Surfactant improves irrigant penetration into unoperated sinuses

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ABSTRACT

Background: Saline irrigations are proving to be a valuable intervention in the treatment of chronic sinusitis. The use of surfactants is a well established additive to topical treatments known to reduce surface tension and may prove to be a simple, nonoperative intervention to improve intrasinus douching penetration.

Methods: Six 30-mL, flat-bottomed medicine cups with circular holes cut through the bottom center and varying in diameter from 1 to 6 mm were created with punch biopsies. Water, saline, saline/dye, and saline/dye/surfactant were compared for maximum holding pressure via these modeled ostia. Holding pressures also were determined for cups with septal mucosa fused to the bottom with holes ranging from 1 to 6 mm. In addition, analysis was carried out with blood and blood/surfactant. Finally, five thawed, fresh-frozen cadaver heads were evaluated before any sinus surgery with water/dye and water/dye/surfactant for intrasinus penetration.

Results: Surfactant significantly improved the ability of all solutions to penetrate ostia in both the plastic cup and fused septal mucosa model. All nonsurfactant-containing solutions were not statistically different from one another, nor did surfactant change the ostial penetration of blood. Surfactant significantly improved the ability of sinus irrigant to penetrate unoperated sinus cavities (3.12 vs 3.5, $p = .021$).

Conclusions: The addition of surfactant to saline irrigation improves ostial penetration in undissected and undiseased cadavers. This has practical implications for unoperated patients seeking care for sinus-related symptoms in that we have now described a method for improving topical treatment of target sinus mucosa prior to surgical intervention.

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Saline irrigation of the nasal cavity and paranasal sinuses plays an integral role in the management of sinusitis. Growing evidence suggests that before performing sinus surgery, it is paramount that an attempt at medical treatment is made that includes nasal douching. In fact, some publications report nasal irrigations in conjunction with oral steroids and antibiotics to be just as effective as surgery for the symptoms of chronic rhinosinusitis.^{1–3} What currently is not clear is the degree of penetration that needs to be achieved to maximize this benefit. Our assumption is that the greater the irrigant distribution throughout the sinonasal cavity, the better the effect. Previous research has shown that the minimum dimension of an ostium is directly related to the ability for nasal irrigants to penetrate a sinus.^{4,5} However, other currently unexplored factors expected to affect penetration include the force required to overcome fluid surface tension and the holding pressure at the ostia, based on this formula: pressure equals surface tension of the fluid divided by the radius of the opening. Surface tension is further related to the boundaries created by the liquid-solid-air interface measured as the angle of contact (Θ).⁶

On the basis of these physical principles, irrigant penetration can be increased and the holding pressure can be reduced by using higher irrigant pressures, decreasing the surface tension, changing the angle of contact, or increasing the ostial radius. Increasing irrigant pressure has limited potential, however, because of constraints by pain and penetration into the eustachian tube and because, before surgery, changing ostial diameter or angle of contact is not readily accomplished. However, the use of surfactants is a well established additive to topical treatments known to reduce surface tension and may prove to be a simple, nonoperative intervention to improve intrasinus douching penetration. The aim of this study is to identify whether water and surfactant composition affect the ability to penetrate a paranasal sinus. Secondarily we plan to see how irrigant composition affects variable material/fluid interfaces.

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METHODS

Exempt status was first obtained from the Wilford Hall Medical Center institutional review board before receipt of cadaveric specimens. The project was divided into two complementary segments:

1. Fluid Physics

Fluid analysis was performed with a series of solutions and modeled ostia. Six 30-mL, flat-bottomed medicine cups with circular holes cut through the bottom center and varying in diameter from 1 to 6 mm were created with punch biopsies (Fig. 1). A second series of medicine cups, all punched with 7-mm holes, were then prepared with 1.5-cm squares of septal mucosa (mucosal side up), dermabonded, and sealed to the plastic overlying the 7-mm hole. Before sealing the mucosa to the cups, holes varying from 1 to 6 mm were punched through the septal squares on a Styrofoam block. The holes were remeasured and were found accurate, excluding the 3-mm hole, which measured at 2.5 mm. The cups were then suspended over secondary collecting cups (Fig. 2). The ostia models were dried thoroughly before creating a fluid column. Using a 5-cc pipette, fluid was slowly added to the suspended medicine cups down the side of the vessel. Column height was recorded when the following three events occurred: the formation of a fluid film over the hole, initiation of fluid drainage, and the residual left after drainage. The cups were then wiped dry with a paper towel, and the process was repeated in triplicate for each hole size and solution. Tested solutions included tap water (W), 0.9% saline irrigant (WS) (not significant; NS) (240 mL), WS plus three drops of McCormick Artificial Food Coloring (McCormick & Co., Sparks, CO) (WSD), dye solution (240 mL) plus 1 mL NeilMed Sinusurf Surfactant (NeilMed Pharmaceuticals, Santa Rosa, CA) (WSDS), and author's blood (J. W. R.) stored in green top (lithium heparinized tubes), and blood (24 mL) plus 0.1 mL surfactant. All experiments were performed under the same conditions at room temperature. Commercial products mentioned in this presentation are not intended to constitute an endorsement by the U.S. Air Force or any other federal governmental entity.

