Comparison of a Novel Hemostatic Agent to Currently Available Agents in a Swine Model of Lethal Arterial Extremity Hemorrhage

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INTRODUCTION

Uncontrolled hemorrhage is a significant cause of morbidity and mortality in both civilian[1] and battlefield trauma[2]. On the battlefield, large vascular injuries of the extremities are a predominant injury pattern, and the leading cause of preventable death[3]. The standard immediate treatment for these injuries is the application of direct pressure via manual compression and external dressings. This method however, is often ineffective and impractical in the battlefield setting[4]. The use of tourniquets, while effective if applied properly, is controversial except as a method of last resort due to the associated risks of reperfusion, limb ischemia, and neurological injury[5]. Therefore, the development of an effective hemostatic agent that can be easily applied in the pre-hospital or battlefield scenario may significantly reduce mortality following trauma.

To this end, several candidate treatments including dressings based on chitosan (HemCon® bandage), zeolite (QuikClot® powder & QuikClot ACS+™ bandage), and fibrin have been developed. Although moderately effective in controlling hemorrhage in various animal models, none of these have proven to be an ideal solution. Only the human fibrin sealant dressing has consistently demonstrated efficacy in reducing mortality, hemorrhage volume, and resuscitation requirements in animal models of severe arterial injury. Fibrin dressings, though effective, are prohibitively expensive and difficult to apply in battlefield conditions. Zeolite-based products, while effective in controlling hemorrhage in several animal models, yield a strong exothermic reaction and have been shown to increase tissue temperatures up to 70.8°C at the site of application, leading to inflammation and local tissue necrosis[6-8].

Super QR (Biolife, LLC) is a newly developed non-zeolite mineral hemostatic agent composed of potassium iron oxyacid salt and hydrophilic polymer. When in contact with blood, Super QR forms a firm physical barrier or seal, which prevents further blood flow and allows a natural blood clot to form beneath. The mechanism for this effect is presumably as follows. The hydrophilic polymer rapidly dehydrates the blood and absorbs exudates, while the iron-based oxyacid salt agglomerates the blood protein. In addition, the byproducts of HA may directly enhance platelet aggregation[9].

OBJECTIVE

To compare the efficacy of Super QR to that of currently available hemostatic agents in a porcine model of lethal arterial injury.

METHODS

Animal model – Anesthetized porcine model of uncontrolled hemorrhage inflicted via 6mm punch biopsy of the left femoral artery.

Instrumentation – Pulmonary artery, arterial, and venous catheters; tissue temperature probes.

Experimental Protocol – Forty swine (31.6±2.9kg) underwent 6mm punch biopsy of the left femoral artery. All animals were allowed to bleed freely for 1 minute, after which they were randomized to 1 of 5 treatment groups:

Group I – Super QR (N=8)
Group II – HemCon® Bandage (N=8)
Group III – QuikClot® Powder (N=8)
Group IV – QuikClot ACS+™ Bandage (N=8)
Group V – Army Field Bandage (N=8)

Enough Super QR and QuickClot® powders were applied to fully cover the entire wound; gauze dressings were then positioned directly over these products. In all groups, 6 kg of force was placed directly over the assigned dressing and held for 4 minutes. After 4 minutes, the force was released and a standard pressure bandage immediately applied.

Resuscitation began 2 minutes after injury with Hextend (max vol = 15mL/kg) and Lactated Ringer's (LR) (max vol = 60mL/kg) infused as needed to maintain mean arterial pressure (MAP) at baseline for the first ten minutes and at 65mmHg thereafter. Animals were observed for 180 minutes or until death.

Outcome Measures – Survival, hemorrhage and resuscitation volumes; continuous monitoring of ECG, HR, MAP, ETCO2, and core body & tissue temperatures; cardiac output, hemoglobin, arterial lactate, and coagulation parameters.

