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Comparison of Buffered and Nonbuffered Nasal Saline Irrigations in Treating Allergic Rhinitis

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Objectives/Hypothesis: We aimed to study the effect of alkalinity of isotonic nasal saline irrigation on nasal symptoms, mucociliary clearance, nasal patency, and patient's preference in patients with allergic rhinitis (AR).

Study Design: A double-blind, randomized, three-arm crossover study.

Methods: Patients with AR were enrolled. Three kinds of isotonic nasal saline irrigations: nonbuffered (pH 6.2–6.4), buffered with mild alkalinity (pH 7.2–7.4), and buffered with alkalinity (pH 8.2–8.4) were given one at a time, in different orders. Patients rinsed their nose with 240 ml of one solution twice daily for 10 days and then swapped to the others. The washout period was at least 5 days. Primary outcomes were nasal symptoms, mucociliary clearance time, and nasal patency. Outcomes were compared between baseline and posttreatment and also between various kinds of solution. Secondary outcomes were patients' preference and adverse events.

Results: Thirty-six subjects entered the study, and there were no dropouts. Overall nasal symptom was significantly improved from baseline ($P = 0.03$) only by buffered solution with mild alkalinity. Sneezing was significantly improved from baseline ($P = 0.04$) only by buffered solution with alkalinity. No other significant improvements were achieved by any solution. When comparing between the three nasal irrigations, there were no differences in all parameters. The patients significantly preferred the buffered solution with mild alkalinity ($P = 0.02$).

Conclusions: Buffered isotonic saline with some degree of alkalinity may improve nasal symptoms. Isotonic saline irrigations, regardless of alkalinity, may not improve mucociliary function and nasal patency. Buffered isotonic saline with mild alkalinity is the most preferred.

Key Words: Nasal saline irrigation, buffered saline, allergic rhinitis, pH, preference, nasal patency, mucociliary function.

Level of Evidence: 1b.

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INTRODUCTION

Nasal saline irrigation has been increasing in popularity. and it has been proven as an effective adjunctive treatment for various sinonasal conditions such as chronic rhinosinusitis, postnasal, or sinus surgery and allergic rhinitis.[1–9] The advantages of nasal saline irrigation in allergic rhinitis may be through direct cleansing of thick mucus, dust particles, or allergens that deposit on the nasal mucosa, or reducing the inflammatory mediators such as histamine, prostaglandins, leukotrienes[10,11] and sICAM-1 in the nasal cavity.[12] Its benefits effect on mucociliary function has been shown.[13–15] The formula used varies from one institution to the other regarding tonicity and alkalinity of the solution. Isotonic saline was found to be the most physiologic saline solution on secretory mucin and cellular morphology of the cultured human nasal epithelial cells.[16] Both buffered hypertonic and buffered isotonic saline nasal spray significantly improved saccharine clearance times.[13,15] Irrigation with isotonic saline improved mucociliary clearance time (MCCT) in acute sinusitis and allergic rhinitis, while hypertonic saline appeared to be more useful in chronic sinusitis patients in one study.[17] Whereas optimal tonicity has been widely explored, few studies investigate the effect of acidity and alkalinity of nasal saline solution on clinical efficacy. Suslu et al. compared buffered hypertonic saline, buffered isotonic saline, and nonbuffered isotonic saline on nasal mucosa after septoplasty. They found that buffered hypertonic seawater improved nasal airway patency more than both buffered isotonic saline and nonbuffered isotonic saline. At the 20th day of using buffered and nonbuffered saline irrigations, the MCCT were longer than the group that was using buffered hypertonic saline.[18] However, another study compared the effect of pH of nonbuffered solution and buffered solution on

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TABLE I.
Median of Post-Treatment Data and Net Changes of Symptoms Scores, MCCT, and Nasal Patency of Patients (visit–visit 1 of each treatment).