2. Cadaver Douching

Five thawed, fresh-frozen cadaver heads were prepared by creating maxillary, frontal, and sphenoid trephinations with a previously published methodology⁴ to facilitate intrasinus observation during douch-

Figure 1. Plastic cups with 1- to 6-mm holes cut through the base (2- to 6-mm cups shown) with fluid residuals for each hole size in place.

Figure 2. View from above showing septal mucosa sealed with Dermabond to the base of a plastic 7-mm cup. Holes in the septum were cut ranging from 1 to 6 mm.

Table 1. Ranked ordinal scale describing nasal irrigant penetration into sinus cavities

0	No penetration
1	Bubbles/mist
2	Drops/dribble
3	Filled up to one-third of sinus
4	Filled up to two-thirds of sinus
5	Completely full, spills out of sinus

ing. Sinus irrigations were carried out on each cadaver in a nose-to-wall orientation by using the Neilmed SinusRinse bottle filled with either water plus dye or water plus dye plus surfactant. All trials were run in duplicate, and no surfactant was used until all of the water plus dye measurements had been taken. All irrigations were performed by the same author blinded to the intrasinus findings while using the same pressure and technique for all attempts. Half of a bottle (~120 mL) was used in each attempt and then suctioned between irrigations. The observations were graded on a previously published ordinal scale⁴ (Table 1).

Statistics

The results were collected and stored in a Microsoft Excel spreadsheet. Using an integration formula based on the shape of the test sample cup, fluid heights at any volume were automatically tabulated for analysis. Graphical and statistical analysis of these results were calculated using SPSS 19 (Chicago, IL). A Mann-Whitney U test was

used for repeated measure analysis for each hole size. A Wilcoxon signed-rank test was used for paired cadaveric results.

RESULTS

Relationship of Pressure to Ostial Diameter

Maximum holding pressure supported over modeled ostia behaved in an exponential fashion with asymptotes as the diameter approached zero and as the ostia increased in size. These relationships were best visualized on log-log axes (Figs. 3–5).

Solution Versus Ostial Penetration

Statistical analysis found no differences between water, water plus salt, and water plus salt plus dye in its ability to penetrate the plastic cup model (Fig. 3). However, the addition of surfactant reduced the holding pressure significantly relative to solutions without surfactant (Fig. 3 and Table 2). This trend remained true for the harvested mucosa sealed to the base of the plastic cup (Fig. 4). Analysis of heparinized blood showed no significant improvement of ostial penetration with addition of surfactant (Fig. 5).

Surfactant Impact on Ostial Penetration in Cadaver Model

Paired analysis of penetration before and after the addition of 1 mL of surfactant to a 240 mL bottle of irrigant showed a significant increase in entry of irrigant into undissected sinuses (3.12 vs 3.5, $p = .021$). Analysis by specific sinus revealed all trended toward improvement with surfactant, but none reached statistical significance.

DISCUSSION

Surface tension arises from the natural tendency of fluid molecules to arrange themselves in the orientation with the smallest surface area to allow a fluid to resist external forces. At the molecular level, Van der Waals forces, intramolecular forces pulling molecules of a fluid toward each other equally in all directions, provide the cohesive force. Macroscopically, this manifests as droplets of water or beads of mercury. Surface tension enables fluids to break Archimedes' principle as demonstrated by a razor blade floating on water or insects walking across water. At the site of an opening in a container of fluid, surface tension creates a holding pressure in a static fluid or fluids with a low Reynolds, Weber, and Froude numbers. The pressure occurring at an ostium is based on fluid density and the height of the fluid above the center of the ostium. In a static system, the hydrostatic fluid pressure must be less than or equal to the surface tension of the fluid at the ostia. Hydrostatic pressure ($P = \rho gh$) is calculated by multiplying density (kg/m^3), gravitational forces (m/s^2), and height (m). For this initial experimental analysis, ostia were considered in the horizontal plane. The maximum height of fluid held at the ostia, determines surface tension.⁷

Surface tension is affected by temperature, fluid heterogeneity, and molecular composition. Surface tension varies with the addition of solutes. Inorganic salts increase surface tension, while alcohols and surfactants decrease surface tension. In the physiologically relevant intranasal temperature ranges, conservatively 15–38 °Celsius, surface tension changes are minimal in water; only 0.0039 N/m difference.⁸ Pure water has a surface tension of 71.97 dynes/cm at 25 °Celsius, while surface tension of normal saline is 68 dynes/cm, blood 53 dynes/cm, and surfactant 32 dynes/cm.

