Dead Sea salt irrigations vs saline irrigations with nasal steroids for symptomatic treatment of chronic rhinosinusitis: a randomized, prospective double-blind study

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Background: **Intranasal steroids are 1 of the most frequently prescribed medications for the treatment of chronic rhinosinusitis (CRS), and saline irrigations are commonly used as an adjunct to medical therapy. We aimed to compare the efficacy of Dead Sea salt (DSS) irrigations and DSS nasal spray vs saline irrigations and topical nasal steroid spray in the treatment of symptoms of CRS.**

Methods: **A total of 145 symptomatic adult patients without acute infection were initially enrolled and 114 completed the study. Patients completed a Sino-Nasal Outcomes Test 20 (SNOT-20) survey (primary outcome metric) and underwent endonasal examination, acoustic rhinometry, and smell testing (secondary outcome metrics). Patients were randomized to 2 groups. The experimental group (n = 59) self-administered hypertonic DSS spray and DSS irrigation; the control group (n = 55) self-administered fluticasone spray and hypertonic saline irrigation and spray. Patients and staff were blinded to group assignment. Outcomes were reassessed at 4 weeks.**

Results: **The 2 groups were homogeneous with respect to pretreatment primary and secondary outcome metrics. Dropout rates were 30% in the DSS group and 36.6% in the control group. Both groups showed significant improvement in mean SNOT-20 scores following treatment; however, the degree of improvement was not significantly different between groups ($p = 0.082$). There were no significant changes in secondary outcome metrics between the 2 groups.**

Conclusion: **For patients with CRS, treatment with DSS irrigations and sprays appears as effective for symptom reduction as a combination of hypertonic saline irrigations and sprays and a topical steroid spray.** © 2011 ARS-AAOA, LLC.

Key Words:
hypertonic saline solution; nasal lavage; nasal saline irrigation; rhinitis; sinusitis; steroid

How to Cite this Article:
Friedman M, Hamilton C, Samuelson CG, et al. Dead Sea salt irrigations vs saline irrigations with nasal steroids for symptomatic treatment of chronic rhinosinusitis: a randomized, prospective double-blind study. *Int Forum Allergy Rhinol*, 2012; 2:522–257

Chronic rhinosinusitis (CRS) affects 31 million Americans each year, with an associated healthcare cost of $5.8 billion. The most commonly used medical treatments are antibiotics, antihistamines, intranasal steroids, and systemic steroids.[1]

The use of topical nasal steroids for the treatment of allergic rhinitis has been studied extensively, and a 2008 meta-analysis also found excellent randomized controlled trial (RCT) evidence for their use in CRS.[2]

Many studies have shown the use of saline solutions to be of benefit for chronic sinusitis or rhinosinusitis,[3–6] with the majority finding hypertonic saline to be more efficacious than buffered physiological saline. Saline irrigations and sprays are now so widely used to alleviate sinonasal symptoms that we should consider them to be another "standard" treatment for rhinosinusitis. Topical saline sprays are often recommended for unrestricted as needed (PRN) use.

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Funding sources for the study: Tricord Pharmaceuticals, manufacturers of Oasis Nasal Wash solution and Oasis Nasal Spray.
Potential conflict of interest: M.F. serves as a consultant for Tricord Pharmaceuticals. M.F.'s unrelated financial relationships include serving as a member of the speaker's bureau for GlaxoSmithKline.

Received: 2 August 2011; Revised: 17 October 2011; Accepted: 11 November 2011
DOI: 10.1002/alr.21003
View this article online at wileyonlinelibrary.com.

