Gelfoam paste in experimental laminectomy and cranial trephination

Hemostasis and bone healing

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The hemostatic properties and effect on osteogenesis of gelatin foam paste and bone wax were compared on surgical bone lesions in experimental animals. Thirty rabbits each received four trephine craniotomies and four lumbar laminectomies. Alternate bone incisions in each animal were treated with either gelatin foam paste or bone wax. Blood loss was measured by absorbing the blood into dry surgical cottonoids weighed before and after use. Bone healing sites of three rabbits were examined histologically to assess the effect of each agent on osteogenesis. The trephination sites of eight rabbits were subjected to fracture force testing at 6 weeks postoperatively to compare the effect to the two agents on bone healing. No significant difference was found between gelatin foam paste and bone wax in either effectiveness of hemostasis or effect on osteogenesis.

KEY WORDS □9 bone hemostasis □9 Gelfoam □9 bone wax

Almost 100 years after its introduction, bone wax is still in wide use despite attempts to find materials with superior properties. The effective hemostasis achieved by bone wax arises from a physical rather than a biochemical effect: when pressed firmly into bleeding bone it blocks blood flow from damaged vessels and allows clotting to occur.

Questions have arisen, however, in regard to the effect of bone wax on bone healing and osteogenesis. A powdered form of gelatin foam is currently available as a topical therapy for decubitus ulcers, and can easily be converted to a paste with a consistency similar to that of bone wax. The parent compound (Gelfoam) is in widespread use as a hemostatic agent in the form of sheets or pledgets, but this form of the product is of only limited usefulness in the control of bone bleeding. Because gelatin foam is resorbable in the human body, the paste form represents a possible answer to problems arising from the osteogenic inhibition reported with bone wax. Since the introduction of gelatin foam paste, reports by Taheri and Harris, et al., suggest that this agent is quite effective and safe for control of bone bleeding. The effect on subsequent bone healing has not been specifically reported in a controlled laboratory situation, nor has a direct comparison of hemostatic effectiveness between bone wax and gelatin foam paste been reported.

The present investigation compares the hemostatic properties and osteogenic effect of gelatin foam paste and bone wax on surgical bone lesions in experimental animals.

Materials and Methods

Thirty New Zealand white rabbits were operated on under combined ketamine-Rampom general anesthesia (Fig. 1). The scalp and lumbar region were shaved and prepared with Betadine as two separate aseptic fields in each rabbit. A midline scalp incision was made with skin and temporalis muscles reflected laterally on both sides. Meticulous hemostasis was obtained in the area, and the wound was temporarily packed open with saline-soaked gauze sponges. A midline lumbar incision was then made. The lumbar dorsal fascia was incised in the midline, and paraspinal muscles were stripped bilaterally from the spines and laminae of four lumbar vertebrae. The yellow ligament and interspinous ligaments and muscles were transected above and below each of the four exposed spinous processes. Meticulous hemostasis was obtained in this area before temporary packing was placed.

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Fig. 1. Operative sites in rabbits. Four trephine openings were made in the skull and four modified lumbar laminectomies were performed. Hemostasis was obtained at alternate trephine sites and alternate laminae with bone wax and Gelfoam paste.

Returning to the cranial incision, a 3/8-in. trephine was used to cut four full-thickness openings through the skull alternately on the right and left sides. Hemostasis was obtained at each trephine opening before proceeding to the next. Bone bleeding from two holes on one side was controlled with Gelfoam paste and bleeding from the contralateral pair was controlled with bone wax. The Gelfoam paste was constituted by mixing 1 gm of sterile powder with 3 or 4 ml of normal saline, then kneading the mixture to a consistency similar to that of warm bone wax. The amount of blood loss was quantitated by absorbing the blood into dry surgical cottonoids weighed before and after use.

In the lumbar region, four spinous processes and their corresponding facets were removed, one lamina at a time. Bone bleeding from cut bone surfaces of alternate laminae was controlled with gelatin foam paste. Bone wax was used on the remaining surfaces. Bleeding was controlled at each site before proceeding to the next, and was again quantitated by using dry surgical cottonoids.

