FloSeal use in endoscopic sinus surgery: effect on postoperative bleeding and synechiae formation

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Abstract

Purpose: The objective of this study is to evaluate the effect of the hemostatic agent, FloSeal (FS), on bleeding and healing after functional endoscopic sinus surgery.

Methods: We performed randomized, double-blinded, controlled study at a tertiary care center. Patient nasal sides were randomized to FS or control. After completion of sinus surgery, FS was placed in the appropriate nasal cavities followed by saline-soaked neuropatties in both nasal cavities. Control sides received saline-soaked neuropatties alone, without FS.

Results: Forty-five patients were enrolled. Mean time to cessation of bleeding in recovery was 16.4 and 30.8 minutes for the FS- and control-treated sides, respectively \((P = .028)\). Patients maintained diaries for 7 days postoperatively and reported similar durations of bleeding at home, but indicated less discomfort on the FS-treated side. Postoperative endoscopic examinations revealed significantly less crusting in FS-treated nasal cavities at 1 week, but significant differences at 1 and 3 months. There were no differences in postoperative scarring or middle turbinate lateralization.

Conclusions: Use of FS after functional endoscopic sinus surgery resulted in less bleeding, immediately postoperatively, and less discomfort, and did not increase the incidence of crusting or scarring compared with control.

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1. Introduction

The use and optimal type of nasal packing after functional endoscopic sinus surgery (FESS) has long been debated [1]. Although every sinus surgeon has in common the goals of excellent hemostasis and rapid postoperative healing with avoidance of scarring or medial turbinate lateralization, there is little agreement on how best to achieve these goals. The advantages of packing the sinonasal cavity at the conclusion of surgery include improved hemostasis, reduced crusting and scarring, and decreased frequency of medialization of the middle turbinate. Nasal obstruction, increased risk of infection, and patient discomfort, especially on removal, are the primary disadvantages of nasal packing [2]. Biodegradable packing agents are thought to offer the advantage of improved hemostasis without added patient discomfort or need for removal.

FloSeal (FS) (Baxter International Inc, Deerfield, Ill) is a bovine collagen-derived gelatin matrix that is combined with bovine thrombin at the time of use. Because of its granular consistency, it conforms to irregular surfaces and ensures direct contact of the thrombin with the hemorrhagic tissue surface. Since the matrix swells, it also provides some tamponading of injured vessels. Because blood permeates between the gelatin granules, clot formation is rapid and is structurally supported by the matrix. Undisturbed, the material is fully resorbed within 6 to 8 weeks [3].

Given the limited data available on the use of FS as a biodegradable hemostatic agent for FESS, we performed a controlled, randomized, double-blinded study to evaluate its effect on postoperative hemostasis, pain, and healing.
2. Methods

2.1. Study design

Forty-five patients scheduled for routine bilateral FESS were enrolled in a controlled, randomized, double-blinded study (institutional review board approved). Informed consent was obtained at the time of preoperative evaluation. All patients had their preoperative sinus computer tomograms graded as per Lund and Mackay [4].

2.2. Surgical technique and postoperative management

All patients were placed under general anesthesia. Topical cocaine solution and/or lidocaine/phenylephrine solution was used for local anesthesia and vasoconstriction in the nasal cavity. One percent lidocaine with epinephrine was injected submucosally at the appropriate surgical sites. Appropriate endoscopic sinus surgery was performed. No cases were altered or discontinued because of excessive bleeding.

When the procedure was completed, each side was randomized to FS or control; prerandomized envelopes were opened sequentially and patients were assigned to a group according to the instructions in the envelope. FloSeal was prepared immediately before use according to the manufacturers instructions. Briefly, the bovine thrombin was reconstituted in sterile saline and mixed with the gelatin matrix. The final thrombin concentration was 1000 U/mL. FloSeal was placed in the appropriate nasal cavities followed by saline-soaked neuropatties in both nasal cavities. Control sides received saline-soaked neuropatties alone without FS. The resident surgeon performed this component of the procedure in the absence of the attending surgeon, so as not to bias his postoperative evaluation of the patient.

