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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 a U.S. Food and Drug Administration (FDA) approved bandage for hemorrhage control. Previous animal data have shown the HemCon® dressing to reduce hemorrhage and improve survival. The purpose of this case series is to report the hemostatic efficacy of the dressing in combat casualties.* ***Methods:*** *A request for case information on use of HemCon® dressings in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) was sent to combat medics, physicians, and physician assistants.* ***Results:*** *Forty-eight uses of the HemCon® dressing were reported and reviewed by two U.S. Army emergency medicine physicians. Four of the 48 cases were determined duplicative resulting in a total of 44 combat uses. Dressings were utilized externally on the chest and abdomen in 19 cases, on extremities in 23 cases, and on neck or facial wounds in 2 cases. Dressings were appropriately utilized after gauze failed 66% of the time. In 42 (95%) of the cases, the use of the HemCon® dressing resulted in a cessation or marked improvement in hemostasis. Dressings were reported to be most useful in areas where a tourniquet 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 were reported.* ***Conclusion:*** *The HemCon® dressing appears to be an effective hemostatic agent for combat casualties.*

Introduction

Uncontrollable hemorrhage accounts for almost 50% of combat fatalities and up to 80% of civilian trauma fatalities within the U.S.[1,2] Standard field dressings and direct pressure for hemorrhage control have been shown to be inadequate in previous combat patients. Therefore, hemorrhage control has been a priority for the U.S. Army Department of Defense Combat Casualty Care Research Program for the last 10 years. Research has focused on the development of various dressings for compressible areas, improved tourniquets, tourniquet guidelines, and the use of systemic agents (rFVIIa) to control hemorrhage and reduce mortality from exsanguination.[3,4]

A number of hemostatic agents and bandages have undergone animal studies to compare hemorrhage control, morbidity and mortality with some success.[3,5-10] Also, there have been reported success in two recent human studies for hemorrhage control with these agents.[11,12] King et al reported that a new dressing, the Modified Rapid Deployment Hemostat, successfully stopped bleeding in nine out of 10 patients with high grade liver injuries who failed conventional hemorrhage control therapies.[11] The results of these studies suggests pre-hospital use of some new hemostatic agents may decrease mortality related to hypovolemia and have led to recommended use in the Pre-Hospital Trauma Life Support textbook.[13]

Currently, military medical personnel are using two of the new hemostatic products in combat operations to include Quickclot and the HemCon® chitosan-based dressing, with reported success. This study describes the use of the HemCon® dressing in current combat operations by military medical personnel for external hemorrhage control.

Materials and Methods

This study describes the results from clinical practice in hemorrhage control in a combat zone. In 2003, just prior to the start of OIF, the HemCon® dressing was approved by the U.S. FDA and 2,500 were distributed to U.S. Special Operations Military medical personnel. Initial distribution was to forward deployed medics and was followed by a more general distribution to physicians and physician assistants located in both Iraq and Afghanistan as more bandages became available. Over 40,000 dressings have now been distributed. 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. Instruction and training on use of the bandage was based largely on review of the packet insert by all providers.

In Nov 03, in an effort to discern any issues related to usage of these dressings, those forward deployed medical personnel

who initially received HemCon® dressings, were contacted by the authors on use and performance of the dressing (Table 1). Initially, six successful cases were reported. 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 38 cases reported. Due to security reasons and combat situations, most of these cases were based on verbal reports of HemCon® dressing usage and success.

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
   Comments_____

Table 1. HemCon® Dressing Data Collection Sheet

The authors received approval to conduct a retrospective review of these cases from the institutional review board at Brooke Army Medical Center, Fort Sam Houston, TX.

Results

A total of 48 cases of HemCon® dressing use was collected over a 1-year period and reviewed by two U.S. Army emergency physicians. Four cases were determined to be duplicate reports of HemCon® dressing experience. Thus, a total of 44 unique cases are described. No adverse effects or complications were noted with dressing use. The anatomical distribution of the HemCon® dressing use in combat patients is summarized in Table 2. The majority, 52%, of dressings were applied to wounds located on patient's extremities while 43% were applied to wounds located on the chest (trunk) and abdomen. The remaining two uses of the HemCon® dressing consisted of a face and a neck wound. Bleeding was from a predominantly venous source in 14 cases, arterial source in four cases, and unknown in 26 cases (Table 3). The dressings were applied in the pre-hospital setting by medics. No dressings were used in a body cavity.

