

Ferric Sulfate Hemostasis: Effect on Osseous Wound Healing. II. With Curettage and Irrigation

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Hemorrhage control is often a problem for the clinician during osseous surgery. Ferric sulfate is an effective hemostatic agent, but with prolonged application to an osseous defect can cause persistent inflammation and delayed healing. The purpose of this investigation was to evaluate the effectiveness of ferric sulfate as a hemostatic agent and to determine its effect on healing after thorough curettage and irrigation from osseous surgical wounds. Standard size osseous defects were created bilaterally in the mandibles of rabbits. Ferric sulfate was placed in one defect until hemostasis was obtained; the contralateral defect was allowed to fill with blood and clot. After 5 min both defects were curetted and irrigated. The repair of the defects was evaluated histologically at 18 and 46 days. There were no significant differences between the ferric sulfate-treated defects and the untreated controls. When adequately curetted and irrigated from the surgical site prior to closure, ferric sulfate did not cause persistent inflammation or delay osseous repair in comparison to controls.

Commercial preparations of ferric sulfate have been advertised for use in periapical surgery (1). However, only two cases using ferric sulfate as a hemostatic agent (2) have been reported in available literature. The authors did not comment on removal of the hemostatic agent prior to wound closure or assessment of wound healing.

In a previous study, we found that ferric sulfate left in situ in surgical osseous defects had adverse effects (3). An intense foreign body reaction and abscess formation was found in some of the experimental specimens after 46 days. The purpose of this study was to determine if the foreign body response and delayed healing caused by the ferric sulfate (Astringent; Ultradent Products, Inc., Salt Lake City, UT) could be reduced or eliminated by curettage and irrigation of the osseous defect prior to wound closure.

MATERIALS AND METHODS

The experiments were performed in 12 New Zealand White rabbits (2.3 to 3.7 kg). Anesthesia was obtained by the intramuscular injection of a combination of xylazine (7 mg/kg), ketamine (30 mg/kg), and atropine (0.3 mg/kg). On both sides of the mandible, an incision was made along the alveolar crest in the naturally edentulous space between the incisor and premolar teeth. An envelope flap was reflected to expose the alveolar cortical bone. An osseous defect (3 mm in diameter, 2 mm into cancellous bone) was created on each side with a #8 round bur. All defects were curetted and irrigated with saline.

Drops of the 15.5% ferric sulfate solution were placed in the osseous defect on the experimental (right) site until complete hemostasis was obtained. Blood was allowed to fill the control (left) site which did not receive ferric sulfate. After 5 min the sites were gently curetted with a small bone curette and irrigated with sterile saline until all visible ferric sulfate coagulum (right) or the blood clot (left) was removed and hemorrhage reestablished. The flaps were repositioned and closed with resorbable sutures.

The rabbits received a combination of penicillin (100,000 units of procaine-G) and streptomycin (base equipment of 125 mg) for 3 days for infection control, and meperidine (5 mg/kg) for pain control. The rabbits were fed a soft diet of crushed rabbit pellets for 1 wk to minimize trauma to the surgical sites.

The rabbits were killed in groups of six at 18 and 46 days postoperatively. After obtaining anesthesia, the animals were killed and perfused with Poly-LEM (Polysciences, Warrington, PA) via the carotid arteries. Specimens were sectioned from the mandibles to include the osseous defects and adjacent bone and fixed in Poly-LEM. The specimens were decalcified in a 10% sodium formate-formic acid solution and processed for routine paraffin embedding. Seven-micrometer sections were cut in a coronal plane through the center of the defect and stained with hematoxylin and eosin.

