Sinus penetration of saline solution irrigation and atomizer in a cadaveric polyp and allergic fungal sinusitis model

Mary Doellman, D.O.,[1] Philip G. Chen, M.D.,[2] Kevin C. McMains, M.D.,[1] Kathleen M. Sarber, M.D.,[1] and Erik K. Weitzel, M.D.[1]

ABSTRACT

Allergic fungal sinusitis (AFS) is a stubborn disease requiring surgical and medical management. Delivery of topical medication is paramount in these patients, but the most difficult to accomplish. We investigated heavy irrigation (nasal douche) and atomized medication delivery potential in a cadaveric sinus model of polypoid AFS disease. Three disease models were created: a control that involved unoperated sinuses and no simulated disease; an unoperated AFS with type II polyposis mode; and an operated model with recurrent allergic fungal sinusitis with type II polyposis. The maxillary sinus showed the best irrigation and overall the heavy irrigator was more efficient than the atomizer.

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Allergic fungal sinusitis often affects a younger population and is more concentrated in warm climates, such as the southern United States[1] and southern Australia.[2] This disease process is unique in its pathophysiology, with extremely thick allergic mucus that fills the sinus cavities and is difficult to remove without surgical assistance.[3,4] This disease process is usually accompanied by polypoid disease that obstructs the natural sinus ostia, by hindering the ability for irrigation to penetrate the nasal sinusitis and thereby inhibiting topical delivery of medications and clearance of the fungal mucus.[5]

Multiple studies evaluated heavy sinus irrigation as a component of postoperative management after sinus surgery.[3–10] Analysis of the results of these studies indicates that sinus penetration is not only important for the removal of residual debris and postoperative crusting but also for delivery of steroids to decrease inflammation. However, it is increasingly evident that delivery system, patient anatomy, and inflammatory process all have significant impact on irrigant distribution.[6] For example, intrasinus penetration with nasal douching was adversely affected in patients with obstructive pathology in the middle meatus.[1] Although there is evidence that demonstrate that nasal atomizers penetrate different subsites of the nose,[11] no studies have been performed to evaluate their effectiveness of sinus cavity penetration for medication delivery and possible removal of debris in an allergic fungal sinusitis (AFS) with a polyposis model.[4,8,12] Our goal was to address the ability of the nasal atomizer and manual squeeze bottle to dispense medications and/or saline solution in patients with severe, obstructive sinus disease by using a cadaveric model.

From the [1]Department of Otolaryngology - Head and Neck Surgery, San Antonio Military Medical Center, Fort Sam, Houston, Texas, and [2]Department of Otolaryngology-Head and Neck Surgery, University of Texas San Antonio Health Science Center at San Antonio, San Antonio, Texas

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Address correspondence to Philip G. Chen, M.D., Department of Otolaryngology-Head and Neck Surgery, 8300 Floyd Curl Drive, MC 7777, San Antonio, TX 78229
E-mail address: P_g_chen@hotmail.com

METHODS

Experimental Setup

Four thawed fresh frozen heads were used for this experiment. None of the maxillary sinuses had a secondary os. Five-millimeter drill holes were created in the canine fossa and anterior frontal bone to allow endoscopic visualization into the maxillary and frontal sinuses, respectively. The sphenoid was not accessible because the brains were *in situ*. A 30° endoscope was placed through the sinus trephinations for an intrasinus visualization of the os during irrigation. Grading was carried out according to a previously published ranked ordinal scale from 0 to 5, depending on the amount of penetration, which constitutes the magnitude of irrigation.[7,9] This scale is as follows: 0, no penetration; 1, bubbles; 2, drops; 3, filled one-third of the sinus; 4, filled two-third sinus; and 5, completely filled sinus. The frequency (regardless of magnitude) with which any irrigation entered a sinus was also collected and was reported as a percentage of attempted trials of medication delivery.

Six drops of green food coloring were mixed in 240 mL of water for the NeilMed squeeze bottle (NeilMed Pharmaceuticals, Santa Rosa, CA), and 6 drops were added to 15 mL of water for use in the NasoNeb (MedInvent, Medina, OH). All irrigations were carried out according to manufacturer specification. All experimentation was carried out in a nose-to-wall position.

