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Original Contributions

EXPERIENCE WITH CHITOSAN DRESSINGS IN A CIVILIAN EMS SYSTEM

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□ **Abstract—The HemCon® Bandage (HemCon Medical Technologies Inc., Portland, OR) is a hemostatic dressing made of chitosan, a complex carbohydrate derived from chitin. The objective of this study was to determine the effectiveness of the HemCon® Bandage in a civilian emergency medical services system. The HemCon® Bandage was added to the trauma kits of a fire agency and data were collected from June 1, 2005 to August 31, 2006. The dressing was to be used when conventional treatment (pressure and gauze dressings) failed to control external bleeding wounds or for obvious arterial bleeding. Paramedics documented time to cessation of bleeding after HemCon® Bandage application as well as wound characteristics and suspected bleeding type. There were 37 uses and complete data were available for 34 cases. Wound location involved the head, neck, or face in 13 subjects and extremities in 18 subjects. There was one case each involving the chest, abdomen, and axilla. The bandage controlled hemorrhage in 27/34 (79%) cases, 25/34 (74%) within 3 min of application. In 25/34 cases, direct pressure had initially failed to control bleeding and the HemCon® Bandage was effective in 19/25 (76%). The HemCon® Bandage failed to stop bleeding within 10 min in 7 cases. User error was a factor in 6 of the 7 failures. The HemCon® Bandage is an effective adjunct for uncontrolled external hemorrhage when traditional measures, such as pressure and gauze dressings, fail. © 2009 Elsevier Inc.**

□ **Keywords—chitosan; hemostasis; bandage; external hemorrhage; EMS**

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INTRODUCTION

Hemorrhage is the second leading cause of death in civilian trauma and the leading cause of death from battlefield trauma in the military (1–4). There has been little advancement in the control of external hemorrhage, as evidenced by our reliance on gauze dressings and direct pressure, which has remained unchanged for hundreds of years. As such, there recently has been a significant interest in the development of new external hemostatic agents to achieve hemostasis when conventional methods fail. One of these products is the HemCon® Bandage (HemCon Medical Technologies, Inc., Portland, OR), which is a 10 cm × 10 cm × ~2 mm-thick square bandage (Figure 1) composed of chitosan and a non-absorbable backing in a vacuum-sealed pouch.

Chitosan is a biodegradable, non-toxic, complex carbohydrate derivative of chitin (poly-β[1→4]-N-acetyl-D-glucosamine), a naturally occurring substance (5). Numerous animal studies have demonstrated its effectiveness as a hemostatic agent in controlling bleeding from both arterial and venous sources, as well as in coagulopathic subjects (6–11). There are several factors that are thought to contribute to the hemostatic function of chitosan, the most important being its inherent mucoadhesive properties. Additional mechanisms thought to be

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Figure 1. Photograph comparing the more pliable and smaller HemCon® Bandages to the original 4"× 4" size. A roll of ChitoFlex™ is also shown.

involved include platelet activation, vasoconstriction, and interactions with red blood cells through ionic forces and cell surface proteins (12–16). Other possible beneficial attributes of chitosan have been proposed as well, including antimicrobial activity and improved wound healing compared with standard dressings (17).

The military has been the first to employ many new hemostatic agents in humans and the HemCon® Bandage has been distributed to medical personnel involved with combat operations in Iraq and Afghanistan. A retrospective review of 64 uses from these two conflicts suggests that the HemCon® Bandage is an effective hemostatic agent for pre-hospital combat casualties when standard methods are unsuccessful (5). Given that significant morbidity and mortality also can result from uncontrolled external hemorrhage in civilian emergency medical services (EMS) systems, it was hypothesized that a chitosan-based dressing also may control hemorrhage in wounds not responding to direct pressure.

METHODS

Study Design

Data for this case series were obtained through a retrospective chart review of prospectively completed data collection forms after each HemCon® Bandage use, as well as the accompanying pre-hospital case record. The data form was adapted from the one used by the military. The institutional review board at the Oregon Health & Science University (OHSU) approved the study, and waived the requirement of informed consent.

