The Effects of Movement on Hemorrhage When QuikClot® Combat Gauze™ Is Used in a Hypothermic Hemodiluted Porcine Model

Jose Garcia-Blanco, MD; Brian Gegel, DNAP; James Burgert, DNAP; Sabine Johnson, MS; Don Johnson, PhD, RN

ABSTRACT

Background: The purpose of this study was to compare the effectiveness of QuikClot® Combat Gauze™ (QCG) to a control wound dressing to withstand movement in a porcine model with hemodilution and hypothermia. Design: This was a prospective study with a between-subjects experimental design. Twenty-six Yorkshire swine were randomly assigned to two groups: QCG (n = 13) or a control dressing (n = 13). **Methods:** The subjects were exsanguinated to 30% of the blood volume; hypothermia was induced for 10 minutes. The hemostatic agent, QCG, was placed into the wound, followed by standard wound packing. If hemostasis was achieved, 5L of crystalloid solution were rapidly administered intravenously, and the wound was again observed for rebleeding. If no bleeding occurred, the extremity on the side of the injury was systematically moved through flexion, extension, abduction, and adduction sequentially 10 times or until rebleeding occurred. Results: An independent t test indicated there were significant differences in the number of movements before rebleeding between the QCG group (mean ± standard deviation [SD], 32.92 ± 14.062) and the control group (mean ± SD, 6.15 ± 15.021) ($p < .0001$). **Conclusion:** QCG produces a robust clot that can withstand more movement than a control dressing.

KEYWORDS: *movement, hemorrhage, QuikClot®, Combat Gauze™, hypothermic hemodiluted porcine model*

Introduction

Trauma is the leading cause of morbidity and mortality in civilian and military populations, with uncontrolled hemorrhage as the major cause of death.[1–5] During the recent conflicts in Iraq and Afghanistan, uncontrolled hemorrhage accounted for about 50% of battlefield deaths prior to evacuation.[6] The mortality rate among trauma patients with isolated systolic hypotension (<90mmHg) is as much as 54%.[7] Furthermore, significant blood loss predisposes individuals to hypothermia, coagulopathy, infection, acidosis, and multiple organ failure.[2,8–10] Therefore, early control of hemorrhage is essential for initial survival and for optimal recovery.

Hemostatic agents may be one of the easiest and most effective methods of treating hemorrhage. They were specifically developed to treat severe, noncompressible hemorrhage in military and prehospital settings. The US military's Committee of Tactical Combat Casualty Care (CoTCCC) is the group responsible for developing guidelines for the management of wounded military personnel. CoTCCC recommends QCG as the first hemostatic agent for use in treatment of severe hemorrhage that cannot be controlled by a tourniquet.[11] QCG is a rayon/polyester gauze impregnated with kaolin, a white, aluminosilicate, inert mineral. Kaolin promotes clotting by activation of factor XII (FXII) and factor XI (FXI) in the intrinsic coagulation pathway. In addition, kaolin promotes the activation of platelet-associated FXI, which activates the intrinsic coagulation pathway in patients without clotting-factor deficiencies and those with FXII deficiency.[12]

QCG has been found effective in controlling massive hemorrhage in normothermic swine.[13–15] However, between 30% and 50% of trauma patients present with hypothermia.[16,17] Hypothermia decreases the enzymatic activity of clotting factors and impairs platelet function.[18] The association of hypothermic coagulopathy in a trauma victim results in increased risk for morbidity and mortality.[13] Furthermore, hemodilution may influence the effectiveness of hemostatic agents. Several researchers have found that hemostatic agents are effective in hemorrhage control but often fail following crystalloid resuscitation.[10,19–27]

A healthcare provider will attempt to minimize the movement in case of injury. However, the patient may move because of pain, the victim may have to be moved out of the line of fire, and movement during evaluation may be necessary. Few studies have investigated the effects of movement when a hemostatic agent is used. Johnson and colleagues found QCG effective for controlling

hemorrhage with aggressive fluid resuscitation and, subsequently, movement.[15] Gegel and colleagues compared the effectiveness of QCG to that of a control treatment in a group of normothermic swine.[28] They found the agent was effective in controlling hemorrhage, and the clot formed was robust enough to withstand more movement than the control.[28] In another study, the same researchers investigated the effectiveness of QCG in a hypothermic scenario. They found QCG was superior to the control treatment relative to hemorrhage control, fluid resuscitation, and movement.[13] No study has compared the effectiveness of QCG in a hypothermic, hemodiluted model with movement.

