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Emergency Medicine

Hydrogel and hemostatic dressings in body injuries

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Summary:

A simple procedure of first aid for burns can be quickly carried out by an amateur, or any person providing first aid, allowing to stop the process of tissue damage by heat and causing a significant pain relief. After applying a hydrogel dressing to a burn wound, cooling of the wound starts (the heat is pulled out from the body to the gel). In case of cooling the patient's body with hydrogel burn dressings, a large loss of body temperature can be avoided in patients who require transport over long distances.

Uncontrolled hemorrhage remains a leading cause of traumatic death. Despite advances in medical intervention and protective equipment, fatal traumatic hemorrhage remains one of the most challenging problems for both military and civilian medicine. As a result, much attention has been focused on the development of alternative methods of controlling hemorrhage, including topical hemostatic dressings. Hemostatic dressing works by interacting directly with red blood cells and platelets to form a cross-linked barrier clot. There have also been concerns related to side effects, specifically thermal injury from the exothermic reaction, although documented occurrences are relatively rare.

Key words: burn, burn dressing, burn wound, hypothermia, hemorrhage, wound, dressing, clot, chitosan.

Thermal injuries of the skin can be substantially reduced by cooling the burned areas. One of the main effects of such a treatment is the inhibition of further and deeper penetration of the heat into the skin. Emergency procedures consist in eliminating the heat accumulated at a deeper level of the skin, by its 'pulling out' towards the surface, which allows for avoiding secondary injuries of these parts of the skin. If no cooling is applied, burn classified initially as a second-degree burn, turns into a third-degree burn, as a result of heat penetration. Shortly after cooling with hydrogel dressings, most of the patients report pain reduction. The anaesthetic effect after applying hydrogel dressings is a result of heat emission to the outside of tissues (which inhibits the penetration of the temperature into the body) and blocking of the release of substances that belong to tissue mediators (e.g. thromboxanes, prostaglandins, and leukotriens). Mediators (intermediating substances) are also a key element in developing the burn syndrome. Their release in high amounts leads to an increased permeability of the capillaries with formation of oedema and hypotension due to vasodilation which may lead to ARDS (acute respiratory distress syndrome).

The most popular burn dressings include hydrogel dressings, e.g. Water Jel – Burn Dressing (Fig. 1). Commercially available hydrogel dressings have a specific composition and properties.

Their matrix is a special gel produced by mixing 94% of demineralised sterile water with a gelling agent. Its consistency is similar to the one of a popular preparation Defi-Gel [1].

Figure 1: Hydrogel dressing – gel in the packet together with the dressing.

Table 1: Bacterial growth among 15 most common microorganisms after a contact with gel enriched with tea tree oil (modified according to Torsov in 1995).

Microorganisms	Bacterial growth after:		
	30 min	60 min	240 min
Staphylococcus aureus	+	+	negative
Streptococcus pyogenes	+	+	negative
Streptococcus agalactiae	+	+	negative
Streptococcus faecalis	+	+	negative
Escherichia coli	+	negative	negative
Klebsiella pneumoniae	+	negative	negative
Enterobacter cloacae	+	negative	negative
Serratia marcescens	+	negative	negative
Proteus vulgaris	+	negative	negative
Pseudomonas aeruginosa	+	negative	negative
Acinetobacter calcoaceticus	+	negative	negative
Clostridium perfringens	+	+	negative
Clostridium difficile	+	(+)	negative
Candida albicans	+	+	negative
Candida tropicalis	+	+	negative

Some of the hydrogel dressings include also natural oils with bacteriostatic properties (oil from tea tree). Their addition reduces the risk of infection of the burn wound, and disinfects the already infected wounds. The spectrum of action of the oil from tee tree includes 15 most common microorganisms [2] (Table 1).