Study Setting and Population

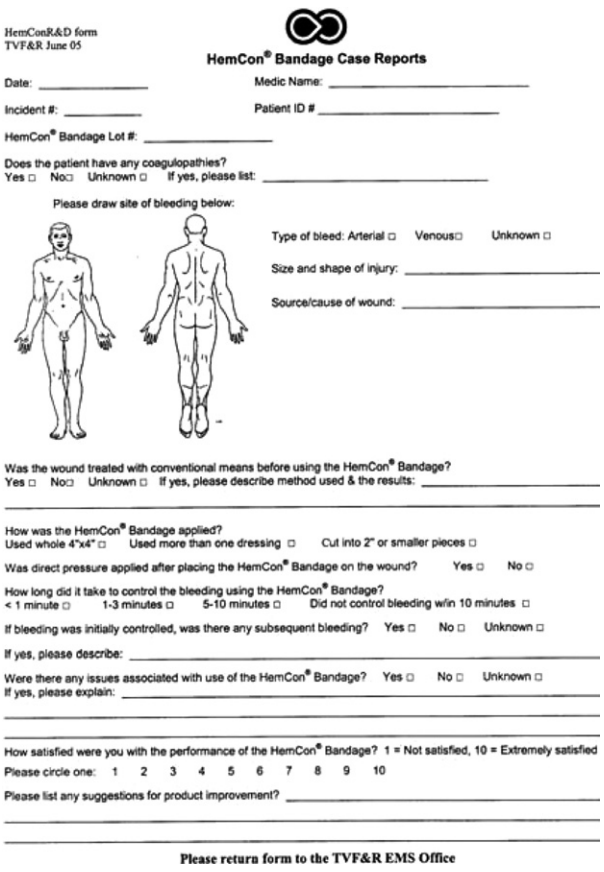
The HemCon® Bandage was added to the trauma kits of all 22 frontline apparatuses of Tualatin Valley Fire & Rescue, a mixed urban-suburban non-transporting fire agency, on June 1, 2005. This agency provides fire protection and first-responder advanced life support (ALS) EMS to over 418,000 citizens in nine incorporated cities. Over 60% of the agency's firefighters also are paramedics. The agency covers an area of 210 square miles and responds to over 23,000 medical EMS calls annually. In 2005, the agency responded to 2338 traumatic incidents, and 226 patients were subsequently transported to a Level 1 trauma center. We estimate that 10–20 of these trauma system patients had hypovolemic shock due to presumed hemorrhage in the EMS setting, almost exclusively from blunt trauma. In the agency's service area, hospital transport is primarily accomplished through a private ALS ambulance agency.

Study Protocol

All EMS personnel were trained, using a multimedia presentation adapted from the military, in the use of the HemCon® bandage. The training presentation included an overall description of the product with directions for application and removal, with picture representation of the steps involved. There was no training with live tissue or hands-on training with the product itself. The initial approach to most external hemorrhage (lacerations, abrasions, puncture wounds) was application of manual pressure with a gauze bandage and elevation of the bleeding area if possible. This is the approach that is traditionally taught to EMS providers and it was not altered for the purpose of the study. If the gauze bandage soaked through with blood, it was to be removed and the HemCon® Bandage applied as directed. The amount of time over which gauze and pressure were applied was not standardized and was left to the discretion of the treating emergency medical technician. For suspected arterial bleeding (large spurts of blood after deep lacerations), personnel were allowed to proceed with the use of the HemCon® Bandage immediately. Crews were encouraged to cut the bandage into pieces as needed to fit the contour of the wound. All receiving hospitals were notified of the removal process for the bandage, which involved irrigating the area with saline.

