

Nasal rinsing with an atomized spray improves mucociliary clearance and clinical symptoms during peak grass pollen season

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ABSTRACT

Background: Nasal rinsing with an atomizer spray was found to be effective in the treatment of allergic rhinitis. Two parameters express the nasal functions: (1) mucociliary clearance (MCC), and (2) the pH and its stability. MCC is the main factor that defines the time of pollen transition on the nasal mucosa and, therefore, the amount of the allergen glycoprotein elution.

Objective: We hypothesized that the nasal wash efficacy could be due to the reduction of contact time of the grass pollen on the nasal mucosa (improving MCC).

Methods: Forty patients with seasonal grass pollen oculorhinitis were randomized in two groups: 20 received three times daily nasal rinsing with hypertonic solution buffered to pH 6.1, before and during the peak pollen season in 2015 (active group), and another 20 patients were allocated to the control group and received no nasal treatment. The daily symptoms score and the use of oral antihistamines when required were evaluated during the grass pollen peak season. All the patients completed the study.

Results: In comparison with the control group, in the active group, a significant decrease of both nasal symptoms ($p = 0.01$) and consumption of antihistamines ($p = 0.035$) was found. Furthermore, the MCC was significantly worse ($p = 0.011$) only in the control group.

Conclusion: The nasal treatment maintained the efficiency of the MCC in the patients in the active group, who showed a significant reduction of symptoms and medication score. The MCC decreased the transit time of the pollen on the nasal mucosa, which favored an elution of the allergenic proteins.

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The hygiene of the nasal cavities is indicated on a daily basis to remove airborne particles, such as aeroallergens and those particles produced by environmental pollution.¹ The importance of the mucociliary clearance (MCC) has been widely demonstrated in both the lower and upper airways.²⁻⁶ MCC is slowed down in all diseases of the upper airways and particularly in the inflammatory diseases of the nasal mucosa.^{7,8} Washing the nasal cavity is a real adjuvant therapy in chronic rhinosinusitis^{9,10} and viral rhinitis,¹¹ and in the postsurgical treatment.^{12,13} A Cochrane review summarized the evidence that the nasal washes not only relieve symptoms but are significantly helpful as an adjunct to conventional treatment.¹⁴ In this respect, the nasal washes were also found to be effective in the treatment of allergic rhinitis.¹⁵⁻¹⁸ Unlike the physiologic solution, the hypertonic saline solution is able to improve the MCC in both healthy subjects and in patients with perennial rhinitis.^{19,20} In this randomized parallel group study, we wanted to assess whether the efficacy of the nasal rinsing with an atomizer spray in the therapy of grass allergic rhinitis was due to an improvement of the MCC.

METHODS

Forty patients (16 female and 24 male patients), ages between 16 and 38 years, with grass pollen rhinoconjunctivitis for at least 2 years, were invited to participate in this prospective randomized study. The patients were allocated to two groups: active and control. The general

characteristics of the sample population are shown in Table 1. The following criteria were adopted for inclusion: (a) a typical clinical history of seasonal allergic rhinoconjunctivitis, and (b) marked positivity of the skin-prick test results (wheal > 5 mm) to grass pollen extracts in a hydroglyceric solution titrated at 30,000 biologic units/mL (Bial Aristegui, Rome, Italy), according to the established guidelines.²¹ Patients were excluded because of (a) the coexistence of nasal polyposis and/or bronchial asthma, (b) sensitization to other allergens, (c) previous specific immunotherapy, (d) chronic use of nasal decongestants or corticosteroids, and (e) smoking.

Study Design and Clinical Assessment

The study design and clinical assessment are illustrated in Fig. 1. The patients were randomly divided into two groups according to the randomization tables.²² The patients in the active group were treated with atomized hypertonic phosphate-buffered solution, at pH 6.1 (Atomix; Tred, Milan, Italy), one puff (0.13 mL) in both nostrils three times per day, whereas the control group did not receive this type of treatment. During the study, the MCC was assessed from April 1 to 7, 2015, and during a grass pollen peak (from April 27 to May 3). Clinical assessment was performed at the start and at the peak of the pollen season. All the patients kept a daily diary of allergic symptoms during the pollen season. The degree of severity of such nasal symptoms as itching, sneezing, discharge, and obstruction as well as such ocular symptoms as itching and epiphora was recorded on a scale of 0 to 2 (0, no symptoms; 1, tolerable symptoms; 2, intolerable symptoms). The patients were instructed to use antihistamines when needed (cetirizine 10 mg once a day) and to record the frequency of administration and dosage as well. To calculate the consumption of antihistamines, four points were arbitrarily allocated for each day in which 10 mg of cetirizine was taken by the patient.

