

A Special Report on the Chitosan-based Hemostatic Dressing: Experience in Current Combat Operations

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Background: Hemorrhage remains a leading cause of death in both civilian and military trauma patients. The HemCon chitosan-based hemostatic dressing is approved by the US Food and Drug Administration (FDA) for hemorrhage control. Animal data have shown the HemCon dressing to reduce hemorrhage and improve survival. The purpose of this article is to report preliminary results of the hemostatic efficacy of the HemCon dressing used in the prehospital setting on combat casualties.

Methods: A request for case information on use of HemCon dressings in Operation Iraqi Freedom and Operation Enduring Freedom was sent to deployed

Special Forces combat medics, physicians, and physician assistants.

Results: Sixty-eight uses of the HemCon dressing were reported and reviewed by two US Army physicians. Four of the 68 cases were determined duplicative resulting in a total of 64 combat uses. Dressings were utilized externally on the chest, groin, buttock, and abdomen in 25 cases; on extremities in 35 cases; and on neck or facial wounds in 4 cases. In 66% of cases, dressings were utilized following gauze failure and were 100% successful. In 62 (97%) of the cases, the use of the HemCon dressing resulted in cessation of bleeding or improvement in hemostasis. There were two reported dressing failures that occurred with blind application of bandages up into large

cavital injuries. Dressings were reported to be most useful on areas where tourniquets could not be applied to control bleeding. The dressings were reported to be most difficult to use in extremity injuries where they could not be placed easily onto or into the wounds. No complications or adverse events were reported.

Conclusion: This report on the field use of the HemCon dressing by medics suggests that it is a useful hemostatic dressing for prehospital combat casualties and supports further study to confirm efficacy.

Key Words: HemCon, Chitosan, Hemorrhage control, Hemostatic dressing, Military.

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Standard gauze field dressings and direct pressure are often inadequate in the control of hemorrhage. In fact, uncontrollable hemorrhage accounts for almost 50% of combat fatalities and up to 80% of civilian trauma fatalities within the United States,^{1,2} making new methods and products for hemorrhage control a research priority of the US Army Department of Defense Combat Casualty Care Research Program. New dressings for compressible areas, improved tourniquets, and improved tourniquet guidelines and systemic agents (i.e., recombinant activated factor VII) have all been part of our research focus.^{3,4} QuikClot (Z-Medica, Newington, CT) and the HemCon chitosan-based dressing (HemCon Inc., Tigard, OR) are two new hemostatic agents among several products that have already been deployed. This report outlines the initial experience using the HemCon dressing as described by far forward military medical person-

nel in the prehospital combat zone during the early stages of current combat operations.

PATIENTS AND METHODS

In 2003, just before the start of Operation Iraqi Freedom, the HemCon dressing was approved by the US Food and Drug Administration and 2,500 were distributed to US Special Operations Military medical personnel. Initial distribution was to forward deployed medics, followed by a more general distribution to physicians and physician assistants located in both Iraq and Afghanistan as more bandages became available. Over 103,000 dressings have now been distributed into combat operations in Iraq and Afghanistan. Providers were instructed to utilize the dressings in cases where other standard techniques had failed or if they thought there was a high likelihood of failure with standard techniques. The use of this dressing is a standard component of the Prehospital Trauma Life Support (PHTLS) military section, and is taught to all Special Operations Forces (SOF) and conventional Army medics in their respective training schools.⁵

In November 2003, in an effort to discern any issues related to usage of HemCon dressings, the authors contacted the forward deployed medical personnel who initially received HemCon dressings and requested a response to a short survey (Table 1). Communication with these widely dispersed and remote SOF teams was necessarily extremely limited, so in-depth reviews were not possible. The authors received approval to conduct a retrospective review of these

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Table 1 HemCon Dressing Data Collection Sheet

