Hemostasis in a Noncompressible Hemorrhage Model: An End-User Evaluation of Hemostatic Agents in a Proximal Arterial Injury

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OBJECTIVE:

1. Evaluate hemostatic bandages by the end user using subjective and objective criteria.
2. Determine if user training and education level impact overall hemostatic outcomes.
3. Our hypothesis was that prior medical training would be directly linked to improved hemostatic outcomes in noncompressible hemorrhage independent of dressing used.

DESIGN: Military personnel were given standardized instruction on hemostatic dressings as part of a tactical combat casualty care course (TC3). Soldiers were randomized to a hemostatic dressing. Proximal arterial (femoral and axillary) injuries were created in extremities of live tissue models (goat or pig). Participants attempted hemostasis through standardized dressing application. Evaluation of hemostasis was performed at 2- and 4-minute intervals by physicians blinded to participants' training level.

SETTING: Military personnel that are due to deploy are given "refresher" instruction by their units as well as participating in the TC3 to further hone their medical skills prior to deployment. The TC3 is simulation training designed to simulate combat environments and real-life trauma scenarios.

PARTICIPANTS: Military personnel due to deploy, physicians (residents and board certified surgeons), animal care technicians, and veterinarian support.

RESULTS: Celox 42 (33%), ChitoGauze 11 (9%), Combat Gauze 45 (35%), and HemCon wafer 28 (22%) bandages were applied in 126 arterial injuries created in 45 animals in a standardized model of hemorrhage. Overall, no significant difference in hemostasis and volume of blood loss was seen between the 4 dressings at 2 or 4 minutes. Combat gauze was the most effective at controlling hemorrhage, achieving 83% hemostasis by 4 minutes. Combat gauze was also rated as the easiest dressing to use by the soldiers ($p < 0.05$). When compared to nonmedical personnel, active duty soldiers with prior medical training improved hemostasis at 4 minutes by 20% ($p = 0.05$).

CONCLUSIONS: There is no significant difference in hemostasis between hemostatic bandages for proximal arterial hemorrhage. Hemostasis significantly improves between 2 and 4 minutes using direct pressure and hemostatic agents. Prior medical training leads to 20% greater efficacy when using hemostatic dressings. (J Surg 70:206-211. Published by Elsevier Inc. on behalf of the Association of Program Directors in Surgery)

KEY WORDS: hemostatic dressing, hemorrhage, simulation, training, education

COMPETENCIES: Patient Care, Medical Knowledge, Practice-Based Learning and Improvement

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INTRODUCTION

Noncompressible torso and proximal extremity hemorrhage are leading causes of preventable deaths on the battlefield.[1-4] A vast array of hemostatic agents have been developed to assist medical and nonmedical first responders in stopping this bleeding. The proper application of hemostatic agents on the battlefield is not addressed in traditional Pre-hospital trauma life support courses.[1] To fill this gap in training, tactical combat casualty care (TC3) courses were developed and instituted specifically for military medical personnel prior to deployment.[5,6] The culminating event is teaching and testing the various tasks in a live tissue model. In addition to airway, breathing, and amputation management, medics learn to treat exsanguinating hemorrhage from a "noncompressible" vascular injury to the groin or axilla. This training allows medics to gain experience in treating a "live and bleeding patient" in a controlled setting prior to encountering a soldier bleeding to death on the battlefield. In addition to training personnel in TC3, we sought to assess employment and efficacy of multiple hemostatic bandages by the actual personnel administering care at the frontlines as well as a subjective evaluation of both the training and the ease of use of the various hemostatic products.

METHODS

Military personnel participating in the TC3 course were selected from units due to deploy within 3 to 6 months. The personnel evaluated had various levels of training. The minimum requirement for participation was combat life saver (CLS) training. CLS is a US Army training program administered at basic combat training for all newly enlisted soldiers. The goal of CLS is to provide all soldiers the ability to increase survival of combat casualties at the point of injury. The basic tenets of CLS are controlling hemorrhage with a tourniquet or other means, administering basic first aid, placing intravenous access, and initiating intravascular fluid to mitigate shock. Combat medics and more advanced medical personnel attend advanced individual training that mirrors emergency medical technician (EMT) training.

