Isotonic saline nasal irrigation is an effective adjunctive therapy to intranasal corticosteroid spray in allergic rhinitis

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ABSTRACT

Background: *This study was designed to determine if the addition of large-volume, low–positive pressure nasal irrigations delivered with isotonic sodium chloride (hereinafter "saline") added to intranasal corticosteroid therapy improves quality of life and objective measures of nasal breathing in patients with allergic rhinitis when compared with intranasal corticosteroid alone.*

Methods: *A prospective, unblinded, single-arm pilot study was performed of patients with allergic rhinitis already on intranasal corticosteroid pharmacotherapy. Patients added large-volume low-pressure saline irrigation twice daily for 8 weeks to their ongoing regiment of nasal corticosteroid. Mini-Rhinoconjunctivitis Quality of life Questionnaire (mRQLQ) assessment and nasal peak inspiratory flow (NPIF) were performed at baseline and at 4 and 8 weeks.*

Results: *A total of 40 patients were enrolled. Twice-daily nasal irrigation with isotonic saline significantly ($p < 0.001$) reduced mRQLQ scores, from 36.7 ± 20.48 (baseline) to 14.9 ± 11.03 (4 weeks) to 10.10 ± 10.65 (8 weeks). No significant changes were seen in NPIF, pattern use of nasal steroid use, or adverse events.*

Conclusion: *Large-volume, low–positive pressure nasal irrigation with isotonic saline is an effective adjunctive therapy to improve quality of life in patients with allergic rhinitis already on intranasal corticosteroid therapy.* This study was a part of the clinical trial NCT01030146 registered at clinicaltrials.gov.

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Allergic rhinitis is a global health problem, affecting between 10 and 40% of the world's population.[1–3] In industrialized countries it is the most common allergic condition affecting ~20% of the population.[4] The prevalence of hay fever (seasonal allergic rhinitis) has increased for many decades but appears to have stabilized in recent years.[5] Current guidelines of the European Academy of Allergy and Clinical Immunology Working Party on the Management of Rhinitis and Allergic Rhinitis and Its Impact on Asthma initiative state that antihistamines and nasal steroids are the first-line therapy for allergic rhinitis.[6,7]

Studies of nasal irrigations continue to report the benefits in managing sinonasal complaints.[8–13] Nasal irrigations may be used for a variety of conditions. Their use is included in the management of acute and chronic rhinosinusitis, allergic and nonallergic rhinitis, nonspecific nasal symptoms (including postnasal drip), septal perforations, and the postoperative care of surgical patients. Apart from improved patient symptomatology, prescription medication use is often decreased. When nasal irrigations are combined with other medical modalities, patients with chronic sinusitis may not require surgical intervention as often.[13] In a recent study, Rabago *et al.*[14] performed a randomized, controlled trial looking at patients with two episodes of acute sinusitis or one episode of chronic sinusitis per year for 2 consecutive years. Fifty-two patients received isotonic saline, whereas 24 patients did not receive any irrigation. When using isotonic nasal irrigations, improvements in quality of life and overall symptom severity scores were statistically significant. Steroid nasal spray use was also decreased. Toomoka *et al.*[15] used pulsatile isotonic saline nasal irrigations for a range of sinonasal conditions, extending from atrophic rhinitis to the symptom of postnasal drainage. They reported that patients who used nasal irrigations for the treatment of sinonasal complaints experienced statistically significant improvements in 23 of 30 nasal symptoms. Nasal irrigations can also be effective in rhinitis,[10,14–16] including allergic and nonallergic rhinitis.

Nasal steroids and antihistamines are the gold standard in treating allergic rhinitis, and the safety and efficacy of saline nasal irrigation in managing sinonasal complaints have shown promising results. We sought to determine if the addition of low-pressure nasal irrigation with isotonic saline to intranasal corticosteroid sprays would improve quality of life in patients with allergic rhinitis.