Study Measures

After each use, paramedics completed a data collection form (Figure 2) in which they were asked to document



HemConR&D form
TVF&R June 05

HemCon® Bandage Case Reports

Date: _____ Medic Name: _____

Incident #: _____ Patient ID # _____

HemCon® Bandage Lot #: _____

Does the patient have any coagulopathies?
Yes □ No□ Unknown □ If yes, please list: _____

Please draw site of bleeding below:

Type of bleed: Arterial □ Venous□ Unknown □

Size and shape of injury: _____

Source/cause of wound: _____

Was the wound treated with conventional means before using the HemCon® Bandage?
Yes □ No□ Unknown □ If yes, please describe method used & the results: _____

How was the HemCon® Bandage applied?
Used whole 4"x4" □ Used more than one dressing □ Cut into 2" or smaller pieces □

Was direct pressure applied after placing the HemCon® Bandage on the wound? Yes □ No □

How long did it take to control the bleeding using the HemCon® Bandage?
< 1 minute □ 1-3 minutes □ 5-10 minutes □ Did not control bleeding w/in 10 minutes □

If bleeding was initially controlled, was there any subsequent bleeding? Yes □ No □ Unknown □

If yes, please describe: _____

Were there any issues associated with use of the HemCon® Bandage? Yes □ No □ Unknown □
If yes, please explain: _____

How satisfied were you with the performance of the HemCon® Bandage? 1 = Not satisfied, 10 = Extremely satisfied
Please circle one: 1 2 3 4 5 6 7 8 9 10

Please list any suggestions for product improvement? _____

Please return form to the TVF&R EMS Office

Figure 2. EMS data collection form.

suspected bleeding type (venous or arterial), history of acquired coagulopathy, wound size and shape, cause of the wound, effectiveness of treatment with conventional methods, application method for the HemCon® Bandage, time to cessation of bleeding, development of any subsequent rebleeding, adverse events or any problems associated with the bandage, satisfaction score (1–10), and any suggestions for product improvement. Unanswered questions were presumed to be unknown. Venous or arterial bleeding was estimated by the EMS personnel based on flow characteristics and was not verified. Wound size estimates were reported in inches or centimeters and converted to inches for consistency. The primary outcome variable was time to cessation of visible external bleeding after placement of the HemCon® Bandage. This was estimated by paramedics in increments of <1 min, 1–3 min, 5–10 min, or >10 min. Hemostasis requiring >10 min was considered to represent a failure of the bandage.

Data Analysis

The data were collected and entered into a secure, password-protected MS Access database (Microsoft, Inc., Redmond, WA). The pre-hospital medical records with patient identifiers removed were retrospectively reviewed to determine patient demographics and additional clinical information that may not have been recorded on the data collection form. Descriptive statistical analyses were performed.

Research Ethics

The HemCon® Bandage is Food and Drug Administration-approved and commercially marketed for control of external hemorrhage. The bandages used in the study were provided free of charge from HemCon Medical Technologies, Inc. as part of a field clinical product trial. The authors of this study do not have any financial interests in HemCon Medical Technologies, Inc. and did not receive grants or funding in support of the research or preparation of this manuscript. HemCon Medical Technologies, Inc. did not have involvement with collection of data, analysis or interpretation of data, writing of the manuscript, or in the decision to submit the manuscript for publication.

RESULTS

Thirty-seven uses of the HemCon® Bandage were reported within the 15-month study time period. Complete data on the primary outcome variable were present for 34 cases (Table 1). In three cases, the time to cessation of bleeding after HemCon® Bandage application was not recorded and these cases were eliminated from further analysis.

Of the 34 uses analyzed, no adverse events or complications were reported. Most of the wounds were extremity wounds (53%) with lacerations to the head, neck, and face the next most frequent (38%). The remainder included one chest wound, one abdominal wound, and one wound to the axilla (9%). The source of bleeding was suspected to be venous in 13 cases, arterial in 12 cases, and unknown in 9 cases. There were five cases where the EMS provider determined a coagulopathy was present, 19 where no coagulopathy was identified, and 10 cases where this information was unknown.

