

ORIGINAL RESEARCH–SINONASAL DISORDERS

Effect of microporous polysaccharide hemospheres (MPH) on bleeding after endoscopic sinus surgery: Randomized controlled study

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

ABSTRACT

OBJECTIVES: Absorbable hemostatic agents are commonly used after endoscopic sinus surgery (ESS). MPH (microporous polysaccharide hemospheres) is a novel hemostatic powder that is rapidly absorbed. The goal of this study was to examine the effects of MPH on bleeding after ESS.

STUDY DESIGN: Randomized, controlled, single-blinded.

SETTING: Tertiary university hospital.

SUBJECTS AND METHODS: Patients undergoing bilateral (symmetric) ESS for CRS by the same surgeon were randomized to unilateral treatment with MPH at surgical conclusion. The untreated opposite side served as a control. All patients received standard postoperative management. Patients completed symptom diaries using visual analog scales (VAS, scored out of 100) at baseline and through postoperative day (POD) 30. Outcomes including bleeding, pain, obstruction, and nasal discharge were recorded separately for left and right sides.

RESULTS: Forty patients (19 men, 21 women) with an average age of 48.3 years were included. There were no complications, and all patients were discharged home the same day. The mean bleeding score on POD one for MPH-treated sides was 22.5 vs 39.0 for untreated controls (mean reduction 16.5, $P < 0.0001$, 95% CI -23.2 to -9.7). The scores for bleeding at baseline and at all other post-treatment days were not significantly different ($P > 0.05$). There were no other significant differences between MPH-treated and control sides in any other variables measured.

CONCLUSION: The use of MPH after ESS results in significantly less bleeding in the early postoperative period with no increase in pain, obstruction, or nasal discharge. Patients treated with MPH follow a normal postoperative recovery otherwise.

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At the conclusion of endoscopic sinus surgery (ESS), important issues include assuring postoperative hemostasis and preventing adhesion formation in critical areas. Historically, nonabsorbable nasal packs were placed in the

middle meatus. However, these are uncomfortable for the patient and reopen the wound during removal.¹ Interestingly, for the purpose of preventing adhesions, a recent review found that there are few data on the benefit of standard nonabsorbable packing over absorbable packs or no packing at all.² Controlled studies have clearly demonstrated that patients have a strong preference for absorbable packing over nonabsorbable.³

The use of an absorbable hemostatic agent following ESS obviates the need for packing removal. Due to their excellent hemostatic properties and superior patient comfort, a number of bioabsorbable agents have been developed and are now routinely used after ESS. These materials differ substantially in their mechanisms of action, composition, method of delivery, and clearance profiles.

Microporous polysaccharide hemospheres (MPH, commercially available as Arista and Hemaderm, Medafor, Inc, Minneapolis, MN) is a novel absorbable hemostatic powder that is rapidly cleared within 24 to 48 hours. Acting as a “molecular sieve” by osmotically extracting fluids from blood, MPH particles (diameter of 30-100 μm) concentrate platelets and other formed elements, promoting the formation of a fibrin clot. MPH does not require any preparation, heating, or mixing prior to use. In comparison to biomaterials derived from animal sources, MPH, which is made from purified potato starch, is hypoallergenic and carries no inherent risk of disease transmission.⁴

Previous studies in other surgical specialties have established the hemostatic properties of this material.⁴⁻⁷ Although MPH was FDA approved for use in otolaryngology in 2005, its use in our specialty was only recently described.⁸ The previous study was a nonrandomized, uncontrolled study in which we reported our initial experience with the safety of this substance in postsurgical human sinuses. The objectives of the present study were to systematically examine the efficacy of MPH in reducing bleeding after sinus surgery and to explore the impact of this sub-

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stance on other sinonasal symptoms during the recovery period.

MATERIALS AND METHODS

Patient Selection

The study population consisted of patients undergoing bilateral, symmetrical ESS by the senior author (R.S.) using standard techniques for CRS with or without nasal polyps. All patients were diagnosed with CRS refractory to maximal medical therapy and had evidence of significant disease on post-therapy CT imaging. Patients meeting inclusion criteria were enrolled consecutively into this randomized, controlled, and blinded study. Patients with massive nasal polyposis (extending to the nasal vestibule), sinonasal neoplasia, personal history of bleeding disorders, or routine use of anticoagulants were excluded. Patients who required septoplasty or any unusual surgical approaches (external techniques or frontal drill-out surgery) were also excluded. Approval from the Saint Louis University Institutional Review Board was obtained.