Dead Sea salt (DSS) solutions differ from standard saline solutions by virtue of their unique mineral content. Dead Sea water treatments have long been used to treat severe dermatologic conditions.[7–10] With their proven clinical value in dermatology, DSS solutions have been theorized to have anti-inflammatory properties not present in standard saline preparations. Previous studies have shown the value of DSS in the treatment of seasonal allergic rhinitis symptoms.[11] Cordray et al.[11] suggest DSS may be used as an effective alternative to an intranasal steroid for treatment of mild to moderate rhinitis. DSS spray was found to be a significantly more effective treatment than saline spray alone. In a previous study by the senior author (M.F.),[12] a regimen of DSS sprays and irrigations is found to be superior to hypertonic saline sprays and irrigations for the symptomatic treatment of CRS. To our knowledge, no previous study has examined the comparative efficacy of DSS solution vs a combination of topical intranasal steroid and hypertonic saline solution for the treatment of CRS.

We considered treatment with a combined regimen of saline irrigations with topical steroids to be a "standard" treatment for CRS. For the purposes of this study, we subjected our "control" group to such a combined regimen, so that we might determine if our experimental intervention of DSS irrigations could achieve comparable symptom improvement and morbidity.

Patients and methods

Participants

The protocol was approved by the Western Institutional Review Board, Olympia, WA. Between January 2008 and January 2011, informed consent was obtained from 145 patients presenting to the outpatient clinic of the senior author (M.F.) with complaints of CRS-related symptoms as outlined in the Rosenfeld criteria for CRS.[13]

Only adult patients (aged 18-90 years) presenting with 2 or more of the following symptoms for greater than 12 weeks were included: (1) mucopurulent drainage; (2) nasal obstruction (congestion); (3) facial pain-pressure-fullness; and (4) decreased sense of smell. The diagnosis for all patients was confirmed with either identification of edema on endonasal examination, or computed tomography (CT) verification of paranasal sinus inflammation. Full endoscopic evaluation was performed on all patients by 1 of 2 otolaryngologists (M.F. and T.K.V.).

Exclusion criteria

Patients with a Lund-Mackay radiological score of 2 for any single sinus or the osteomeatal complex were excluded. Patients with air fluid levels within 1 or more sinuses on CT, fever, or otherwise not meeting Rosenfeld criteria for CRS were also excluded.[13] Patients with significant nasal airway obstruction resulting from mucocele, extensive polyposis causing >90% nasal obstruction, or severe septal deformity causing >90% nasal obstruction were referred for surgical treatment and excluded from the study. It should be noted that patients with polyposis or septal defects that did not meet criteria for surgical intervention were included in the study population. In addition, patients with active allergic fungal sinusitis, cystic fibrosis, or a known systemic immunodeficiency condition were excluded (including all patients with diagnosed diabetes). Finally, patients known to be pregnant, found pregnant on urine testing, or those refusing to commit to acceptable birth control methods for the duration of the study were excluded. Patients not fluent in the English language were also excluded.

Randomization

Participants were randomly assigned (using computerized random numbers 1 or 2) into either the "experimental" or "control" group.

Blinding

Blinding was strictly maintained for both researchers (including clinical staff) and participants. Study medications were prepackaged by the sponsor's pharmacists (located at a distant site) into anonymous kits and numbered accordingly. Kit contents were based on the ratio of 1:1 group assignment using computer-generated random numbers. Kits were dispensed in numerical order based on subject accession number. The group assignment list was kept by the study pharmacist, who never met the researchers or patients. A copy of this list was stored in a locked location at each treatment site for emergency unblinding purposes.

Interventions

Included patients were instructed on how to perform nasal irrigations and were asked to do so every morning and every night with the supplied solution. Nasal irrigation was performed using a syringe to flush 20 mL of solution per naris. This volume of irrigant was chosen for practical reasons only, as patients were provided with the full volume required for the duration of the study at the outset. Patients were supplied with unlabeled and identical spray bottles and were instructed to administer 2 sprays per naris 3 times daily. Patients from both groups were given supplies sufficient to last 30 days.

The experimental group received DSS solution (1.8 N) for all spray and irrigation bottles. Controls received hypertonic saline (1.8 N) for all irrigation along with midday and bedtime spray bottles. The morning spray bottle in this group contained fluticasone 50 μg/per actuation.