The HemCon® Bandage controlled external hemorrhage in 27/34 (79%) cases, 25/34 (74%) within 3 min of application. In 25/34 cases, direct pressure had failed to control bleeding and the HemCon® Bandage was effective in 19/25 (76%). In 7 cases, the HemCon® Bandage failed to stop bleeding within 10 min. In six of the seven failures, user error was determined to be a contributing factor. This included two cases where the wrong side of the bandage was applied against the wound. In another

Table 1. Summary of 34 Cases of HemCon® Bandage Use

Case #	Sex	Age (years)	Coagulopathy	Type	Location	Size (inches)	Shape	Mechanism	Pretreatment	Bandage Application	Time to Hemostasis	Paramedic Satisfaction
1	M	29	No	Venous	Bicep	1	Linear	Knife	Direct pressure	Whole	<1 min	10
2	M	38	No	Unknown	Forearm	3	Linear	Knife	Direct pressure	Whole	1–3 min	9
3	M	45	No	Unknown	Thigh	3	Linear	Grinder	Direct pressure	Cut to fit	>10 min	8
4	M	85	Yes	Arterial	Scalp	3	Linear	Fall	Towel	Whole	1–3 min	8
5	M	61	Unknown	Arterial	Scalp	8	Linear	Fall	Towel	Cut to fit	1–3 min	10
6	M	NA	Unknown	Unknown	Face	2	Linear	Fall	Direct pressure	Whole	>10 min	NA
7	F	91	Yes	Arterial	Scalp	1.5	Linear	Fall	Direct pressure	Whole	1–3 min	8
8	M	63	Unknown	Venous	Scalp	6	Avulsion	MVC	Direct pressure	Whole	>10 min	2
9	M	49	No	Unknown	Chest	0.79	Puncture	Knife	Direct pressure	Cut to fit	<1 min	9
10	M	35	Unknown	Arterial	Scalp	2	Linear	Knife	No	Cut to fit	<1 min	10
11	M	60	No	Arterial	Scalp	1–2	Linear	Unknown	Direct pressure	Whole	1–3 min	9
12	M	32	No	Arterial	Thigh	2	Puncture	Knife	Direct pressure	Cut to fit	>10 min	1
13	F	21	No	Venous	Scalp	1.5	Linear	MVC	Direct pressure	Cut to fit	<1 min	10
14	M	59	No	Venous	Knee amputation	Torn stitch	Linear	Fall	No	Whole	5–10 min	6
15	F	85	Yes	Venous	Scalp	Quarter size	Round	Fall	Direct pressure	Cut to fit	1–3 min	6
16	M	38	Unknown	Venous	Neck	3 × 3	Linear	Saw	No	Whole (m)	1–3 min	4
17	M	21	Unknown	Venous	Face	4 × 2	Linear	MVC	Direct pressure	Cut to fit	1–3 min	7
18	F	62	Yes	Venous	Thigh	5 × 5	Irregular	NA	Direct pressure	Whole	1–3 min	10
19	M	46	No	Arterial	Axilla	1	Puncture	Knife	Direct pressure	Whole	>10 min	2
20	M	69	No	Venous	Lower leg	0.5	Linear	Fingernail	Direct pressure	Cut to fit	1–3 min	NA
21	F	NA	No	Arterial	Wrist	7	Linear	Knife	No	Whole	<1 min	10
22	F	84	Yes	Arterial	Thigh	Small circle	Round	Unknown	Direct pressure	Whole	<1 min	10
23	F	93	Unknown	Venous	Scalp	2–3	Linear	Fall	Direct pressure	Cut to fit	1–3 min	7
24	F	36	Unknown	Unknown	Wrist	2 × 0.5	Linear	Knife	Direct pressure	Whole	<1 min	8
25	M	52	No	Unknown	Lower leg	Open Fracture	Irregular	MVC	No	Whole	1–3 min	NA
26	M	26	Unknown	Unknown	Scalp	2 × 0.5	Linear	MVC	No	Whole	<1 min	10
27	F	83	No	Venous	Foot	0.5	Puncture	Shears	Gauze	Whole	<1 min	9
28	M	75	No	Venous	Lower leg	10	Linear	Lawnmower	Towel	Whole (m)	<1 min	8
29	M	16	No	Unknown	Wrist	2 × 3	Linear	Ice skate	Direct pressure	Whole	<1 min	10
30	M	48	No	Arterial	Palm	5–6	Linear	Glass bottle	No	Whole	>10 min	7
31	F	58	No	Arterial	Knee	8	Linear	Surgical incision	Direct pressure	Whole	1–3 min	8
32	M	29	Unknown	Unknown	Abdomen	6	Puncture	Knife	No	Whole	<1 min	6
33	F	32	No	Venous	Forearm	2.5 × 4.5	Linear	Glass window	Towel	Whole	>10 min	6
34	M	28	No	Arterial	Forearm	3 × 1	Linear	Glass window	No	Whole	5–10 min	8