At the conclusion of this portion of the procedure, the trephine buttons and excised spinal processes were replaced in their original positions. They were not fixed in place by any means. The cranial and lumbar regions were closed in layers, and the animals were housed singly to recover from the procedure. Ten animals were lost prior to sacrifice: three rabbits died under anesthesia; three rabbits died postoperatively after extensive epidural bleeding at a trephination site; one affected site had been treated with gelatin foam paste and two with bone wax; and four rabbits died of idiopathic causes at 1, 5, 8, and 13 days postoperatively.

The remaining animals were sacrificed in three experimental groups as follows: In Group 1, nine animals were sacrificed within 48 hours postoperatively, after data had been gathered on the effectiveness of hemostasis of the two test agents. In Group 2, three animals were sacrificed for histological processing, one each at 1, 4, and 6 weeks postoperatively. After fixation in Bovin's Picroformic fixative, the bones were decalcified with Decal,* sectioned, and stained with hematoxylin and eosin. In Group 3, eight animals were sacrificed at 6 weeks postoperatively, and their trephination sites prepared for fracture force testing, using a similar technique to that employed by Evans and Lissner. After sacrifice, healed trephination sites were removed with an electric bone saw. Each specimen was mounted on a support under which was centered a ½-in. diameter cylinder. The resulting unit was centered on an Instron materials testing instrument.† The machine drove a ¾-in. diameter piston onto the fracture site at a speed of 2 mm/min. A strip chart recorder connected to the instrument recorded the force applied to the fracture site. A sudden negative slope on the recorder line indicated that a fracture had occurred and the machine was shut down.

Results

Effectiveness of Hemostasis

Four groups of data were analyzed: 1) trephination treated with Gelfoam, 2) trephination treated with bone wax, 3) modified laminectomy treated with Gelfoam, and 4) modified laminectomy treated with bone wax. These results are summarized in Fig. 2 and Table 1. The effectiveness on hemostasis of the two agents was compared at the two operative sites in terms of volume of blood lost intraoperatively at each site. Gelfoam was slightly more effective in hemostasis than bone wax in the comparison of trephination. However, there was no significant difference in effectiveness of hemostasis between the two agents at either site.

Histological Examination

At 1 week postoperatively, there was no significant difference in the appearance of fracture sites treated with Gelfoam or bone wax. Abundant numbers of osteoblasts were observed in each specimen, although neither specimen showed any inflammatory reaction to the hemostatic agent used. At 4 weeks postoperatively, only the Gelfoam-treated site specimens were satisfactorily processed. New bone formation was

*Decal manufactured by Scientific Products, Evanston, Illinois.
†Instron materials testing instrument (Model TT) manufactured by Instron Corp., Canton, Massachusetts.
WEIGHT OF BLOOD IN COTTONOIDS (grams)

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<tr>
<th>Feature</th>
<th>Trephine Craniotomy</th>
<th>Lumbar Laminectomy</th>
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<tr>
<td></td>
<td>Bone Wax</td>
<td>Gelfoam Paste</td>
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<tr>
<td>no. of rabbits</td>
<td>27</td>
<td>27</td>
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<tr>
<td>mean blood loss (gm)</td>
<td>0.307 ± 0.068</td>
<td>0.233 ± 0.066</td>
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<tr>
<td>p value*</td>
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*Neither comparison was statistically significant.

**Discussion**

Howard and Kelley studied the effect of bone wax on bone healing and osteogenesis in Albino rats. Their experimental model called for the drilling of a $\frac{3}{16}$-in. hole through the anterior cortex into the marrow space of the left tibia in each animal. The experimenters blocked each hole with bone wax, removed excess wax, and irrigated the area with saline before closing the wound. Similar holes in the same or opposite tibia were simply irrigated before closing, and served as control lesions. Animals were sacrificed after 12 hours to 60 days. The authors reported that bone wax "almost completely inhibited the formation of new bone." They hypothesized that bone wax is an inert physical barrier to fracture repair that inhibits osteogenesis locally involving the immediate area of fusion. Their study suggests that bone wax may be contraindicated in operations where fusion is the desired result.