A 1 hour block of standardized training on the use and application of hemostatic bandages was given, focusing on life-threatening penetrating vascular injuries to the axilla and groin. This training stressed immediate compression, exposure of the wound by removing debris or blood from the injury site, and application of the hemostatic dressing. This was derived from an expert panel convened to establish guidelines for use of hemostatic agents in the military in 2003 and 2004.[1] Familiarization with materials and practice scenarios on mannequins were performed prior to the culminating event: live tissue training using goat models (*Capra hircus)*. Instructors leading and evaluating the live tissue lab included physician assistants, 3rd-year general surgery residents, and board-certified general surgeons. The training protocol and data collection methods were approved by the Institutional Review Board and Institutional Animal Care and Use Committee.

We evaluated 4 hemostatic bandages currently deployed in combat units: Celox, ChitoGauze, Combat Gauze, and HemCon wafer. The ChitoGauze and HemCon wafer, developed by the Oregon Medical Laser Center, is derived from deacetylation of naturally occurring chitin, which is a carbohydrate complex found in shellfish. It is a nontoxic, biodegradable molecule with strong mucoadhesive properties that received US Food and Drug Administration clearance for human use in 2002.[7] Its primary mechanism of action is by tissue adherence and mechanical sealing of the injury. On contact with blood, it stops bleeding by absorbing water and transforming into an adhesive material that binds to the underlying damaged tissue.[7,8] Initially manufactured as a single-sided, 4×4 inch wafer, the HemCon wafer, it was transformed into ChitoGauze bandages which is a dual-sided, flexible, 3×28 inch roll. The purported benefits of the newer dressing are that it is flexible, thinner, and more versatile allowing for application to a wider range of injuries. Unfortunately, manufacturing of ChitoGauze was restricted pending intellectual property and only 11 products were used. Celox is a chitosan based powder (Medtrade Biopolymers Inc., Seattle, WA) that functions identically to ChitoGauze and was initially manufactured as a powder. The Celox bandage we used incorporates chitosan powder into a rolled 3 inch wide gauze bandage. Combat Gauze is impregnated by kaolin, an inert silicate particle that has procoagulant properties affecting the intrinsic pathway.

Soldiers were randomized to using 1 of the 4 hemostatic dressings (sometimes depending on availability of the dressings on a particular training day), similar to our group's prior reported method.[9,10] Briefly, instructors were blinded to the level of training of each of the medics taking the course. Femoral and axillary arteries were exposed surgically prior to injury. A standardized vascular injury was created by 50% partial transaction with an 11-blade scalpel. Active hemorrhage was allowed for at least 5 seconds prior to bandage application. Compression, exposure, and direct application of the hemostatic bandage were performed by the student. Sterile gauze was typically applied over the hemostatic dressing to fill the wound cavity and aid compression. Compression was held for a period of 2 minutes. A wound without active hemorrhage from around the dressing was determined to be "hemostatic." The volume of hemorrhage from each event was estimated by the attending physician. Compression was reapplied by the student and the wound was reevaluated at 4 minutes following vascular injury. The student was then immediately interviewed following the intervention for level of training, their subjective interpretation of bandage effectiveness, and "ease of use." This was recorded on a scale of 1 to 5, where 5 was regarded as the best. Data was recorded on a standardized form.

Statistical analysis was performed using IBM SPSS PASW statistics software version 18. ANOVA analysis was used for comparing bandages on overall efficacy, ease of use, hemostasis, and hemorrhaged blood volumes at 2 and 4 minutes. Paired T test was used to determine improvement in hemostasis at 2 and 4 minutes for each bandage type. Pearson's coefficient was used to determine correlation between ease of use, efficacy, medical training, and hemostasis.