The senior author (E.K.W.) performed all irrigations and was blinded to the cadaver's operated condition. A single observer (M.S.D.) carried out all observations. For each method and operated state, the methodology described by Abadie *et al.*[7] was used. When addressing the squeeze bottle, the observer graded two squeezes of the bottle to replicate how actual patients use the device. The NasoNeb was used only once, according to manufacturer specifications. This method was repeated for each of the four sinuses being evaluated.

Simulated Surgical Disease States

Previous research established reasonable simulations of severe chronic disease.[4,12] In this study, raw oyster fragments were used to replicate nasal polyps. The fragments were cut and placed endoscopically to completely fill the middle meatus without extension below the inferior edge of the middle turbinate. Wet cat food was used to mimic AFS and was spread like a pate in the medial half of the maxillary sinus to completely obstruct the sinus os, yet allow enough space laterally for a 30° endoscope to maintain intrasinus visualization.

Surgical Conditions

Three surgical disease conditions were used for this project. Condition 1 was a control that involved unoperated sinuses and no simulated disease. Condition 2 involved placement of raw oyster fragments (~5 × 20 mm) into the middle meatus to simulate type II polyposis with placement of cat food with a Toomey syringe into the medial half of the maxillary sinus to completely obstruct the ostium. Condition 3 involved a Draf IIA frontal sinusotomy, total sphenoethmoidectomy, and largest possible maxillary antrostomy. The middle turbinates were suture medialized to the septum. Simulated polyps were placed to fill the middle meatus to the inferior border of the middle turbinate. Finally, simulated fungal debris was squeezed into the medial maxillary sinus cavity.

Statistics

All ranked ordinal data were analyzed with nonparametric analysis (Friedman test with a *post hoc* Wilcoxon test). Statistical significance was set at $\alpha = .05$. Data were recorded into Microsoft Excel 12.2.7 (Microsoft Corp, Redmond, WA), and all statistics were performed in SPSS 17 (IBM Corp, Armonk, NY).

RESULTS

Frontal Sinus. Analysis of penetration magnitude data (Fig. 1) showed increased irrigation penetration for both irrigation ($p = 0.001$) and atomizer ($p = 0.05$). *Post hoc* testing revealed a significant increase in penetration between conditions 1 and 2 ($p = 0.016$) and conditions 1 and 3 ($p = 0.016$) for heavy irrigator penetration. Analysis of atomizer data did not demonstrate statistically significant penetration potential on *post hoc* testing between conditions 1 and 2 ($p = 0.083$) or conditions 1 and 3 ($p = 0.083$). Frequency data (Fig. 2) similarly displayed increased irrigation potential for both irrigation ($p = 0.004$) and atomizer ($p = 0.05$). Results of *post hoc* testing on irrigation data again showed significantly greater irrigation penetration in condition 1 than in condition 2 ($p = 0.025$) and condition 1 than in condition 3 ($p = 0.008$). Results of *post hoc* testing for the atomizer demonstrated significant differences between conditions 1 and 2 ($p = 0.083$) and conditions 1 and 3 ($p = 0.083$). Magnitude or frequency that compared the two diseased states (conditions 2 and 3) failed to show statistically significant differences in frontal penetration for either atomizer or irrigation.

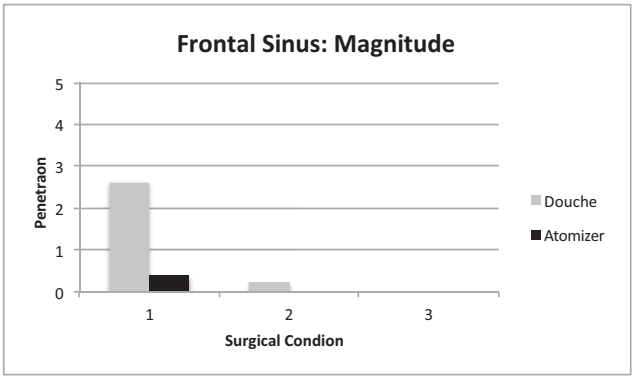

Figure 1. *Degree of penetration for frontal sinuses subtyped by irrigation system, based on a 0–5 visual scale.*