The carrier material of the gel, used in hydrogel dressings, should be resistant to tearing and allow a simple application of the dressing on the wound. Water Jel dressings use a special knitted material made of polyester, highly resistant to tearing and allowing a simple application of the dressing on the burn. In dressings of large sizes, i.e. emergency blanket, the carrier material is sheep worsted wool, with properties that allow for carrying large amounts of gel on its surface. Due to that, such dressings are heavy and must be carried in special tubes allowing for their easy use, when needed. Other producers of dressings for burns usually use a carrier material made of polyurethane foam which is not as resistant as polyester. Another disadvantage is that any compression squeezes nearly the whole gel out of the dressing. As a result, a dry polyurethane foam covers the wound, and the gel is squeezed out onto the surface of the dressing. All dressings are sterile and packed in disposable packaging; some of the products are labeled with information on the percent of body surface that can be protected with the dressing, with a classification into adults and children. The most common size of the available dressings is: 5x15 cm (e.g. small burn wounds), 10x10 cm (e.g. hand), 10x40 cm (e.g. the upper or the lower limb), 20x45 cm (e.g. back or stomach), 20x55 cm (e.g. hand with protection of the burned fingers) and rescue blankets from 91x76 to 244x183 cm (Fig. 2).

Figure 2: Hydrogel dressing.

There are also special dressings for specific body parts, as in case of burn wounds of the face

causing problems with cooling; there is a special dressing in the form of a face mask, size 30x40 cm, allowing the protection of the injured ears, which often get burned as a result of the influence of such factors as high temperature in the region of the head (Fig. 3). The structure of this type of hydrogel dressing (properly placed openings for eyes, nose, and mouth) allows for using it in intubated patients as well [1].

Figure 3: Hydrogel face mask dressing.

Figure 6: . Application of a hydrogel dressing on a burned body area.

The most common and effective cooling system used in hydrogel dressings acts by collecting the heat from the skin surface and transferring it to the hydrogel layer (Fig. 4). The heat is transferred directly from the burn to the gel, by means of thermal conductivity. This leads to thermal dissipation over the whole surface of the gel, and thus the surface conducting the heat to the outside increases, which was marked with blue arrows in Fig. 5. The "buffering" effect of the gel layer allows for a faster and more effective heat removal directly from the burn wound, with a lower loss of heat of the adjacent tissues. As a result of this process, the temperature of the tissue under the burn wound is becoming much reduced, which in turn leads to a decrease in tissue damage, inhibition of burn spreading into the tissues and soothing effect on pain (Fig. 5). In the gel layer, the heat spreads – thermal convection, marked with yellow arrows in Fig. 5.

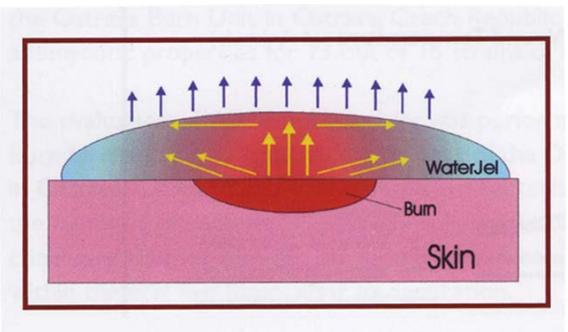

Figure 5: The principle of operation of the „Water Jel" system.

The most common cooling technique has so far been the use of cold (15-20°), preferably running water, for at least 15 minutes. The indication for water use is the fact that this is a factor quickly and effectively reducing the temperature of the skin subjected to heat damage. A major disadvantage of the traditional method (cold water) as the first aid in burn wounds is a high risk of local hypothermia, which can expand. The cooling time of up to 15 minutes is supposed to limit hypothermia and its expansion. This rule is not true for burned surface of more than 10%, because this situation requires large quantities of cold water. The use of large quantities of cold water as a cooling factor may lead to a sudden body temperature drop due to large amounts of heat being removed from the body in a manner difficult to control. Using water as a cooling factor requires also a free access to the cooling substance itself, which is often difficult to achieve in pre-hospital conditions. Apart from newborns and small children, there are also other groups of patients with an increased risk of hypothermia after the use of cold water as a method advised in first aid of burn wounds:

- Patients with extensive burns.
- Patients with burns of the back.
- Elderly patients
- Patients in the state of shock.
- Multiple injuries.

In case of these groups of patients, cooling of burns should be very careful, with constant monitoring of vital signs and body temperature. Cooling with hydrogel dressings allows for

hypothermia control by gradual thermal conduction from deeper layers towards the body surface, until stabilisation of the temperature at 36.6°C. Hypothermia is a common phenomenon in case of burns covering larger body surfaces and with longer times of heat conduction [3, 4].

