Review Article Oral rehydration solutions for burn management in the field and underdeveloped regions: a review

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Abstract: Burn injuries are the fourth most common type of trauma worldwide, and the appropriate care of burn injuries in resource-limited settings such as the battlefield, underdeveloped nations, or in mass casualtiesremains a significant challenge. Rehydration constitutes the primary treatment of the systemic effects of burns and is a major factor in patient recovery. The standard of care for the replenishment of fluid and electrolyte losses in burn injury remains intravenous fluid therapy, but oral rehydration solution therapy (ORST) demonstrates beneficial utility in saving the lives of burn patients when they are applied in the acute phase of burn injuries, especially when intravenous rehydration is unavailable or inaccessible. Advantages of ORST as compared to intravenous therapy include availability, ease of administration in the field, low risk of infections and complications, low cost, and no requirement for accessory or specialized equipment. These benefits position ORST very attractively for the provision of interim first aid until definitive medical assistance arrives. Extensive and comprehensive investigation may be warranted to elucidate, account for and quantify individual burn patient biochemical variables toward the potential realization of such an "omniuse" oral rehydration solution for the benefit of burn injuries worldwide.

Keywords: Oral rehydration solution therapy, ORST, burns, burn management

Introduction

The appropriate care of burn injuries in combat field environments or other resource limited settings remains a significant challenge. Burn injuries are commonplace events in disasters and during military conflicts. Currently, in war afflicted regions, civilians account for over 80% of those who are killed or wounded. Burn injuries remain an ubiquitous threat in the military theatre and thus a major complicating factor associated with armed conflict. The availability and application of state of the art modalities to facilitate burn management in these resource deficient settings can be expected to have positive impacts on victim morbidity and mortality [1].

Rehydration constitutes the primary treatment of the systemic effects of burns and is a major factor toward patient recovery. The standard of care for the replenishment of fluid and electrolyte losses in burn injury remains intravenous fluid therapy. The minimum volume of fluids should be provided immediately for restoration of homeostasis and avoidance of edema. Since the 1960's, oral rehydration solution therapy (ORST) has been employed to treat the loss of fluid and electrolytes resulting from diarrhea. As an alternative to intravenous fluid resuscitation, ORST has also been found to be beneficial in the resuscitation of children with moderate burns [2].

The addition of appropriate levels of sodium can make ORST as efficacious as intravenous therapy. In situations of mass casualty or in resource-poor settings where intravenous fluid therapy is not readily available for all patients, ORST can be a potentially life-saving therapy. There are a number of advantages inherent to ORST over IV therapies, which include: ease of administration in the field; compactness and modularity (does not require accessory intravenous equipment); physiological non-invasiveness with little risk of infection since dermal penetration is not required; low cost. Cumulatively, these practical benefits position ORST very attractively for the provision of interim first aid until more well equipped medical assistance arrives. Studies are currently underway to determine if the use of ORST might serve as a viable alternative to IV fluid therapy in the resuscitation of burns. This paper will review the current literature as relates to the use of ORST in addressing burn injuries.

Burn injury epidemiology

The World Health Organization (WHO) reports that in the United States, over 410,000 burn injuries occurred in 2008 that required medical attention. Of these, ~50,000 cases necessitated hospitalization, of which ~20,000 comprised major burns that involved at least 25% of the total body surface area, with ~4,500 of these individuals succumbing to their injuries [3]. Burn injuries represent the fourth most common type of trauma worldwide. The incidence of fire-related injuries in 2004 was estimated to be 1.1 per 100,000 population, with the highest rate existing in Southeast Asia and the lowest in the Americas. The incidence of burns in low and moderate-income countries is 1.3 per 100.000 population, compared with an incidence of 0.14 per 100,000 population in high-income countries. The incidence of burn injuries that are severe enough to require medical attention is almost 20 times higher in the Western Pacific than in the Americas. Infants in Africa have an incidence of fire-related burns that is three times the world average for this age group [4].

Worldwide, an estimated 195,000 deaths every year are caused by burns with the vast majority occurring in low- and middle-income countries. Women in the WHO Southeast Asia region have the highest rate of burns, accounting for 27% of global burn deaths and nearly 70% of the burn deaths in the region. Burns occur mainly in the home and workplace and are preventable injuries.

Severe burn injuries affect approximately 5 to 20% of survivors of war-time conflicts, civilian mass disasters or terrorist attacks. Burns are reported to be more common during wars at sea and wars that involve armored vehicles. Of these burn injury survivors, 80% sustain less than 20% total body surface area burns (TBSA). As relates to civilian fire disasters, there have

been 73 in the U.S. spanning the 20th century. Every incident has resulted in the improvement of building codes and/or fire regulations. As a result, subsequent disasters have resulted in fewer than 25 to 50 patients that have required inpatient burn care [5]. The majority of severely burned patients die at the scene or within the initial 24 hours following the injury [6-11].