NA = data not available; MVC = motor vehicle crash; Whole (m) = multiple whole bandages used.

two cases, there was incomplete coverage of the wound and areas not in contact with the bandage continued to bleed. In the fifth case, the wound was covered with cooking oil as part of the incident. The cooking oil was not removed before application of the bandage, resulting in a failure of adherence. In the sixth failure, the bandage was not applied as directed to a deep groin wound. The etiology of failure in the final case could not be determined. Excluding cases in post hoc analysis where the source of bleeding or outcome was unknown, the HemCon® Bandage was effective in 5/5 cases of possible coagulopathy, 9/12 suspected arterial injuries, and 11/13 suspected venous injuries. Satisfaction scores were reported in 31 of the 34 cases, with a mean score of 7.6 (range 1–10).

DISCUSSION

In recent years, the U.S. Food and Drug Administration has approved several hemostatic agents and bandages for hemorrhage control. Unfortunately, human clinical data are lacking and most of these products have been tested only in animal models of severe hemorrhage. Chitosan-based dressings have been successfully used in swine models of splenic trauma, liver lacerations, and aortic perforation. (7,8,10). The only reported human experience to date comes from use in Operation Iraqi Freedom and Operation Enduring Freedom. Every U.S. Army Combat Lifesaver and medic serving in these conflicts is mandated to carry at least one bandage. Wedmore et al. reported that use of the HemCon® Bandage in 64 cases resulted in cessation of bleeding or improved hemostasis in 97% (5).

The overall success rate for the HemCon® Bandage in our series was 79% and the bandage was most effective in simple linear lacerations of the scalp and extremities. This is lower than the military success rate reported by Wedmore et al. (5). The discrepancy may be due to several factors. Military trauma produces a different distribution of wound type, mechanism, and location. All of the injuries in the military study were caused by improvised explosive devices, gunshot wounds, or indirect fire (fragments) except for a foot laceration. Similar penetrating injuries such as gunshot wounds were much less frequent in our civilian study sample. The majority of injuries were caused by low-energy lacerations involving sharp objects or ground-level falls. The bandage may be more appropriate in high-velocity projectile injuries due to the increased morbidity and mortality risk with uncontrolled external hemorrhage in these cases. Use of the HemCon® Bandage by EMS providers may therefore be more appropriate in populations with a higher incidence of penetrating trauma. Of note, Wedmore et al. reported that extremity injuries were the most difficult to control. In our study, extremity injuries accounted for 53% of the injuries and 4/7 bandage failures. There also was a higher estimation of suspected arterial injuries in our series. There may have been more recall and selection bias in the military study because data collection was delayed due to ongoing combat operations. Finally, the primary outcome variable of effective hemostasis was defined differently in these two studies. In the military study, effectiveness was defined as complete, partial, or none compared to the time estimation used in our study. Thus, the results are not directly comparable.