	pH 6.2–6.4			pH 7.2–7.4			pH 8.2–8.4		
Parameters	Median	Net changes	*P* value	Median	Net changes	*P* value	Median	Net changes	*P* value
Nasal blockage	2.65	−0.65	0.36	2.9	0.05	0.42	2.45	−0.85	0.14
Rhinorrhea	1.65	−0.35	0.11	1.9	−0.5	0.46	2.15	0.35	0.49
Sneezing	2.6	−0.5	0.19	2	−0.4	0.21	1.95	−1.25	0.03*
Itchy nose	1.3	−1.15	0.07	1	−0.65	0.07	1.25	−0.7	0.14
Overall nasal symptoms	2.4	−1.05	0.06	2.8	−0.4	0.03*	2.75	−0.15	0.29
MCCT (s)	422	15	0.55	437	10	0.81	468	−5	0.31
MCA1 (cm^2)	0.38	0.02	0.20	0.37	0.02	0.76	0.35	−0.02	0.62
MCA2 (cm^2)	0.33	0.003	0.44	0.34	−0.02	0.81	0.37	−0.01	0.93
Nasal Flow (Pa s/cm^3)	0.92	−0.16	0.86	1.02	0.03	0.36	1.22	−0.2	0.72

mucociliary clearance in normal subjects and did not show any difference.[14] Few studies investigated the effect of acidity and alkalinity of nasal saline solution on clinical efficacy; we hereby aimed to study the effect of alkalinity of isotonic nasal saline irrigation on nasal symptoms, mucociliary clearance, nasal patency, adverse effects, and patient's preference in patients with allergic rhinitis.

MATERIALS AND METHODS

Thirty-six subjects from our outpatient clinic with clinical symptoms of allergic rhinitis (median age 37 years; range 18–59 years old; 28 female subjects) were recruited. All had positive skin prick test with inhalant allergens. Exclusion criteria were: acute upper and lower respiratory tract infection, nasal polyps, markedly deviated nasal septum, asthma, pregnancy, severe underlying diseases, history of allergen specific immunotherapy, and history of taking intranasal corticosteroids within 2 weeks and antihistamines within 1 week. The Ethics Committee or institutional review board has approved the study and all subjects gave their written informed consent.

We performed a double-blind, randomized, three-arm crossover study comparing the treatment with three various kinds of isotonic nasal saline irrigations: nonbuffered (pH 6.2–6.4), buffered with mild alkalinity (pH 7.2–7.4), and buffered with alkalinity (pH 8.2–8.4). The nasal irrigations were given one at a time, in different order as randomized by using the 3 × 3 crossover trial of Williams design. Patients were requested to rinse their nose with 240 ml of each solution twice daily for 10 days with a commercial positive-pressure nasal irrigation device, and then swap to the other until they experienced all three solutions. The washout period was at least 5 days before undertaking the next solution. Primary outcomes were nasal symptom visual analog scale (rhinorrhea, nasal blockage, sneezing, itchy nose, and 10-day overall nasal symptoms), mucociliary clearance time, and nasal patency. The outcomes were compared between baseline and posttreatment, and also between various kinds of solution. Secondary outcomes were patients' preference and adverse events.

At the first visit, the nasal symptoms and objective measurements of nasal patency and mucociliary clearance were recorded as baseline. Rhinorrhea, nasal blockage, sneezing, itchy nose, and 5-day overall nasal symptoms before their first visit were recorded on a 10- cm visual analog scale (VAS) (0–10): 0, no symptoms and 10, very severe symptoms. Acoustic rhinometry and anterior rhinomanometry (RhinoMetrics, Assens, Denmark) were used to measure the nasal patency. As for acoustic rhinometry, the data recorded were the minimal cross sectional area (MCA) 1 and MCA 2. The mean value of both sides of nostril was calculated. Anterior rhinometry was used to measure nasal resistance. The mean value of the recorded airflow during the inspiration of the right and left nostril at a pressure difference of 150 Pascal across the nasal passage was calculated. Four airflow measurements were performed in each subject. Then, saccharin test was performed to measure bilateral mucociliary clearance times (MCCTs). The subject sat in an upright position. Approximately 2-mm of saccharin powder was placed on the anterior end of the inferior turbinate, 1 cm below from the top of the inferior concha. The subjects were asked to avoid sneezing or sniffing during the test. The subject's first perception of a sweet taste was recorded. The test was repeated on the other side. The mean value of MCCT was calculated.