It should be noted that a "standard" treatment regimen for rhinosinusitis would typically involve twice-daily saline irrigation (per the above protocol), and use of a steroid spray once daily only. The manufacturer's recommendations for use of DSS are that the intranasal spray be used 3 times per day in addition to irrigations to achieve the best possible symptomatic benefit for patients. In order to make the performance of this double-blinded study viable, the use of a hypertonic saline intranasal spray twice daily in

addition to the once-daily steroid spray was added so that the blinded treatment protocols might be identical.

Outcomes

The primary outcome measure of this study was improvement in rhinosinusitis-related quality of life, measured by the SNOT-20 questionnaire. This is a validated, self-administered questionnaire that uses a 5-point Likert scale to assess how severely a patient's rhinosinusitis symptoms affect their quality of life.[14] Secondary outcome measures included the University of Pennsylvania Smell Identification Test (UPSIT), a 40-item, self-administered, validated instrument to assess a patient's sense of smell.[15] Findings on nasal endoscopy and acoustic rhinometry were also recorded as clinical and numeric measures of nasal-mucosal inflammation.

Upon their return visit following 4 weeks of daily treatment, patients underwent repeat nasal endoscopy and acoustic rhinometry, and completed a repeat UPSIT and SNOT-20. Patients who did not return for review within 6 weeks of their initial visit were dropped from the study. Only after all the data had been collected was the seal broken to identify the control vs the experimental groups.

Statistical analysis

An intention-to-treat and per-protocol analysis was performed on all participants who were randomized. Primary outcome measurement was improvement in rhinosinusitis-related quality of life, measured by the SNOT-20 questionnaire. Secondary outcomes included the UPSIT, nasal endoscopy findings, and acoustic rhinometry values. Sample size was determined using an a priori power analysis based on the only data available—a previous study by Cordray et al.[11] This study compared DSS, isotonic saline, and intranasal steroid use for allergic rhinitis, with a similar primary outcome measurement to the SNOT-20 (Rhinoconjunctivitis Quality of Life Questionnaire [RQLQ]). Based on this analysis, we determined a minimum sample size of 41 per group would be required to reach a power of 0.95.

All statistical analyses were performed using SPSS Version 18.0 (SPSS, Inc., Chicago, IL). Continuous data is displayed as mean ± standard deviation. Statistical significance was accepted when $p < 0.05$. Levene's test for equality of variances was used to determine statistically significant variances. The paired Student t test was used to compare rhinosinusitis severity scores and quality of life (QOL) scores before and after treatment. The 2-tailed Student t test was used to identify differences in rhinitis severity scores and QOL scores between treatment groups. The χ^2 test was used to test the association between categorical variables.

Results

A total of 145 patients were enrolled in the study and were randomized to either the Control group or the Experimental group. Thirty-one (31) patients (17 steroid/hypertonic saline and 14 hypertonic DSS) were dropped from the study because of failure to comply with the treatment protocol or failure to follow-up satisfactorily. Reasons for dropout included: worsening symptoms (10 patients), bloody nasal discharge (1), epistaxis (2), and fear of epistaxis (2). In the intention-to-treat analysis, these dropouts were considered treatment failures. The 114 remaining patients (44 males, 70 females, mean age 43.5 ± 12.8 years) were treated with either steroid/hypertonic saline (n = 55) or hypertonic DSS (n = 59) and completed the 4 week study. Complete baseline data for the 2 groups is listed in Table 1.

Data from both primary and secondary outcome metrics is described in Table 2. The primary outcome metric in the study was change in SNOT-20 score following the treatment phase of the study. The steroid/hypertonic saline-treated patients had a pre-treatment mean SNOT-20 score of 1.85 ± 0.80. The hypertonic DSS solution patients had a pretreatment mean SNOT-20 score of 2.0 ± 0.80. These scores were not significantly different from each other ($p = 0.315$). Following treatment, the mean SNOT-20 score for the steroid/hypertonic saline-treated patients (1.29 ± 0.74) was significantly reduced from the pretreatment score ($p < 0.0001$). In the hypertonic DSS solution-treated patients, the posttreatment mean SNOT-20 score (1.21 ± 0.52) was also significantly reduced from the pretreatment score ($p < 0.001$). The posttreatment mean SNOT-20 scores were not significantly different between the 2 treatment groups ($p = 0.785$).