1. Anatomical area of injury			
Extremities	Trunk/Abdomen	Groin	Head/Neck
2. Type of bleeding			
Arterial	Venous/mixed	Unknown	
3. Other hemostatic measures attempted first?			
Gauze	Pressure dressings	Other	
4. Was the HemCon dressing applied before other measures?			
Yes	No		
Comment			
5. Was the HemCon dressing effective in hemorrhage control?			
Complete	Partial	None	
Comment			

cases from the institutional review board at Brooke Army Medical Center, Fort Sam Houston, TX. Initially, respondents reported six successful cases. A second larger-scale request was put out in early 2004 requesting information on hemorrhage control success and failure for the HemCon dressing. This request resulted in another 62 cases reported. Due to security reasons and combat situations, most reported cases were based on verbal reports of HemCon dressing use from the involved medics. The information on the clinical utility of the HemCon dressing was obtained several days to weeks after the casualty was treated.

RESULTS

Two US Army emergency physicians collected and reviewed a total of 68 cases of HemCon dressing use over a 1-year period. Four cases were determined to be duplicate reports; thus, a total of 64 unique cases are described. No adverse effects or complications were noted. The majority of dressings (35 of 64 [55%]) were applied to wounds located on patient extremities, whereas 25 of 64 (39%) were applied to wounds located on the chest (trunk), groin (including one penile wound), buttocks, and abdomen. The remaining four uses of the HemCon dressing consisted of face and a neck wounds. Bleeding was predominantly from a venous source in 33 cases, arterial source in 7 cases, and unknown in 24 cases. Medics applied dressings in the prehospital setting. The dressings were not placed into any abdominal or chest cavity wounds.

In 42 (66%) of the cases, the HemCon dressings were used after failure of traditional dressings such as gauze Kerlex and pressure dressings such as an ace wrap. In the remaining 22 cases, it was unclear if any methods had been tried before HemCon application. In 62 (97%) of the cases reported, the HemCon dressing completely stopped or greatly improved bleeding. There were two cases where the bandage failed to slow or stop bleeding. In both cases, the bandage was placed blindly up into large cavitation wounds. In one case, it stopped the bleeding but when the medic removed his hand the dressing came out with his hand as a large clot covered mass. In the second, it was placed up into a large cavitation wound and bleeding continued. However, where

medics were able to visually see the application of the dressing, hemostasis was achieved in all cases. Finally, in one other case, the HemCon dressing initially failed on a foot laceration from broken glass. The dressing was ineffective because the bandage could not be applied into the small wound. However, when the dressing was torn into small pieces and placed into the laceration, hemostasis was attained. Other than the foot laceration all other wounds were due to improvised explosive devices, gunshot wounds, and indirect fire (fragments).

DISCUSSION

The HemCon dressing is an FDA-approved hemostatic agent currently used in the combat environment for the external temporary control of severely bleeding wounds, and also has demonstrated efficacy based on animal work.⁶⁻⁸ Chitosan is a biodegradable, nontoxic, complex carbohydrate derived from chitin (poly β (1 to 4)-N-acetyl D-glucosamine), a naturally occurring substance. Chitosan is the deacetylated form of chitin. The generic term "chitosan" generally is applied when the extent of deacetylation is above 70% and the generic term "chitin" is used when the extent of deacetylation is insignificant, or below 20%. In the form of an acid salt, chitosan demonstrates mucoadhesive activity.⁹ This makes it an ideal candidate for a hemostatic agent. Different forms of chitosans have been used to enhance hemostasis in animal studies involving bleeding from esophageal varices, arterial catheter puncture sites, peritoneal abrasions, or similar experimental insults.¹⁰⁻¹⁴

The HemCon dressing is a freeze-dried chitosan-based dressing designed to optimize the mucoadhesive surface density and structural integrity of chitosan at the site of injury. The current version of this dressing is sold commercially as a 10 cm \times 10 cm \times ~2-mm thick square dressing with nonabsorbable backing, and is packaged in a vacuum-sealed aluminum pouch (Fig. 1). The prototype version of this dressing significantly reduced blood loss and resuscitation fluid use, and improved hemostasis and survival in an experimental model of severe hepatic injury and hemorrhage in swine.⁸ In a subsequent study that employed the commercial version of the dressing, the HemCon dressing controlled bleeding in



