Celox (chitosan) for haemostasis in massive traumatic bleeding: experience in Afghanistan

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The use of Celox, a chitosan-based haemostatic agent, for the control of massive traumatic bleeding in patients arriving at a ROLE 2 (Enhanced Care) Facility in southwestern Afghanistan is described. Twenty-one soldiers with gunshot wounds were treated with successful haemostasis in 18 at the first application and in three after further applications. Celox is an effective haemostatic agent and a useful adjunct for the treatment of massive traumatic bleeding. ***European Journal of Emergency Medicine*** **00:000–000 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Since ancient times, loss of blood has been the single most common cause of death on the battlefield. Uncontrolled bleeding continues to be the leading cause of death on the battlefields of modern warfare as well [1] and is among the main causes of death in the civilian environment [2]. It is also one of the most feared complications after surgery [3].

In recent years, new medical equipment and methods have been developed to control moderate-to-severe bleeding as the standard gauze supplied to individual soldiers and direct pressure are often insufficient to achieve haemostasis [4]. The Tactical Combat Casualty Care protocol outlines the carrying of a tourniquet and haemostatic agents in each soldier's personal medical equipment for use in first aid [5].

The majority of the injuries sustained on the battlefield are to the upper and lower limbs, neck and head and finally to the chest and abdomen. The anatomical distribution of injuries is influenced by the type of conflict, by the weapons used on the field as well as by the protective equipment worn by individual soldiers when deployed in the field [6]. To address these issues, haemostatic agents have been developed to treat massive bleeding in areas of the body where tourniquets cannot be used, such as the neck, the groin and the axilla. In addition, these haemostatic agents can be used to allow the removal or loosening of tourniquets when long delays occur during the evacuation of the injured from the battlefield, thereby reducing the risk of tissue damage due to the tourniquet. These newer haemostatic agents have evolved into products that are effective in stopping bleeding, ranging from minor to massive, in a very short time while reducing the problems attributed to their earlier use [7].

Celox is a chitosan, an entirely biodegradable and biocompatible substance [8], which is a pearly coloured, odourless and nontoxic derivative of chitin. Structurally, chitosan is a linear polysaccharide composed of randomly distributed β (1–4)-linked 2-amino-2-deoxy-D-glucose (D-glucosamine) and 2-acetamide-2-deoxy-D-glucose (*N*-acetyl-D-glucosamine). The generic term of chitosan is used when the percentage of deacetylation of chitin is higher than 70%.

The positively charged Celox reacts on direct contact with blood, binding with the negatively charged red blood cells. This leads to clotting without exothermic reaction and without damaging the surrounding tissue. It works in states of hypothermia, in patients taking anticoagulants or antiplatelets [9] and does not cause a clot remote from the site of application. Once clotting has occurred, Celox can be removed by irrigating the wound with water or saline. Numerous studies conducted *in vitro* and on animals have shown the effectiveness of chitosans as haemostatic agents for even massive bleeding.

Materials and methods

Between April and October 2008 in a U.S. ROLE 2 (Enhanced Care) Facility in Southwestern Afghanistan during an International Security Assistance Force mission, 21 soldiers suffering from gunshot wounds (GSWs) were treated with Celox (SAM Medical Products, Newport, Oregon, USA), a granulated form of chitosan.

The patients were all male and between the ages of 18 and 45 years. None of the injured was taking anticoagulant therapy or had been treated with another haemostatic agent before arrival at ROLE 2. The majority of these injuries were located in the limbs; 13 patients had lower limb injuries, four patients had upper limb injuries, three patients had injuries to the shoulders and one patient had sustained an injury to the neck (Table 1). Of the 13 GSWs to the lower limbs, five had associated

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Table 1 Nature of wounds

Site	Number of patients	Type of projectile	Exit wounds	Tourniquet in place on arrival	Life-threatening bleeding	Outcome
Upper limb	4	4 HVGSW	4	4	3	All transferred to role 3, no feedback available
Lower limb	13	11 HVGSW 2 LVGSW	11	11	9	2 Fasciotomies on site, 9 transferred to role 3 without feedback
Shoulders	3	3 HVGSW	2	0	3	All transferred to role 3, no feedback available
Neck	1	1 HVGSW	1	1	0	Surgery on site then transferred to role 3

HVGSW, high-velocity gunshot wound; LVGSW, low-velocity gunshot wound.

fractures, two femoral, two combined tibia and fibula and one combined femur and tibia. Two of the patients with fractures required fasciotomies for compartment syndrome before onward transfer. Of the patients with GSWs to the upper limb, three suffered fractures: two to the humerous and one to combined humerous and radius. One patient with a GSW to the shoulder suffered a clavicular fracture. The patient with a GSW to the neck suffered mandibular fracture as part of the exit wound.