METHODS

Subjects

This was a prospective, single-arm, pilot study approved by the Medical University of South Carolina Institutional Review Board (HR 19154). All patients were evaluated at the Medical University of South Carolina Sinus Clinic. Inclusion criteria were (1) patients (18–99 years of age) diagnosed with allergic rhinitis with positive allergy testing (either skin-prick test or elevated IgE measured by modified radioallergosorbent test) who have completed 1 month of pharmacotherapy consisting exclusively of nasal steroids and remained symptomatic and (2) patients able to provide informed consent and perform scale assessment. Exclusion criteria were (1) a diagnosis of sinusitis, cystic fibrosis, or immune deficiency or those unable or unwilling to perform saline irrigations for 2 months and (2) use of oral or topical antihistamines, eye drops, leukotriene inhibitors, other nonsteroidal sprays, or oral steroids.

This was a prospective, single-arm pilot study of 40 patients. After having been on nasal steroids for at least 30 days, as per standard treatment protocol, patients underwent allergy testing with the skin-prick test, a baseline nasal peak inspiratory flow (NPIF) measurement, and a baseline assessment with the Mini-Rhinoconjunctivitis Quality of Life Questionnaire (mRQLQ; Fig. 1). Patients continued pharmacotherapy with nasal steroid sprays with the addition of

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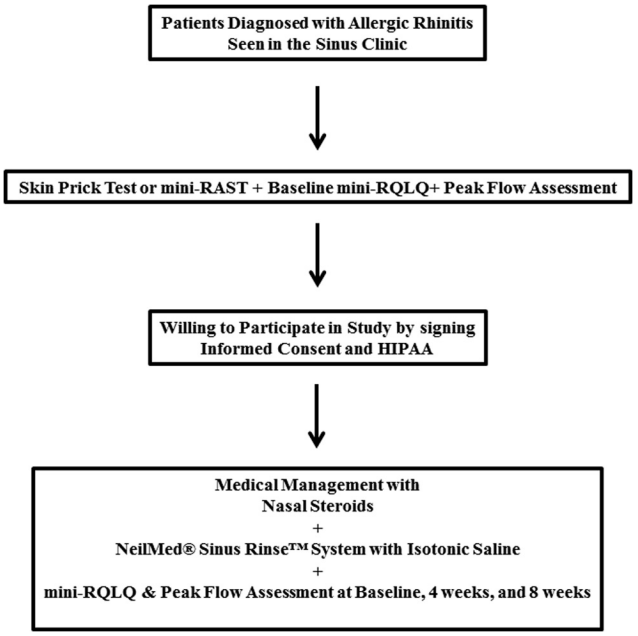

Figure 1. *Flowchart detailing study procedures.*

low-pressure nasal irrigation with isotonic saline as an adjunctive therapy. Those who enrolled were given NeilMed Sinus Rinse bottles (NeilMed Pharmaceuticals, Inc., Santa Rosa, CA) and instructions on the use of a low-pressure squeeze bottle with isotonic saline to be performed twice a day for 8 weeks. At the end of 4 and 8 weeks, patients then completed another mRQLQ and NPIF assessment.

Disease information and demographic variables, such as age, ethnic group, and sex, were collected.

Outcomes

The mRQLQ[17] is a validated shortened version of the Juniper rhinoconjunctivitis quality-of-life questionnaire.[18] There are 14 questions in five domains (activities, practical problems, nose, eye, and other symptoms). Each question is scored as an integer from 0 (not troubled) to 6 (extremely troubled). The questionnaire was able to be completed in <2 minutes by most adults.

Nasal Peak Inspiratory Flow

A peak flowmeter with a purpose-built face mask measures the patient's maximum flow of inspiration (NPIF). Patients were instructed to ensure that the face mask forms an air-tight seal around the nose, close their mouth, and inhale forcefully through their nose (sniff). Each patient was given two practice sniffs. Three satisfactory maximal inspirations were obtained, and the highest of the three results was taken as the NPIF.