Fig. 1. HemCon chitosan-based hemostatic dressing courtesy of HemCon, Inc. HemCon bandage instructions for use: 1. Apply dressing with pressure for 1–2 minutes or until dressing adheres and bleeding is stopped. 2. Apply outer bandage to secure dressing on wound site. 3. Remove dressing within 48 hours. Caution: For external use only. Do not implant. Not for consumption. Do not eat. Single use only. Do not sterilize. Do not apply over eyes.

five of seven attempts in an experimental model that included transection of the femoral artery and vein in pigs.⁶ The authors of the latter study noted that the dressing resulted in “superb hemorrhage control” in five instances but failed completely in two others, raising issues with dressing-to-dressing variability. It now appears that the company has solved the issue of dressing variability.¹⁵ There is evidence suggesting that the HemCon dressing may act by enhancing platelet function¹⁶ and by incorporating red blood cells into the clot¹³ that forms at the site of the wound. However, it currently appears that the principal cause behind the hemostatic effects of HemCon dressing are its mucoadhesive properties.⁸

In this report, the medical providers felt the bandages were most beneficial in 29 (45%) of the cases where a tourniquet could not be utilized due to the proximity of the injuries (i.e. groin, axilla) or inability to otherwise apply a tourniquet such as a neck or face wound. In one case, the bandage was placed on a leg wound in lieu of a tourniquet to allow an injured soldier to return briefly to an ongoing combat operation. The bandage was felt to be of less utility in

small extremity injuries where standard treatment alone would have been effective. In 12 extremity cases, the supervising physicians who eventually received these casualties felt the HemCon dressing may have been utilized “overzealously” and that standard dressings alone may have been as effective as the \$90 bandage. Due to the stiffness of the bandage, it was also found to be more difficult to apply into small wounds without cutting or tearing it to fit.

The need for hemorrhage control is not limited to combat medicine. Uncontrolled hemorrhage accounts for up to 80% of early civilian trauma deaths, although there are few deaths from isolated extremity trauma in the civilian community.¹⁷ The ideal hemostatic dressing will require little training; be nonperishable, durable, flexible and inexpensive; adhere to the wound only; pose no direct risk of disease; not induce a tissue reaction; and effectively control hemorrhage from arterial, venous and soft tissue bleeding. As described in this small case series and in animal studies,^{6–8} the HemCon dressing seems to meet many—but not all—of these requirements, with the main issue relating to flexibility of the current dressing. Although we did not evaluate efficacy beyond initial use of the dressing, there were no reports of adverse effects. This is the first report to document “real-world” use and efficacy of the HemCon chitosan-based hemostatic dressing for external hemorrhage on human patients.

This study is retrospective and observational by design and thus has several limitations. Data were collected and based on verbal and written accounts of HemCon dressing use, rather than complete patient records due to security reasons and the combat situation. Thus, selection and recall bias may affect the results reported. Also, because this study focused only on acute hemorrhage control in a combat environment, the long-term follow-up was absent. Although no adverse outcomes reports have arisen, it is possible that hemostatic failure occurred after the initial application as well as other possible complications from bandage use such as infection, delayed wound healing and increased scarring. Data collection in the prehospital military environment is notoriously difficult, and in this series the ongoing combat operations posed severe limitations on data collection and follow-up. Although obviously not ideal, the data collected do represent the largest case series of reports describing a new hemostatic modality introduced during a war.

Previously, gauze was the only bandage used to control hemorrhage in the prehospital combat environment. However, based on the above data the US Army has recently decided to supply one HemCon dressing to every deployed soldier, three for every Combat Life Saver, and five to every medic in the combat theater. These dressings now join the new tourniquets carried by all soldiers as the individual and medic carried hemostatic devices of choice for severe combat injuries. Finally, the HemCon bandage is now being utilized in civilian emergency medical services for moderate to severe hemorrhage.