RESULTS

In total, 42 Celox (33%), 11 ChitoGauze (9%), 45 Combat Gauze 45 (35%), and 28 HemCon wafer (22%) bandages were used to control hemorrhage in 126 arterial injuries created in 45 animals (average weight 35.9 ± 8.6 kg) in a standardized model of hemorrhage.

Hemostasis: Bandage Comparison

"Hemostasis" was defined as cessation of visible hemorrhage within the wound by the physician proctors who evaluated dressing application at 2 and 4 minute intervals. All 4 dressings were marginally effective at controlling hemorrhage at 2 minutes regardless of training. Although not statistically significant, Combat Gauze was the most effective at controlling hemorrhage, achieving 83% hemostasis by 4 minutes. As independent bandages, there was no significant difference in mean hemostasis at 2 or 4 minutes (Fig. 1).

Efficacy and Ease of Use: Bandage Comparison

"Efficacy" and "ease of use" were graded scales of perceived effectiveness and usability annotated by the soldier immediately following application. Combat Gauze was the only

TABLE 1. Bandage Efficacy and Ease of Use

Bandage	Mean Efficacy*	Mean Ease of Use*
Combat Gauze	4.20 ± 0.16	4.51 ± 0.12
ChitoGauze	3.82 ± 0.35	4.36 ± 0.15
Celox	3.78 ± 0.21	3.90 ± 0.18
HemCon	3.33 ± 0.27	3.78 ± 0.24

*Standard error.

bandage that was significantly superior to the HemCon wafer in perceived efficacy ($p < 0.05$). Combat Gauze was also superior to Celox and HemCon wafer in ease of use ($p < 0.05$) (Table 1). Overall efficacy and ease of use had a significant positive correlation 0.33 $p = 0.001$ using Pearson's coefficient. Therefore, if a bandage was perceived as being easy to use it was also perceived as being effective and vice versa.

Medical vs. NonMedical Training

Level of training was blinded to the physician prior to application of hemostatic dressing. There were 36 personnel with CLT. The remaining 37 personnel were either trained at a minimum of EMT training, had a medical occupation, or had nursing degrees. There was no difference in hemorrhage volume between trained and untrained personnel at 2 and 4 minutes and total (30.2 mL total $p = 0.08$, 14.8 mL $p = 0.097$ for 2 minutes, 11.8 mL $p = 0.08$ for 4 minutes). There was no significant difference in hemostasis at 2 minutes between trained and untrained personnel (12.2% $p = 0.30$). However, at 4 minutes, medically trained soldiers improved hemostasis 19.9% ($p < 0.05$) (Fig. 2) compared to soldiers with CLS training only.

Training appeared to affect correlation in bandage evaluation and hemostasis (Table 2). Medically trained soldiers had a positive correlation between ease of use and efficacy of bandage at 2 and 4 minutes. Nonmedically