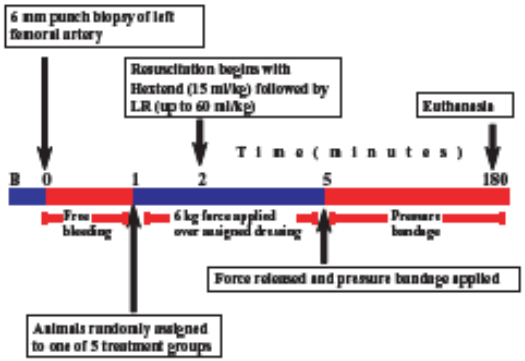

Figure 1 - The experimental timeline

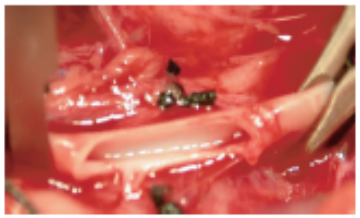

Figure 2 -Left femoral artery injury via punch biopsy.

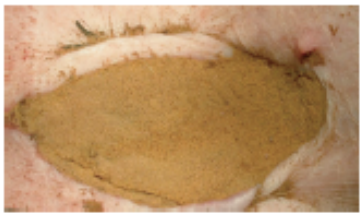

Figure 3 -Super QR powder: stopped bleeding completely, picture taken at 180 minutes.

RESULTS

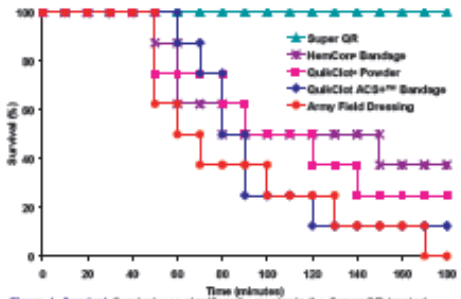

Figure 4 -Survival: Survival was significantly greater in the Super QR treated animals as compared to all other groups ($P < 0.001$).

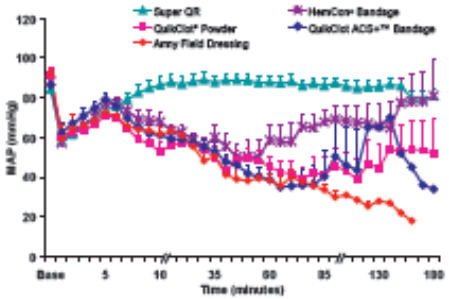

Figure 5 - Mean Arterial Pressure: MAP in the Super QR treated animals returned to baseline levels and remained significantly greater as compared to all other treatment groups ($P < 0.05$; mANOVA).

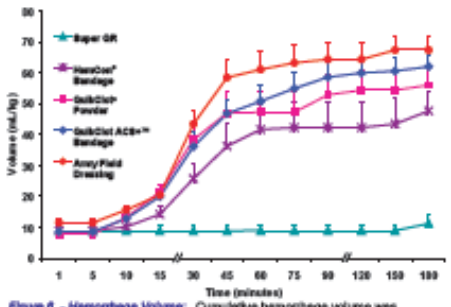

Figure 6 - Hemorrhage Volume: Cumulative hemorrhage volume was significantly lower in the Super QR treated animals as compared to all other groups ($P < 0.001$; mANOVA).

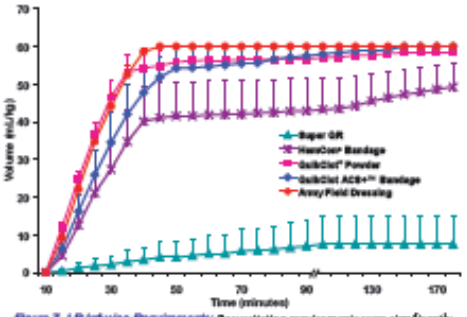

Figure 7- LR Infusion Requirements: Resuscitation requirements were significantly lower in the Super QR treated animals as compared to all other groups ($P < 0.001$; mANOVA).

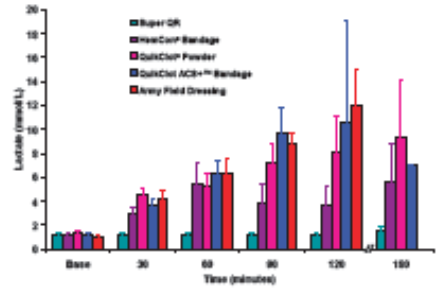

Figure 8 - Arterial Lactate: Arterial lactate was significantly lower in the Super QR treated animals as compared to all other groups throughout the experimental protocol ($P = 0.009$; mANOVA).