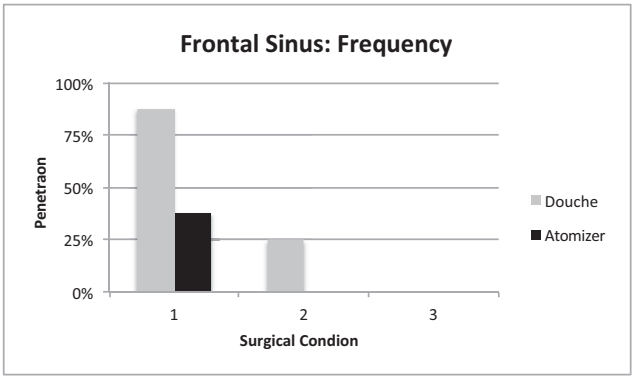

Figure 2. *Percentage of trials with successful irrigant penetration into the frontal sinuses by irrigation system.*

Maxillary Sinus. Analysis of penetration magnitude data (Fig. 3) showed increased irrigation penetration for both irrigation ($p = 0.002$) and atomizer ($p = 0.01$). Results of *post hoc* testing revealed significant differences between conditions 1 and 2 ($p = 0.016$) and conditions 2 and 3 ($p = 0.016$) for heavy irrigator penetration. Atomizer data exhibited statistically sig-

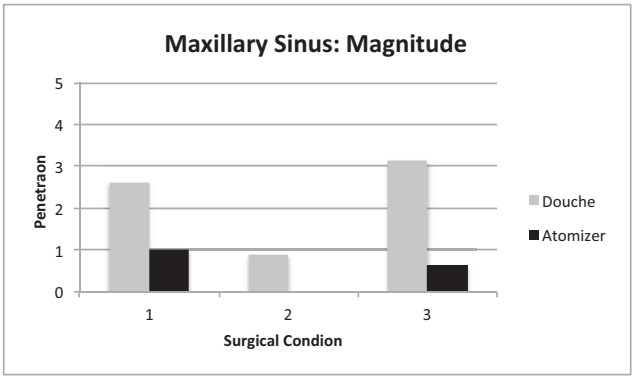

Figure 3. Degree of penetration for maxillary sinuses subtyped by irrigation system, based on a 0–5 visual scale.

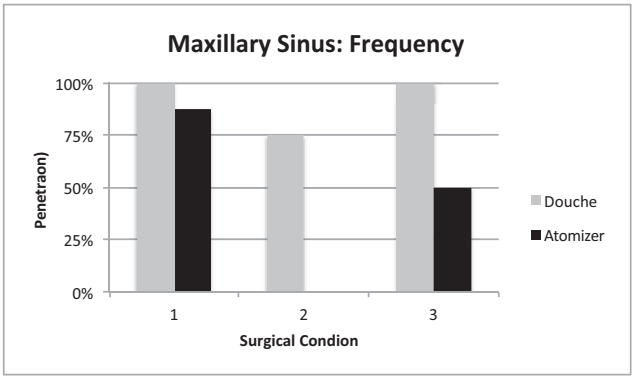

Figure 4. Percentage of trials with successful irrigant penetration into the maxillary sinuses by irrigation system.

nificant penetration potential on *post hoc* testing between conditions 1 and 2 ($p = 0.011$). Frequency data (Fig. 4) similarly displayed increased irrigation for atomizer ($p = 0.01$). Results of *post hoc* testing on atomizer data showed significantly increased irrigation penetration between conditions 1 and 2 ($p = 0.008$) and conditions 2 and 3 ($p = 0.046$). Magnitude or frequency that compared the unoperated nondiseased condition[1] and operated diseased states (condition 3) failed to show statistically significant differences in frontal penetration for either atomizer or irrigation.