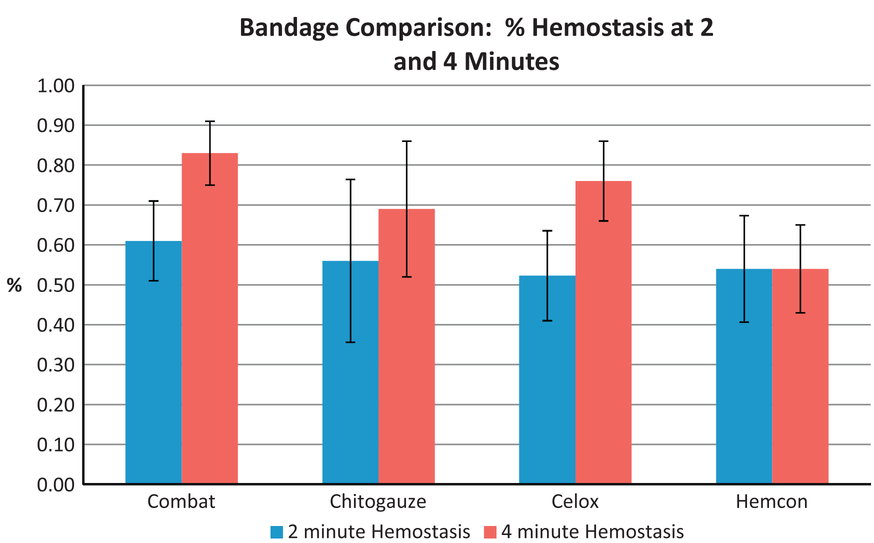

FIGURE 1. Bandage comparison: % hemostasis at 2 and 4 minutes.

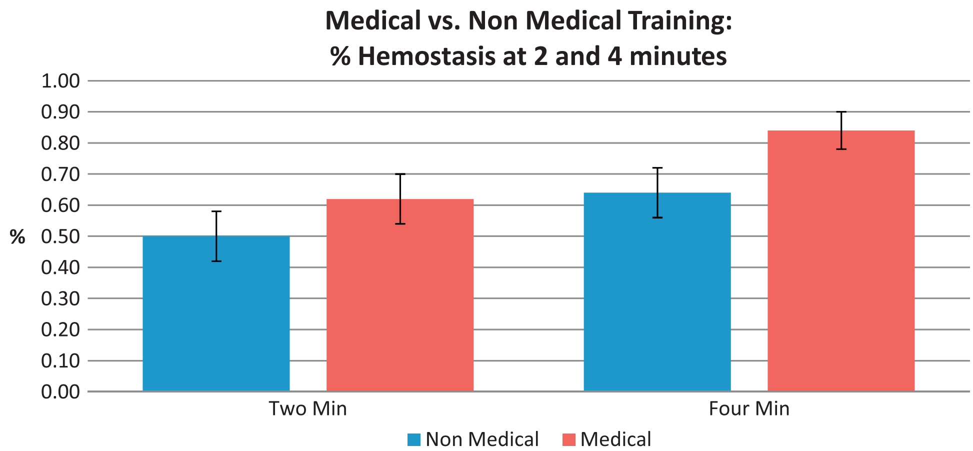

FIGURE 2. Hemostasis at 2 and 4 minutes with medical vs. nonmedical training.

trained personnel displayed no significant correlation between ease of use and efficacy. Therefore, if an EMT thought a bandage was easy to use, it was also perceived as effective. Whereas if CLS trained personnel thought a bandage was easy to use, it may or may not have correlated with efficacy. Both groups had a significant negative correlation between efficacy and hemostasis. A negative value meant less blood loss and greater hemostasis. Thus, both groups could effectively evaluate if a bandage was hemostatic at 2 and 4 minutes. However, only medical personnel could correlate bandage ease of use with efficacy and hemostasis.

DISCUSSION

Recently, the National Trauma Institute has appealed for congressional awareness for greater advancements in hemostatic dressings to address military need. There are multiple hemostatic dressings currently deployed with no clear advantage in hemostasis. Dressings using chitosan, chitin, kaolin, and thrombin are most prevalent. Although the superiority to regular cotton gauze is apparent, clear differences between hemostatic bandages have been difficult to ascertain.[11-15] Mortality, volume of blood loss, rates of survival, re-bleeding, and overall effectiveness have been evaluated in multiple live-tissue studies without a superior agent.[9,11-17] Furthermore, the combat environment, rapid evolution in chemical composition, and delivery make bandage evaluation challenging.[18-20]

Combat Gauze was rated as the easiest to use and most effective by the US Army soldiers in our training facility. In our findings, Combat gauze (CR) also has the best rate of hemostasis at 2 and 4 minutes of compression. CG has been shown to be more effective than gauze at controlling hemostasis in multiple experiments when applied by resident surgeons and scientists in the lab setting; however, subjective comparison is laden with bias. CG is currently the approved hemostatic dressing deployed with US Army personnel. Previous experience and familiarity may improve the margin of effectiveness when compared with employing dressings with different physical properties such as pliability, packaging, and overall composition. Therefore, training may be the primary factor in overall effectiveness with hemostatic bandages.