In evaluating the bandage failure rate of 21% in our series, user error was a contributing factor in most of the cases. Many of these may be correctable through improved product design, education, and training. In two cases, the providers could not determine which side of the bandage to apply to the wound, indicating that adding such instructions may be helpful. This suggestion has, in fact, been implemented by the manufacturer in their most recent product line. In addition, some providers did not understand the importance of cutting or folding the bandage to fit the shape and depth of wounds. This is extremely important because the bandage material must come into close contact with the hemorrhaging tissue to activate its mucoadhesive properties. When cases with user error are removed in post hoc analysis, the success rate increases to 97%, which is the same as that reported by Wedmore et al. (5).

To address these issues, it may be useful to have hands-on training with the bandage. The military training model involves more hands-on experience, and the soldiers also are required to complete a post-test after training. Such training, which was not included in this study, may allow the providers to become more familiar with the product and its correct application. An important challenge with regard to training is the infrequency of bandage use. Based on our findings, we estimate that the bandage will be used once per 1000 EMS medical calls and once for every 100 trauma calls. Thus, it is likely that most providers will lose skills with time and require ongoing training to remain knowledgeable and proficient.

However, training issues are not the only explanations for bandage failure. Limited pliability of the product makes it difficult to apply to irregularly contoured wounds. This limitation has recently been addressed with the release of newer, more pliable bandages in 2” × 4” and 2” × 2” sizes. An additional product line called ChitoFlex™ also has been developed to specifically address difficult-to-reach penetrating injuries. ChitoFlex™ is prepared as a gauze roll and designed to be packed along a wound track to stop bleeding. This may improve success with

deep wounds in difficult-to-apply areas such as the groin and axilla.

Pusateri et al. have suggested that the ideal hemostatic dressing for pre-hospital use should fulfill the following criteria (18). First, it should be able to stop large-vessel arterial and venous bleeding within minutes of application, even when applied to an actively bleeding site. Second, it should be ready to use, with no requirement for mixing or special preparation. Third, it should be simple to apply with minimal training required. Fourth, it should be lightweight and durable. Fifth, it should be stable and functional at room temperature for at least 2 years. Sixth, it should be safe to use, posing no risk of either injury in the tissue to which it is applied or of bacterial or viral transmission. Finally, it should be inexpensive. The HemCon® Bandage fulfills many but not all of the requirements outlined by Pusateri et al. Our experience suggests that a chitosan-based hemostatic dressing such as the HemCon® Bandage is effective in controlling external hemorrhage when gauze and direct pressure fail in civilian EMS systems. The primary limitations with the original bandage in regards to the Pusateri et al. criteria were flexibility and the cost of approximately $100 for each 4" × 4" bandage. Despite recent improvements, we feel that the bandage is unlikely to replace pressure and gauze in civilian EMS systems but would seem to be an excellent second-line agent when traditional measures fail.

LIMITATIONS

Due to the observational nature of this study, there are several limitations that deserve attention. Our findings are limited by the small sample size and factors inherently present in EMS studies. Data collection was based on written accounts by the EMS providers and could not be independently verified. For example, we could not confirm whether the sources of bleeding were indeed venous or arterial. In addition, the amount of pressure and duration of compression used with gauze dressing application was not standardized. However, because the data collection forms were filled promptly after bandage use, recall bias was minimized. Some of the outcome variables, including the primary outcome variable of time to cessation of bleeding after the application of the HemCon® Bandage, were not rigidly standardized and inter-rater reliability was not addressed. In addition, the study was not designed to evaluate gauze and pressure with the HemCon® Bandage in a direct head-to-head comparison. Despite these limitations, we feel that this was a clinically important primary outcome measure because it reflects real-time effectiveness of the bandage as desired in the pre-hospital setting. Although three cases were omitted from the final analysis due to incomplete data, we feel that the selection bias is minimal.

The EMS personnel involved in the study were fire first responders and usually not involved with transport. Transport data were not available and it is possible that the patients' conditions may have changed en route to the hospital. Data on recurrence of bleeding after initial control also was not consistently available. In the absence of hospital follow-up data, we cannot comment on any short-term or long-term complications. We do wish to note that on several occasions, providers at receiving hospitals commented that wounds appeared to be cleaner than similar wounds that were managed with gauze and pressure.