The sections were examined for inflammation and evidence of healing and were scored based upon the following scale: 0 = complete healing with surgical site filled with healthy cancellous bone; 1 = fibrosis with dense collagen, with or without early bone formation; 2 = granulation tissue filling the surgical site, with or without chronic inflammation; 3 = acute inflam-

TABLE 1. Histological scores

	18-Day Specimens						46-Day Specimens					
	1	2	3	4	5	6	7	8	9	10	11	12
Control	0	1	1	—	0	1	1	1	0	0	0	0
Experimental	0	1	—	1	0	1	1	0	0	0	0	0

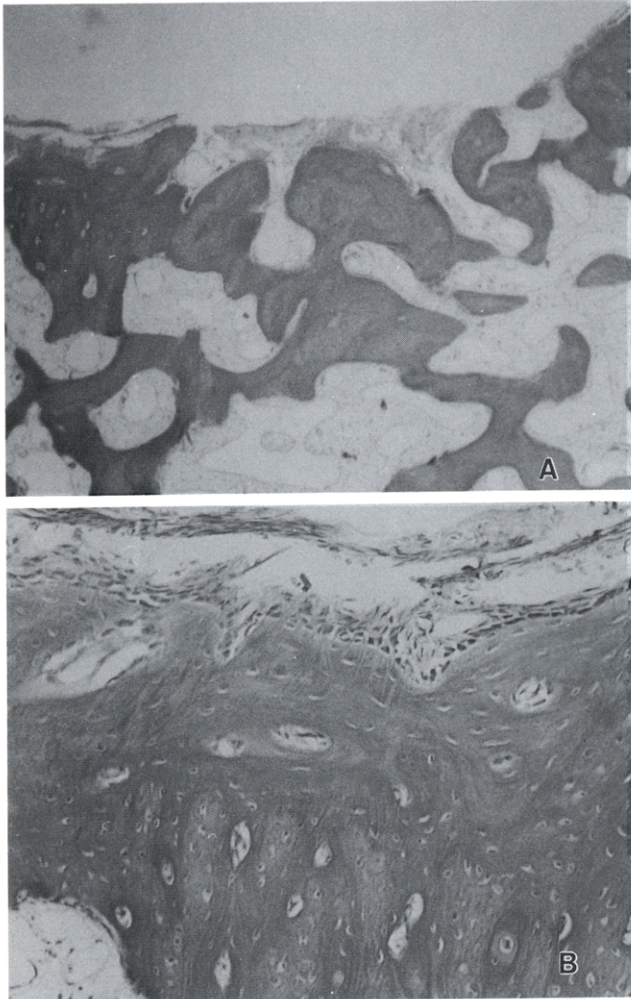


FIG 1. Photomicrograph of an 18-day control specimen. A, New bone trabeculae almost fill the defect. Original bone surface is on the left. B, Enlarged area of box in A: very active bone formation with plump osteoblasts is seen on all surfaces of the trabeculae (hematoxylin and eosin; original magnifications $\times 12$ and $\times 25$, respectively).

mation, with or without granulation tissue; and 4 = abscess formation.

The scores were analyzed by nonparametric *t* tests (Wilcoxon rank sum test and Wilcoxon signed rank test) to determine whether significant differences exist between the experimental and control groups or specimens.

RESULTS

Hemostasis was achieved in less than 1 min with the ferric sulfate. The dark color of the coagulum contrasted with any red areas of residual hemorrhage. Spot application of additional ferric sulfate provided complete hemostasis. Hemostasis