Tourniquets could not be applied to six of the 21 injured patients because of the anatomical location of the injuries (two patients sustained wounds to the buttocks, three to the shoulders and one to the neck). Celox was used in all cases in which haemostasis was not achieved through simple pressure and with the use of gauzes where bleeding was moderate-to-severe. Where necessary for penetrating wounds, applicators were created for the Celox granules using 10-ml or 20-ml plastic syringes with the ends cut off. Syringes of varying diameters were used so that they could be adapted to the different sizes of the wounds, allowing the Celox to be pushed deep into the wound (the Celox-A applicator was not available in the field at that time).

The application of the improvised device in the field proved extremely effective and easy to use. Using this simple system, it was possible to compact the Celox deep inside the wound leading to quick haemostasis. We observed that in all cases haemostasis was far more effective when Celox was applied deep into the wound rather than only to the surface. After applying Celox, pressure was applied to all patients using 4×4 cotton gauzes (Curity, Tyco Healthcare Group LP, Mansfield, Massachusetts, USA) and rolled gauze (Kerlix, Tyco Healthcare Group LP) for a period of at least 2 min. In 18 patients, clotting occurred in less than a minute while in three cases, in which arterial bleeding was severe, further applications of Celox were necessary. Once clotting had occurred, all the treated injuries were bandaged tightly. For the 15 soldiers with limb injuries, who were treated with a tourniquet on the battlefield, these tourniquets were left on during the application of Celox and the following 2 min of compression. The tourniquets were slowly removed only after clotting occurred. In all these cases, bleeding was controlled and it was not necessary to replace the tourniquets. No patient reported pain during or after the administering of Celox and no changes to the tissue surrounding the injuries were noted. All were transferred to ROLE 3 Facilities. There was no feedback on late outcomes; however, Celox is easily irrigated out after definitive treatment.

During the same period 12 other GSWs were not treated with Celox. These comprised two GSWs to the feet, six to the chest, of whom two died within the facility and four GSWs to the head, of whom three died within the facility.

Discussion

Celox has been approved by the American Food and Drug Administration [501 (k)], CE (Class 3) and by the North Atlantic Treaty Organization as a haemostatic agent. Celox is produced in three different sterile formulations, in granular form (Celox), in rolled gauze (Celox Gauze) and in a prefilled cylindrical applicator (Celox-A). This is the first published series from the field of its use in the military setting of high-velocity GSWs and the success of the initial uses reported here is gratifying. Follow-up from this setting is difficult and it is to be hoped that others will be able to report sequential assessments of casualties and their final outcomes in detail in due course. However, so far, Celox seems to be completely safe and has not shown significant side-effects. It has shown superior effectiveness when compared with other haemostatic agents when tested in research settings [10]. In a general context, chitosans have been used in the emergency field for some time. There has been earlier anecdotal evidence of the successful use of Celox in medical emergencies, both in the military and civilian fields. Celox has also been used successfully during cardiothoracic surgery and the use of chitosans has been well documented in other general surgical procedures. It is currently used both by the U.S. Armed Forces and a number of European Forces including the Italian Armed Forces engaged in Afghanistan.

Conclusion

The experience reported here shows that Celox granules have a quick and efficient haemostatic action producing a stable clot. The use of improvised applicators enabled good haemostasis to be achieved by pushing Celox deep into the wound. Ready-prepared cylindrical applicators (Celox-A) can be used to treat deep wounds, particularly

those caused by firearms or blade weapons, by compacting the Celox granules inside the wound and facilitating haemostasis. This device can be used successfully in the battlefield setting, in field hospitals and in the civilian emergency environment. Furthermore, it can be used not only by medical personnel and paramedics, but also by the injured soldiers themselves.

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