Secondary outcome metrics included UPSIT and acoustic rhinometry data. The pretreatment UPSIT for the steroid/hypertonic saline-treated patients (30.9 ± 5.6) remained unchanged after treatment (31.3 ± 4.9, $p = 0.778$). Similarly, the pretreatment UPSIT for the hypertonic DSS-treated patients (31.4 ± 6.1) did not change following treatment (31.5 ± 7.2, $p = 0.898$). Again, no significant difference existed between the 2 treatment groups ($p = 0.888$ pretreatment and $p = 0.924$ posttreatment).

Bilateral acoustic rhinometry measurements (cross-sectional area in cm^2 [CSA-2]) were recorded for each patient. The pretreatment means for CSA-2 were similar for both groups (see Table 2). These values did not change significantly following treatment in either group.

Discussion

Nasal irrigation has been prescribed by otolaryngologists and rhinologists for centuries as an adjunctive treatment for allergic rhinitis and CRS.[16] Today, nasal irrigations and sprays (typically saline) are even more frequently used for these indications,[17,18] as well as in the postoperative period following endoscopic sinus surgery.[19] Although the exact mechanism of action by which saline nasal irrigations improve nasal function is not fully understood, most theories suggest that they: (1) improve the mucociliary function of the respiratory mucosa; (2) have a protective role on the sinonasal mucosa; (3) decrease mucosal edema; (4) clear

TABLE 1. Comparison of baseline data from 55 patients treated with steroids/hypertonic saline and 59 patients treated with hypertonic Dead Sea salt solution

	Steroids/hypertonic saline	Dead Sea salt solution	*p*
n	55	59	
Age (years), mean ± SD	41.2 ± 12.5	41.0 ± 13.7	0.953
Males, n (%)	20 (36.4%)	24 (40.7%)	0.676
Females, n (%)	35 (63.6%)	35 (59.3%)	
BMI (kg/m), mean ± SD	28.3 ± 6.3	25.6 ± 3.1	0.085
Medical history			
History of fungal sinusitis, n (%)	6 (10.9%)	3 (5.1%)	0.237
Rx with antibiotics, n (%)	22 (40.0%)	25 (42.3%)	0.623
Courses in past year, mean ± SD	2.5 ± 1.9	1.9 ± 1.4	
Rx with steroids	13 (23.6%)	16 (27.1%)	0.457
Courses in past year, mean ± SD	0.51 ± 0.91	0.61 ± 1.1	
Surgical history, n (%)			
Rhinoplasty	5 (9.1%)	8 (13.6%)	0.578
Septoplasty	22 (40%)	29 (49.2%)	0.098
SMR	21 (38.2%)	26 (44.1%)	0.221
ESS	19 (34.5%)	17 (28.8%)	0.124
Endoscopy			
Polyps	11 (20%)	13 (22.0%)	0.755
Deviated septum	31 (56.4%)	39 (66.1%)	0.472
Turbinate hypertrophy	45 (81.8%)	50 (84.7%)	0.608
Purulence	6 (10.9%)	11 (18.6%)	0.429
Polypoid mucosa	12 (21.8%)	14 (23.7%)	0.210

ESS = endoscopic sinus surgery; BMI = body mass index; Rx = treatment; SD = standard deviation; SMR = submucosal resection of the septum.