Sample Size

The study design was a two-treatment, parallel design. The statistical power was assumed to be 80 percent with the needed significance level (two-tailed alpha error) assumed to be 5 percent. Using previous data collected on a similar population using the same visual analog scales (VAS) for postoperative bleeding, the mean on day one was 46.1 with a SD of 15.1. To assume clinical relevance, a sample difference of 30 percent (difference between means of the two groups = 14) was used. Sample size was determined to be 40 patients using the Harvard method (http://hedwig.mgh.harvard.edu/sample_size/quant_measur/para_quant.html).

Outcome Measures

Patient-centered outcomes of this study were evaluated using a standardized symptom diary created to track postsurgical symptoms experienced from each side of the nose. Standardized questionnaires using visual analog scales (scored from 0 to 100) were completed preoperatively for baseline measurements as well as on postoperative days (POD) one, seven, 14, and 30. Symptoms evaluated included bleeding, obstruction, pain, and anterior nasal discharge, which were each scored separately for left and right sides. Clear and simple definitions for the VAS for each symptom were provided both verbally and in writing. Descriptive anchors for bleeding were 0 = no bleeding, 50 = moderate bleeding requiring occasional changing of drip pad, and 100 = severe or constant bleeding requiring medical intervention. Descriptives for secondary outcomes were pain: 0 = no pain, 30 = mild (relieved with over-the-counter medication), 60 = moderate (relieved with narcotic pain medication), and 100 = severe (requiring intravenous pain medication); obstruction: 0 = breathe easily through the side, 50 = able to breathe with difficulty, and 100 =

totally blocked; and discharge: 0 = no discharge, 50 = requiring frequent use of tissue, and 100 = constant discharge. The diaries were collected during postoperative visits and analyzed at the conclusion of the study. All data were entered into a standard spreadsheet (Microsoft Excel, Version 2003, Redmond, WA). Comparisons were made using univariate (paired Student *t* test) analysis.

Surgery

Following induction of general anesthesia, the nose was prepared with oxymetazoline (0.05%) spray, submucosal injection of one percent lidocaine with 1/100,000 epinephrine, and cocaine (4%)-soaked pledgets. ESS was then performed bilaterally with the same sinuses addressed on each side using conventional techniques. At the conclusion of the procedure, MPH was applied per manufacturer's instructions to *only one side*. The MPH powder was used to coat all areas of the operated field (Fig 1). The opposite side was left untreated. No other forms of packing or splints were used. The side to be treated was assigned preoperatively by using a randomly generated number scheme based on patients' date of birth. Patients were unaware of which side was to receive treatment intraoperatively. All patients were discharged home postoperatively with pain medication, a seven-day course of antibiotics, and instructions to begin saline irrigations on POD two. They were reminded to complete their symptom diaries for POD one at 24 hours after surgery, and to bring their diaries with them to all subsequent follow-up visits. Standard postsurgical debridements were performed bilaterally on POD seven. No residual MPH substance was identifiable in any of the sinus cavities.

RESULTS

Forty consecutive patients (19 men, 21 women) with a mean (SD) age of 48.3 (13.6) years (range, 21–79 years) comprised the study group. All patients completed symptom diaries for the entire study period. The demographics of the patient population are highlighted in Table 1. As shown, the mean (SD) preoperative Harvard CT stage was 3.1 (0.8); inter-quartile ranges were: 11 study patients in stage 2, 14 patients in stage 3, 15 patients in stage 4. Forty-five percent of the procedures were revisions, and a majority of cases were performed using image-guidance technology. The average estimated intraoperative blood loss (SD) was 66.5 mL (28.8). There were no intraoperative complications.

The mean bleeding score on POD 1 for the MPH-treated sides was 22.5 vs 39.0 for untreated controls (mean reduction 16.5, $P < 0.0001$, 95% CI –23.2 to –9.7). This was a highly significant reduction in bleeding, as illustrated in Figure 2. The patient scores for bleeding at baseline and at all other post-treatment days were not significantly different between MPH-treated and untreated sides ($P > 0.05$). Postoperative bleeding scores continued to decrease between

