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EVALUATION OF CHRONIC COAGULOPATHIC DAMAGE IN GRADE V LIVERS USING HYPOTHERMIC CHITOSAN DRESSINGS

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ABSTRACT

Acidosis, coagulopathy, and hypothermia are lethal triads that can exacerbate exsanguination from hepatic trauma. Hypothermic coagulopathic liver damage model with modified chitosan dressings was tested. As a result of hypothermic coagulopathy, subject swine underwent standardized grade V liver injuries. It was compared with a standard packing with a modified chitosan dressing. Blood loss and pre-treatment temperature were similar between groups. The modified chitosan group displayed a significant reduction in post-treatment blood loss and an increase in resuscitation mean arterial pressure ($P < 0.0001$ and $P < 0.018$, respectively). Compared to the control group, the modified chitosan group had a significantly lower mean fluid resuscitative volume ($P < 0.0056$). As compared to standard packing, modified chitosan achieved haemostasis on average in 5.2 minutes. Half of treatment animals survived an hour after injury compared to all control animals. Injuries to the liver can be treated using modified chitosan dressings in a simple and rapid manner.

Key words: Advanced haemostasis; Haemorrhage; Chitosan.

INTRODUCTION

Haemorrhage can become fatal through exsanguination in the battlefield or from civilian trauma, which can be compounded by hypothermia, acidosis, and coagulopathy. Both civilians and soldiers are at risk following this lethal triad [1]. Topical hemostatic agents have recently been developed and researched for the control of life-threatening hemorrhages. Fibrin patches, Rapid Deployment Hemostats, and Modified Rapid Deployment Hemostats are also available at the company in addition to fluid fibrin sealants, chitosan dressings, and fibrin patches from Marine Polymer Technologies [2]. Based on study, several hemostatic agents may be effective in treating trauma. Chitosan dressings are among these agents. Despite promising results showed, there are certain limitations regarding intracavitary hemorrhage adhesive capabilities and weak models of lethal extremities [3]. Although they are light in weight, their application is easy, they are stable in harsh environments, and they are quick to prepare. Dry fibrin sealants and chitosan dressings are well tolerated by animals, reduce fluid resuscitation and blood loss, and ensure good hemostasis [4]. There has been research done on the Excel Arrest patch in the non-coagulopathic, non-hypothermic liver injury model previously. Blood loss reduction and resuscitation fluid management are indispensable on the battlefield today. Standard gauze packing has been shown to reduce total blood loss, fluid resuscitation, time to hemostasis, and mortality in a previous study [5]. The same MCP was assessed for hemostatic efficacy in this study using Pig liver injury caused by hypothermic coagulopathy.

METHODS AND SOURCES

Surgery of Animals

The study involved 18 crossbred pigs weighing 39.6 kg x 2.8kg. Each animal underwent a veterinary examination. The night before the experiment, commercial food and water were not available to the animals.

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The IACUC approved it according to the protocol. The concentration of glycopyrrolate at 0.01 mg/kg was anesthetic, it was discovered that telazol is an effective anesthetic at a dose of 6 mg/kg. A successful intubation was performed, mechanical ventilation was administered at a rate of 10 breaths per minute, 12 mL of tidal volume per kilogram of body weight, and 100% oxygen was administered. When isoflurane was used under anesthesia, the pCO2 reached 40mm Hg.

In addition to monitoring vital signs, veins were cannulated, resuscitation fluids are infused. Induction of dilutional coagulopathy and controlled hemorrhage were also achieved by cannulating the right femoral artery. Animals underwent splenectomies. A spleen of three times the weight of Lactated Ringer's (37°C) should be used instead. Ringer's was infused to compensate for blood loss during the procedure. Splenectomies are performed in swine hemorrhage models because sequestration of blood fluctuates. We performed a hemologic laboratory analysis first after injury, and then 60 minutes after death.

Induction of Coagulopathy

Hextend solution was then injected into the femoral catheter after 60 percent of the estimated blood volume of the animal had been removed. In order to calculate blood volume (mL/kg), use the following equation: 161.475 51 + 0.2197 (body weight in kg). Between each 10-minute period, there was a 2-minute break. Temperatures of 32°C and 0.5°C were maintained via external cooling. A 4°C lactated Ringer's solution was injected into the abdominal cavity of the animal in the event that its core temperature exceeded 32.5°C after the controlled hemorrhage.