CONCLUSIONS

The chitosan-based HemCon® Bandage is beneficial in stopping uncontrolled external hemorrhage in the civilian EMS setting when traditional methods such as pressure and gauze fail. Proper training in the use of the bandage is essential because user error was a contributing factor in most of the documented failures. Future trials should attempt to address the differences in morbidity and mortality using traditional methods vs. the HemCon® Bandage.

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REFERENCES

1. Acosta JA, Yang JC, Winchell RJ, et al. Lethal injuries and time to death in a level I trauma center. J Am Coll Surg 1998;186:528–33.
2. Sauaia A, Moore FA, Moore EE, et al. Epidemiology of trauma deaths: a reassessment. J Trauma 1995;38:185–93.
3. Shackford SR, Mackersie RC, Holbrook TL, et al. The epidemiology of traumatic death. A population-based analysis. Arch Surg 1993;128:571–5.
4. Bellamy RF. The causes of death in conventional land warfare: implications for combat casualty care research. Mil Med 1984;149: 55–62.
5. Wedmore I, McManus JG, Pusateri AE, Holcomb JB. A special report on the chitosan-based hemostatic dressing: experience in current combat operations. J Trauma 2006;60:655–8.
6. Acheson EM, Kheirabadi BS, Deguzman R, Dick EJ Jr, Holcomb JB. Comparison of hemorrhage control agents applied to lethal extremity arterial hemorrhages in swine. J Trauma 2005; 59:865–74.
7. 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;54:177–82.
8. Schwaitzberg SD, Chan MW, Cole DJ, et al. Comparison of poly-N-acetyl glucosamine with commercially available topical

hemostats for achieving hemostasis in coagulopathic models of splenic hemorrhage. J Trauma 2004;57:S29–32.
9. Klokkevold PR, Fukayama H, Sung EC, Bertolami CN. The effect of chitosan (poly-N-acetyl glucosamine) on lingual hemostasis in heparinized rabbits. J Oral Maxillofac Surg 1999;57:49–52.
10. Sondeen JL, Pusateri AE, Coppes VG, Gaddy CE, Holcomb JB. Comparison of 10 different hemostatic dressings in an aortic injury. J Trauma 2003;54:280–5.
11. Alam HB, Uy GB, Miller D, et al. Comparative analysis of hemostatic agents in a swine model of lethal groin injury. J Trauma 2003;54:1077–82.
12. Chou TC, Fu E, Wu CJ, Yeh JH. Chitosan enhances platelet adhesion and aggregation. Biochem Biophys Res Commun 2003; 302:480–3.
13. Rao SB, Sharma CP. Use of chitosan as a biomaterial: studies on its safety and hemostatic potential. J Biomed Mater Res 1997;34:21–8.
14. Thatte HS, Zagarins S, Khuri SF, Fischer TH. Mechanisms of poly-N-acetyl glucosamine polymer-mediated hemostasis: platelet interactions. J Trauma 2004;57:S13–21.
15. Thatte HS, Zagarins SE, Amiji M, Khuri SF. Poly-N-acetyl glucosamine-mediated red blood cell interactions. J Trauma 2004; 57:S7–12.
16. Fischer TH, Thatte HS, Nichols TC, Bender-Neal DE, Bellinger AD, Vournakis JN. Synergistic platelet integrin signaling and factor XII activation in poly-N-acetyl glucosamine fiber-mediated hemostasis. Biomaterials 2005;26:5433–43.
17. Stone CA, Wright H, Clarke T, Powell R, Devaraj VS. Healing at skin graft donor sites dressed with chitosan. Br J Plast Surg 2000;53:601–6.
18. Pusateri AE, Holcomb JB, Kheirabadi BS, Alam HB, Wade CE, Ryan KL. Making sense of the pre-clinical literature on advanced hemostatic products. J Trauma 2006;60:674–82.