Modified Rapid Deployment Hemostat Bandage Terminates Bleeding in Coagulopathic Patients with Severe Visceral Injuries

David R. King, MD, Stephen M. Cohn, MD, FACS, Kenneth G. Proctor, PhD, and the Miami Clinical Trials Group

Background: We recently reported that a new dressing, the Modified Rapid Deployment Hemostat (MRDH) controlled bleeding in hypothermic coagulopathic swine after traumatic liver avulsion. The purpose of this study was to evaluate the MRDH in coagulopathic trauma patients undergoing abbreviated laparotomy.

Methods: A prospective, observational clinical trial of the MRDH dressing was performed at our Level One Trauma Center in patients with high-grade visceral injuries with coagulopathy who failed conventional therapy and required packing. Attending surgeons graded the injury and the adequacy of hemostasis following application of the dressing. Patients were followed until discharge or death.

Results: Ten patients were enrolled: nine severe hepatic injuries, and one major abdominal vascular injury. All patients were hypothermic, acidic, and clinically coagulopathic. Intraoperative hemostasis was immediately obtained after MRDH placement in all cases except one. There was one death.

Conclusion: The Modified Rapid Deployment Hemostat terminates bleeding from severe visceral injuries in coagulopathic patients undergoing abbreviated laparotomy.

Key Words: Trauma, Liver, RDH, MRDH, Hemostasis, Hypothermia, Acidosis.

The United States Food and Drug Administration (FDA) recently cleared (as a Class I medical device) a novel hemostatic dressing for use on extremity bleeding from trauma, called the Rapid Deployment Hemostat (RDH, Marine Polymer Technologies, Inc., Danvers, MA). The RDH contains the chemical hemostat fully acetylated poly-N-acetyl glucosamine. In association with the manufacturer, our laboratory reengineered and then studied a new lyophilized version of this bandage for intra-abdominal use (called the Modified Rapid Deployment Hemostat, MRDH). The MRDH differs from the RDH in multiple ways. Most importantly, the active ingredient, fully acetylated poly-N-acetyl glucosamine, has been increased from 5 mg/cm² in the RDH to 16 mg/cm² in the MRDH by a lyophilization process. The MRDH also has a different size, improved consistency, and more durable backing. The MRDH consists of a 1 cm layer of active ingredient bonded to one side of a 4-by-4 inch gauze pad with a radiopaque stripe (Fig. 1). It is pure white in appearance, with a slightly firm, yet pliable, consistency. This device was found to be effective in an animal model of severe traumatic liver injury with acidosis, hypothermia, and coagulopathy. The MRDH reduced blood loss, reduced crystalloid requirement, and improved mean arterial pressure. Mortality was reduced from 100% in the standard abdominal packing group to 20% in the MRDH group. This dressing facilitated rapid and effective hemostasis in these severe hepatic injuries. Other trials have shown efficacy of similar polymer containing devices from the same manufacturer in controlling lethal hemorrhage, even in fully anticoagulated animals. This newest version, the MRDH, is also cleared by the FDA for intra-abdominal placement for up to 30 days to control bleed-
ing, but has never been tested in severely injured trauma patients with coagulopathy, hypothermia, and acidosis.

The purpose of this clinical trial was to prospectively evaluate the MRDH in severe visceral bleeding. We hypothesized that the MRDH would control bleeding from severe visceral injuries in coagulopathic trauma patients undergoing abbreviated laparotomy with packing.

MATERIALS AND METHODS

During a 12 month period from January 2003 to December 2003, patients over 18 years old with traumatic high-grade visceral injuries were enrolled into a prospective observational trial with waiver of consent at our Level One trauma center. The University of Miami Institutional Review Board approved this trial and the waiver of consent.

Any patient presenting with hemoperitoneum requiring surgical exploration was considered for enrollment. During exploration for intra-abdominal hemorrhage, patients were enrolled if the following criteria were met: 1) a high-grade visceral injury was identified, 2) control of bleeding failed conventional management strategies (defined as control of surgical and non-surgical bleeding by any technique in the attending surgeon’s armamentarium), 3) the patient required abbreviated laparotomy with packing, and 4) the patient was judged to be clinically coagulopathic. Enrollment also required that the attending trauma surgeon grade the liver injury. All patients meeting these criteria were included regardless of severity of injury, comorbidities, or associated injuries. Enrollment also required pager notification of an on-call fellow who would release the MRDH for use.