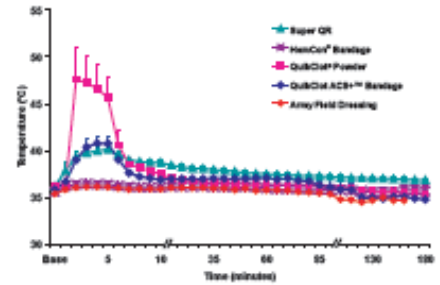

Figure 9 - Tissue temperature: Tissue temperature increased after product application in the Super QR, QuikClot Powder, and QuikClot ACS+ treated animals. This increase was significantly greater in the QuikClot Powder group as compared to all other groups ($P < 0.001$; mANOVA).

Table 1. Survival, Hemorrhage and Resuscitation Volumes

Group	Survival(%)	Mean Survival Time (minutes)	Hemorrhage Volume (mL/kg)	LR Infusion Volume (mL/kg)
Super QR	100	180 (0)	11 (3)	8 (8)
HemCon® Bandage	37.5	116 (22)	40 (5)	46 (7)
QuikClot® Powder	25	107 (15)	35 (5)	58 (2)
QuikClot ACS+™ Bandage	12.5	91 (14)	62 (3)	66 (0)
Army Field Dressing	0	79 (15)	67 (4)	66 (0)
P-Value	<0.001	0.004	<0.001	<0.001

Table 2. Coagulation Profile

Group	PT (seconds) Base	PT (seconds) Final	PT (seconds) P-Value*	PTT (seconds) Base	PTT (seconds) Final	PTT (seconds) P-Value*	Platelets (10^3/µL) Base	Platelets (10^3/µL) Final	Platelets (10^3/µL) P-Value*	Fibrinogen (mg/dL) Base	Fibrinogen (mg/dL) Final	Fibrinogen (mg/dL) P-Value*
Super QR	14.3 (2.4)	14.2 (1.8)	<0.001	13.7 (1.4)	13.9 (1.2)	0.885	291 (79)	273 (79)	0.172	148 (21)	134 (22)	<0.001
HemCon® Bandage	15.4 (0.8)	15.8 (1.4)		13.8 (1.2)	15.1 (1.6)		362 (107)	254 (138)		154 (36)	91 (31)	
QuikClot® Powder	16.2 (0.8)	17.7 (2.6)		14.3 (1.6)	19.4 (4.9)		349 (82)	309 (88)		144 (17)	68 (17)	
QuikClot ACS+™ Bandage	15.1 (1.4)	17.8 (3.7)		14.6 (2.1)	16.6 (2.6)		314 (200)	192 (54)		135 (37)	58 (14)	
Army Field Dressing	15.8 (0.8)	17.8 (1.8)		16.3 (2.7)	18.6 (2.6)		327 (166)	164 (69)		147 (38)	64 (13)	

*P-Values are ANOVA for final values

DISCUSSION

- In a porcine model of lethal arterial injury, Super QR significantly reduced 180-minute mortality, total hemorrhage volume, and LR infusion needs as compared to the HemCon® Bandage, QuikClot® Powder, QuikClot ACS+™ Bandage, and Army Field Dressing.
- Super QR provided effective hemostasis even in the setting of significant increases in arterial pressure.
- The coagulation profile was significantly more favorable in the Super QR treated animals, likely due to the reduced fluid needs.
- While application of Super QR increased tissue temperature, this increase was not statistically significant as compared to the other groups and more importantly, was not to a degree or of duration sufficient to cause thermal injury[10].

LIMITATIONS

- This study included only short-term mortality.
- This model included only arterial injury. Therefore the data can not be generalized to other types and mechanisms of injury.

CONCLUSIONS

In a clinically relevant model of lethal arterial hemorrhage, the application of the new hemostatic agent, Super QR, significantly reduced mortality, hemorrhage volume, and resuscitation requirements as compared to all other hemostatic agents tested in this study. Additionally, Super QR did not result in the marked increase in tissue temperature characteristic of zeolite-based products.

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