IMPROVING ON ARMY FIELD GAUZE FOR LETHAL VASCULAR INJURIES: CHALLENGES IN DRESSING DEVELOPMENT

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Abstract

Accounting for half of all deaths, uncontrolled hemorrhage remains the leading cause of death on the battlefield. Gaining hemostatic control of lethal vascular injuries sustained in combat using topical agents remains a challenge. Recent animal testing using a lethal arterial injury model compared a variety of woven and non woven products with granular products, and found only one product (WoundStat) gave consistent animal survival (J Trauma. 2007;63:276-284). This product is a granular substance which seals the hemorrhaging wound in 30 seconds. However, the Army Institute for Surgical Research has put forth the challenge to develop an intact dressing with comparable hemostatic properties. The challenges in developing this type of product from woven and non woven cotton-based materials will be discussed.

Introduction

The development of smart interactive fabrics is increasing at an accelerated rate (34% growth rate, 2004 – 2009). Four classes of biologically active molecules including enzymes, peptides, carbohydrates, and lipids have demonstrated activity on cotton for a variety of potential uses including wound dressings, decontamination wipes, decubitus prevention bed sheets, and skin care materials (1). We have previously shown that the attachment of enzymes including lysozyme has robust antibacterial activity (2), and we have demonstrated that protease binding peptides (3) and protein binding lipids (4) attached to cotton have potential as wound healing agents. Our interest in agents to stop lethal arterial hemorrhages arose from our work on the hemostatic properties of chitosan. Chitosan is a biopolymer derivative of chitin which is derived predominantly from shellfish. Chitosan is characterized for its relative percent level of acetylation. The development of improved hemostatic agents for use in lethal extremity arterial hemorrhages has increased over recent years. The hemostatic properties of chitosan derive in part from its positively charged surface, which initiates aggregation of negatively charged red blood cells (5,6). Thus the ability of chitosan to initiate coagulation is related to the percent of deacetylated chitosan. Chitosan has been developed as a sponge for use in lethal extremity arterial hemorrhages and it is used in battlefield casualties for that purpose. Chitosan is among a number of currently deployed hemostatic agents used within the armed services to treat hemorrhaging wounds.

We have examined the blood flow and clotting properties of chitosan-treated nonwoven spunlaced cotton. Nonwoven designs can provide as many design opportunities for blood adsorption and platelet adherence, stopping blood flow, and stimulating coagulation as wovens. The chitosan-treated nonwoven, spunlaced cotton was subject to a blood adsorption test which consisted of placing a drop of citrated sheep blood on the treated cotton and measuring the diffusion of blood flow into the fabric with time. Figure 1 shows the results of this study using a 2% chitosan/BTCA-treated spunlaced cotton non-woven. Chitosan was grafted onto the fabric using a butane-tetracarboxylic acid crosslinking reagent. The results of this experiment show that a 2% chitosan treated fabric is effective in stopping blood flow into the fabric. The activity appears to be based on the gelling properties of the chitosan. Citrate-treated blood will attenuate clotting, and visual assessment of the fabric bound blood suggested the absence of fibrin mediated clotting.

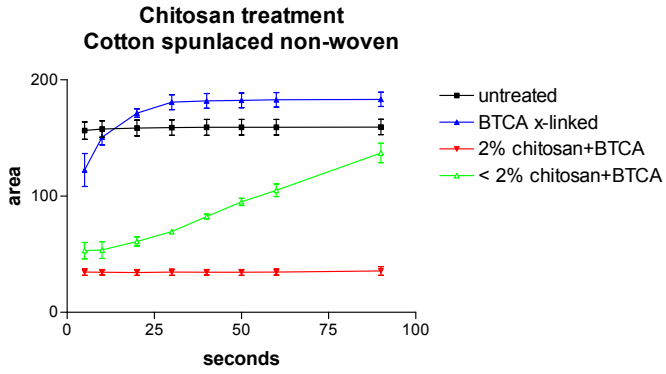

Figure 1. Plot of diffusion of blood across an area of chitosan-treated spunlaced nonwoven, and comparison with less chitosan.