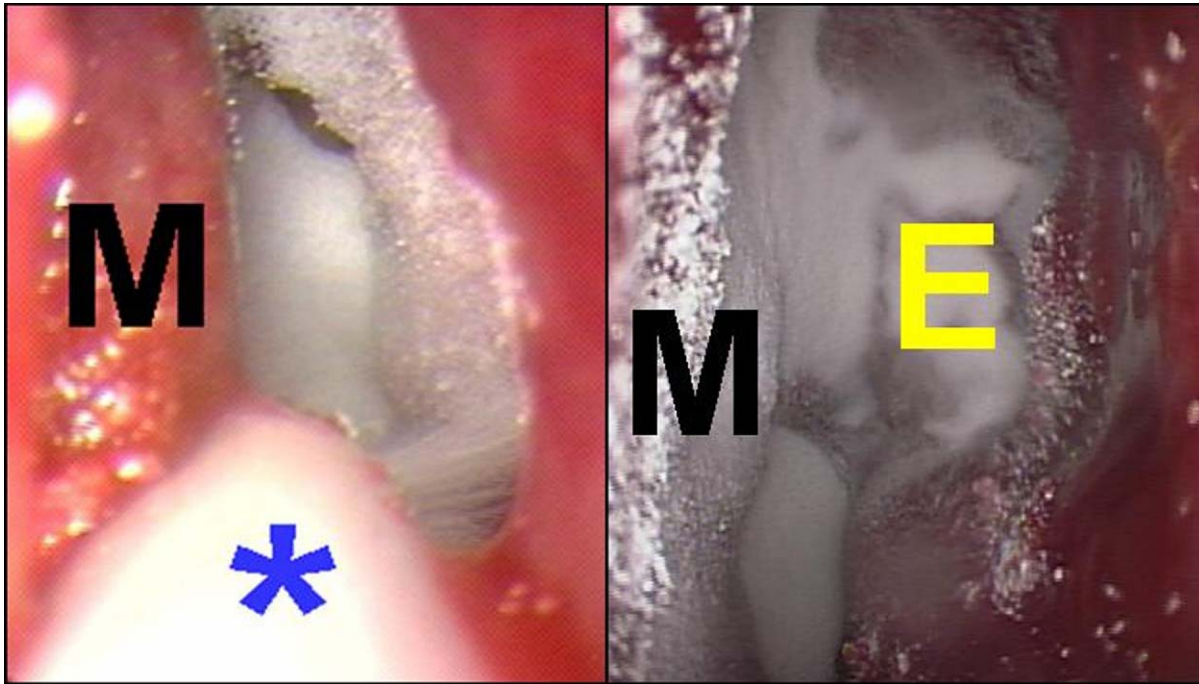


Figure 1 Endoscopic view of left middle meatus during (left panel) and after (right panel) application of MPH at the conclusion of surgery (M, middle turbinate; E, ethmoid cavity; *, MPH applicator).

time points in a significant fashion until day 14, where the trend leveled (Fig 3). By POD 30, bleeding bilaterally returned to below baseline levels.

There were no significant differences detected in pain, obstruction, and nasal discharge between MPH-treated and untreated sides at any time point of the study. As expected, pain significantly increased on POD one bilaterally compared to baseline ($P < 0.0001$), but then significantly decreased between each time point following, and continued to decrease to below preoperative levels by POD 30 ($P = 0.0002$), as demonstrated in Figure 4. During the postoperative period, nasal obstruction on both sides followed a steadily declining course (Fig 5). Obstruction decreased significantly between PODs one and seven ($P < 0.0001$) and PODs seven and 14 ($P = 0.017$), on both sides. Improvement then tapered, but POD 30 scores for obstruction were greatly improved on both sides vs baseline ($P < 0.0001$). Anterior nasal drainage increased slightly on POD one compared to baseline ($P >$

0.05), but between PODs one and seven it decreased significantly ($P = 0.0006$) on both treated and untreated sides. Patient scores for pain ($P = 0.0002$), obstruction ($P < 0.0001$), and drainage ($P < 0.0001$) improved significantly compared to preoperative baseline levels by POD 30.

DISCUSSION

The choice of packing materials, or whether packing is used at all after ESS, is dependent upon the individual surgeon

Table 1
Patient characteristics

Study patients	40
Age	48.3 y
Male sex	19 (47.5%)
CRS without polyps	31 (77.5%)
CRS with polyps	9 (22.5%)
Harvard CT Stage	3.1
Primary ESS	22 (55.0%)
Revision ESS	18 (45.0%)
Use of image guidance	24 (60.0%)