The nonbuffered isotonic saline (pH 6.2–6.4) was commercial sterile normal saline (Thai Otsuka, Bangkok, Thailand) 1000 ml. Buffered isotonic saline with mild alkalinity (pH 7.2–7.4) was prepared by adding sodium bicarbonate 14 milligram into 1000 ml of normal saline. Buffered isotonic saline with alkalinity (pH 8.2–8.4) was prepared by adding 1 teaspoon of sodium bicarbonate into 1,000 ml of normal saline. The pH measurements were performed by the pH meter (PerpHect, Thermo scientific, Waltham, MA, USA) at 25° Celsius room temperature. Randomization was achieved according to a computer-generated sequential list. The study irrigations were prepared by a doctor who knew the randomization codes. All solutions looked alike. The patients and all investigators were blinded. Five bottles of 1,000 ml of saline irrigation were given to each subject for 10-day treatment. Subjects had to stop antiallergic medications during the study. At the second visit (posttreatment), after a 10-day nasal saline irrigation, subjects returned for recording their nasal symptoms and the same procedures were repeated as on the first visit. The patients were asked for scoring the severity of nasal and otologic adverse events (nasal burning, ear fullness, or ear pain) based on a 10-cm VAS. At the last visit, after the subjects finished all three solutions, they had to choose the most preferred nasal saline solution.

Statistical Analysis

The variables were the VAS of nasal symptoms and overall nasal symptom, MCCT, MCA1, MCA2, and nasal resistance. When data were not normally distributed, nonparametric statistics were used for analysis and data were presented as median.

TABLE II.
Number of Patients Experiencing Nasal and Otologic Adverse Effects by Each Formula of Irrigations.

	pH 6.2–6.4		pH 7.2–7.4		pH 8.2–8.4	
Adverse Effects	Number (%)	Median (Range)	Number (%)	Median (Range)	Number (%)	Median (Range)
Nasal Burning	13 (36.1)	1.2 (0.1–4.7)	7 (19.4)	0.6 (0.1–1.81)	9 (25)	0.8 (0.2–2.8)
Ear Fullness/Pain	11 (30.6)	0.9 (0.1–6.2)	12 (33.33)	0.8 (0.1–4.8)	9 (25)	1.7 (0.3–8.1)

The net changes in VAS of nasal and overall symptoms, MCCT, MCA1, MCA2, and nasal resistance were compared by Wilcoxon signed rank test between two treatments. All data were analyzed using Wilcoxon signed rank test to compare the baseline and posttreatment within each treatment group. The severities of adverse effects were compared by McNemar's test. The numbers of patients' preference of each solution were compared by Chi-square test. *P* values lower than 0.05 were considered significant. All statistic analysis was run using Stata software package (Stata Corp, College station, TX, USA).

RESULTS

A total of 36 subjects entered the study and there were no dropout. The overall nasal symptoms were significantly improved from baseline ($P = 0.03$) only by buffered solution with mild alkalinity (pH7.2–7.4). Sneezing was significantly reduced from baseline ($P = 0.04$) only by buffered solution with alkalinity (pH 8.2–8.4). No other parameters significant improvements were achieved by any solution. The data are shown in Table I. When comparing the outcomes of posttreatment between three nasal irrigations, there were no differences in all parameters. There were no significant differences in nasal and otologic adverse effects between each treatment. The data of adverse effects was shown in Table II. The number of patients' preference in each solution is shown in Figure 1. The patients significantly preferred buffered with mild alkalinity (pH 7.2–7.4) ($P = 0.02$).