All patients were discharged the same day on a 2-week antibiotic regimen along with a nasal steroid spray and high-dose guaifenesin. Patients were instructed to initiate aggressive nasal saline irrigations on postoperative day 1 as per our routine postoperative protocol. They returned for follow-up endoscopic examination in clinic at 1 week, 1 month, and 3 months postoperatively. During these examinations, patients were evaluated for significant crusting and scarring that required debridement and division of scar tissue, respectively. At the time of follow-up, the primary surgeon could not distinguish nasal cavities treated with FS from controls.

2.3. Reporting

Nursing staff in the Post-Anesthesia Care Unit (PACU) carefully monitored all the patients, and the time to cessation of bleeding was noted for each side. Patients were discharged with a postoperative diary to make daily records during their recovery. On a daily basis, the degree of bleeding, number of dressing changes, and relative right vs left discomfort were recorded. Patients were asked to report the nasal side with greater pain compared with the opposite side. If pain was not different between sides, they reported “same.” This reported technique attempted to correct for the postoperative pain associated with the surgery itself as much as possible and to allow a comparison between tested and controlled sides.

3. Results

3.1. Patients and treatments

Twenty-one men and 24 women enrolled into the study. Their average age was 46 years (range, 18–72 years). The average age of the male group was slightly but significantly greater than the female group (50.4 vs 43.2 years, \( P = .046 \)). The preoperative Lund and Mackay radiological scores [4] were similar for sinuses treated with either FS or control.

At the time of the operation, each side was randomized to treatment with FS or control. Forty-seven sides were assigned...
to the control group (25 left, 22 right), and 43 sides were assigned to the FS group (20 left, 23 right). Twenty patients received same treatment on both sides, whereas 25 patients received different treatments on each side.

3.2. Postoperative bleeding

The average time to cessation of bleeding after arrival in the PACU was 16.4 minutes for the sinuses treated with FS and 30.8 minutes for the control sinuses ($P = .028$). Fig. 1 shows the cumulative percentage of patients in each group still bleeding at time of arrival in the PACU (39.4% FS, 61.5% control) and after 30 (12.1% FS, 33.3% control), 60 (3.0% FS, 7.7% control), and 90 minutes (0% in both groups). Thus, by 30 minutes after completion of the operation, 88% of FS sinuses were hemostatic vs only 67% of the control group.

When patients’ postoperative diaries were reviewed, there was no difference in time to complete cessation of bloody discharge (average 2.9 days in both groups). Fig. 2 shows the cumulative percentage of patients in each group with bloody discharge on each postoperative day. Patients treated with FS on both sides reported a slightly lower number of nasal-drip-dressing changes (average, 5.4; range, 1–19) than patients in the bilateral control group (average 6.6, range 1–20), before cessation of bleeding, but this was not significant and is obviously a very subjective measure.

3.3. Postoperative pain

The postoperative diaries of patients treated with FS on one side and control on the other were used to assess relative postoperative pain. Fig. 3 shows how these patients localized the pain on each postoperative day. Over the first postoperative week, an average of 20.8% of these patients complained of greater pain on the FS side, whereas 34.8% noted greater pain on the control side. On average, 44.4% could not perceive a difference. Based on $\chi^2$ analysis, patients experienced, on average, significantly less pain on the FS-treated side ($\chi^2 = 4.88, P = .027$).

3.4. Postoperative crusting and scarring

Patients were evaluated for crusting and scarring/lateralization of the middle turbinates at 1 week, 1 month, and 3 months. Patient compliance with these strict follow-
up times was only 95%, 88%, and 45%, respectively. All patients had relatively equal but small amounts of bloody debris present in the sinuses that required removal under endoscopic guidance in the office 1 week after surgery. At the 1-week follow-up (Fig. 4), sinuses treated with FS were significantly less likely to exhibit crusting (2.4% vs 18.6% control, \( P = .015 \)). Differences at 1 and 3 months were not statistically significant. There was no significant difference in scarring or medial turbinate lateralization at any follow-up (Fig. 5).