In a search for a superior hemostatic agent for bone bleeding that would not impair bone healing, Taheri began using powdered gelatin foam in patients on whom he had performed anterior cervical fusions. He mixed the powder into a paste and applied this to the interbody drill hole during drilling and prior to placing the bone dowel. Initially, he mixed the powdered Gelfoam with sterile thrombin solution but discontinued this practice after two patients developed anaphylactic reactions. In 1971, he published a brief report of his experience with gelatin foam paste in over 300 anterior cervical operations during an 8-year period. There were no anaphylactic reactions or other serious complications. He reported that follow-up x-ray films showed no difference in bone healing from that experienced in the previous 4 years, during which surgery was performed without the use of Gelfoam paste. Weiss has subsequently confirmed the clinical utility of this technique. Rengachary and Manguoglu reported using a combination of gelatin foam sponge and powdered bovine thrombin for hemostasis, also during anterior cervical fusions, and did not encounter any problems with anaphylactic reactions to the thrombin.

Following Taheri's report, Harris et al. reported a controlled operative study of gelatin foam paste used as a topical hemostatic agent to control bleeding from...
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the cancellous surface of femoral osteotomies done during the course of total hip replacement operations in a series of 45 patients. This study compared the hemostatic effectiveness of gelatin foam paste, Gelfoam sponge plus bovine thrombin, and microfibrillar collagen, using a dry sponge technique for quantification of blood loss. They reported that bleeding decreased spontaneously by 11% over a 3-minute interval in eight patients whose raw bone surfaces were not treated with a hemostatic agent. By contrast, microfibrillar collagen effected a reduction of 47%, gelatin sponge soaked in thrombin gave a reduction of 75%, and gelatin paste gave a reduction of 85%. Follow-up clinical and x-ray studies showed no apparent difference in bone healing between the three groups of patients.

Brightmore1 found evidence that bone wax formed a physical barrier to bone healing in sternotomized goats, inhibiting osteogenesis and causing absorption of cancellous bone. Geary and Frantz,4 and Lattes and Frantz,5 studying experimental rib and radius fractures in dogs, found that lesions treated with bone wax generated the same or somewhat greater amount of calcified callus as did untreated controls, but union of the fracture was prevented by physical interposition of wax particles. They noted that bone wax produced a characteristic foreign-body reaction, consisting of giant cells, monocytes, and phagocytes.

Perhaps surprisingly, there have been no reported studies in animals specifically comparing the hemostatic effectiveness or effect on bone healing of Gelfoam paste and bone wax. In our study, we found the Gelfoam paste to be as easy to use as bone wax, which it resembled in consistency. In addition, we found the agent to be at least as effective as bone wax in experimental craniotomy and laminectomy, and perhaps slightly more so. The effect on bone healing was assessed both histologically and in terms of tensile strength of healed bone, and again we could find no significant difference. Since this portion of the study did not include control areas treated with no topical hemostatics, we cannot comment on whether or not both agents impaired bone healing to a similar degree or whether neither caused significant impairment in healing. Grossly, however, bone healing seemed to be consistent with what would normally be expected in the course of experimental animal surgery.

Conclusions

We conclude that Gelfoam paste provided an effective alternative to bone wax for the control of bone bleeding. The agent is easy to use and seems to have no significant deleterious effect on bone healing.

Acknowledgments

The authors would like to thank Dr. Bennet Gordon of the Department of Materials Engineering, Worcester Polytechnic Institute, Worcester, Massachusetts, for his generous aid with the fracture force testing portion of this study.

References


Fig. 3. Effect on bone healing of bone wax and Gelfoam paste at 6 weeks after craniotomy in eight rabbits. The mean force (in pounds) necessary to fracture healed trephine buttons was 44.4 ± 12.0 lb for bone wax, and 42.3 ± 12.3 lb for Gelfoam paste. The results did not differ significantly (p = 0.9).

The Upjohn Co., Kalamazoo, Michigan, kindly supplied financial assistance and powdered Gelfoam for this project. Address reprint requests to: Harold A. Wilkinson, M.D., Ph.D., Department of Neurosurgery, University of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, Massachusetts 01605.