TABLE 2. Data from both primary and secondary outcome metrics on 55 patients treated with steroids/hypertonic saline and 59 patients treated with hypertonic Dead Sea salt solution

	Steroids/hypertonic saline	Dead Sea salt solution	*p*
Pretreatment SNOT-20	1.85 ± 0.80	2.00 ± 0.80	0.315
Posttreatment SNOT-20	1.29 ± 0.74	1.21 ± 0.52	0.785
p	<0.0001[a]	<0.0001[a]	
SNOT-20 Change Score	−0.56	−0.79	0.082
Pre-UPSIT	30.9 ± 5.6	31.4 ± 6.1	0.888
Post-UPSIT	31.3 ± 4.9	31.5 ± 7.2	0.924
p	0.778	0.898	
Pre-AR CSA-2 right (mm^2)	1.41 ± 1.20	1.22 ± 0.73	0.638
Post-AR CSA-2 right (mm^2)	1.52 ± 1.99	1.67 ± 1.09	0.756
p	0.834	0.102	
Pre-AR CSA-2 left (mm^2)	1.11 ± 0.77	1.61 ± 1.88	0.201
Post-AR CSA-2 left (mm^2)	1.81 ± 2.15	1.85 ± 1.55	0.899
p	0.105	0.605	

[a]Denotes statistically significant difference when $p < 0.05$.

AR = acoustic rhinometry; CSA = cross-sectional area; SNOT = Sino-Nasal Outcome Test; UPSIT = University of Pennsylvania Smell Identification Test.

mucus and static secretions; (5) clear infective debris; (6) remove allergens or inflammatory mediators; and (7) minimize crusting.[17,18]

Numerous studies have been designed to study the efficacy of these solutions and compare various types and concentrations of saline. While most studies demonstrate clinical improvement with saline irrigation,[17] conclusions about the type or concentration of saline that should be used have been conflicting and inconsistent. Saline solutions of different compositions and concentrations have been described in the past. Physiological saline (normal saline, 0.9% NS), lactated Ringer's solution (LR) and various concentrations of hypertonic saline have been used with varying results.[4,5,16,20,21]

Isotonic saline nasal irrigation is one of the oldest and most effective methods used in the treatment of rhinosinusitis and allergic rhinitis.[3] Solutions are easily prepared and inexpensive. Proponents of isotonic saline nasal irrigation, argue its superiority due to its lesser side effect profile compared with hypertonic saline. The most commonly reported adverse effect from the use of hypertonic saline is nasal mucosal irritation. Transient increases of inflammatory mediators (leukotrienes and prostaglandins) result in further nasal hypersecretion and hyperactivity.[21] Additionally, the release of substance P, a neurotransmitter responsible for the production of pain, has been reported with hypertonic saline use. Reported side effects frequently include a burning or stinging sensation. However, few studies report patients experiencing side effects to a degree that causes them to stop using the solution, and many show only minor differences in reported side effects between patients using hypertonic vs normal saline.[3,5,6] Serious side effects have not been reported with the use of either hypertonic or normal saline nasal sprays or irrigations.

On the other hand, the benefits of hypertonic saline use have been well-described.[3–6,16] Various authors have demonstrated the mucolytic properties of hypertonic saline.[19,22] Studies by Hauptman and Ryan,[3] Keojampa et al.,[5] and Talbot et al.[6] demonstrated that using hypertonic saline, in contrast to normal saline, provides a greater improvement in mucociliary clearance. The rheological alterations caused by hypertonic saline are suggested to be the most important factor. It is believed that an acidic milieu causes mucus to exist in a "gel" or "viscous" phase (a semisolid system in which particles take a more solid form), whereas an alkaline environment causes mucus to exist in a "sol" phase (a fluid colloidal system in which the continuous phase is a liquid).[6] Hypertonic saline is a mildly alkaline solution; hence, it keeps mucus in sol phase and thereby reduces the mucociliary transit time.

