DEVELOPMENT OF A PORCINE MODEL OF NONCOMPRESSIBLE HEMORRHAGE

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Abstract:

This research seeks to develop technologies to address the challenging problem of exsanguinating hemorrhage on the battlefield, particularly truncal (noncompressible) hemorrhage. Exsanguination is the first or second most common cause of battlefield mortality and noncompressible hemorrhage have been especially problematic. A research priority of the US Army is to develop effective treatment for traumatic hemorrhage in subjects with noncompressible injuries. We believe that bleeding from complex wound topographies in noncompressible, truncal injuries can be treated with a resorbable synthetic polymeric matrix combined with human clotting factors. In contrast to previous hemostatic devices, we believe our engineering approach will maximize efficacy while decreasing both polymer and biologic usage, thus providing a cost-effective device. Accordingly, we have developed the ability to engineer a variety of synthetic, resorbable prototypes at nano- and micro-scales (fiber and particulate) using minimal amounts of polymer and clotting factors. Prototype configurations range from a cotton gauze analogue to an expandable polymer. In addition, we have developed economical, abundant sources of human fibrin sealant components that are kinetically faster than commercially-available sealants.

Introduction:

The first part of the study is to create a hemorrhagic model which reciprocates the bleeding problems currently existing in the battlefield. In this attempt we tried to create a bleeding model which exsanguinates to death in one hour when no biologics are supplied.

Methods

Each animal was fasted for 12-18 hours before surgery, with free access to water. Premedication was done with a combination of telazol (4.4mg/kg), ketamine (2.2 mg/kg), and xylazine (2.2 mg/kg), given as a single IM shot. An IV line was established in a marginal ear vein to provide supplemental medication (telazol 4.4mg/kg, ketamine 2.2 mg/kg,
and xylazine 2.2 mg/kg IV as needed), and euthanasia solution at the end of the procedure. The animal was masked with isoflurane (3-4%) and supplemented with oxygen (3-5 L/min) to achieve relaxation for endotracheal intubation. Once intubation was accomplished, the animal
was maintained with isoflurane (1-2%) supplemented with oxygen (1-2 L/min) throughout the procedure. A rectal temperature probe, pulse oximeter and EKG (cardiac) monitors were placed. The animal rested on a warming blanket. Mechanical ventilation was provided at a rate of 12-15 breaths per minute and a tidal volume of 5-10 mL/kg. End-tidal pCO2 was maintained at 35-45 mm Hg. The equipment required for these and subsequent procedures included an anesthesia machine, a ventilator, an end-tidal CO2 monitor, a rectal-temperature monitor, a warming blanket, an arterial
pressure monitor, a Foley catheter, laparotomy and vascular surgical instruments, and a suction apparatus. Continuous vital sign data were digitally captured by a Bionet monitor.

Fig. 1: Anesthesia equipment and the vital signs monitor used during operating procedures.

Model

A carotid arterial catheter for pressure monitoring and blood sampling, and a jugular venous catheter for fluid and medication administration was placed via surgical cut down in the right neck. A midline laparotomy and splenectomy was performed to minimize autotransfusion by the contractile porcine spleen.
A calculated injury is made to the left lateral lobe of the liver involving 1 portal vein branch, 1 hepatic vein and hepatic artery branches. Control animals gets no treatment where as the test group gets the firm alginate foam directed into the abdomen away from the injury site to prevent any foam embolization into the heart. The incision is then closed and the animal is allowed to recover for 1 hour with warm saline infusions whenever the MAP falls by 20% of its pre-injured state. After 1 hour the animals are sacrificed by

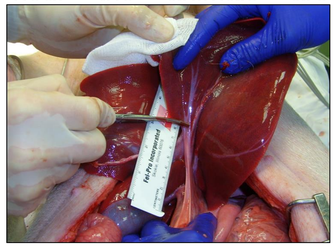

Fig. 2: . Liver in situ of a swine model, immediately prior to injury. Tips of scissors indicate 2nd branch of left main Portal Vein to Left Lateral lobe. (Injury Site)

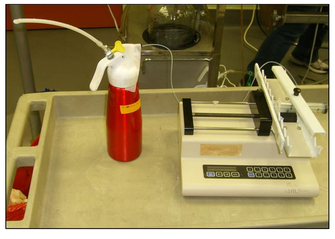

Fig. 3: Alginate Foam Injecting Equipment.

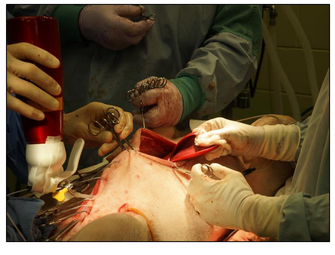

Fig. 4: Injecting mechanism. (Note the injecting site is away from the injury site). Left Lobe of Liver is also seen in the picture. Picture taken before injury.

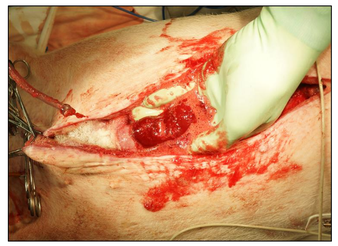

Fig. 5:. Reopening of midline incision 20 min after injury & treatment, Right is cephalad. Alginate foam in inferior portion of wound; C lot mixed with foam from superior portion of wound

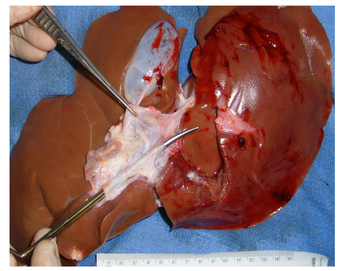

Fig. 6: Liver ex vivo, inferior view showing PV system & injury. This injury was a partial transection of the LLL at its base, Scissors has been inserted in the orifice of the main PV, into the left main branch, and the tips are emerging through the cut proximal end of the 2nd branch to the LL lobe.

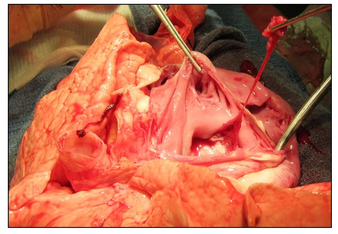

Fig. 7: Stringy red colored clot recovered from the right ventricle of the heart showing the risk of embolization when alginate foam is injected close to the injury site.

Conclusion

1. The current model works as a reliable hemorrhagic subject as without any medical aid the controls die in a 30-60 minutes window.
2. The above delivery system has provided some preliminary evidence of effective drug delivery system in swine hemorrhagic models
3. The firm alginate foam delivering mechanism can be combined with other clotting factors for more effective hemostasis.