Patients with burns in whom the body temperature decreases due to cooling to 30°C or less, should be protected at intensive care units. This fact has been observed by many physicians all over the world who deal with treating burns and it led to their questioning of the need to use the method of cooling with cold water as a means of first aid for burns. The risk of hypothermia and further health complications which may occur, cause an increased mortality among patients treated at burn units. The meaning of body temperature in the context of burn management was clearly stated in the data from studies conducted at burn treatment centres in the whole world. The studies showed that body temperature reduction by 1°C below 36.6°C on admission to hospital is the cause of increased mortality among patients by 43%.

There have been studies in which a series of measurements of body temperature were conducted in young and healthy individuals and in real cases – patients with burns, brought in by Emergency Medical Services, provided with hydrogel dressings [5]. The observations showed that using hydrogel dressings causes a gradual reduction in body temperature, up to 36.6°C, in burn casualties. The observed effect was also present in case of covering large body surfaces with a rescue blanket, with no hypothermia noticed in those patients (Table 2).

An indisputable advantage of hydrogel dressings is their long storage period, with expiry date of 5 years from the moment of production. The possibility of storing at -5 - +35°C. A long shelf life and a high amplitude of temperatures at which it can be stored allow for equipping the ambulances with these dressings. Owing to that, it is possible to act quickly and effectively at the site of occurrence and to fully secure the burned patients in pre-hospital conditions.

Despite advances in interventional medicine and protective equipment, massive haemorrhages caused by injuries remain one of the main causes

Table 2: Time of cooling the burn wound to the level of the body temperature, with the use of a hydrogel dressing.

Cooling time	Temperature in the burn wound
	Hydrogel dressings
Start	80.5 °C
after 30 seconds	78.4 °C
after 1 minute	71.2 °C
after 2 minutes	52.1 °C
after 3 minutes	44.7 °C
after 4 minutes	**36.6** °C

Figure 6: Different forms of haemostatic dressings

of death of such patients and thus one of the main challenges to the current civilian and military medicine. Uncontrolled bleedings are at present the cause of almost 50% of fatalities among soldiers, on the battlefield, before evacuation to hospital. Mortal haemorrhages due to injury are the cause of 80% of deaths among civilians (studies conducted on the territory of the USA).

The constantly increasing number of hostilities in hardly accessible areas and an increasing number of cases with the use of guns in civil conditions requires an effective protection of the haemorrhages as a part of the first aid (Fig. 5). In order to meet these requirements, our effort was focused on developing alternative methods of bleeding control, including special dressings for haemorrhage control. A few preparations have been developed which were mostly introduced for use on battlefields, in military conditions: a standard dressing containing chitosan (HemCon), powder dressing including zeolite (QuickClot) and dressing with granulated chitosan (Celox). The dressing with chitosan

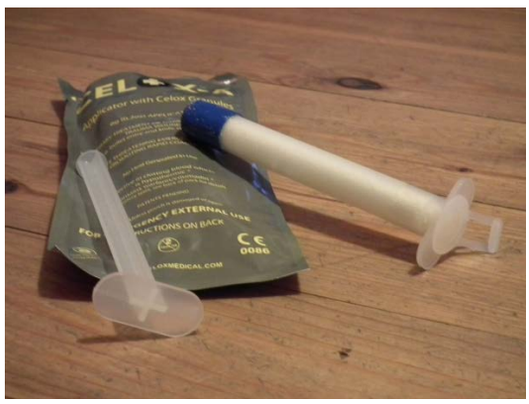

Figure 7: Haemostatic dressing with an applicator

Figure 8: haemostatic powder

Figure 9: Haemostatic gauze.

is a quite rigid plate forming a mucoadhesive physical barrier at injury site. Zeolite is a hard granulate, quickly absorbing water from blood and concentrating natural coagulation factors at bleeding site. The dressing with granulated chitosan acts through a direct interaction with red blood cells and platelets, forming a cross-linked barrier clot, irrespective of the application conditions (irrespective of the blood clotting factors) [6, 7, 8].