In conclusion, the HemCon chitosan-based hemostatic dressing as used by medics appears to be a safe and useful adjunct for the control of external hemorrhage in this case series of prehospital combat patients. Further human prospective controlled studies are warranted.

REFERENCES

1. Sauaia A, Moore FA, Moore EE, et al. Epidemiology of trauma deaths: a reassessment. *J Trauma*. 1995;38:185–193.
2. Carey ME. Analysis of wounds incurred by U.S. Army Seventh Corps personnel treated in Corps hospitals during Operation Desert Storm, February 20 to March 10, 1991. *J Trauma*. 1996;40:S165–S169.
3. Holcomb J, Pusateri A, MacPhee M, et al. New technologies in hemorrhage control. *Curr Opin Crit Care*. 1997;3:488–493.
4. Pusateri AE, Modrow HE, Harris RA, et al. Advanced hemostatic dressing development program: animal model selection criteria and results of a study of nine hemostatic dressings in a model of severe large venous hemorrhage and hepatic injury in swine. *J Trauma*. 2003;55:518–526.
5. National Association of Emergency Medical Technicians. PHTLS Basic and Advanced Prehospital Trauma Life Support. St. Louis: Mosby, 2003.
6. Alam HB, Chen Z, Jaskille A, et al. Application of a zeolite hemostatic agent achieves 100% survival in a lethal model of complex groin injury in Swine. *J Trauma*. 2004;56:974–983.
7. Kheirabadi BS, Acheson EM, Deguzman R, et al. Hemostatic efficacy of two advanced dressings in an aortic hemorrhage model in Swine. *J Trauma*. 2005;59:25–34.
8. Pusateri AE, McCarthy SJ, Gregory KW, et al. Effect of a chitosan-based hemostatic dressing on blood loss and survival in a model of severe venous hemorrhage and hepatic injury in swine. *J Trauma*. 2003;54:177–182.
9. Evans EE, Kent SP. The use of basic polysaccharides in histochemistry and cytochemistry: IV. Precipitation and agglutination of biological materials by aspergillus polysaccharide and deacetylated chitin. *J Histochem Cytochem*. 1962;10:24–28.
10. Brandenburg G, Leibrock LG, Shuman R, et al. Chitosan: a new topical hemostatic agent for diffuse capillary bleeding in brain tissue. *Neurosurgery*. 1984;15:9–13.
11. Fukasawa M, Abe H, Masaoka T, et al. The hemostatic effect of deacetylated chitin membrane on peritoneal injury in rabbit model. *Surg Today*. 1992;22:333–338.
12. Klokkevold PR, Fukayama H, Sung EC, et al. The effect of chitosan (poly-N-acetyl glucosamine) on lingual hemostasis in heparinized rabbits. *J Oral Maxillofac Surg*. 1999;57:49–52.
13. Klokkevold PR, Lew DS, Ellis DG, et al. Effect of chitosan on lingual hemostasis in rabbits. *J Oral Maxillofac Surg*. 1991;49:858–863.
14. Klokkevold PR, Subar P, Fukayama H, et al. Effect of chitosan on lingual hemostasis in rabbits with platelet dysfunction induced by epoprostenol. *J Oral Maxillofac Surg*. 1992;50:41–45.
15. Pusateri AE, Holcomb JB, Kheirabadi BS, et al. Making sense of the preclinical literature on advanced hemostatic dressings. *J Trauma*. 2005 (in press).
16. Chou TC, Fu E, Wu CJ, et al. Chitosan enhances platelet adhesion and aggregation. *Biochem Biophys Res Commun*. 2003;302:480–483.
17. Dorlac WC, DeBakey ME, Holcomb JB, et al. Mortality from isolated civilian penetrating extremity injury. *J Trauma*. 2005; 59:217–222.