Measurement of MCC

The saccharin test was first described by Andersen *et al.*²³ It is a simple and widely used test to evaluate the MCC. We measured the nasal saccharine transit time to assess the MCC.²⁴ The patients remained seated with their head tipped slightly forward while breathing normally (not forcefully), without sneezing or blowing their nose,

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Table 1 General characteristics of studied population

	Active	Control	
Age, mean $\pm$ SD, y	25.0 $\pm$ 5.3	27.0 $\pm$ 6.8	n.s.
M/F	7/13	9/11	n.s.
Years of disease, mean $\pm$ SD	9.7 $\pm$ 7.3	7.5 $\pm$ 6.8	n.s.
Preseasonal MCC, mean $\pm$ SD	12.97 $\pm$ 5.24	14.86 $\pm$ 4.90	n.s.

SD = Standard deviation; n.s. = not significant; MCC = mucociliary clearance.

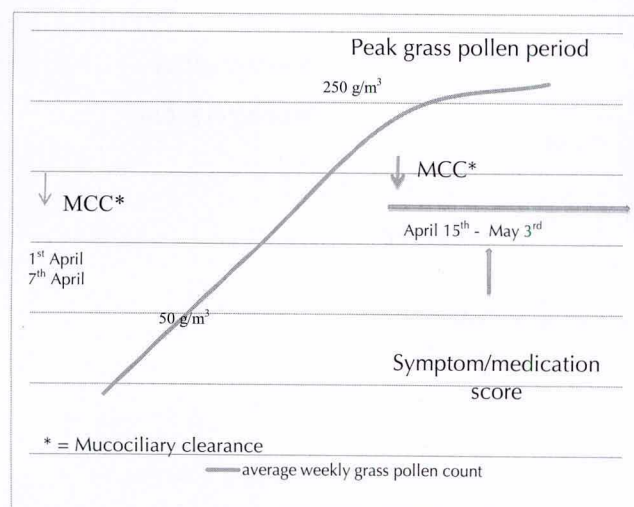


Figure 1. Study design and pollen count.

and without taking any substances that might interfere with the test. Saccharine particles (2.5 mg) were deposited 2 cm behind the tip of the inferior nasal turbinate of the unobstructed nostril; the timer was stopped at the first perception of sweet taste (the subjects were asked to report the exact time that they detected the taste of saccharin). The taste they were to expect was not specified to avoid false-positive results. The saccharine particles were carried backward by the physiologic ciliary transport along the entire nasal cavity until it reached the rhinopharynx and the oropharynx, where a characteristic sweet taste could be perceived. The time was recorded in seconds by using a stopwatch. The nostril with lower resistance to physiologic airflow confirmed by rhinomanometry was chosen for measurement of MCC. The maximum delay between the deposition and perception after which the saccharin taste was considered "not detected" was set at 30 minutes.

Pollen Count

The pollen count was carried out by using a volumetric Zamboni device (VPPS 2000, Lanzoni, Bologna, Italy) during April and May 2015; the peak pollen period has been defined as the interval (from April 27 to May 3), during which grass pollen counts exceeded 200 grains/ m^3 (F. Ottoboni, unpublished data, April/May 2015).

Statistical Analysis

Differences between the two groups about the above-mentioned characteristics, the symptoms, and medications scores were calculated by using the Mann-Whitney *U* test. MCC differences within the same group before or during the grass pollen peak were analyzed by using the Wilcoxon test.

Ethical Standards

All procedures that contributed to this work complied with the ethical standards of the relevant national and institutional guidelines

Table 2 Weekly symptoms and medication score during the peak pollen period (from April 27 to May 3)

	Active Group	Control Group	<i>p</i> Value
Nasal symptoms, mean $\pm$ SD	13.60 $\pm$ 10.00	29.60 $\pm$ 16.50	0.011
Ocular symptoms, mean $\pm$ SD	3.63 $\pm$ 3.13	3.23 $\pm$ 2.50	n.s.
Medication score, mean $\pm$ SD	4.80 $\pm$ 5.20	14.80 $\pm$ 14.52	0.035

n.s. = Not significant.

on human experimentation (institutional review board of the ethics committee of Fondazione Istituti di Ricovero e Cura a Carattere Scientifico (I.R.C.C.S.) Ca' Granda Ospedale Maggiore Policlinico of Milan, Italy) and with the Helsinki Declaration of 1975, as revised in 2008. The patients gave signed written consent for submitting to the tests and for the publication of the results.