Statistical Analysis

All analyses and graphs were performed with Sigma Stat 3.5, Sample Power 2.0, and Sigma Plot 10.0 (SPSS, Inc., Chicago, IL). Disease information and demographic variables, such as age, ethnic group, and gender, were summarized by means of summary statistics. Continuous variables were summarized by mean ± SD. Categorical variables were summarized by frequency and percentage. All continuous variables were tested for normal distribution as determined by Kolmogorov-Smirnov test. Peak flow assessment and mRQLQ were compared at baseline and 4 and 8 weeks. Continuous variables were compared by using a one-way ANOVA with repeated measures (normal distribution) or a one-way ANOVA on ranks with repeated measures (without normal distribution). When an analysis of variance model was found to indicate a significant difference ($p < 0.05$), further Duncan's *post hoc* comparison tests were performed to compare among baseline and 4 and 8 weeks. A value of $p < 0.05$ was considered indicative of statistical significance. Sample size was not performed, considering this was a pilot study.

RESULTS

A total of 40 patients participated in the study from December 2009 to April 2012. Eleven men (27.5%) and 29 women (72.5%) with a mean age of 38 years (range, 21–71 years) enrolled in this study. Of the 40 patients, 6 (15.0%) were classified as "others," 10 (25.0%) were African Americans, and 24 (60.0%) patients were white. All but six (15.0%) of the patients were nonsmokers. There were 3 (7.5%) patients that were classified with having seasonal allergies, 11 (27.5%) were perennial, and 26 (65.0%) were classified as mixed. Twice-daily nasal irrigation (Table 1; Fig. 2) significantly ($F_{(2,116)} = 48.478$; $p < 0.001$) reduced mRQLQ scores from 36.7 ± 20.48 (baseline) to 14.9 ± 11.03 (4 weeks) to 10.1 ± 10.65 (8 weeks). *Post hoc* Duncan's multiple comparison tests indicated that mean RQLQ values were statistically significantly lower at 4 and 8 weeks when comparing with baseline ($p < 0.05$). There was no significant difference when comparing mRQLQ scores between 8 and 4 weeks. There were no significant ($F_{(2,116)} = 0.507$; $p = 0.604$) changes with NPIF from baseline (237.1 ± 123.4) and at 4 (224.9 ± 95.2) and 8 weeks (232.9 ± 97.6). There were no significant changes with pattern use of nasal steroids. All 40 patients completed the study and had no adverse effect.

Table 1 **mRQLQ changes in mRQLQ scores**

Domain	Baseline	4 wk after Baseline	8 wk after Baseline
Activities			
Regular activities at home and at work	2.5 ± 1.47	1.3 ± 1.14	0.9 ± 1.03
Recreational activities	2.7 ± 1.58	1.3 ± 1.17	0.9 ± 1.18
Sleep	2.6 ± 1.60	1.3 ± 1.09	0.6 ± 0.84
Practical problems			
Need to rub nose/eyes	3.1 ± 1.89	1.2 ± 0.96	0.9 ± 1.08
Need to blow nose repeatedly	2.9 ± 1.73	1.2 ± 1.21	0.9 ± 1.18
Nose symptoms			
Sneezing	2.7 ± 1.61	1.1 ± 1.28	0.7 ± 0.88
Stuffy blocked nose	3.4 ± 1.69	1.3 ± 1.22	1.1 ± 1.03
Runny nose	2.9 ± 2.04	1.1 ± 1.11	0.7 ± 0.93
Eye symptoms			
Itchy eyes	2.9 ± 1.76	0.9 ± 1.01	0.5 ± 0.82
Sore eyes	2.2 ± 1.97	0.6 ± 0.93	0.4 ± 0.74
Watery eyes	2.4 ± 1.80	0.7 ± 0.97	0.5 ± 0.76
Other symptoms			
Tiredness and/or fatigue	2.8 ± 1.74	1.1 ± 0.88	0.9 ± 0.96
Thirst	1.9 ± 1.81	0.9 ± 1.01	0.5 ± 0.82
Feeling irritable	2.1 ± 1.76	0.8 ± 0.97	0.6 ± 0.99
Total score (mean score)	36.7 ± 20.48	14.9 ± 11.03	10.1 ± 10.6

mRQLQ = Mini-Rhinoconjunctivitis Quality of Life Questionnaire.