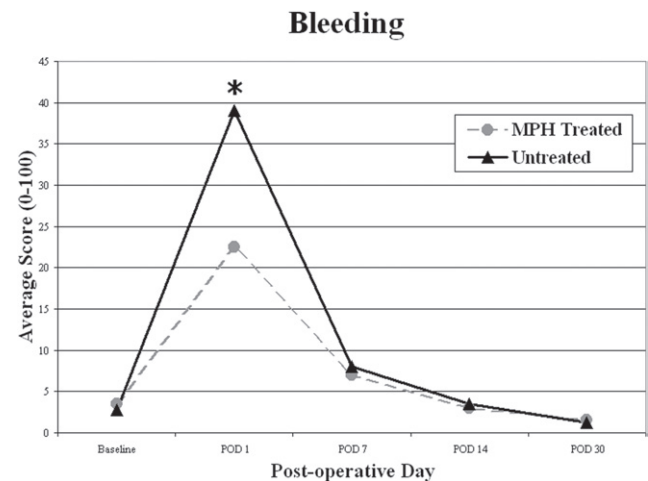


Figure 2 Postoperative bleeding scores showing significant difference between treated and untreated sides on POD one. Note no difference between MPH-treated and untreated sides at baseline and at PODs seven, 14, and 30.

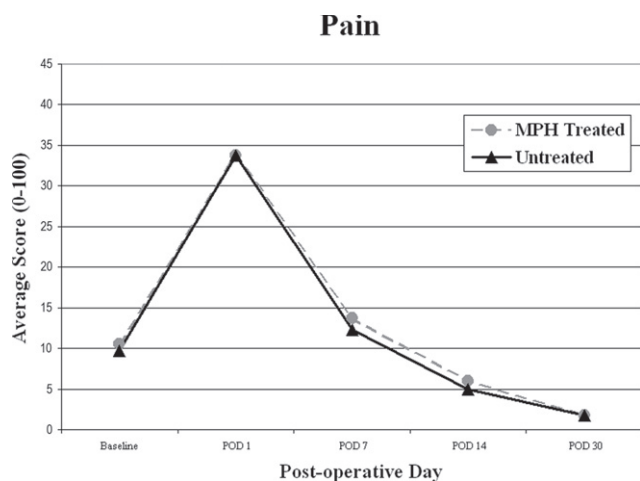


Figure 3 Postoperative pain scores showing similar curves for MPH-treated and untreated sides.

and the particular details of the case. Although the risk of significant hemorrhage following ESS is quite small,⁹ some degree of epistaxis is encountered postoperatively when no nasal packing is placed. The extent of bleeding that is to be expected following ESS has been shown to be significantly underestimated by patients.¹⁰ The “nuisance bleeding” experienced for a few days after surgery can be a source of significant anxiety and may negatively impact the patient’s sense of overall recovery from the procedure.¹⁰ This study was designed, therefore, to examine the efficacy of MPH after sinus surgery, from the *patient’s* perspective.

MPH was found to be effective in reducing the amount of bleeding experienced during the early recovery period after ESS. On POD one severe bleeding was rarely encountered from either treated or untreated sides, and most patients reported moderate bleeding only (mean 39/100 VAS) from the untreated side. Comparatively, there was a 40 percent reduction in bleeding on the side treated with MPH. In light of patients’ concerns over postoperative bleeding,

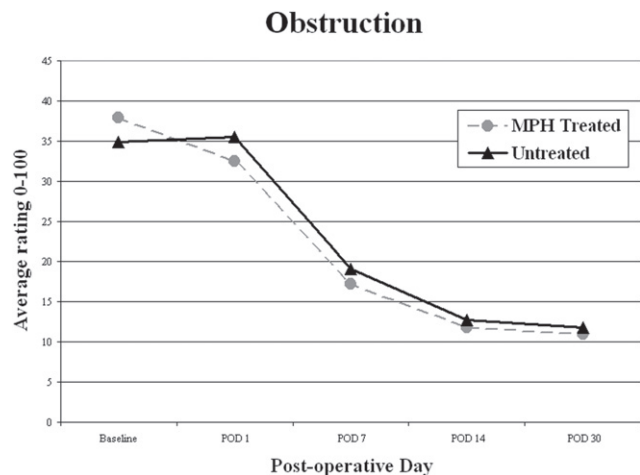


Figure 4 Postoperative obstruction scores showing bilateral improvement from baseline following recovery from surgery.