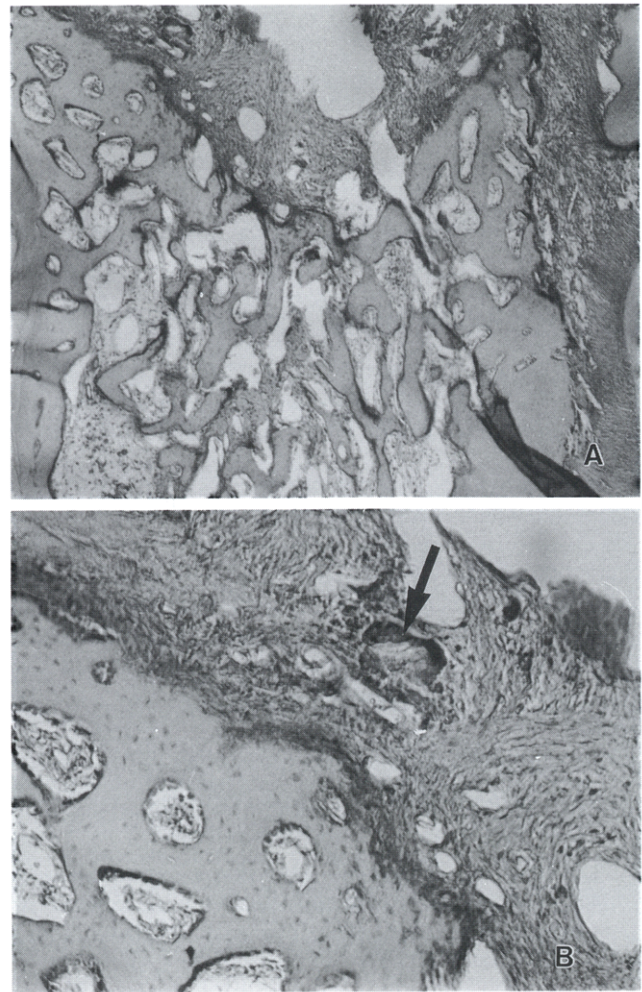


FIG 2. Photomicrograph of an 18-day experimental specimen. A, Active bone formation with new trabeculae fills the defect. Original cortical bone is to the left. B, Enlarged area of upper left of A: isolated foreign body giant cell (arrow) adjacent to an area of new bone formation (hematoxylin and eosin; original magnifications $\times 12$ and $\times 25$, respectively).

was maintained without additional applications for 5 min. The ferric sulfate coagulum was removed by gentle curettage and irrigation with saline.

One set of poor quality histological sections in the 18-day experimental group and one set in the 18-day control group were eliminated from grading. All scores for the 22 graded specimens were either "0" (complete healing with the surgical site filled with healthy cancellous bone) or "1" (fibrosis with dense collagen with bone formation (Table 1). Both the experimental and control sites demonstrated active cancellous bony trabeculae with numerous plump osteoblasts. Interspersed were focal areas of loose to dense fibrous connective tissue (Figs. 1 and 2).

All 46-day specimens demonstrated either complete healing or fibrosis with bone formation. Although the general healing of the 18-day and 46-day experimental and control groups were scored equally, there were histological findings in the 18-day experimental group not found in the controls. Aggregates of ferric sulfate residue were found in association with

foreign body giant cells (Fig. 2). Inflammatory infiltrates were limited to a few focal collections of lymphocytes, but no significant collection of granulation tissue was seen. None of the 46-day experimental group demonstrated ferric sulfate aggregates or foreign body giant cells.

Statistical analysis of the scores showed no significant difference ($p > 0.05$) between any of the specimens or groups (experimental versus control and 18-day versus 46-day).

DISCUSSION

In studies of dermatological use, ferric sulfate solution was not removed from the soft tissue surgical site and considerable acute inflammation, foreign body reaction, and delayed healing was reported (4–7). The same response was found in our previous study when ferric sulfate was not removed from osseous defects (3).

In this investigation, intraosseous hemostasis with a ferric sulfate solution followed by curettage and irrigation with sterile saline produced a transient, mild foreign body reaction but did not delay osseous wound healing. The foreign body reaction found in the 18-day specimens was minimal and was not observed in any of the 46-day specimens.

The long-lasting foreign body reactions and delayed wound healing associated with the use of bone wax (Ethicon, Somerville, NJ) (8, 9), Gelfoam (Upjohn Co., Kalamazoo, MI) (8, 10), Absele (Ethnor, Division of Ethicon, Somerville, NJ) (11), and Hemofibrine (Septodont, France) (12) were not found in this study. The results of this investigation appear to compare favorably with the mild, transient foreign body reaction reported with polylactic acid (10) and Avitene (MedChem Products, Inc., Woburn, MA) (13, 14). However, Avitene is expensive and somewhat difficult to place (15). In contrast, ferric sulfate is inexpensive, easy to place, and readily removed by curettage and irrigation.

The results of this study show that ferric sulfate provides effective hemostasis and, with curettage and irrigation of the surgical osseous defect prior to closure, does not delay healing.

Further studies comparing the biocompatibility of curetted ferric sulfate with resorbable hemostatic agents are being conducted.

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You Might Be Interested to Know

A recent study (Thorax 46:807) concluded that men who snore a lot may have diminished daytime function because the reduced quality of sleep from snoring causes substantial daytime drowsiness.

They needed a research study to prove that? Couldn't they have just asked their wives' opinion?

Eugene Fulton