Once patients were enrolled, an unlimited number of MRDH bandages were applied onto any exposed parenchymal surface, over large open vessels, or after suture ligation of these vessels. The decision to suture ligate or to directly apply the dressing to the open vessels was made by the attending trauma surgeon. Additionally, dressings were packed into deep crevices where active bleeding was identified from within those wounds. Direct pressure was held on the MRDH for no less than 5 minutes. Standard laparotomy pad packing was placed over the MRDH, followed by a temporary abdominal closure, and the patient was transported to the trauma intensive care unit. At the discretion of the surgical team, patients were returned to the operating room for re-exploration and unpacking. Removal of the MRDH proceeded by first soaking the entire bandage with warmed saline, which un-bonds the active ingredient from the gauze backing. The bandage was then carefully and slowly peeled off the injured surface. If bleeding was noted following re-exploration for any reason, the MRDH was made available again for re-packing.

Data were collected from time of admission until discharge or death, and included type of visceral injury, grade of injury (if applicable), transfusion requirement before and after application of MRDH, arterial blood gas analysis, and number of MRDH bandages used. Additional data included age, sex, past medical and surgical history, and medications. Patients were followed to assess rate of postclosure intra-abdominal sepsis and mortality.

RESULTS

Ten patients were enrolled; age was 38 ± 5 years. There were nine blunt hepatic injuries: two Grade-III, five Grade-IV, and two Grade-V lacerations. All patients were hemodynamically unstable and had active ongoing bleeding from significantly disrupted hepatic parenchymal vessels. There was also one major abdominal vascular injury: an iliac vein laceration due to a gun-shot wound to the abdomen. One patient with a traumatic upper-extremity amputation at the level of the acromial-clavicular joint had the MRDH used outside of the study protocol and was excluded from data analysis. All were clinically coagulopathic and had failed conventional interventions to achieve complete hemostasis. Failed attempts at complete hemostasis included perihepatic packing, suture ligation (with and without finger fracture), liver mattress sutures, manual liver compression, temporary Pringle maneuver, and temporary supra-hepatic and infrahepatic vena-caval occlusion. In two cases, recombinant Factor VIIa was also administered without effect. The intraoperative condition of the patients immediately before use of the MRDH is described in Table 1.

Following placement of the MRDH, complete cessation of bleeding was noted in nine patients within 5 minutes. One patient had good hemostasis of liver parenchymal bleeding, but had a missed retrohepatic vein laceration and later died from wounds. All others survived. In one patient with a severe liver laceration, bleeding slowed but did not completely stop. The patient with the iliac vein laceration had the MRDH placed over the bleeding venotomy suture line with immediate hemostasis.

The number of MRDH bandages used ranged from 4 to 15 per case. Overall mortality was 10%. Median PRBC and FFP transfusion requirement following MRDH placement was 10.5 and 0 units, respectively. During re-exploration, no
Table 1 Intraoperative Condition Immediately before MRDH Placement (Mean ± SE)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH</td>
<td>7.19 ± 0.04 units</td>
</tr>
<tr>
<td>Base excess</td>
<td>-10 ± 3 mEq/L</td>
</tr>
<tr>
<td>PT</td>
<td>16.6 ± 1.1 seconds</td>
</tr>
<tr>
<td>PTT</td>
<td>51.0 ± 9 seconds</td>
</tr>
<tr>
<td>Temperature</td>
<td>35.2 ± 0.3°C</td>
</tr>
<tr>
<td>Median PRBC Transfusion Requirement</td>
<td>18 units*</td>
</tr>
<tr>
<td>Median FFP Transfusion Requirement</td>
<td>19 units*</td>
</tr>
<tr>
<td>Time in OR</td>
<td>112 ± 17 minutes</td>
</tr>
</tbody>
</table>

Values are mean ± standard error. *Indicates median values. PT is prothrombin time. PTT is activated partial thromboplastin time. PRBC is packed red blood cells. FFP is fresh frozen plasma. OR is operating room.

DISCUSSION

This initial experience in humans showed that the MRDH terminated bleeding in nine of 10 severely injured patients with visceral hemorrhage and coagulopathy who failed conventional therapies.

After controlling frank surgical exsanguination, the exposed liver parenchyma frequently continues to bleed from smaller vessels. Control of these smaller vessels is often difficult and would require additional operative time when the patient is already hypothermic. Prudence dictates the surgeon perform an abbreviated operation and transport the patient to the intensive care unit. This small vessel parenchymal bleeding is exacerbated by coagulation abnormalities and results in an ongoing blood product requirement until coagulation parameters are corrected. The MRDH arrests this bleeding. Rapid and complete hemostasis will eliminate ongoing dynamic consumption of soluble coagulation factors, allowing the coagulopathy to correct, and limit the need for blood products.