Historical efficacy of oral rehydration solution therapy

In the mid 1940's, National Institutes of Health (NIH) research pharmacologist, Sanford Rosenthal, conducted extensive trials with mouse models that involved the resuscitation of burns and associated trauma. His work is significant in that it confirmed the efficacy of enteral resuscitation for severe burns [12, 13]. Charles Fox published one of the original human studies that described the exclusive use of ORST for both partial and full thickness burns. Four children (TBSA 23%-80%) and five adults (TBSA 19%-41%) who presented with full thickness burns and shock were resuscitated with chilled isotonic sodium lactate (100-150 mL/kg over 24 hours) in accordance with the Parkland formula, which was introduced immediately on admission [14]. In 1949 Carl Moyer utilized ORST in the treatment of 30 children and adults with severe burns. He learned that the use of NaCl solely led to acidosis, hence, more buffered and balanced solutions containing bicarbonate, lactate or citrate were utilized which also lowered the incidence of nausea and vomiting [15].

In 1950, a NIH Surgery Study Section strongly advocated that in the event of a large-scale civilian catastrophe: "The use of oral saline solution is adopted as standard procedure in the treatment of shock due to burns and other serious injuries ... " [16]. Markley, et al., conducted a NIH sponsored comparison of intravenously infused plasma and blood versus orally administered isotonic bicarbonated saline. The study enrolled 55 children and 56 adults with a mean Body Surface Area Burn (BSAB) of ~35%. It was found that after 48 hours, the mortality rate for oral resuscitation (110 mL/kg/first 24 hours) was equivalent to, or superior, in contrast with intravenous resuscitation, showing improved volume expansion (determined by hematocrit and urine output) and hemodynamics. Also elucidated was that ORST was relatively ineffective at >50% BSAB [17].

A comparative study involving 142 burn patients (15-60% BSAB) was conducted by Wilson and Stirman in 1960 to determine the best outcomes between the oral administration of isotonic saline and saline in conjunction with blood [18]. In 1964, Franke and Kock-Marburn published the earliest clinical application (involving 19 children) of an oral electrolyte solution combined with glucose for the successful management of severe burns (8-38% BSAB) [19].

El-Sonbaty reported that children with moderate burns of 10% to 20% TBSA may be resuscitated via oral rehydration in the form of an electrolyte solution. Their recovery appears similar to those who receive intravenous therapy; however, ORST avoids some of the problems that are associated with intravenous intake, including fluid overload. El-Sonbaty found that using ORST had the following advantages: "Simplicity of use, low cost, possibility of use as a first-aid treatment until the patient arrives at a hospital, no risk of fluid overload, and the avoidance of all the difficulties and complications of intravenous infusions [20]".

Kramer, et al. reviewed twelve studies in the literature, which involved over 700 burn patients who were treated via enteral resuscitation. They characterized enteral, as either oral or gastric infusion with salt solutions. These investigations put forward that, in cases where IV therapy is delayed or is not available, "...enteral resuscitation can be an effective treatment for burn shock... in patients with moderate (10-40% TBSA) and in some patients with more severe injuries." Enteral resuscitation can be used exclusively in some patients, while others may benefit from enteral resuscitation as an initial alternative and supplement to IV therapy. Although delayed gastric emptying (vomiting) and aspiration can be relative contraindications, saline fluids might continue to be administered via nasogastric tubes [2] in conjunction with anti-emetics and motility agents.

Studies have been conducted regarding the type of intravenous solutions best suited to treat burn shock, but "the role of enteral resuscitation in initial resuscitation has not yet been tested against modern resuscitative regimens." Intestinal absorption rates after burn injury are sufficient to resuscitate a 40% TBSA burn, and oral rehydration solution therapy could be a

viable option for burn and burn shock resuscitation when IV therapy is unavailable [2, 21]. Thus, this technique lends itself to use in austere environments, such as in the battlefield, underdeveloped nations or in mass casualty situations.

Physiology of oral fluid rehydration

Hypovolemic shock remains the greatest challenge subsequent to major burn injuries. The goal in major burn treatment is to maintain tissue perfusion in the early phase of burn shock. Burn injuries of less than 20% TBSA are associated with minimal fluid shifts and can generally be resuscitated via oral hydration [22-25]. Enteral resuscitation has been attempted in the treatment of even major burns; however, vomiting has been indicated as an issue over the initial 48 hours, which may limit its effectiveness in this application. There is no documentation as yet, however, that pertains to the incidence of this occurring. Nevertheless, in situations where access to care is limited. enteral resuscitation with balanced salt solutions may be initiated [26, 27].

