms as reddening and itching, was recorded on a scale of 0–3 (0 = none; 1 = mild; 2 = moderate; 3 = severe). A total score (ranging from 0 to 16), representing the sum of the scores of these four symptoms, was used to calculate a mean daily rhinitis score per patient for each week of the pollen season. Patients of both groups were also allowed to use oral antihistamines when needed and to record the relative intake. This information was used to calculate the mean number of daily antihistamine treatments per patient per week. Finally, patients and their parents were invited to record adverse effects, if present.

Statistical analysis was performed using unpaired Student's *t* test to compare rhinitis scores and antihistamine use. Differences were always confirmed using the non-parametric Wilcoxon's test for unpaired data, too. Basal characteristics of the two groups were compared using Fisher's exact test or unpaired Student's *t* test, as appropriate. $p < 0.05$ was considered significant in all comparisons. Calculation of the sample size a priori was not performed since this type of calculation is strongly determined by the rate of the event (symptoms of allergic rhinitis and use of oral antihistamines) in the control group. Unfortunately, the allergen concentration is influenced by weather and may thus vary widely from one year to the other. As a consequence, frequency and severity of symptoms of allergic rhinitis also vary widely from one year to the other.

Results

The trial profile is shown in figure 1. Forty patients, 20 males and 20 females, aged 5–14 years (9.1 \pm 2.5), completed the study. They were assigned to the active ($n = 20$) or control group ($n = 20$). Basal characteristics of these two groups were similar. No significant differences were found in terms of age, sex and duration of rhinoconjunctivitis (table 1).

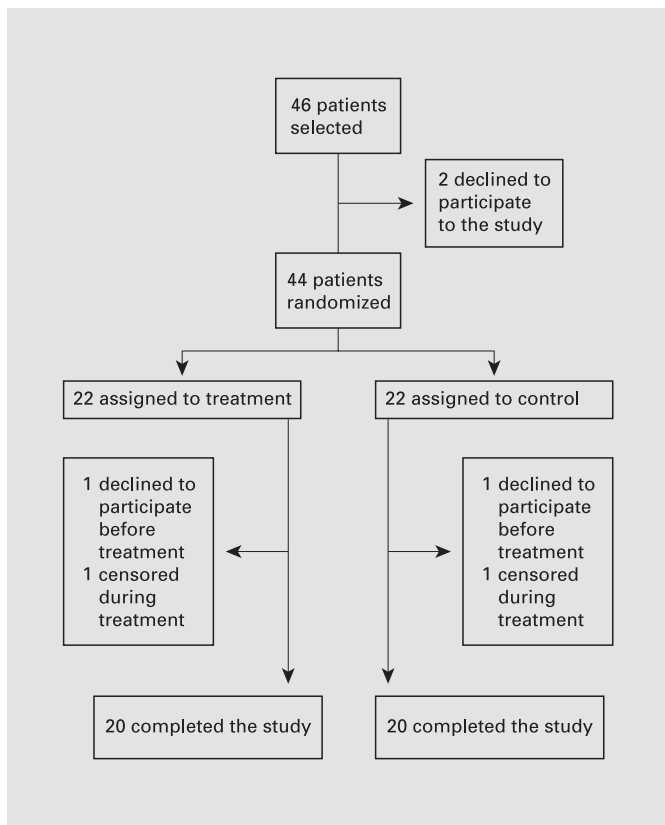


Fig. 1. Trial profile. Forty-six patients were invited to enter the study, 2 refused to participate. Forty-four patients were thus recruited and assigned alternately to the active ($n = 22$) or control group ($n = 22$). One patient per group declined to participate after randomization but before initiation of the study period. One subject in the control group had chickenpox few days after initiation of treatment and was thus censored. One patient in the active treatment was lost to follow-up. Results were therefore available in 40 subjects (20 children receiving nasal irrigation and 20 control subjects).