The U.S. Army Institute for Surgical Research (USISR) and the Uniformed Services University of the Health Sciences have outlined ideal properties needed in a battlefield dressing. These include the following properties 1) being able to rapidly stop large vessel arterial and venous bleeding 2 minutes after application when applied to an actively bleeding wound through a pool of blood. 2) no requirement for mixing or preapplication preparation; 3) simplicity of application by wounded victim, buddy, or medic; 4) light weight and durable; 5) long self life in extreme environments; 6) safe to use with no risk of injury to tissues or transmission of infection; and 7) inexpensive (9). With this list of ideal properties the question arises: Is there any deployed product capable of stopping or reducing groin arterial bleeding and preventing exsanguination that otherwise could not be controlled by the standard gauze dressing? To evaluate this question the USISR compared three deployed hemostatic agents with a fibrin sealant, which is a combination of fibrinogen and thrombin and currently has a prohibitive price ($500 – $1000 per dressing) for purchase. The dressings evaluated were the Army Field Dressing (a cotton product of long-standing use), Quickclot, HemCon, and Fibrin Sealant. The Army Field Dressing, which is the standard field dressing used by the military consists of two layers of gauze that wrap densely packed cotton. It absorbs a large volume of blood, and the cotton strands stimulate platelet aggregation. Quickclot is a granular mineral zeolite that rapidly absorbs water in an exothermic reaction (7). In a wound the reaction may concentrate clotting factors and it promotes hemostasis. Chitosan as previously described has strong tissue adhesive properties that seal the wound and stop bleeding.

To assess these dressings the Swine Femoral Artery assay was employed (8). This assay is a challenging arterial bleeding assay that employs anethesized pigs, which are splenectomized and instrumented. The right femoral artery is exposed and a 6-mm hole is created. Pressure and blood volume loss is measured. In this assay only Fibrin Sealant (a fibrinogen/thrombin composite used as a standard of comparison) gave significant survival rates (9). Mortality was 25% with Fibrin Sealant. Whereas mortality for the other dressings was 100 percent. The results of this assay show only HemCon increased survival over the other hemostatic agents.

More recently Ward et al (10). have reported that a new hemostatic agent consisting of a granular combination of a smectite mineral and a polymer (Woundstat) gave 100 percent survival in the swine femoral artery assay. The substance acts to rapidly seal the hemorrhaging artery, and aggregated red blood cells and the formation of fibrin matrix were noted 1 minute following application. The authors note that Woundstat adheres well, without becoming inextricably linked to tissue, and there is no exothermic reaction. The results of the blood loss before and after application are shown in Table 1.

Table 1. Blood loss parameters for dressings compared to WoundStat. TBL refers to total blood loss. Thus, pre-TBL is preapplication total blood loss, and post application total blood loss.

	Wound-Stat	Quickclot	HemCon	Army Field Gauze
Pre-TBL (mL/kg)	8.3 ± 3.9	12.1 ± 4.7	7.1 ± 2.4	10.4 ± 3.2
Post-TBL (mL/kg)	1.9 ± 1	54 ± 15.3	76 ± 23	59 ± 19

With the development of new granular substances as described above, which improve on survival the application to a solid dressing matrix for delivery will be the next challenge to fulfill ease of application and simplicity. Development of new materials that would consist of composites of the mineral/polymer matrix is worth considering. Other hemostatic powder-like substances that have shown promise which were not tested in these studies and have undergone limited use by the armed forces i.e. TraumaDex would also be candidates for dressing matrix application development. TaumaDex employs starch microspheres which seal blood flow upon application through a molecular sieve-like mechanism. Surface area coverage, sealant efficacy, adherence, and adsorption capacity are all important factors in this challenging area of hemostasis since the geometry and anatomical location of the wounds can vary greatly, and factors into the success of patient survival. Thus it is important that a hemostatic dressing that combines all of the above listed properties be developed with both fabric engineering innovation and cutting edge delivery technology. As exsanguninating hemorrhage remains the leading cause of battlefield death from both Vietnam and current conflicts in Iraq and Afganistan there is indication that a number of casualties killed in action could be saved by more effective control of bleeding. Expeditious development of new agents employing a cotton-based delivery and pressure application dressings using some of these promising technolgies has promise for improving the future prospects of obtaining more effective battlefield dressings that fulfill all of the requirements.

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