The standard of care for military personnel mirrors that which is established for the civilian population; however, options for civilian intervention in wartime are limited. "Of all pre-hospital transports of civilian victims, 70% are done by lay public and 93% receive in the field, or during transport some form of basic first aid administered by relatives, friends, or other first responder not trained for such interventions [28]".

Following thermal injury, immediate local and systemic inflammatory reactions cause changes in vascular permeability, resulting in rapid shift of intravascular fluid to the interstitial space. Burns initiate the rapid depletion of bodily fluids and electrolytes, sodium, in particular. If more than 10% of the body's fluid should be lost, death will ensue. Water is absorbed and passively secreted within the human body following the movement of salts, based on the principle of osmosis. Following burn injuries, the body can absorb simple solutions containing both sugar and salt. There is a continuous exchange of water through the intestinal wall, which allows soluble metabolites to be absorbed into the bloodstream.

The store of sodium within the human body resides almost entirely in solution within bodily fluids and in blood plasma. In contrast, ~98% of the body's entire potassium complement is retained within cells. The concentration of sodium within extracellular fluids must be held within specific parameters in order for human physiological processes to maintain proper functionality. Normally this sodium concentration is precisely controlled by kidney function. However, under dehydrated conditions, water is conserved; thus urine production is absent and sodium regulation is inefficient. It is critical to rehydrate with solutions that contain electrolytes, especially sodium and potassium, so that electrolyte disturbances may be avoided. Supplementation with phosphate has also been reported to be beneficial in offsetting hypophosphatemia, which is a "common phenomenon in patients with massive burn injury [29]"

Sugar is an important element for enhancing the absorption of electrolytes and water. However, if too much is present in ORST, fluid loss is exacerbated. When glucose is added to a saline solution it is absorbed through the intestinal wall and in conjunction with sodium, is carried by a co-transport coupling mechanism. Glucose does not co-transport water; rather it is the increased relative concentration of sodium ions, with their associated hydration shells that facilitate the traversal of water across the intestinal wall [30].

Interestingly, Kahn *et al.* have reported that high doses of ascorbic acid (vitamin C) may reduce fluid requirements, with its purported effects encompassing a reduction in tissue edema and weight gain, as well as decreased respiratory impairment and thus a reduced necessity for mechanical ventilation [31].

Potential benefits of ORST burn management in the field

In 2011 Milner, *et al.* stated that, "Oral rehydration therapy has the potential of saving many lives in the event of mass thermal casualties or in resource-poor settings where transport, intensive care, and definitive surgical care may be delayed [32]." In their review of the literature they found only one report regarding the use of ORST for burn resuscitation in children, yet abundant documentation in support of the safety and effectiveness of ORST as an alternative to IV resuscitation in epidemic cholera. The WHO has estimated that greater than three million lives are saved through the use of ORST in addressing diarrheal diseases every year [33].

Treatment of combat casualties presents a unique opportunity for the use of enteral resuscitation [34]. Due to the uniqueness of combat care, including long evacuation times, new recommendations for initial fluid resuscitation of combat casualties have been proposed [35]. Krausz noted that Advanced Trauma Life Support guidelines provide a systematic standardized approach for the treatment of trauma casualties, which is very successful in civilian trauma, however, on the battlefield, these have required modification in order to align with the combat environment [36]. Since medics have limited options for burn treatment in combat zones, approaches are being sought that will have important implications toward the development of optimal fluid resuscitation strategies for the stabilization of combat casualties [37].

Partial or even complete oral resuscitation might be accomplished by utilizing WHO sanctioned formulations, packets combined with potable water or sports drink ration packets. These interventions can effectively restore plasma volume following thermal injuries when no other alternatives exist. Oral resuscitation alone may be used for many patients, and the supplementation or replacement of IV fluids can be employed for those with more severe injuries. Although the optimal composition of oral replacement fluids has yet to be determined, the belief is that any form of oral resuscitation is preferable to no resuscitation at all [38].