Extremity	23
Chest/Abdomen/Groin/Buttock	19
Head/Neck	2

Table 2. Anatomical Location of Injury

Arterial	4
Venous/Mixed	14
Unknown	26

Table 3. Probable Source of Bleeding

In 29 (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 15 cases, it was unclear if any methods had been tried prior to HemCon® application. In 42 (95%) of the cases reported, the use of the HemCon® dressing resulted in complete cessation or marked improvement in bleeding. One unsuccessful case described attempted dressing use on an extensive face wound that had persistent bleeding from areas where the dressing could not cover. However, where the dressing was able to be applied, hemostasis was achieved. The other unsuccessful case involved use of the HemCon® dressing on a foot laceration from broken glass. The dressing initially was ineffective because the bandage could not be applied effectively onto the small wound. However, when the dressing was then torn into small pieces and placed into the laceration, hemostasis was attained.

Discussion

The two hemostatic agents used currently in combat operations are QuickClot and the HemCon® dressing. QuickClot, which has been used in combat operations since 2002, is an FDA-approved product that uses zeolite granules for hemorrhage control and has demonstrated potential in animal models.[6,8,9] QuickClot was also reported to be successful in a human case of severe hemorrhage from multiple gunshot wounds.[12] The granules were applied to three external wounds which resulted in cessation of bleeding from these sites. However, a potential side effect of the granules is the production of an exothermic reaction in the wound, which potentially could cause collateral organ and tissue damage.[7,8]

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 potential based on animal work.[9,10,14] Chitosan is a biodegradable, nontoxic, complex carbohydrate derived from chitin (poly ? [1 to 40]-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.[15] This makes it an ideal candidate for a hemostatic agent. A variety of 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 [16-21]

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 x 10 cm x ~2 mm thick square dressing with nonabsorbable backing, and is packaged in a vacuum sealed aluminum pouch (figure). 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.[10] In a subsequent study that employed the commercial version of the dressing, the HemCon® dressing controlled bleeding in five of seven attempts in an experimental model that included transection of the femoral artery and vein in pigs.[9] 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. There is evidence suggesting that the HemCon® dressing may act by enhancing platelet function and by incorporating red blood cells into the clot that forms at the site of the wound.[17,22] However, it currently appears that the hemostatic effects of the HemCon® dressing are due principally to its mucoadhesive properties.[10]

Fig. HemCon® chitosan-based hemostatic dressing courtesy of HemCon, Inc.

In this case series, the medical providers felt the bandages were most beneficial in cases where a tourniquet could not be utilized due to the proximity of the injuries (groin, axilla) or inability to otherwise apply a tourniquet such as a neck or face wound. Also, in one case, the bandage was utilized successfully on a leg wound in lieu of a tourniquet to allow the 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 be effective. It was reported that the HemCon® dressing may have been utilized "overzealously" in 12 extremity cases. In these injuries, the supervising physicians who eventually received these casualties felt that gauze dressings alone may have been as effective as the $100 bandage. Due to the stiffness of the bandage, it was also found to be more difficult to apply in small extremity wounds.

The need for hemorrhage control is not limited to combat medicine. Uncontrolled hemorrhage accounts for up to 80% of early civilian trauma deaths. The ideal hemostatic dressing would 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, the HemCon® dressing seems to meet many of these requirements.[9,10,14] Although we did not evaluate efficacy beyond initial use of the dressing, there were no reports of adverse effects with bandage use. This is the first case series 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 combat situations. Thus, selection and recall bias may affect the results reported. Also, because this study focused only on acute hemorrhage control, the long-term follow-up was absent. While no adverse outcome 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 scaring.

In conclusion, the HemCon® chitosan-based hemostatic dressing appeared to be an effective adjunct for the control of external hemorrhage in this case series of combat injuries. No other adjuncts were required to control bleeding in 95% of the reported cases. Further human prospective controlled studies are warranted.

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