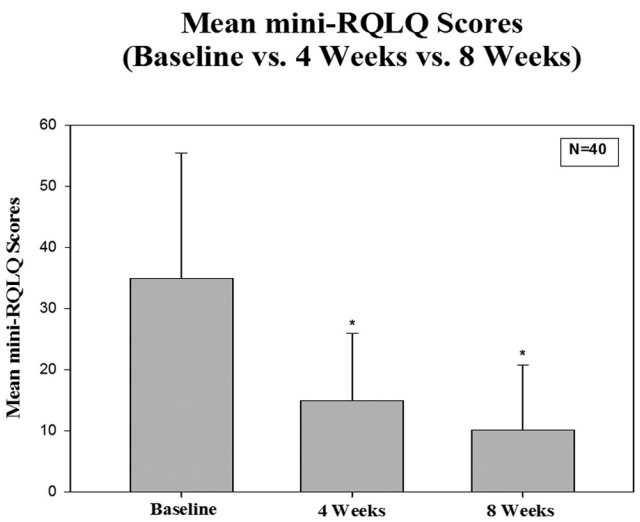

Figure 2. Mean Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores—baseline versus 4 weeks versus 8 weeks. One-way ANOVA ($F_{(2,116)} = 48.478$; $p < 0.001$) post hoc Duncan's = baseline of >4 and 8 weeks ($p < 0.05$).

DISCUSSION

Topical nasal steroids are recommended as first-line pharmacotherapy for allergic rhinitis.[19] Despite their efficacy, roughly one-half of U.S. adults report persistent symptoms or limited duration of efficacy.[20] This study examined patients with allergic rhinitis, who remained symptomatic despite compliance with nasal steroids, found that the addition of nasal irrigation with isotonic saline is effective in improving the quality of life. This further validates studies in acute and chronic rhinosinusitis that nasal irrigations are effective in improving quality of life.[21–24]

The mechanism of symptom improvement with saline irrigations is not fully understood. Numerous studies have hypothesized that nasal irrigation promotes improvement of nasal symptoms *via* various mechanisms: (1) increasing mucociliary function,[23] (2) decreasing mucosal edema,[24] (3) decreasing inflammatory mediators,[25] and (4) clearing inspissated mucus and exogenous inflammatory triggers.[26] We were unable to identify any objective differences in nasal airway patency using NPIF.

Numerous clinical studies have used various tonicities of sodium chloride (NaCl) solution. In this study, isotonic saline irrigation was shown to be effective for patients with allergic rhinitis. Shoseyov *et al.*[27] discovered that hypertonic saline (1 mL) three times per day for 1 month was associated with side effects due to local irritation of the swollen and inflamed mucosa. Patients had burning and itching symptoms of the nostrils during the initial study. Baraniuk *et al.*[28] showed that hypertonic saline nasal irrigation leads to substance P release and glandular secretion by means of stimulation of nociceptive nerves, which eventually can induce pain in patients. Comparably, in this pilot study, there were no side effects with patients on isotonic saline (240 mL) twice a day for 8 weeks.

This study was conducted with the use of high volumes (240 mL) of isotonic saline dispensed by way of a squeezed bottle irrigating the nostrils. Heatley *et al.*[29] compared sinonasal symptom scores after daily nasal irrigation with either a bulb syringe or a nasal irrigation pot and found that they were equally effective. A study by Seppey *et al.* found that stream delivery was significantly more effective than passive instillation of saline.[30] Other studies have recommended that patients use isotonic saline, 5 drops in each nostril at least four times a day, until symptoms subside. Isotonic saline solution nasal irrigation certainly expedites nasal drainage and cleans the airway from any postnasal secretion.[31,32] It is unknown if similar benefits would result from lower-volume delivery devices.

Limitations of this pilot study include the relatively small sample size, not sufficiently powered, lack of blinding and a control arm, varying severity of allergic rhinitis, type of nasal steroid, and having only one subjective scale (mRQLQ). The strengths of this study include its prospective nature, no missing data, no dropouts, objective NPIF measures, and a diverse demographic of age and race. Overall, we were able to show that the addition of nasal irrigation with isotonic saline to intranasal corticosteroid spray improves the quality of life in patients with allergic rhinitis without any adverse effects.

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