Resuscitation and injury

The American Association for the Surgery of Trauma Organ Injury Scaling system was used to create a grade V injury from a previously reported liver clamp [6]. In this case, the liver was penetrated on both sides of the diaphragmatic lobe and the right medial lobe. When the clamp was repositioned, the major hepatic veins were penetrated a second time. Suction was used to collect shed blood, which was labeled as pretreatment blood loss after free bleeding for 30 seconds. In the event of bleeding, A 37°C Hextend solution was used to resuscitate the individual until his or her mean arterial pressure reached 80% of his pre-injury value at a rate of 150 mL/minute. To maintain target, mean arterial pressure, resuscitation was maintained throughout the observation period.

Treatment of liver injuries

As part of the treatment, resuscitation was performed. Hepatic packing with gauze or MCP was randomly assigned to the animals. MCPs were placed on both the anterior and posterior injured livers in the treatment group. Two patches were placed between the liver injuries, and both surgeons' hands applied manual compression for 3 minutes in both planes. A visual check of hemostasis was conducted between periods of compression. Upon achieving hemostasis, compression was stopped. Continuing bleeding was treated with compression again. Another patch was applied if necessary. Compressions could not exceed 12 minutes in duration. Following hemostasis, perihepatic packing was avoided for a 60-minute period.

Hepatic injury areas were compressed with sterile gauze for 6 Using standard hepatic packing, the second group underwent the procedure for minutes. A standard perihepatic packing technique was used following the 6-minute compression period. A 60-minute monitoring period followed the closure of the abdomen and the death of the animal. Each animal's abdomen was examined after the study period. A suction device was used to suction liquid blood.

Results

A 60-minute survival study was conducted with 18 animals. The following table summarizes preinjury and baseline parameters. Statistical difference in the variables was not found, but the coagulation laboratory values showed a difference between the two groups (P = .0001) for postinduction of hypothermic coagulopathy.

TABlE 1: Defining baselines and preinjuries

Observations (N = 18)	14	4
Mean arterial pressure (mPa) at pre-injury temperature (°C)	32.7	32.8
Clotting time (s) prior to injury (mm Hg)	63	91
Normative	64	64
Prior to injury	89	85
Baseline hemocrit (%)	62	52
Before injury	25	22
(103/L) Baseline platelet count	252	247
Injury prevention	98	69

Approximately 10 cm by 8 cm by 4 cm of stellate wounds covered the liver. Blood losses in both MCP and gauze groups after free bleeding for 30 seconds were similar. Within 30 seconds of free bleeding, both groups

experienced similar arterial pressure. Of the 3 animals treated, two needed additional MCPs. Six minutes after injection, all MCP animals had been hemostasised, except one. A 12-minute interval was required to achieve hemostasis on the remaining animal. According to MCP analysis, hemostasis took 5.2 minutes x 2.7 minutes in this group. All standard packing groups did not achieve hemostasis. After injury, MCPs and standard gauze packs significantly differed in terms of injury severity at 30 and 60 minutes. There was a significant reduction in blood loss in the MCP group following treatment. MCP-treated animals also stabilized their mean arterial pressure more quickly after injury than animals whose skin was wrapped in gauze. The mean fluid resuscitation rate for the gauze packing group was expressed in milliliters per minute because animals did not survive for the full observation period. In contrast, 50% of standard participants died by 60 minutes, whereas all MCP participants survived.