RESULTS

As shown in Table 1, the active and control groups of the patients were well matched at baseline according to the inclusion criteria of the trial. In both groups, there was no consumption of antihistamines before the pollen season. The mean weekly symptom medication scores and drug scores for each group during the peak pollen period are shown in Table 2. Compared with the untreated group, the active group had a significantly lower nasal symptoms score ($p = 0.011$) as well as medication score ($p = 0.035$), whereas the two groups did not differ in terms of ocular symptoms. The MCC (time, mean $\pm$ SD) (Fig. 2) was significantly ($p < 0.0001$) longer in the controls (23.72 $\pm$ 6.65 minutes) than in the active group (14.30 $\pm$ 5.58 minutes) during the grass pollen peak, which meant that an efficient MCC was maintained in the active group but significantly worsened in the control untreated group during the season ($p < 0.0001$). Because the MCC is expressed by the nasal saccharine transit time, in the control group, with a longer transit, the pollen elution should be reduced, thus the concentration of pollen was presumably higher. In fact, the results of our study seemed to confirm this hypothesis: the active group maintained a normal MCC function and derived a beneficial effect in terms of symptomatology and the need of drug intake; conversely, the control group showed an increase in the saccharin transit time (and of the pollen), which resulted in a significant increase of both nasal symptoms and consumption of antihistamines. (Table 2).

DISCUSSION

Atomized sprays for rinsing of the nasal cavities are well-established adjuvant treatments in many upper airways diseases. Unlike simple washing, they can be considered a selective aerosol therapy of the upper airways. An initial study¹¹ in 2005 supported this concept: the atomized nasal douche by means of a compressor-micronizer chamber system proved to be more effective in restoring all the physiologic nasal functions than traditional nasal lavages with a 20-mL syringe when using the same isotonic sodium chloride solution. In a study by Passali *et al.*,¹¹ only atomized nasal douches were able to normalize the MCC to a physiologic level in acute viral rhinitis. Another work, published in 2012, provided evidence that an atomized hypertonic saline solution increased the efficiency of the MCC in healthy subjects, with normal baseline levels of nasal clearance by reducing the saccharin transit time.²⁵ Therefore, in the current study, we decided to test this method on patients with seasonal allergic rhinitis.

Beyond the positive evidence of benefit, there is no consensus in the literature about the daily schedule (total dosage, fractionation, con-