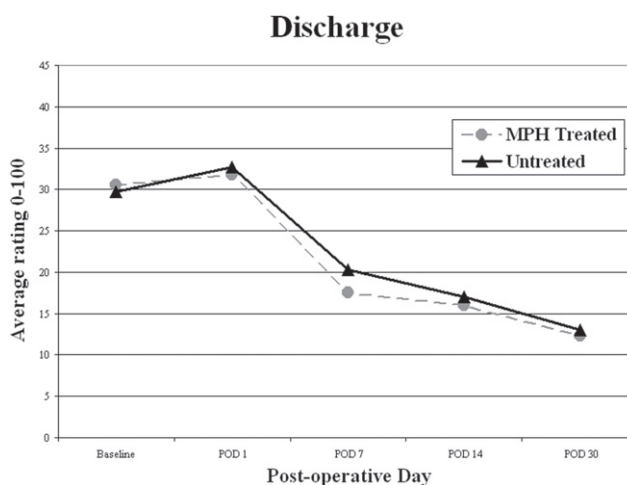


Figure 5 Postoperative anterior nasal discharge scores demonstrating bilateral improvement over recovery period.

this reduction was clearly distinguishable by the patient (each patient served as his or her own untreated control) and likely significant enough that it would be meaningful clinically.

Since MPH is quickly and completely cleared from post-surgical sinus cavities, it follows that the hemostatic effects of this substance are pronounced for only a few days after application, when most postoperative bleeding tends to occur. The “no treatment” control used in this study permits comparison to what the patient would otherwise have experienced as “normal recovery” from surgery. A noteworthy negative finding was that the use of MPH did not significantly alter the pain, obstruction, or anterior nasal drainage that patients experienced during recovery from ESS. There were no differences in MPH-treated vs MPH-untreated sides at any time point for these other symptoms. These sinonasal symptoms were additionally studied to more thoroughly explore the impact of this packing material. A substance that occupies the middle meatus for a variable length of time postoperatively could potentially contribute to a number of sinonasal complaints during the recovery period. The effect of packing materials on other symptoms, besides epistaxis, has not been routinely evaluated in other studies.

Available hemostatic agents function by either providing actual clotting components (eg, fibrin glues) or a surface for clotting to be stimulated (eg, collagen, gelatin sponge, oxidized cellulose). Key distinguishing features among absorbable agents include cost, ease of use, the presence of animal products, and importantly, clearance profiles. Although biomaterials are all resorbed over time, the large majority persist for weeks, exposing regenerating mucosal elements to foreign materials. Animal studies evaluating the effects of prolonged exposure of these substances on healing sinus mucosa have shown that they can impair mucosal regeneration, inciting an inflammatory reaction with frank incorporation of foreign materials noted.^{11,12} Investigations in human subjects following ESS have further demonstrated an increased risk of adhesion and granulation formation

with the use of longer-lasting biomaterials such as FloSeal (Fusion Medical Technologies, Mountain View, CA).^{13,14}

Starch-based MPH comes in a ready-to-use container with a flexible tip applicator permitting product delivery into various regions of the sinonasal tract. Its mechanism of action and clearance kinetics are unique among available biomaterials. Importantly, animal studies have demonstrated that this substance does not interfere with healing or intact sinus mucosa and is quickly cleared from the sinonasal tract.¹¹ Early experience in human patients suggests that there is no increased risk of postoperative synechiae, although controlled studies are required to substantiate these initial observations.⁸

This study is limited by its sample size and reliance on patient self-reporting of symptoms. We attempted to mitigate the biases associated with patient-centered reporting by blinding patients to the side of treatment and by providing clear instructions on when and how to complete the standardized diaries. Whether or not patients actually followed through with these instructions rigorously is of course unknown. In addition, the VAS used is not validated and is not objective. It is possible that in the early postoperative period the cause(s) of some of the symptoms examined may not be directly related to the effect of the packing material used or not used. It is also appreciated that patients may not be able to reliably differentiate and report upon the left- vs right-“sidedness” of a particular symptom (such as facial pain, for example), although this clearly was not an issue with epistaxis, the primary endpoint of the study. A final limitation is that the control side had no packing at all. Many surgeons do use other forms of packing and if comparing MPH to some other packing (ie, nonabsorbable sponge) bleeding outcomes may have been different.

CONCLUSION

MPH is a novel absorbable hemostatic agent with a unique mechanism of action and rapid clearance profile. The use of MPH after ESS results in significantly less bleeding in the early postoperative period with no increase in pain, obstruction, or nasal discharge. Patients treated with MPH follow a normal postoperative recovery otherwise.

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AUTHOR CONTRIBUTIONS

Jastin Antisdel, study design, data management, writer; **Jackie West-Denning**, data management, graph creation; **Raj Sindwani**, study design, data management, writer.

DISCLOSURES

Competing interests: This project was funded in part by an unrestricted educational grant from Medafor, Inc (Minneapolis, MN, manufacturer of MPH). The company had no role in the study design, data analysis, interpretation, or the decision to publish the findings of this study.

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