DISCUSSION

We are able to generate a consistent hemorrhagic, hypothermic, and coagulopathic traumatic model using this animal model. Previous studies have shown similar results. A hemostatic bandage was tested for use in severe solid organ injuries where the hematocrit decreased by 41% on average, similar to a previous study [7.8]. It is generally recommended that patients be stabilized in the operating room before being transferred to an intensive care unit for further resuscitation, and then be evaluated within 24 hours of the surgery. If hemostatic bandages are applied in this scenario, hemorrhage may be reduced. Advanced hemostatic agents are being developed and utilized has become a major research focus in recent years [9]. It is also more difficult to mix and deliver liquid fibrin sealants because of their longer preparation times. Additionally, they are limited by the requirement for a temperature-controlled environment before application, which makes them unsuitable for use in trauma emergency settings and in modern combat theaters [10]. As well as dry dressings, hemostatic powders are available. The chitosan dressings, the dry fibrin sealants, the rapid deployment hemostats, and QuikClot are among the agents that have been reviewed [11]. The importance and potential of these agents are highlighted in a recent review. However, QuikClot's exothermic reaction and inability to remain in the wound raised concerns despite it being the cheapest. Those issues have now been addressed with QuikClot's porous bandage. Although the dressings discussed in this study had varying abilities to control hemorrhage, they all controlled hemorrhage well [12]. Dry fibrin sealant dressings were found to be the most expensive when compared to chitosan dressings. As chitin (poly-N-acetyl glucosamine) is derived from chitin, some chitosan dressings are approved for external use by the US Food and Drug Administration [13]. Several studies have found that tissues are rarely reactive, that exothermic damage is minimal, and that inflammation is minimal [14]. After failing standard gauze dressings, 97 percent of patients received the dressing, which stopped or significantly slowed bleeding. Using chitopsan dressings to treat grade V liver injuries has shown to reduce posttreatment blood loss, survival, and resuscitation volumes. The same dressings also perform well in high-pressure, high-flow Although the dressing initially controlled arterial bleeding after aortotomy hemorrhage, it failed to control bleeding within 2 hours of the injury, raising questions about its use in environments with high pressure [15]. Chitosan bandages were also found to be ineffective in controlling hemostatic control for lethal extremity injuries in two studies. As part of a comparative study on coagulopathic splenic hemorrhage (ChitoSeal, Abbott Laboratories, Abbott Park, IL), a new chitosan patch (ChitoSeal, Abbott Laboratories, Abbott Park, IL) was examined [16]. According to the authors, standard gauze pads provided better hemorrhage control than chitosan dressings. This concern led to Excel Arrest's creation. By exchanging organic vapor with the surface of chitosan, the dressing is cured. As a result of this process, a pliable and adhesive dressing is created. In a non-coagulopathic normothermic model for grade V liver injuries, it showed a significant difference in hemorrhage control and resuscitation reduction [17]. In 180 minutes of observation, there were no failures of the MCP. Tests on the performance of the product were conducted using a hypothermic, coagulopathic hemorrhage model. The mortality rate for trauma patients using this model has been shown to be very high. There is evidence that damage control laparotomies increase survival rates both in civilian trauma and in modern warfare [18]. A perihepatic packing with gauze padding and manual compression is used to control hepatic hemorrhage following damage control laparotomy. Among early trauma deaths, eighty-two percent are caused by controlled hemorrhages and fifty-five percent are caused by liver injuries, according to a study. In order to prevent hemorrhage, perihepatic packs help correct hypothermia, acidosis, and coagulopathy so that further resuscitation can be carried out. A number of studies indicate that perihepatic packing does not come without complications. These include a hemorrhage rate that cannot be stopped, a liver necrosis, a rebleed, an abscess in the abdomen, or cardiac complications. It may be possible to minimize risks and maximize benefits with an advanced hemostatic dressing.

Previous studies have used this animal model. Dry fibrin sealant dressings, not gauze packers, were used to compress the liver in this study [19]. Dry fibrin sealant dressing was found to have improved survival, less blood loss after treatment, and fewer resuscitations compared with standard gauze packing. It has been questioned why no manual hepatic compression was applied in the control group and how it was treated. Our study did not use manual hepatic compression after perihepatic packing.

Manual compression, which is closer to clinical practice, had better effects than modified chitosan dressing. In this study, 50% of the participants survived because of manual compression.

A study in which hypothermic coagulopathic animals were treated with fibrin patches also examined the effects of the patches. A control group and a treatment group were formed sequentially compressed with gauze or fibrin patches for three minutes before perihepatic packing was applied [20]. A survival model might have revealed fewer adverse outcomes in our treatment group without perihepatic packing at 5.2 minutes. Although resuscitation was administered very soon after injury, we did not examine the effects of that procedure. A prolonged period of observation and resuscitation may be necessary after a resuscitation, intensive care unit resuscitation, or an operation. MCPs reduce posttraumatic bleeding, increase mean arterial pressure during resuscitation, and decrease fluid requirements during resuscitation. A selectively administered environment would result in a decrease in the need for blood products and resuscitation fluids. A study showed that MCP can reduce the risks associated with perihepatic injury without perihepatic packing. An MCP can be used to treat dangerous liver injuries in a quick and simple manner.