The angle of contact or θ is obtained from the interaction between the air/fluid/solid interface. At contact angles less than 90°, the surface is hydrophilic and a fluid will wet the surface, while larger contact angles represent hydrophobicity and result in bead formation. The contact angle is a combination of fluid and surface properties in thermodynamic equilibrium. Surface or fluid property alterations change the contact angle and, ultimately, the surface tension at an opening. Research has demonstrated that dry oral mucosa is a hydrophobic surface.⁹

Our research reveals that in an experimental model, surfactant significantly reduces the holding pressure of an ostia relative to

Figure 3. Log-log relationship of the penetration of various solutions through holes created in the base of plastic medicine cups. The holding pressure (y axis) is inversely related to the diameter of the hole (x axis). The addition of surfactant (dashed line) leads to a significant reduction in holding pressure required to penetrate the simulated ostia. There were no differences noted between nonsurfactant-containing solutions (dotted line).

Figure 4. Log-log relationship of holding pressure (y axis) to simulated ostial diameter (x axis) for dried nasal septum. Addition of surfactant (dashed line) significantly reduced holding pressure required to penetrate ostia relative to the water plus dye solution (dotted line).

water, saline, or saline plus dye. Extrapolated further, when tested in an undissected cadaver model, surfactant improves intrasinus penetration during nasal douching. Because treatment of sinus disease is moving toward topical medications, most research on improving the penetration of irrigants has been tied to surgical intervention.^{4,5} This research is the first evidence that by merely adjusting the physical properties of the irrigant, increased topicalization can be achieved. Due to the nature of our cadaveric model there is no ability to assess outcome efficacy; however, our results seen together with Chiu's

report of improved chronic rhinosinusitis symptoms with the addition of surfactant may actually be evidence that the benefit reported by Chiu et al¹⁰ may in fact be due to increased penetration of the saline irrigant in addition to biofilm displacing effect.

Another perhaps less remarkable but important discovery is that water, saline, and blue dye do not significantly change the ability of irrigant to penetrate ostia. This provides justification for methodologies that use any of these solutions in a laboratory setting, which requires coloration of fluid to make it visible, and transposing the

Figure 5. Log-log relationship of holding pressure (y axis) to simulated ostial diameter (x axis) for plastic medicine cups tested with blood. The addition of surfactant did not change the holding pressure.

Table 2. Mann-Whitney U comparison of the column of water supported by varying hole size versus saline (WS), saline plus dye (WSD), and saline, dye, and surfactant (WSDS). Addition of surfactant caused a statistically significant change at all hole sizes for the solution relative to water, saline, and saline plus dye

	6 mm	5 mm	4 mm	3 mm	2 mm	1 mm
W vs WS	NS	NS	NS	NS	NS	NS
W vs WSD	NS	NS	NS	NS	NS	NS
W vs WSDS	0.043	0.046	0.037	0.046	0.046	0.050
WS vs WSDS	0.046	0.046	0.037	0.043	0.043	0.050
WSD vs WSDS	0.043	0.043	0.050	0.043	0.043	0.050

findings into a clinical application, which will not use dyes. The inclusion of the blood data is meaningful in that as we search for methods to improve sinus irrigation immediately postoperative, functional endoscopic sinus surgery FESS blood is a component of the nasal mieu. Improved irrigation may help decrease dependent blood and clot burden from the operated sinuses and thereby decrease the inflammatory cascade in the immediate postoperative FESS setting. Our data do not support this hypothesis as a useful intervention at this surfactant concentration.

CONCLUSION

The addition of surfactant to saline irrigation improves ostial penetration in undissected and undiseased cadavers. This has practical implications for unoperated patients seeking care for sinus-related symptoms in that we have now described a method for improving topical treatment of target sinus mucosa before surgical intervention. Addition of the studied concentration of surfactant to blood does not appear to change its surface tension and therefore may not be a useful addition to the immediate postoperative sinus rinse.

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