Few studies have focused on the individual applying the hemostatic bandage. HemCon was found to be the most useful by special forces' soldiers and trained EMT personnel; failures were attributed to improper application—though this was a retrospective and subjective assessment.[21,22] Hemostatic rates at 2 minutes of application in our study were a dismal 50% to 60% with all 4 dressings. Although not significant, continued compression does show improvement in hemostasis at 4 minutes and has

TABLE 2. Medical Training Correlation with Hemostasis

Time	Correlation	Medical		NonMedical	
		Pearson	Sig	Pearson	Sig
2 minutes	Ease/efficacy	**0.344**	**0.003**	0.264	0.053
	Efficacy/hemostasis	**−0.612**	**0**	**0.597**	**0**
4 minutes	Ease/efficacy	**0.344**	**0.003**	0.264	0.053
	Efficacy/hemostasis	**−0.547**	**0.001**	**−0.552**	**0.001**

Bold indicates statistical significance.

been supported in previous models.[9] Of primary interest is the significant increase in hemostasis at 4 minutes among medically trained and experienced medical personnel regardless of hemostatic agent.

EMT training was the level of training and experience noted for improved hemostasis in noncompressible wounds. Adequate exposure and direct application with hemostatic dressings mirror tenants of surgical principles. The 5 to 6 year training programs for board-certified surgeons is neither feasible nor expected. However, repeated exposure to live surgical wounds alone may be a factor. In the absence of operating experience, live tissue models and simulation of human exsanguinations may be the formative experience in improving preventable death on the battlefield.

This study was limited in that individuals were not blinded to the bandages they were using. There were no controls for training (i.e. untrained individual given a dressing to apply). There were only 11 bandages of ChitoGauze utilized in the study, significantly less number than the other groups. These bandages were randomized from the beginning of the experiment until they were removed from market. Generally, hemostasis in a surgical setting is largely based on clinical exam. Perhaps a more objective method such as serial hematocrit or to weigh bandages before and after employment would be an improvement.

The strength of this study is based on education. Not only is our primary objective met by training medical personnel, but it also establishes a model for didactics, simulation, and then tissue application. Evaluation of TC3 and medical education has only raised more questions about disparity in education: what level of medical training is appropriate to soldiers? When to institute it? Notwithstanding, how can medical training be improved? Perhaps an improved study evaluating when and what medical education would be a double blinded prospective trial comparing students directly from basic combat training.

Multiple studies confirm that hemostasis in a noncompressible wound to the axilla or groin is improved with modern hemostatic agents. However, the rapid advancement of hemostatic agents makes evaluation of their efficacy challenging. Training in application may be just as beneficial as new technology. Our data suggest that medical training and experience improve the effectiveness of these dressings by 20%. Further, our data suggest that there is a correlation between medical training, subjective evaluation of hemostatic bandages, and hemostasis. Field evidence of bandage failure in "blind applications" by personnel without advanced medical training supports our assertion.[21,22] Additionally, our study suggests this training does not seem to be conferred by a single course of didactics and mannequin simulation alone. Repeated simulations may be the only method for conferring benefit. Individuals with EMT training or experience in surgical environments show improved hemostatic efficacy in live tissue hemorrhage. Standardized, reproducible simulation training with hemostatic agents may be comparable to repeated real-world exposure and experience. Further controlled studies are required. Our data indicates that prior medical training and experience when using hemostatic dressings may have a beneficial effect in reducing preventable deaths from noncompressible hemorrhage on the battlefield.

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