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, 186, 1998, 528 –33.
2. Alam HB, Burris D, DaCorta JA, *et al*. Hemorrhage control in the battlefield: role of new hemostatic agents. Mil Med, 170, 2005, 63–9.
3. Champion HR, Bellamy RF, Roberts CP, et al. A profile of combat injury. J Trauma, 54, 2003,13-19.
4. Sauaia A, Moore FA, Moore EE, *et al*. Epidemiology of trauma deaths: a reassessment. J Trauma, 38,1995,185–93.
5. MacLeod JB, Lynn M, McKenney MG, *et al.* Early coagulopathy predicts mortality in trauma. J Trauma, 55,2003,39 – 44.
6. Niles SE, McLaughlin DF, Perkins JG, *et al*. Increased mortality associated with the early coagulopathy of trauma in combat casualties. J Trauma, 64, 2008, 1459 – 63.
7. Pusateri AE, Holcomb JB, Kheirabadi BS, *et al.* Making sense of the preclinical literature on advanced hemostatic products. J Trauma, 60, 2006, 674 – 82.
8. Wedmore I, McManus JG, Pusateri AE, *et al.* A special report on the chitosan-based hemostatic dressing: experience in current combat operations. J Trauma, 60, 2006, 655– 8.
9. Acheson EM, Kheirabadi BS, Deguzman R, *et al.* Comparison of hemorrhage control agents applied to lethal extremity arterial hemorrhages in swine. J Trauma, 59, 2005, 865–74.
10. Fischer TH, Connolly R, Thatte HS, *et al*. Comparison of structural and hemostatic properties of the poly-N-acetyl glucosamine Syvek patch with products containing chitosan. Microsc Res Techn, 63, 2004, 168 –74.
11. Kheirabadi BS, Acheson EM, Deguzman R, *et al.* Hemostatic efficacy of two advanced dressings in an aortic hemorrhage model in swine. J Trauma, 59, 2005, 25–34.
12. Ward KR, Tiba MH, Holbert WH, *et al.* Comparison of a new haemostatic agent to current combat hemostatic agents in a swine model of lethal extremity arterial hemorrhage. J Trauma, 63, 2007, 276 – 83.
13. Holcomb JB, Pusateri AE, Harris RA, *et al.* Effect of dry fibrin sealant dressings versus gauze packing on blood loss in grade V liver injuries in resuscitated swine. J Trauma, 46, 1999, 49 –57.
14. 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, 54, 2003, 177–82.
15. Bochicchio GV, Kilbourne MJ, Keledjian K, *et al.* Evaluation of a new hemostatic agent in a porcine grade V liver injury model. Am Surg [In press].
16. Delgado AV, Kheirabadi BS, Fruchterman TM, *et al.* A novel biologic hemostatic dressing (fibrin patch) reduces blood loss and resuscitation volume and improves survival in hypothermic, coagulopathic swine with grade V liver injury. J Trauma, 64, 2008, 75– 80.
17. Moore EE, Cogbill TH, Jurkovich GJ, *et al.* Organ injury scaling: spleen and liver (1994 revision). J Trauma, 38, 1995, 323–324.
18. Holcomb JB, Pusateri AE, Harris RA, *et al.* Dry fibrin sealant dressings reduce blood loss, resuscitation volume, and improve survival in hypo- thermic coagulopathic swine with grade V liver injuries. J Trauma, 47, 1999, 233– 40.
19. Recinos G, Inaba K, Dubose J, *et al.* Local and systemic hemostatics in trauma: a review. Ulus Travma Acil Cerrahi Derg, 14, 2008, 175– 81.
20. VandeVord PJ, Matthew HW, DeSilva SP, *et al.* Evaluation of the biocompatibility of a chitosan scaffold in mice. J Biomed Mat Res, 59, 2002, 585–90.