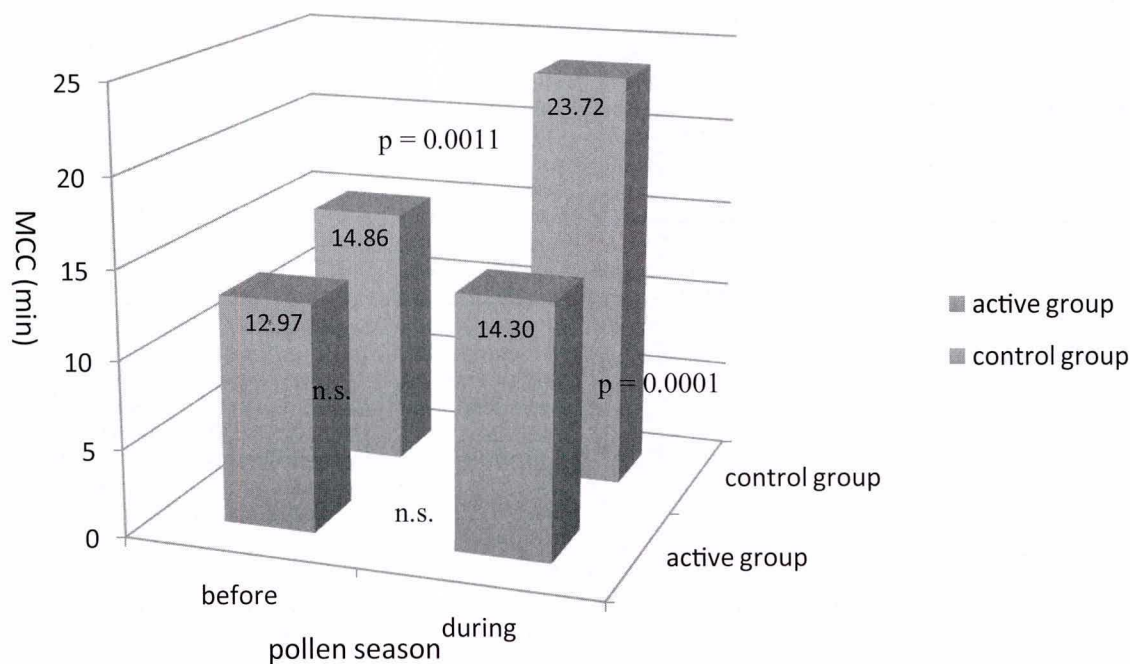


Figure 2. Mucociliary clearance before (from April 1 to 7) and during the peak of the grass pollen season (from April 27 to May 3).

centration of solute) of the administered amounts of atomized nasal spray. In this study, the administration protocol involved the use of one puff (0.13 mL) in both nostrils three times per day, as we had already used in a previous study. The use of MCC as a parameter for indicating proper nasal mucosa function has been previously investigated in many studies.^{2-5,10} In the present trial, nasal symptoms and consumption of antihistamines were found to be significantly lower in the active group compared with the control group. The saccharin transit time, and indirect measure of the MCC, is lengthened in the control group; it is highly likely that the clinical benefit for patients in the active group, who received nasal rinsing three times per day with the atomized spray, may be due to the preserved MCC, which reduced the pollen contact time on the nasal mucosa and, consequently, boosted the amount of the allergen glycoprotein elution.

The nasal mucosa plays a key role in quality control and in conditioning the flow of inspired air. A relationship between the rheologic properties of the nasal mucus and the nasal MCC function was documented many years ago.²⁶ In this work, we decided to use an hypertonic phosphate-buffered solution at pH 6.1. The acknowledgment of the role of hypertonic saline solution, and that of the pH, recently related with the efficiency of MCC,²⁷⁻²⁹ created the basis to understand this complex phenomenon. Unfortunately, in this study, the nasal pH values were not systematically collected and, therefore, were not included in the results; we were unable to draw conclusions on its role in nasal homeostasis.

CONCLUSION

The proposed nasal treatment with hypertonic phosphate-buffered solution at pH 6.1 by means of an atomizer spray restored the MCC impaired by allergic inflammation and could be considered responsible for the observed clinical benefits.

REFERENCES

- Middleton E Jr. Chronic rhinitis in adults. *J Allergy Clin Immunol* 81:971-975, 1988.
- Corbo GM, Foresi A, and Bonfitto P. Measurement of nasal mucociliary clearance. *Arch Dis Child* 64:546-550, 1989.
- Homer JJ, England RJ, Wilde AD, et al. The effect of pH of douching solutions on mucociliary clearance. *Clin Otolaryngol* 24:312-315, 1999.
- Inanli S, Oztürk O, Korkmaz M, et al. The effects of topical agents of fluticasone propionate, oxymetazoline, and 3% and 0.9% sodium chloride solutions on mucociliary clearance in the therapy of acute bacterial rhinosinusitis in vivo. *Laryngoscope* 112:320-325, 2002.
- Hauptman G, and Ryan MW. The effect of saline solutions on nasal patency and mucociliary clearance in rhinosinusitis patients. *Otolaryngol Head Neck Surg* 137:815-821, 2007.
- Yazici H, Soy FK, Kulduk E, et al. Comparison of nasal mucociliary clearance in adenoid hypertrophy with or without otitis media with effusion. *Int J Pediatr Otorhinolaryngol* 78:1143-1146, 2014.
- Wigand ME, Steiner W, and Jaumann MP. Endonasal sinus surgery with endoscopic control: From radical operation to rehabilitation of the mucosa. *Endoscopy* 10:255-260, 1978.
- Ural A, Oktemer TK, Kizil Y, et al. Impact of isotonic and hypertonic saline solutions on mucociliary activity in various nasal pathologies: Clinical study. *J Laryngol Otol* 123:517-521, 2009.
- Huang A, and Govindaraj S. Topical therapy in the management of chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg* 21:31-38, 2013.
- Rabago D, Pasic T, Zgierska A, et al. The efficacy of hypertonic saline nasal irrigation for chronic sinonasal symptoms. *Otolaryngol Head Neck Surg* 133:3-8, 2005.
- Passali D, Damiani V, Passali FM, et al. Atomized nasal douche vs nasal lavage in acute viral rhinitis. *Arch Otolaryngol Head Neck Surg* 131:788-790, 2005.
- Süslü N, Bajin MD, Süslü AE, and Ogretmenoglu O. Effects of buffered 2.3%, buffered 0.9%, and non-buffered 0.9% irrigation solutions on nasal mucosa after septoplasty. *Eur Arch Otorhinolaryngol* 266:685-689, 2009.
- Farag AA, Deal AM, McKinney KA, et al. Single-blind randomized controlled trial of surfactant vs hypertonic saline irrigation following endoscopic endonasal surgery. *Int Forum Allergy Rhinol* 3:276-280, 2013.
- Harvey RJ, Hannan SA, Badia L, Scadding G. WITHDRAWN: Nasal saline irrigations for the symptoms of chronic rhinosinusitis. *Cochrane Database Syst Rev* 25:CD006394, 2016.
- Garavento W, Di Berardino F, Romagnoli M, et al. Nasal rinsing with hypertonic solution: An adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis. *Int Arch Allergy Immunol* 137:310-314, 2005.