The purpose of this study was to compare the effectiveness QCG to a control group relative to movements. Specifically, this study was guided by the following research question: Is there a significant difference between QCG and control groups in number of movements in a porcine model of hemodilution and hypothermia before hemorrhage occurs?

Methods

This was a prospective study with a between-subjects experimental design using a porcine model. The protocol was approved by the Institutional Animal Care and Use Committee and the animals received care in compliance with the Animal Welfare Act and the "Guide for the Use of Laboratory Animals."

The investigators calculated a large effect size of 0.6 based on the previous work from Gegel and Johnson.[15,28] Using an effect size of 0.6, a power of 0.80, and an α of .05, the researchers determined that 26 swine were needed for the study. The investigators used a computer-based randomized-number generator to assign Yorkshire swine to either the QCG group (n = 13) or the control group (n = 13). The mean weight of the swine was 71.3kg (the mean plus or minus the standard deviation [SD] was 70.19 ± 8.94kg in the QCG group and 72.57 ± 11.9kg in the control group), which represents the average weight of the US Army Soldier.[29]

Swine were administered a preoperative intramuscular injection of ketamine (20mg/kg) and atropine (0.04mg/kg). Subjects were placed supine on a litter and administered inhaled isoflurane (4% to 5%). After placement of an endotracheal tube, a peripheral intravenous (IV) catheter was inserted and the isoflurane concentration was reduced to between 1% and 2% for the remainder of the experiment. The subjects were ventilated with a standard Narkomed anesthesia machine (Dräger, Telford, PA, USA; http://www.dremed.com/em_drager_narkomed.shtml).

Heart rate, electrocardiography, blood pressure, oxygen saturation, end-tidal carbon dioxide level, and rectal temperatures were continuously monitored for the remainder of the experiment. The left carotid artery was cannulated with a 20-gauge angiocatheter using a cut-down technique. It was attached to a hemodynamic monitoring system (Hewlett Packard, Palo Alto, CA, USA; http://www.hpl.hp.com) for continuous monitoring of the arterial blood pressures. A central venous catheter was inserted in the subclavian vein using the modified Seldinger technique. The activated clotting time (ACT) test was used to screen all subjects for preexisting coagulopathy. Subjects were further monitored for 30 minutes to ensure hemodynamic stability. Temperature was monitored via rectal probe. All swine were hemodynamically stable prior to intervention.

Thirty percent of each animal's blood volume was exsanguinated by gravity by a central line into the subclavian vein. Swine have the same volume of blood as humans (70mL/kg); therefore, a pig that weighs 70kg has 4900mL of blood. Thirty percent of that volume is 1470mL. A 3:1 replacement of lactated Ringer's solution was administered to dilute the remaining blood.

Hypothermia (<34.0°C) was induced by three methods: cooling blanket, ice packs, and cold isopropyl alcohol spray. Once the temperature reached ≤34°C, the investigators created a complex groin injury to simulate a penetrating inguinal wound. Following the 30-minute stabilization period and 10 minutes of hypothermia, a complex groin injury was created (transection of femoral artery and vein).[30] A complex groin injury was created to simulate a penetrating, traumatic battlefield injury. Specifically, the proximal thigh soft tissues (skin, quadriceps, and adductor muscles) were dissected to expose the femoral artery and vein below the inguinal ligament within the femoral crease.

The femoral artery and vein were transected, and the swine were allowed to bleed for 1 minute, simulating the response time of a battlefield healthcare provider. Blood was collected through the use of 4" × 4" gauze, absorbent pads placed underneath the animals, and by suction-tip catheter placed in the distal portion of the wound per manufacturer's guidelines. After 1 minute of uncontrolled hemorrhage, proximal pressure was applied to the transected femoral vessels, and 4" × 4" gauze was used to blot the blood from the wound per the hemostatic agent manufacturer's guidelines. QCG was packed into the wound, making direct contact with the transected vessels. An overlying layer of petroleum gauze was applied to prevent adhesion of QCG to wound packing materials, allowing for later dressing removal. Standard wound packing, using roller gauze

(Covidien, Mansfield, MA), was placed until the wound cavity was filled. The same procedures were used for the control group with the deletion of the QCG.