DISCUSSION

AFS remains an incompletely described phenomenon; however, the combination of severe nasal polyposis and thick, eosinophilic mucus yields a condition that is often recalcitrant to standard treatment modalities. Surgery is the mainstay of treatment with three primary goals: remove diseased tissue, provide access for hygiene, and afford unobstructed access for topical delivery of medications. The latter two goals are paramount to the continued medical management these patients require.[13] Yet, although the benefits of postoperative sinonasal irrigation in chronic rhinosinusitis (CRS) have been well established,[14–16] the defined benefit of saline solution irrigation in patients with AFS remains unexplored.

Widely patent sinus ostia are beneficial in improving saline solution penetration[5] as well as placement of instruments within the sinus for debridement. The patent ostia are also thought to be beneficial in delivering topical medications. Albeit off-label, the benefits of steroids, *e.g.*, budesonide, in nasal irrigations have been supported in the CRS literature,[17] but there are few data that specifically pertain to AFS.

Although the current study did not evaluate the clinical effects of irrigation (with or without steroids) in patients with AFS, analysis of these data indicates that topical delivery of medication to the sinus cavities can be achieved, even when polyps and mucus are present. Further, saline solution entered the maxillary sinus well in the model, simulating return of polyps after endoscopic sinus surgery (ESS). Thus, heavy irrigation generally penetrated the maxillary sinus, regardless of condition. Previous ESS demonstrated a significantly higher volume of irrigant even in a diseased state. By contrast, penetration was completely inhibited in the frontal sinus in the simulated postoperative recurrence (condition 3), which showed how disruptive polyps and thick mucus are to effective irrigation. One unexpected finding was the larger amount of saline solution penetration in the frontal sinus in condition 2 (unoperated diseased) compared with condition 3. One possible explanation is that the back pressure present in the nonoperated condition improves the ability of saline solution to reach the frontal sinus. However, clinical conclusions from these observations should be drawn with caution.

There is good evidence that nebulizers deliver saline solution to the sinus cavities, especially after ESS.[11] However, these tend to be low-volume systems (10–20 mL) rather than high-volume (200–300 mL) systems such as the various sinus irrigation methods. When delivery devices are compared, results of this study indicated that the penetration of saline solution within the observed sinus was universally poor when the atomizer was used. This has been demonstrated previously in a non-AFS model.[7] However, it is arguable that the purpose of atomizers is to deliver highly concentrated topical medicines to target mucosa, whereas heavy irrigators serve to replace the function of diseased cilia. Benefits from budesonide in nasal atomizers have been supported in the CRS literature,[18,19] although a paucity of data exists that specifically regards use in the management of AFS.

In each experimental condition, the atomizer underperformed with respect to the frontal sinus. No fluid entered any sinus in the unoperated diseased condition (condition 2), and only a small amount of saline solution was seen in the maxillary sinus after ESS and disease recurrence (condition 3). Thus, this model of-

fers little support for using atomizers to irrigate or provide medicine to the paranasal sinuses in the patient with preoperative AFS.

Two principal limitations of this study arise. First, the use of cadaver material did not allow reporting of clinical outcomes. Although penetration of the sinuses differs, this did not necessarily translate into clinical benefits. Second, although the simulated nasal polyp material and fungal debris material have good face validity, they may have slightly different mechanical properties compared with actual human tissue, which may influence these results. It is plausible that the simulated polyp and mucus obstruct the sinus ostia completely during certain trials, although incompletely during other trials. Therefore, conditions would not be perfectly identical during each trial. However, we believe that this simulation is also realistic, and the physician has no way of knowing, in a real patient, whether or not an os is completely obstructed. It is also worthy to note that the physical properties of nasal polyps and fungal debris differ significantly among patients.

CONCLUSIONS

This study compared paranasal sinus penetration by using low-volume atomizers and high-volume irrigators in a simulated AFS model. Although previous surgery seems to improve the heavy irrigation potential in simulated recurrent severe chronic sinusitis of the maxillary sinus, the frontal sinus does not show the same benefit from previous Draf IIA sinusotomy. Thus, in recurrence of disease after thorough sinus surgery, early surgical intervention or aggressive medical management to reduce polyp burden may be warranted to allow continued effective irrigations.

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