One patient receiving nasal irrigation was lost to follow-up. No adverse effect was reported in the active group. Evidence from patients' diary cards showed significant clinical benefits in those children who received a regimen of three-times daily nasal rinsing with hypertonic saline solution during the pollen season (fig. 2). The mean weekly rhinitis score in the active group was reduced during the whole pollen period. More specifically, this difference was statistically significant in the 6th and 7th week of therapy. Concerning the use of oral antihistamines, a markedly reduced intake was observed in patients allocated to nasal rinsing (fig. 3). A statistically significant difference was noted in 5 of the 7 weeks of the study period.

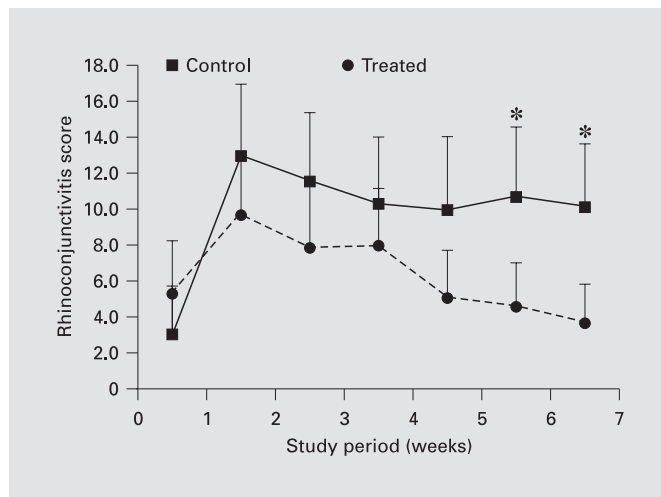


Fig. 2. Mean \pm SD of the rhinoconjunctivitis score during the 7-week period of the grass pollen season for both patients treated with nasal irrigation and controls. The total score (ranging from 0 to 16) was calculated as the sum of scores of four different symptoms (nasal discharge, nasal obstruction, ocular reddening and itching). This score was reduced in 6 of the 7 weeks in patients who were prescribed nasal irrigation. This difference was statistically significant in the 6th and 7th week of therapy.

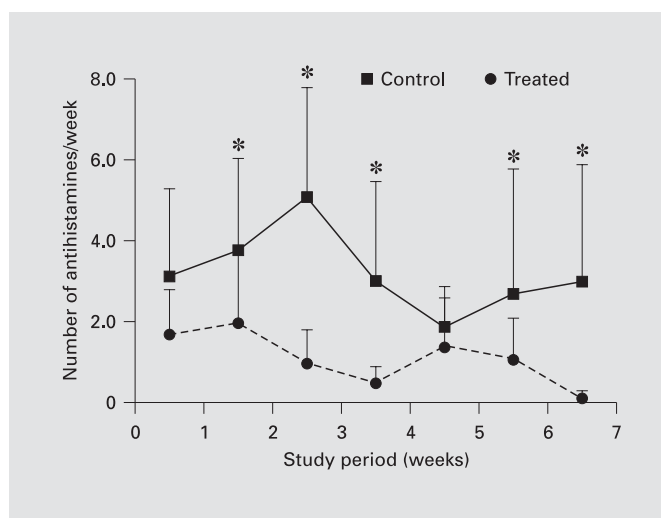


Fig. 3. Mean \pm SD number of oral intake of antihistamines per week for each week of the grass pollen season in both patients treated with nasal irrigation and in controls. Drug treatment was reduced among patients allocated to nasal irrigation. This reduction was statistically significant during the 1st, 2nd, 4th, 6th and 7th week of the study period.

Discussion

The results of this randomized study demonstrate that nasal rinsing with hypertonic saline solution is effective in controlling grass-pollen-allergic symptoms in the pediatric patient. Using a daily symptom score that evaluates the intensity of rhinoconjunctivitis symptoms, significant clinical benefits were observed in children who were prescribed nasal rinsing. The efficacy of this local treatment is also supported by the significant decrease in the use of antihistamine drugs and by the absence of relevant side effects.