4. Discussion

The present study evaluates the utility of a dissolvable hemostatic agent, FS, in the immediate and extended postoperative period after FESS. In this double-blinded, controlled, randomized study, FS was noted to result in a significantly reduced bleeding in the immediate postoperative period. However, there were no significant differences in bleeding between FS-treated and control sinuses during the first postoperative week, as assessed by patients. Thus, FS offers a significant hemostatic advantage in cases where immediate postoperative bleeding is a concern. Studies in other surgical fields have shown FS to be extremely effective in controlling intraoperative and postoperative bleeding [3,5,6]. A preliminary report of FS used intraoperatively during FESS demonstrated adequate control of postoperative bleeding without apparent adverse effect on healing [7]. However, this study was not randomized or controlled. Taken together, these data and the present study suggest that FS may be of particular use in cases with greater than normal intraoperative bleeding or coagulation deficits.

Patients treated with FS on one side and control noted significantly less pain on the FS-treated side. The basis for this is unclear but may simply represent a protective effect of the FS matrix on the region of damaged mucosa with exposed submucosal tissue. Neither the present study nor any data in the literature suggest an action of FS to reduce inflammation, which is a presumed mechanism of postoperative intranasal pain. However, postoperative endoscopic examination revealed reduced crusting in sinuses treated with FS compared with controls. This is not unexpected because crusting likely results from persistent oozing and mucosal irritation, both of which FS is likely to prevent. This may also contribute to the reduced discomfort experienced by patients treated with FS. In our study, there were no differences in postoperative healing at 1 and 3 months based on endoscopic exam. This is consistent with the findings of Gall et al [7] who noted no adverse effects on healing 30 days postoperatively. However, Chandra et al [8] have recently reported increased granulation tissue and adhesions 6 to 8 weeks postoperatively in FS-treated patients compared with patients treated with thrombin-soaked gelatin foam. The 2 agents worked equally well as hemostatic agents in the 20 patients they studied, each of whom had one ethmoid cavity packed with FS and the other with thrombin-soaked gelatin foam. In this study [8], the authors were not blinded to the treatment, which may have introduced some bias into the results. In addition, matched controls were used, which may have artificially enhanced the statistical difference between the 2 groups, especially because the control was a thrombin-soaked gelatin foam, which would be expected to decrease the rate of crusting compared with an untreated sinus (the control in the present study). Moreover, the average adhesion score for the 20 sinuses treated with FS in this study was 1.9; a score of 2 as defined by the authors represented “obvious adhesions not associated with turbinate lateralization or the accumulation of mucopurulent secretions [8].” In the present study, a patient was noted to have adhesions if they appeared clinically significant, and division was warranted; usually, this involved middle turbinate lateralization or obstruction. Perhaps the most important difference in the 2 studies is the more aggressive use of postoperative irrigation in the present study, which the authors believe results in a significantly lower rate of granulation and adhesion formation. In another study, Maccabee et al [9] reported that FS appeared to increase reactionary fibrosis of healing mucosa. The problem with this study is that the maxillary sinuses of the rabbits we filled with FS and were then sealed closed for 2 weeks. This model does not resemble a real clinical situation and traps material in a closed sinus cavity during the healing process. In our study, patients irrigated their sinonasal cavities aggressively, as per our routine protocol after endoscopic sinus surgery. This debridement helps maintain sinus drainage and ventilation after surgery and perhaps result in a lower rate of inflammation and tissue fibrosis.

The use of bovine thrombin (the procoagulant agent in FS) in humans has been criticized because of the possibility of predisposition to future anaphylaxis as a result of formation of antibodies to bovine thrombin or factor Va. Oz et al [3] used FS to control hemorrhage in cardiac surgery and noted no postoperative coagulopathies. A more recent prospective study of 309 patients treated with FS intraoperatively by Winterbottom et al [10] demonstrated an incidence of 19% and 30% postoperative antibodies to bovine factor Va and bovine thrombin, respectively. This patient group also had a 0% and 2.6% incidence of postoperative antibodies to human factor Va and human thrombin, respectively. None of these patients had a demonstrable coagulopathy. There were no alterations in the typical complication profiles, including 5 patients with previous exposure to bovine thrombin. FloSeal has been used in hundreds of thousands of patients, and to date, not a single complication involving coagulation abnormalities has ever been reported.

A final point worth mentioning is that a cost analysis was not performed with this study. Future studies incorporating cost-benefit analysis are necessary to provide us with some guidance.
5. Conclusion

Use of FS after FESS resulted in less bleeding, immediately postoperatively, and reduced discomfort. In addition, FS did not increase the incidence of crusting or scarring compared with controls.

References