Rabago et al.[16] performed a randomized, controlled trial showing hypertonic (2%) saline significantly improves symptoms and QOL initially, with continued gains in QOL over a 12-month follow-up period. Clinical studies also demonstrate that the use of hypertonic saline irrigation for 3 to 6 weeks in patients with rhinosinusitis leads to significant improvement in 70% of patients.[18] A further study reports that 38% of patients who used hypertonic nasal saline irrigation decreased or completely eliminated their use of other nasal medications such as nasal steroids and antihistamines.[4]

The concept of substituting hypertonic DSS for normal hypertonic saline is based on the observed therapeutic value of DSS solutions as anti-inflammatory agents in the treatment of various dermatologic conditions, such as allergic dermatitis, atopic dermatitis, and psoriatic dermatitis.[7–10] The various minerals (such as Ca, K, Br, Zn, and Mg salts) that comprise DSS are known to exhibit favorable effects in the treatment of inflammatory diseases.[11] Magnesium salts, which comprise approximately 35% of DSS, have the ability to bind water, enabling them to influence epidermal proliferation as well as differentiation and to enhance permeability barrier repair.[8] Skin bathed in the Dead Sea or in simulated DSS solutions demonstrates decreased inflammation, increased hydration, and decreased redness.[8]

Very few studies have compared the efficacy of topical intranasal steroid to saline nasal spray or irrigation. In a study by Inanli et al.,[23] no significant difference in mucociliary clearance times was found between subjects treated with 3 weeks of daily fluticasone propionate nasal spray, 3% saline nasal spray, or 0.9% saline irrigation. However, that study compared only mucociliary clearance, and did not evaluate patient quality of life or clinical changes in the nasal mucosa. Cordray et al.[11] found that the use of triamcinolone nasal spray, resulted in a greater improvement in rhinoconjunctivitis (seasonal allergic rhinitis) quality of life than DSS spray or normal saline spray. That study, however, did not look at the effectiveness of nasal irrigations in conjunction with sprays, and only had a small number of patients (5 per treatment group).[11]

We feel that there is sufficient evidence to conclude that hypertonic solutions are more efficacious than isotonic solutions for the treatment of CRS. For this reason, we chose to use a hypertonic mixture in both the experimental and control arms of our study. We used a 1.8% DSS solution as both spray and irrigation in the experimental arm, and our results showed significant improvement in terms of nasal symptoms and rhinosinusitis-related QOL. The control arm used a topical steroid spray and 1.8% hypertonic saline irrigation/spray, and also demonstrated significant improvement in symptoms and QOL. The results seen in the control arm of our study are not surprising. There is considerable evidence in the literature to support the use of nasal steroids for CRS[2] and they are 1 of the 3 most frequently prescribed medications for CRS across the United States.[1] That the use of DSS alone achieved a comparable level of improvement to the use of steroid and hypertonic saline, might be explained by the additional anti-inflammatory properties of DSS compared with other hypertonic solutions. It should be noted that neither treatment group demonstrated any improvement in sense of smell or rhinometric parameters. This observed improvement in symptoms without objective improvement in mucosal inflammation may be explained by the relatively short treatment period of 4 weeks. A

longer-term study would be useful to assess these objective measures. Further studies could also be conducted to assess the effect of DSS on the mucociliary clearance time in comparison with hypertonic and isotonic saline solutions.

While no therapeutic superiority was noted between treatment groups, these results suggest that DSS solutions/spray alone may be used as a viable alternative to intranasal steroid spray and hypertonic saline solutions. Indications to use 1 treatment or another may be determined on a case by case basis, and may include factors such as cost, availability, and patient preferences/attitudes regarding the use of steroids.

Conclusion

In our short-term study, treatment with DSS irrigations and sprays provides significant improvement in symptoms and QOL for patients with CRS, and appears to be as effective as using a combination of a topical intranasal steroid and hypertonic saline solution in achieving these symptomatic benefits.

Acknowledgments

Aside from the listed authors, we acknowledge the contributions of the following people involved in the execution of this study: Kanwar Kelley, MD; Tanya Pulver, MD; and the physicians, nursing staff, technical, and support staff at Advanced Center for Specialty Care (Advocate Illinois Masonic Medical Center, Chicago, IL). Tricord Pharmaceuticals supplied all solutions (DSS, hypertonic saline, and fluticasone) used in the treatment arm of the study. Tricord Pharmaceuticals had no involvement in the study design, collection, analysis, and interpretation of data or in the writing of the report, or in the decision to submit the paper for publication.

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