Studies on the effectiveness of these agents show that some products have their adverse effects, especially heat injuries caused by exothermic reactions after using preparations from zeolite. However, documented cases of such injuries are infrequent. Preparations including granulated chitosan (Celox) bond to the surface of red blood cells and platelets and to produce a gel-like clot or plug without producing high energy (this is not an exothermic reaction). They work independently of the body's normal clotting mechanism and can hypothermic or even heparinised blood. An additional advantage of dressings with granulated chitosan (Celox) is the fact that they do not cause allergic reactions in the users. It is possible because chitosan is a natural polymer extracted from the shells of shrimp and is subjected to the process of deep purification (rafination) during which proteins causing potential allergic reactions are removed. Possible penetration of the granulate to the blood flow causes its biodegradation because chitosan is a natural polysaccharide (polymer consisting of sugars) under the influence of lysozyme (enzyme naturally occurring in the body) (Fig. 7, 8, 9).

Comparative parallel studies of Celox produced on the base of chitosan with two haemostatic agents commonly used in the military (HemCon and QuickClot) were conducted, with the use of a standard dressing from gauze. The experiments were conducted under conditions of a fatal wound with bleeding from groin in 48 adult pigs fed and prepared for surgery in standardised conditions.

It was decided to use the model of haemostatic study, which is the closest to the conditions of groin injury on a battlefield and procedures of first aid. The reason for recreating the groin wound was the current tendencies among injuries on the battlefield, where the majority of wounds includes the lower limb, especially in the region of groin, and the upper limb, in the region of groin. Some wounds are only superficial and can be easily controlled (limited) by a direct compression, application of a compression dressing or other conventional techniques of bleeding control. The greatest difficulties are connected with wounds with anatomical structure making it difficult to control bleeding. An example of such injuries is groin wound and thus it was decided to use such a wound in these studies.

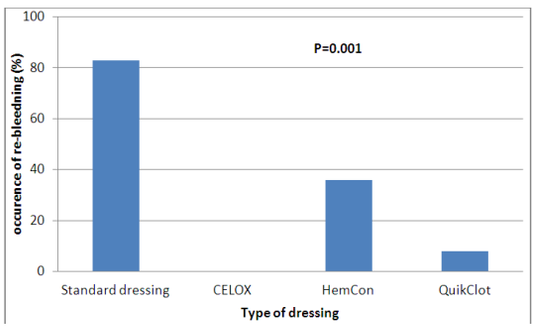

Figure 10: Percent of cases of re-bleeding during studies.

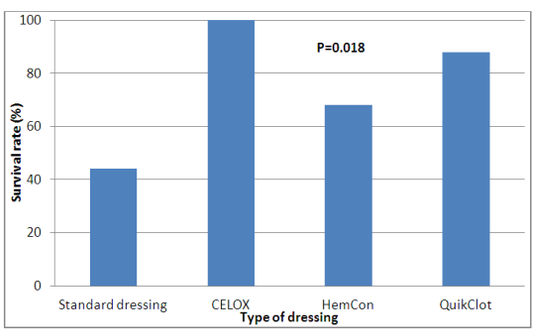

Figure 11: Survival rate for the whole study time.

Additionally, the adopted model was supposed to create a fatal bleeding wound with the fastest possible recreation of methods of first aid on the battlefield. It was decided to recreate a 3-minute bleeding, before protecting it, which reflects the realities of a fatal wound. There are no uniform data on the mean time until protection (the first aid) from the moment of bleeding onset, under the conditions of a battlefield. Adapting a 3-minute bleeding time allowed the researchers to reflect the time of waiting for the first aid team in battlefield conditions.

In the conducted study, the dressing with granulated chitosan (Celox) was performing similar to other dressings with chitosan. It did not produce any significant heat during application. The wound temperature was 37.2°C. Moreover, similarly to other dressings with chitosan, Celox was easy to remove. After coming into interaction with blood, it produces a soft, slightly viscous, gel-like mass, which can be easily removed with hand, without the use of tools. The remaining material can be easily washed off the wound by means of saline solution. One of the main advantages of this agent is the possibility to use it in the form of granulate. In some situations, non-exothermic dressing is very useful, which can easily adapt to the shape of the wound. In many aspects, Celox seems to be combining the advantages of HemCon and QuicClot, without revealing the disadvantages of those two. It was found that this agent is as effective as HemCon and QuickClot in controlling the bleeding, and this is the only dressing which significantly increases the survival rate as compared to a standard dressing from gauze.