Burn resuscitation in underdeveloped countries

Burn resuscitation in underdeveloped countries (where ~85% of burns occur in low and middle income regions) remains especially challenging in view of very limited, or completely lacking medical infrastructures in these regions. Further hampering efforts to address and potentially improve this state of affairs, as noted by Ahuja *et al.*, is the acute lack of studies that examine the "cost of burn care in the developing world...". As they observe, the perception of modern burn care is that it is an

expensive, resource intensive enterprise, which necessitates "specialized equipment, personnel and facilities to provide optimum care." At minimum, it is suggested that, in addition to the benefits imparted by education and prevention, burn centers should be established that can provide "reasonable" burn care "in face of resource constraints." The criteria for what is deemed reasonable encompasses "adequate resuscitation, daily topical dressings, appropriate surgery (escharotomy, debridement, and skin grafting), adequate nutrition and physical therapy", the results of which may be measured in terms of patient outcomes and mortality [39].

Several recent articles describe the status of burn care in developing countries. In a review of nine patients with massive burns (>50% TBSA) of which four died, Onuba et al. (University of Calabar Teaching Hospital, Nigeria) cited that, in these cases, the primary factors for morbidity and mortality were "Delay and inadequate fluid resuscitation and overwhelming infection [40]." Ahuja and Goswami reported (from the results of a one year study conducted at a 50 bed burn unit at the Lok Nayak Hospital in North India) that 15 of 161 patients with greater than 70% TBSA survived. The primary causes of mortality were cited as "sepsis and respiratory complications". The researchers reveal, "Financial and infrastructure constraints often dictate treatment modalities and outcomes [39]. Sun et al. reported on bath-related burns (1-60% TBSA) endured by neonates in hospitals in developing countries, and attributed these to careless (likely inexperienced) nursing. Due to the complex nature of neonate burns, they recommended that the course of treatment here should include the close cooperation of burn surgeons; the formation of an interdisciplinary team; timely and aggressive fluid resuscitation; early provision of oxygen and patient warmth; appropriate biological dressing; recombinant human growth hormone (if necessary); and prompt removal of necrotic tissue. Also deemed critical were steps toward the prevention of neonate burns in developing countries [41].

A four year retrospective of 269 burn patients at the Tenwek Hospital, Bomet, Kenya (one of the small number of hospitals in East Africa that offer quality burn care) revealed that more than half (59%) of the patients were children under the age of five. Of all cases, 76% comprised second degree burns, where 55% were generated by scalding and 13% were epileptic seizure-related. Otteni *et al.* recommended that preventative measures should be taken to minimize exposure of children to boiling liquids and open flames in the home in conjunction with early presentation following burn events.

The rate of mortality at Tenwek was found to be 12%, with sepsis, cardiac arrest and respiratory failure and pneumonia being cited as the primary causes. Fluid resuscitation at Tenwek for patients with major burns (>10-15% TBSA) relies on the Parkland formula. The impact of financial constraints on burn treatment translates to the very limited provision of early excision and grafting and restricted access to blood products. Hence, "with the exception of facial burns and burns over joints, granulation tissue development is allowed with daily dressing changes." Less costly, albeit less efficacious ointments are utilized in the absence of Silvadene, and Bacitracin is employed for burns affecting the face. When wounds are at the proper condition, skin grafting is conducted; however, timelines for their performance may be hampered by the financial situation of the patient [42]. Thus, in developing regions, as illustrated above, financial constraints can impose significant restrictions on the quality of burn care. Hence, the utilization of advanced oral hydration products and techniques may facilitate increases in positive patient outcomes, at a reasonable expenditure.

Envisaged strategies for the future treatment of burn patients may emerge as advanced oral rehydration solutions are developed. The elements of such orally administered resuscitants might encompass chemically mediated selfregulating "smart encapsulants", which would be activated only under specific chemical conditions within set parameters that are present within their localized in vivo environment. If a portion of the encapsulants are not utilized due to particular unsuitable in vivo conditions, they would be eliminated by natural physiological processes. Extensive and comprehensive investigations are warranted to elucidate, account for and quantify personalized biochemical variables toward the potential realization of such "omniuse" oral rehydration solutions for the benefit of burn patients worldwide.

Conclusion

As is apparent from the contents of this brief review, there exists no optimal or "universal" oral rehydration solution that has yet been conceived or formulated. Patients presenting with varying levels of burn severity, coverage and depth, inhalation injury, associated injuries, and age, require individually tailored treatments insofar as resuscitation solution composition, volumes and administration times. Whether used alone or in conjunction with intravenous hydration, specific constituents of oral rehydration solutions may serve to remedy particular physiological aspects of burn trauma. Oral rehydration solutions demonstrate beneficial utility in saving the lives of burn patients when they are applied in the acute phase of burn injuries, in lieu of intravenous rehydration, when intravenous rehydration is unavailable or inaccessible.

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