Performance of a Dextran-only Dressing Versus SurgiClot® to Achieve Hemostasis in a Swine Injury Model of Cancellous Bone Bleeding

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INTRODUCTION

SurgiClot® is a novel hemostatic dressing that can control vigorous arterial and venous bleeding, and leaves no residual foreign material to elicit an inflammatory or foreign body response. SurgiClot® is comprised of lyophilized human thrombin and fibrinogen embedded in a soluble, electrospun nanofiber dextran dressing. The design of the dressing allows for initial tamponade by the dextran component, followed by formation of a fibrin clot to maintain hemostasis. The purpose of this study was to compare the hemostatic efficacy of a dextran-only dressing to that of the SurgiClot® dressing in the swine iliac-crest and spine injury model of cancellous bone bleeding.

METHODS

Three swine female (Yorkshire cross) weighing 51, 45, and 24 kg were used in this study. Animals were housed in accordance with criteria outlined in the "Guide for the Care and Use of Laboratory Animals" (National Academy Press, 1996), and were provided food and water *ad libitum* except prior to any anesthetized procedure.

The study was designed as a prospective, intent to treat study, that compared the hemostatic efficacy of a dextran-only dressing to that of the SurgiClot® dressing. Both dextran- and SurgiClot®-treated injuries were also compared to the pre-treatment free-bleeding injury (control). The free-bleeding injury arm was added to demonstrate that spine and iliac crest bone bleeding injuries could not achieve hemostasis in a timely manner without intervention. Sterile samples of SurgiClot® and dextran-only dressings, were provided by St Teresa Medical (St. Paul, MN) prior to the start of the study.

On the day of surgery, animals were sedated and anesthetized with Telazol (4.0-6.0mg/kg IM), and if needed, Xylazine (0.5-5.0mg/kg IM). Animals were intubated and maintained under anesthesia with inhalant isofluorane (0.5-5%), and positioned to a prone position. Incisions and dissections were performed to access the target bone structures (right and left iliac crests and L6-L4 vertebrae). Upon creation of a blood-oozing bone decortication injury, either a 2 or 5 minute pre-treatment free-bleed was observed prior to treating with either a dextran-only dressing or SurgiClot®. The viable decortication injury was treated with the dextran-only or SurgiClot® dressing. Treatment with either the dextran-only or SurgiClot® dressings were randomized in a balanced fashion to control for bias. Following the initial dressing application, injuries were assessed for hemostasis at 2-minutes. If hemostasis did not occur after the initial 2-minute application, the dressing was re-applied for an additional 2-minutes. No injury was treated for longer than a total of 4minutes. The time to hemostasis, or the failure to achieve hemostasis after 4 minutes, was recorded. The procedure was repeated until up to n = 8 injuries were treated for each animal. Following completion of the study procedures, all animals were euthanized with an overdose of a barbiturate-based euthanasia solution.

The data were constructed into a contingency table, and analyzed statistically using a cumulative logistic regression model. The statistical equation for this model was $logit[\Pr(Y \leq j)] = \alpha_j + \beta_i x_i$, where j is each possible outcome, i is the treatment group, and x_i is an indicator for the treatment group. There were three treatment groups: Free-Bleed, Dextran, and SurgiClot®, and three possible outcomes: hemostasis after 2 minutes ("After2"), hemostasis after an additional 2 minutes with re-application ("After4"), and hemostasis after 5 minutes ("NoHemo"). The variables were logically ordered with "NoHemo" as the worst possible outcome, "After 4" the next worst, and "After2" as the best possible outcome. Thus, the probability of having a worse treatment outcome was modeled overall.

RESULTS

All injuries were considered to be comparable in size and in blood-flow. None of the free-bleeding injuries achieved hemostasis after 5 minutes. Following the 5 minute free-bleed, treatment with either the dextran-only or SurgiClot® dressing achieved hemostasis at all injury sites. All injuries treated with the dextran-only bandage achieved hemostasis by the 4-minute observation. Sixty percent (6 of 10) of injuries treated with the dextran-only dressing achieved hemostasis after 4 minutes, while the remaining forty percent (4 of 10 injuries) achieved hemostasis after 2 minutes. All injuries treated with the SurgiClot® dressing achieved hemostasis after the 2-minute application (10 of 10 injuries).

Results of the statistical analysis using a cumulative logistic regression model are shown in the table below.

	Estimate	Exp. (Estimate)	P-Value
α_1	1.8200	6.1719	0.014484
α_2	3.7077	40.77	0.000104
$\beta_{Dextran}$	-3.4696	0.03113	0.000572
$\beta_{SurgiClot}$	-5.3516	0.004741	0.00000899

These p-values indicate that the treatment (Dextran-only or SurgiClot®) effect was highly significant compared to that of free-bleed. In particular, $\exp(\beta_{Dextran}) = 0.03$ indicated that the odds of having a worse outcome than any fixed level j, in the Dextran treatment group is only 3.1% of the Free-Bleed group. Similarly, $\exp(\beta_{SurgiClot}) = 0.004741$, which indicates that the odds of having a worse outcome than any fixed level j, in the SurgiClot® treatment group is only 0.47% of the Free Bleed group. This clearly indicates that the two treatments are both much less likely to result in longer bleeding times than the Free-Blood group, and that in comparison with the Dextran treatment, the SurgiClot® treatment is stronger. To verify this model was a good fit, the residual deviance was tested. Here, the null hypothesis that this is a good fitting model was tested. The p-value for this model was 0.16 (much greater than the usual 0.05 cut-off), which indicates that the null hypothesis cannot be rejected. Thus the model is a good fit

DISCUSSION

This study was successful in assessing the hemostatic efficacy of the dextran-only dressing when compared to bleeding without intervention. Additionally, SurgiClot® was shown to decrease the time to hemostasis as compared to that of the dextran-only dressing, which indicates an ancillary effect of the clotting proteins to achieve hemostasis.

SIGNIFICANCE

SurgiClot's initial and primary mode of action appears to be the physical effect of tamponade by the solid dextran component.