A conclusion from observation was that the real reactional layer of Celox is only 1 mm thick. This ability helps in creating a capsule of unabsorbed preparation around a soft "dome" made of the agent bonded to blood. The remaining agent, not bonded to the wound, can be used again for controlling the next haemorrhage. The possibility of a "multiple use" allowing for potential control of re-bleeding is a feature of haemostatic agents, not possessed by the currently used agents.

In this study of objects treated with the use of HeHcon, there was a higher incidence of re-bleeding and a higher mortality than in case of Celox and QuickClot, and a lower incidence of re-bleeding and mortality than in case of a standard gauze. It was found that when used in accordance with its purpose, the haemostatic agent HemCon in the form of a layered plate was very effective, but in some situations this form was completely ineffective, with potential fatal results. The basic reason for such a wide range of effectiveness figures, is the physical form of that dressing. The use of HemCon was more difficult than of other materials. It seems to follow from the rigidity of the layered plate, applied to a narrow wound in conditions of a poor visibility of its contents.

In spite of the repeatability of the application method, the dressing did not always adhere to incised blood vessels. Instead of that, it adhered to the surrounding tissue. However, in case of a proper adherence to blood vessels, the application was effective. Difficulties with applying the HemCon dressing suggest that wide and flat wounds are be more appropriate than the deep and narrow ones, when the application follows the indications. No possibility of a universal use of the dressing may require more precise trainings. Generally, 8 out of 12 (67%) animals subjected to therapy with HemCon survived until the end of the study, but no statistically significant result was achieved, as compared to standard dressings from gauze.

The QuickClot dressing acts through exothermic reaction. This is the heat generated in the region of QuickClot application that causes problem of thermal damage to tissues of human organs as a result of increased body temperature, up to 61.0°C on average. The Z-Medica company developed a new composition of the preparation, which does not produce such an exothermic reaction any more. Studies on the new formula (preparation) have shown that it does not cause such thermal damage. According to the studies, the agent proved to be very effective; 11 of 12 (92%) animals survived the time of the study and one remaining case was connected with the occurrence of re-bleeding. The survival rate of animals treated with QuickClot (as compared to a standard dressing from gauze) was substantial ($p = 0.072$).

During autopsy of the mentioned fatal case, it was found that the majority of the preparation moved to a cavity in the tissue, running across the bundle of blood vessels; only a small amount of the agent was left in place, acting directly on the incised vessels. Although the dressing was applied in accordance with the manufacturer's instructions, the dislocation of the substance was a probable cause of death. The QuickClot preparation is mechanically relatively easy to use. However, it may require some additional training in order to make the right decision on its use, taking into consideration the risk of thermal damage.

It is commonly believed that early control of bleeding may limit the early and late mortality by reducing a substantial loss of blood, hypotension, coagulopathy, and abnormal metabolism or infections [9, 10]. The results of this study, conducted on a model of uncontrolled bleeding in pigs showed that Celox improved bleeding control and increases the survival rate. Celox is a preparation substantially increasing the possibility of managing severe bleeding owing to its easy application. It should be placed directly on the wound and then compressed. The wound should be pressed for a short time, in order to squeeze the granulated chitosan out into the wound and to stop blood outflow. During that time, Celox will form a clot and obtain an appropriate endurance.

The required time and compression force depend on the pressure of outflowing blood. In case of less severe wounds, it is enough to compress the dressing with a finger for a few seconds. In case of more severe wounds, it is advised to compress it strongly for 5 minutes, or as long as it is required by the circumstances. If the blood starts flowing again from the wound (and we are sure that Celox covers the whole surface of the wound), one should just hold pressure for a longer time, and when necessary, use additional amounts of Celox preparation. Owing to its properties and easy application, this dressing from granulated chitosan is close to a perfect haemostatic dressing.

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