Limitations of our study may be ascribed to the study design since our trial was not blinded and we did not use placebo. Although such a study design would have been preferable, the extreme specificity of the way of administration hampers its application. In this context, it should be noted that none of the available studies on this topic have conducted a true double-blinded placebo-controlled trial. At present, we are unable to assess the importance of the placebo effect in determining nasal symptom control observed in our study. At least, three considerations have to be done in this regard. First, a striking difference has emerged between the active and the control group. We believe that it is highly debatable to ascribe such a marked difference solely to a placebo effect. Second, differences in both symptom scores and antihistamine drug use tended to increase with time. This observation does not support a relevant placebo effect considering that this effect is typically expected to be more relevant during the first weeks of treatment. Third, the control group also received medical treatment (oral antihistamines if needed). A more significant placebo effect would have been expected if no therapy rather than medical therapy were prescribed. Overall, although a role for the placebo effect cannot be ruled out, it is unlikely that this effect may exclusively explain the results observed in this trial. Of note, in our study, compliance with the study protocol was extremely high, patients were under the care of only two experienced physicians, and basal characteristics of the two study groups were similar. In this regard, it has to be noted that symptom scores and use of oral antihistamines were similar in the two groups during the first week of treatment when the grass pollen count was still low. Therefore, in our opinion, other important sources of bias in our trial can be excluded.

Tamooka et al. [13] have previously reported that nasal washing is effective in the treatment of seasonal allergic rhinitis in adults. These authors, employing a patient-reported nasal-disease-specific questionnaire, documented

a significant improvement in the symptom score after nasal irrigation with hypertonic saline [13]. Subsequently, Klimek et al. [14] confirmed this finding. They documented that nasal rinsing with isotonic solution in adult patients with allergic rhinitis reduces the intake of other anti-allergic drugs by more than 30%. In a previous preliminary randomized study, we have documented that this approach is also effective in the prevention of symptoms in pediatric patients with allergic rhinitis to *Parietaria* [11]. The results of the present study are in line with these previous reports. Specifically, the present study supports a beneficial effect of nasal rinsing also in children with seasonal grass pollen rhinoconjunctivitis. The mechanism by which this improvement could be effected in this field as well as in other sinonasal diseases has not been fully clarified. It has been hypothesized that nasal lavage promotes improvement of nasal symptoms in different ways. Specifically, it seems that this local treatment may mechanically clear inspissated mucus, minimize crusting and decrease both mucosal edema and inflammatory mediator concentration [7, 15]. In this regard, recent evidence accumulated showing that an even higher efficacy could be effected using hypertonic saline instead of normal saline [6, 7, 9, 10]. Indeed, a hypertonic solution may reduce edema more efficiently through diffusion of osmolar gradients. Moreover, studies *in vitro* and *in vivo* have documented a marked increase in mucociliary clearance using hypertonic solutions while normal saline has no such effects [6, 7]. Of note, however, hypertonicity should not be above 3% since negative effects may appear with higher concentrations [16, 17]. Based on experimental evidence, nasal irrigation with hypertonic saline was chosen in the present study since this protocol appeared to be simple, and patient adherence with both the way of administration and the use of a drug-free solution was high. In this context, it is worthwhile noting that the present study does not rule out the possibility that similar results could be obtained using isotonic rather than hypertonic saline. Moreover, the possibility to use a two-times or even a one-time daily administration of hypertonic saline in patients with allergic rhinitis remains to be investigated since such a simpler protocol might to be as effective as the longer one whereas patient adherence could be further increased.

In conclusion, this study supports the possibility to use a three-times daily regimen of nasal rinsing with hypertonic saline as an adjunctive therapy in the pediatric patient with seasonal grass pollen rhinoconjunctivitis. The treatment is tolerable, inexpensive and effective. Further studies are required to determine its precise role in the armamentarium of allergic rhinitis drugs.

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