Although obvious surgical bleeding was controlled in all hepatic injury cases, the MRDH terminated bleeding in one patient with a large iliac vein laceration that had continued aggressive oozing from the suture line. In this case, there was significant bleeding from the venotomy suture line, the adjacent injured vertebral body, and the surrounding venous plexus. Our original intention was not to use the MRDH on any potential surgical bleeding sites, however use in this circumstance is not without merit. In our animal experience, the MRDH terminated surgical bleeding from all exposed hepatic vessels after subtotal liver avulsion. Other groups have also described control of other types of surgical bleeding with the previous RDH bandage.7,10,16

It is noteworthy that the MRDH is not the same hemostat tested by other investigators.17 Additionally, it has been our cumulative animal and human experience that this dressing is effective only if placed in direct contact with the bleeding vessel, with direct pressure.

The polymer on the MRDH bandage is poly-N-acetyl glucosamine,10 and is derived from a marine microalgae grown in an ultrapurified form.11 Following processing, the polymer is a fully-acetylated linear structure consisting of approximately 2000 N-acetyl glucosamine residues, with a molecular weight of approximately 3 × 106 Daltons and is free of proteinaceous debris and contaminants.19,20 It can be formulated into membranes, fibers, sponges or gels that can be directly applied to wound surfaces. Gel formulations are effective as hemostats in rabbit and canine models of variceal bleeding.12,13 Another formulation, the Syvek Patch, is commercially available and is efficacious at arresting bleeding from vascular puncture sites following cardiac catheterization, even under complete heparinization.14 Poly-N-acetyl glucosamine alone is fully biodegradable and can be left in place on a bleeding surface to provide continued hemostasis after wound closure.

This bandage is easy to use, has a long shelf-life, does not require special storage conditions, pre-mixing of reagents, or use of donated blood products, in contrast to other hemostatic adjuncts such as fibrin glue. The MRDH does not contaminate the surgical field with small particulate matter and has no exothermic heating associated with its use, in contrast to the hemostatic agent granular zeolite (QuickClot™). Thus it is safe to handle with a gloved-hand in the wound.

Other available alternative hemostatic dressings are chitosan-based. Chitosan is a heterogeneous water-soluble substance containing variable compositions of N-acetyl glucosamine and glucosamine residues, depending on its source and mode of manufacture. Chitosans generally have molecular weights in the 40,000–100,000 Dalton range. Typical chitosans are deacetylated, with between 75–90% glucosamine residues, and are thus cationic polymers. The primary hemostatic mechanism is by electrostatic interaction with blood elements.18 Furthermore, none of the other chitosan dressings are cleared for internal use.

The older RDH and the new MRDH contain the same active ingredient, but in higher concentration in the MRDH. Additionally, the MRDH is prepared in a slightly different process for bonding to the gauze backing, but this proprietary process does not affect the hemostatic properties of poly-N-acetyl glucosamine. The exact mechanism(s) of action remain to be elucidated. Earlier investigations have demonstrated discrete platelet and red blood cell poly-N-acetyl glucosamine interactions.10 These interactions appear to be receptor mediated, as compared with the electrostatic interactions by chitosan, and are consequently high affinity and high specificity.19,20,21 Other investigators have demonstrated efficacy of this polymer in fully anticoagulated animal models,10,14,15 suggesting a multi-faceted hemostatic mechanism independent of direct receptor-mediated platelet or red blood cell interactions. It has subsequently been shown to control puncture wound hemorrhage in isolated rat aortic vessels with significant bleeding.10
rings in the absence of any formed elements of blood. The mechanism of action was speculated to be via polymer-induced local endothelin release, however this particular mechanism has been questioned. It is clear that there are multiple in vivo dynamic interactions with this substance, but additional work is necessary.

The major limitation of this study is that no comparison could be made to the current “standard of care” in a randomized placebo-controlled fashion. Florida law prohibits a randomized placebo-controlled clinical trial with waiver of consent unless the two interventions are both considered “standards of care.” Therefore, only a prospective observational investigation could be undertaken with waiver of consent. The waiver of consent was necessary because the instability of these patients upon presentation prohibited any attempts at informed consent. In fact, these patients arrived at our center already intubated by pre-hospital providers and in need of emergent laparotomy. Clearly it was impossible for the surgical staff to be blinded to this investigation because of the obvious differences in the physical properties of standard laparotomy pads and the MRDH.

Based upon this small clinical experience, a large randomized placebo-controlled trial is necessary to fully evaluate the hemostatic potential of this new bandage. Additional clinical trials are warranted to evaluate the MRDH for other specific severely bleeding wounds. There is potential for this device to be used in the pre-hospital or military combat casualty care setting for control of non-cavitary hemorrhage as well. The results of this study suggest that the MRDH may be specifically indicated in traumatic hepatic bleeding with coagulopathy.

In summary, the MRDH terminated bleeding in this small population of coagulopathic hypothermic trauma patients with severe visceral injuries. Control of visceral bleeding with the MRDH resulted in a low postoperative transfusion requirement and a low mortality rate. Additional multicenter clinical trials are indicated for this promising new hemostatic device.

REFERENCES


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