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Case Series

Hemostasis and Safety of a Novel Fibrin Dressing Versus Standard Gauze in Bleeding Cancellous Bone in a Caprine Spine Surgery Model

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Abstract

Background: Decorticated bone is a significant source of blood loss in scoliosis surgery. Current hemostatic methods include packed gauze (GS), physical barriers such as bone wax, and xenograft collagen-based materials. We assessed the safety and efficacy of a novel fibrin dressing (dextran-thrombin-fibrinogen [DTF]) compared to GS. This dressing comprises lyophilized thrombin and fibrinogen embedded in an elastic electrospun nanofiber dextran matrix.
Purpose: The study tests the hypothesis that DTF is more efficacious than GS in control of bleeding from cancellous bone.
Study Design: A preclinical Good Laboratory Practices (GLP) study.
Methods: We enrolled 10 goats that were followed for 28 ± 1 days. Each animal was randomly assigned to the test or control group. Both test and control animals had 4 cancellous bone injuries. Test animal injuries were treated with DTF, whereas standard GS was used to control bleeding in the control animals. Bleeding at the bone injury site was characterized as either none, oozing, flowing, or pulsatile and was assessed at 4 and 8 minutes after dressing application. Goats were survived 28 ± 1 days and then necropsied.
Results: Application of the fibrin dressing to bleeding cancellous bone, both posterior spinal lamina, and iliac crest graft sites, resulted in control of bleeding within 4 minutes at all injury sites. Eighty percent of control injury sites continued to bleed after 8 minutes and required application of bone wax to control bleeding. There were no differences in prothrombin time, partial thromboplastin time, or fibrinogen levels between test and control animals at 1 or 28 days. We observed no adverse histologic reactions at 28 days.
Conclusion: The fibrin dressing is an efficacious and safe method of controlling blood loss from cancellous bone in a spine surgery model.

Keywords: Hemostasis; Fibrin dressing; Bleeding cancellous bone

Introduction

Spine deformity surgery generally involves decortication and exposure of large surfaces of cancellous bone that can lead to significant blood loss. Various strategies have been developed to minimize blood loss and associated morbidities including hypotensive anesthesia [1], injection of epinephrine into the soft tissues, and preoperative administration of tranexamic acid [2]. Blood loss from bone can be reduced by direct physical application of topical hemostatic agents (eg, Gelfoam and FloSeal) [3-5], bone wax, and gauze.

Currently available topical hemostatic agents are not ideal for use in bleeding cancellous bone, and package inserts specifically require their removal prior to wound closure. Porcine or bovine collagen/gelatin products, whether in sheets or in a slurry form with thrombin, interfere with bone healing. Allografts can elicit an inflammatory response. Although the material can temporarily control bleeding, it cannot be left in the fusion bed for continued hemostasis. Further, the large bleeding surface areas exposed in deformity surgery make use of agents such as FloSeal impractical because of cost. Bone wax, while effective, also can interfere with bone healing or successful arthrodesis. Bone wax can be removed from the surface, but

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not from cancellous spaces without further resection of bone.

Gauze sponges, packed into areas of bleeding cancellous bone temporarily tamponade the bleeding, but must be removed prior to wound closure. Sponge packing is the most common strategy used to control hemostasis during spine surgery, but it does not allow for continued hemostasis after surgery.

Fibrin sealants are another strategy to control blood loss and are available either in a frozen liquid form or as lyophilized proteins combined with a backing dressing generally derived from mammalian collagen. Liquid fibrin does not reduce blood loss from decorticated transverse processes during spine fusion surgery [6]. Collagen-backed fibrin sealants have not been tested on bleeding bone and may impede healing [7].

A novel fibrin dressing that stops arterial bleeding [8-10] also may be useful in control of hemorrhage from other tissues, including bone. This dressing comprises lyophilized thrombin and fibrinogen embedded in a fully absorbable matrix of electrospun dextran nanofibers. Prototype dressings used salmon proteins, whereas the current dressing uses human proteins. The solid physical state of the dressing provides initial hemostasis by tamponade [11]. Further contact with fluid (eg, blood) completely dissolves the electrospun dextran carrier and solubilizes the proteins, which then interact to form a fibrin seal.