In both groups, firm manual pressure of 25lb/in^2, as measured with an electronic TIF scale (Thermal Industries of Florida/Robinair, Owatonna, MN, USA; http://www.robinair.com/), was applied for 5 minutes to the injury site. The TIF scale is precise to within 0.5 oz and accurate to within 0.5%.[31] The scale was placed between the combat litter and the operating room table and zeroed in accordance with manufacturer's instructions. Thereafter, 500mL of Hextend (Hospira, Inc, Lake Forest, IL, USA; http://www.hospira.com) was administered to all the subjects in accordance with current battlefield resuscitation protocol recommended by the CoTCCC. Hextend is a formulation of 6% hetastarch combined with a physiologically balanced crystalloid carrier that more closely mirrors plasma electrolyte balance than 6% hetastarch in 0.9% sodium chloride. After 5 minutes of direct pressure, a 10-lb sandbag was applied to the wound for additional 30 minutes. After 35 minutes of pressure (5 minutes of manual pressure plus 30 minutes with the sandbag), the standard pressure dressing was removed. It was not possible to blind the investigator relative to the use of QCQ or a standard dressing. However, the subsequent researchers were blinded to group assignment relative to observation of hemorrhage after the 30 minutes. In addition, the individual conducting the movement of the extremities was blinded.

For the purposes of this study, hemostasis was defined as a clot formation with oozing of 2% or less of the swine's total blood volume over a 5-minute period (100mL in a 70kg pig). The investigators consulted with three experts (trauma surgeons) relative to what they believed to be clinically important relative to the definition. After discussion, they were unanimous that hemostasis should be defined as 2% or less of the swine's total blood volume over a 5-minute period. For the swine with hemostasis, the clot was further challenged with 5 L IV crystalloid solution rapidly administered through the central venous catheter over 5 minutes. If rebleeding occurred during crystalloid infusion, the experiment was terminated.

For the subjects that achieved hemostasis, the investigators systematically moved the leg on the side of the injury. On a real battlefield, personnel would take significant precautions when moving combat casualties. For this study movement consisted of the following: flexion, extension, abduction, and adduction 10 times sequentially or until rebleeding occurred. The movements consisted of a full range of motion. The number of movements were counted up to 40 (10 of each movement) or until there was bleeding (2% of blood volume).

Results

There were no statistically significant differences between the groups in reference to the amount of initial 1-minute hemorrhage, body weight, core body temperatures, arterial blood pressure, pulse, mean arterial pressure, blood volume, amount of fluid resuscitation, or the amount of initial hemorrhage (p = .292). The mean volume of fluid replacement was 4454.86mL (mean ± SD was 4338.18 ± 673.48mL in the QCG group and 4571.55 ± 750.32mL in the control group). The mean temperature was 33.31°C (mean ±SD was 33.05°C ± 0.64°C in the QCG group and 33.57°C ± 0.34°C in the control group). The ACT was within normal limits for all subjects. An independent t test was used to determine if there was a statistically significant difference in the number of movements before hemorrhage occurred. The QCG group was able to tolerate movements more than the control group (p < .0001) (Table 1).

Table 1 *Summary of Extremity Movements Before Rebleeding*

Group	Movements, No.	p value
QCG	32.92 ± 14.062	<.0001
Control	6.15 ± 15.021	<.0001

Discussion

QCG is used by the US Military and in many civilian sectors for management of massive hemorrhage in trauma casualties. The US Military's CoTCCC is responsible for developing guidelines for the management of wounded military personnel. It recommends QCG as the first-line hemostatic agent for use in treatment of severe hemorrhage. The findings of this study support the recommendations.

One goal of the US Army is that each soldier carries a hemostatic agent. QCG produces a robust clot that can withstand significant movement. The movements were completed to a maximum range of motion, but this should be avoided in patients with an inguinal injury. In this study, however, the investigators wanted reproducible movements that would test the robustness of newly formed clot.

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Disclosures

The authors declare no conflicts of interest.

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Dr Garcia-Blanco is an associate investigator for the Geneva Foundation, Tacoma, Washington.

Dr Gegel is affiliated with Veteran Anesthesia Services, San Antonio, Texas.

Dr Burgert is affiliated with the Department of the Army Academy of Health Sciences, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Ms Johnson is affiliated with the Department of the Army Academy of Health Sciences, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas.

Dr Johnson is director of research, Department of the Army Academy of Health Sciences, US Army Graduate Program in Anesthesia Nursing, Fort Sam Houston, Texas. E-mail: arthur.d.johnson14.civ@mail.mil OR arthurjohnso@gmail.com.