16. Satdhabudha A, and Poachanukoon O. Efficacy of buffered hypertonic saline nasal irrigation in children with symptomatic allergic rhinitis: A randomized double-blind study. *Int J Pediatr Otorhinolaryngol* 76:583–588, 2012.
17. Hermelingmeier KE, Weber RK, Hellmich M, et al. Nasal irrigation as an adjunctive treatment in allergic rhinitis: A systematic review and meta-analysis. *Am J Rhinol Allergy* 26:e119–e125, 2012.
18. Nguyen SA, Psaltis AJ, and Schlosser RJ. Isotonic saline nasal irrigation is an effective adjunctive therapy to intranasal corticosteroid spray in allergic rhinitis. *Am J Rhinol Allergy* 28:308–311, 2014.
19. Talbot AR, Herr TM, and Parsons DS. Mucociliary clearance and buffered hypertonic saline solution. *Laryngoscope* 107:4:500–503, 1997.
20. Keojampa BK, Nguyen MH, and Ryan MW. Effects of buffered saline solution on nasal mucociliary clearance and nasal airway patency. *Otolaryngol Head Neck Surg* 131:679–682, 2004.
21. Bousquet J, Heinzerling L, Bachert C, et al. Practical guide to skin prick tests in allergy to aeroallergens. *Allergy* 67:18–24, 2012.
22. Glantz SA. *Primer of Biostatistics*. 2nd ed. San Francisco: McGraw-Hill, 1988.
23. Andersen I, Camner P, Jensen PL, et al. Nasal clearance in monozygotic twins. *Am Rev Respir Dis* 110:301–305, 1974.
24. de Oliveira-Maul JP, de Carvalho HB, Miyuki Goto D, et al. Aging, diabetes, and hypertension are associated with decreased nasal mucociliary clearance. *Chest* 143:1091–1097, 2013.
25. Bencova A, Vidan J, Rozborilova E, and Kocan I. The impact of hypertonic saline inhalation on mucociliary clearance and nasal nitric oxide. *J Physiol Pharmacol* 63:309–313, 2012.
26. Salah B, Dinh Xuan AT, Fouilladieu JL, et al. Nasal mucociliary transport in healthy subjects is slower when breathing dry air. *Eur Respir J* 1:852–855, 1988.
27. Magomedov MM, and Magomedov GM. Acid-base equilibrium and mucociliary clearance in the nasal cavity in the patients with chronic rhinitis and inflammatory diseases of paranasal sinuses [in Russian with English abstract]. *Vestn Otorinolaringol* (2):43–45, 2013.
28. Kotan D, Tatar A, Aygul R, and Ulvi H. Assessment of nasal parameters in determination of olfactory dysfunction in Parkinson's disease. *J Int Med Res* 41:334–339, 2013.
29. Berkebile AR, and McCray PB Jr. Effects of airway surface liquid pH on host defense in cystic fibrosis. *Int J Biochem Cell Biol* 52:124–129, 2014. □

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