Given the various strategies to control bleeding, we wanted to test the new fibrin dressing against the most commonly used hemostatic method. We tested the hypothesis that this dextran-thrombin-fibrinogen (DTF) dressing would be more efficacious than packed gauze sponges (GSs) at achieving hemostasis in bleeding cancellous bone in a posterior lumbar fusion and iliac crest graft model.

Materials and Methods

Ten dairy-bred goats (5 castrated male, 5 female) weighing 35.5 to 58.0 kg were used in this study. Ages ranged between 14 and 29 months. The animals were housed and cared for in a USDA registered facility in accordance with standard criteria (facility Registration Number 41-R-0084) [12]. The study was conducted in accordance with FDA Regulations on Good Laboratory Practices (GLP) for Nonclinical Laboratory Studies CFR Title 21 Part 58 [13]. The original protocol and all changes to the protocol were approved by the NAMSA Institutional Animal Care and Use Committee (IACUC). The number of experimental animals was kept to the minimum but adequate to ensure statistical significance [14].

The test article, DTF, was provided by the manufacturer (St. Teresa Medical, Inc., Eagan, MN). These were finished (packaged, sterilized) dressings with lyophilized human thrombin and fibrinogen embedded in a 7 × 7 cm sheet of electrospun USP-grade dextran. The control article, 10 × 10 cm sterile cotton gauze sponges (GS), was procured independently from the manufacturer (Merit Medical, Chester, VA).

A physical examination of each animal was performed by the facility veterinarian before proceeding with the study. Animals were anesthetized with atropine (0.005−0.02 mg/kg, intramuscular), buprenorphine (0.01 mg/kg, intramuscular), ketamine (2.2−5.5 mg/kg, intravenous), and diazepam (0.3−0.5 mg/kg, intravenous). On occasion, propofol (1−8 mg/kg, intravenous) was used to aid induction. Anesthesia was maintained using isoflurane (0.5% to 5.0%, inhalant). Each animal received penicillin G (30,000 U/kg, intramuscular) preoperatively. Blood pressure was monitored via an intra-arterial catheter and transducer.

Strict sterile technique, including gown, gloves, and drapes, was used for the surgical procedures. A posterior approach to the lumbar spine was performed, as well as separate skin and fascial incisions over both iliac crests, creating 3 separate skin wounds exposing 4 bone test sites per animal. Hemostasis of the muscle was obtained with electrocautery. The lamina of two lumbar vertebrae and the iliac crests were decorticated with a chisel. To avoid cross-contamination, the right L4 lamina and the left L5 lamina were decorticated with the spinous processes and interspinous ligament left intact. The cancellous bone bleeding was graded as either pulsatile, flowing, oozing, or none. The animals had been randomized to either control or test article which the surgeon learned at this stage of the procedure.

The randomized dressing (gauze only or test article plus gauze) was applied directly to the bleeding surface. A cotton gauze backing was used behind the DTF dressings because the test article dissolved after application. Light manual pressure to keep the dressing in place was maintained by the surgeon for 4 minutes. After 4 minutes, the gauze was removed and bone bleeding was again graded by the surgeon. If bleeding continued, a second identical dressing was applied with 4 minutes of compression, and then the bone was observed and bleeding was graded. If bleeding persisted after the second dressing application, the surgeon sealed the surface with bone wax.

All gauze dressings were collected, weighed, and compared to an equal number of unused gauzes to estimate blood loss. Results were analyzed using Student *t* test.

Performance of the test article was assessed by presence of controlled bleeding within 4 minutes, blood loss, and the need for dressing reapplication. Four data points were obtained from each animal: right L4 lamina, left L5 lamina, and the right and left iliac crests. Results were analyzed statistically using a Student *t* test (blood loss) and a simple chi-squared test (dressing performance).

Each animal was then recovered, survived, and maintained in the FDA-registered facility for 28 days, at the end of which time they were again anesthetized in a similar manner and then euthanized by barbiturate overdose.