DISCUSSION

The baseline pH in human nasal cavity is 6.4 in the anterior and 6.27 in the posterior of the nose.[19] Mildly acidic solution sprayed into the nostril produced an increase pH in the anterior part of nasal cavity in the first minute, presumably due to reflux bicarbonate secretion, while pH7.2 unbuffered saline solution produced an increase in pH and reach a maximum 7.06 in 11.25 minute.[19] The pH can be altered by air temperature, sleep, emotion, and food ingestion.[19]

The improvement of the overall nasal symptoms and sneezing after alkaline nasal saline irrigations was found in this study. These effects were not found when rinsing with nonbuffered solution. Up to our knowledge, this is the first study investigating how various alkalinities of nasal irrigations affects nasal symptoms of the patients with allergic rhinitis. Although most homemade nasal irrigations are buffered with sodium bicarbonate, resulting in alkalinity of saline solution, the advantages of buffering nasal solution with alkalinity are not clear[14] and optimal pH for nasal irrigation is not known.[7] In agreement with the previous study, there was no significant change in the nasal patency[15,20] and mucociliary clearance[21] in isotonic nasal saline solution treatment. However, hypertonicity may improve mucociliary function.[14,21] The ciliary beat frequency of trachea was shown not influenced by fluid with pH value of 7–10 in the animal study but decreased by the higher and lower values.[22]

In contrast to this study, the study on nasal drug delivery system suggested an adjustment of the pH of nasal formula to 4.5–6.5 to avoid nasal irritation and prevents of growth of bacteria. Lysozyme in nasal secretions destroys bacteria at acidic pH. Under alkaline conditions, lysozyme is inactivated and the tissue is susceptible to microbial infection.[23] Nevertheless, that concern may be kept in mind when treating patients with rhinosinusitis other than allergic rhinitis.

Nasal saline irrigation have been shown for its benefits as noninvasive adjunctive treatment for sinonasal diseases. Some patients rinse their nose as long-term treatment. This may change the properties or contents of the gel or the sol layer in nasal mucus blanket, and the changes may different depending on the osmolarity and pH of the solutions. So far, there is no study of adverse effects of long-term use of nasal saline irrigation on nasal mucosa, mucociliary clearance, lysozyme, or level of secretory IgA in nasal secretions. Those kinds of study will prove the safety of nasal irrigation in long-term management.

Although few minor adverse events similarly occurred in all three solutions, most patients preferred the saline solution with mild alkalinity, maybe resulting from a pH 7.2 that is similar to the physiological pH of cellular cytoplasm, which is suitable for the environment of nasal mucosa cells and reduced the patients' overall nasal symptoms. Based on our findings, we suggest that

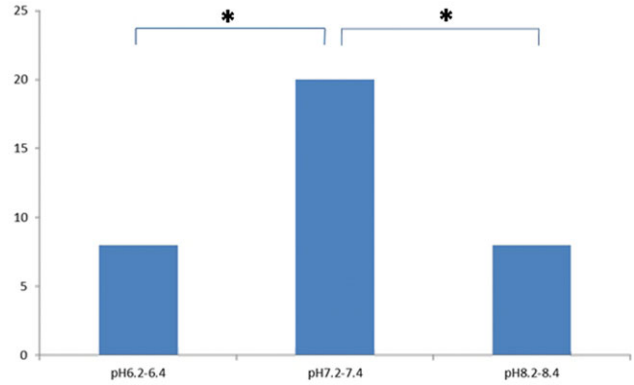

Fig. 1. The number of patients' preference in each treatment (*$P = 0.02$). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

patients with allergic rhinitis rinse their noses with isotonic saline with mild alkalinity. The homemade recipe for this is to add just a pinch of sodium bicarbonate to 1 liter of saline solution.

The advantages of the crossover design in this study include the following; the participant variation is eliminated, fewer participants are required to obtain the same power, and every patient receives every kind of solution, which allows the determination of the preference for an individual participant. The possible weak point of this study is that the duration of 10-day irrigations may not be long enough to see improvement of more symptoms, while the duration of 6-week irrigations may be required in the other study[1] to show significant improvement in allergic rhinitis.

CONCLUSION

The differences in pH of isotonic saline irrigations affect some of nasal symptom reliefs but do not affect mucociliary function, nasal patency, and adverse effects in allergic rhinitis. Buffered isotonic saline with mild alkalinity (pH7.2–7.4) is the most preferred.

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