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Resuscitation in Extensive Burn in Pediatrics and Fluid Creep: an Update

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Abstract

Purpose of review Excessive administration of crystalloid and the abandonment of colloid replenishment at certain point of resuscitation are the major contributors to fluid overload, leading to a phenomenon termed fluid creep. Over-resuscitation in burn pediatric patients often results in fluid overload and many complications characterized by anasarca, orbital compartment syndrome, extremity compartment syndrome, bloodstream infections, pneumonia, abdominal compartment syndrome, and pulmonary edema requiring a prolonged and potentially complicated hospital stay.
Recent findings Permissive hypovolemia has been shown to effectively reduce organ dysfunction, when applied a rigorous control of diuresis. More recently, a urine output target of 0.5 to 1 ml/kg/h in the first 48 h of fluid resuscitation has become a trend in the monitoring of pediatric patients. Colloids appear to be an essential component for the resuscitation of severely burned patients.
Summary Many strategies were developed to optimize fluid resuscitation in burn patients, and until current days there are controversies regarding the most efficient method to determine the ideal volume of fluid to avoid hypovolemic shock and complications from over resuscitation as well. The success of resuscitation is related to the administration of lower fluid volumes. Some centers have demonstrated that selection of more strict protocols of fluid resuscitation, rigorous diuresis control, moderate use of opioids, and early and regular use of albumin are correlated to positive outcomes and thus may attenuate the urgence of fluid creep.

Introduction

Burns are important traumatic events that, besides preventable, are relatively common in pediatric populations, accounting for a substantial proportion of hospital admissions. Burn causes considerable morbidity and mortality among patients, being males most affected (proportion of 1.6:1 against female); however, mortality rate are higher among females [1]. Burn induced metabolic and hormonal changes may persist for long periods after the traumatic event, and represents an economic burden to health systems due to the high costs of its treatment, that requires long hospitalization time and rehabilitation. Thermal traumas are most prevalent in low-income and under development regions. The steep growing of world economic conditions, however, may decrease the number of burn accidents in a global perspective [2–7].

Burns are preventable. Educational programs, fire alarms, smoke detectors, and water temperature control systems contributed significantly to decrease burn accident rates in some countries over the last years. Culture and political characteristics in different regions over the world impact the epidemiology of burn prevalence. Most of the burn accidents in pediatric age groups are due to scalds with overheated liquids in the domestic environment. In their development period, children display an exploration behavior and are not capable to distinguish dangerous situations [8, 9].

According to the CDC (Centers for Disease Control and Prevention) statics between 2007 and 2016, burn accidents are classified as the fourth cause of death by unintentional injuries in children under 1 year of age in the USA, the third cause among children with one to 9 years of age, and the fourth cause among children with 10 to 14 years. Additionally, 16 to 20% of children admitted with burn accidents are victims of abuse. The mortality is proportional to the age group—when younger, the higher the mortality is—due to the incomplete development of multiple systems including an immature immune system. Approximately 10,000 children develop permanent sequel as a result of thermal injury every year. In 2010, the total cost of pediatric burn treatments was around one billion dollars [10].

The survival rate of children with burns regards on age, extension and depth of the lesion, causal agent and the management of the injury. In young children, particularly under 2 years of age, the mortality rate is higher for the same body surface area when compared to older children and adults. Most common causes of death in burn children are smoke inhalation and hypoxic-ischemic encephalopathy.

Adequate fluid resuscitation is still the critical aspect in the initial management of the burn patient, being fundamental to prevent shock and other complications from thermal injuries [11, 12••].

Many strategies were developed to optimize fluid resuscitation in burn patients and until current days there are controversies regarding the most efficient method to determine the ideal volume of fluid to avoid hypovolemic shock complications [12••].

Resuscitation formulas were developed based on body weight and burn extension, with a variety of fluid combinations. Cope and Moore, in 1942, observed that patients' fluid requirement was associated to weight and burn extension area [13]. This conclusion was fortified and upgraded by Cancio et al., providing evidence that the burn extension (positively) and weight (negatively) were associated to higher volume demand for an appropriate resuscitation [14]. However, the most broadly strategy used is the Parkland Formula, reported by Charles Baxter and Tom Shires in 1968. They described the use of 3.5 to 4.5 ml/kg/TBSA% of an isotonic crystalloid solution in the first 24 h, associated to a colloid infusion as a plasma formate of 0.3 to 0.5 ml/kg/BSA% in the second 24 h period. The volume should be adjusted according to the diuresis [15].

Further studies by Baxter verified that 12% of adults required more volume than preconized by the Parkland Formula, while others needed 18% less volume. This observation deflagrated a discussion in 1979 at the National Health Sponsored Conference on Burn Healthcare. At this Conference, it was determined that patients must receive the minimum amount of liquid possible to maintain organic perfusion. The initial fluid therapy would now consist on isotonic saline solution with a volume between 2 and 4 ml/kg/BSA% in the first 24 h and titrated to maintain the urine output between 30 and 50 ml/h in adult patients. The colloid used after the 24th hour was excluded. This recommendation was universally accepted as a consensus to resuscitation among burn healthcare providers and is still currently the most used [16].

Aggressive fluid resuscitation with Ringer Lactate proposed by Baxter and Shires, added to the advanced in surgical techniques of excision, antibiotic therapies, together with adequate monitorization and intensive therapy support, modified the evolution of burn patients that previously had a premature death due to Burn Shock and kidney injury [17]. Currently, patients survive to the initial burn phase and sepsis became the leader cause of morbidity and mortality in burn patients. Due to the loss of the primary barrier against microorganisms, patients are constantly exposed to the environment, specifically to hospital flora—and, consequently, they are considered to be at high risk for nosocomial infections [18].

Etiology of fluid creep

Increased fluid load, a phenomenon called "fluid creep", can lead to excessive edema and organ failure [19].

Many reports have revealed that very large resuscitation volumes are being given even in otherwise "uncomplicated" patients, with none of the recognized factors of increased fluid requirements such as inhalation injury, use of alcohol or drugs, overestimation of burned BSA, delay in resuscitation, severe trauma, or high-voltage electrical contact. Larger fluid volumes, as much as 5 to 8 ml/% TBSA/kg, are being required for successful burn resuscitation in an increasing number of burn patients [20].

The lipoprotein complex that builds up on scars has a significant effect on cytokines release and leads to an important systemic inflammatory response syndrome (SIRS) and to an immune dysfunction with multiple aspects. Late excision and complex removal may perpetuate the SIRS state and raise the need of liquids during this period [21].

The classic Starling model to describe fluid movement due to transendothelial differences in hydrostatic and osmotic pressures inside the vascular lumen and surrounding tissue was reviewed in recent studies regarding the endothelial glycocalyx. The glycocalyx is a carbohydrate rich layer that coats the vascular endothelium. Its capacity to control the capillary overflow of colloids and fluids has been a focus of recent research. Apart from its ability to restrict the contact of some molecules with the endothelium and to modulate the interaction with other cells, recent studies emphasize the importance of the endothelial glycocalyx as one of the main determinants on vascular permeability, that can be modified in a systemic inflammatory condition [22].

Endothelium instability and imbalance of Starling forces result in an important effusion of fluids, electrolytes, and proteins to the extravascular territory, with rapid balance of the intravascular and interstitial compartments. These changes result in loss of circulating plasmatic volume, with the resulting hemoconcentration, development of important edema and reduction of urine output, contributing to cardiovascular function depression. Finally, there is a change over the volume distribution in each compartment: augmentation of the interstitial and intracellular volumes and reduction in blood and plasmatic volumes [23].

Edema appears locally in the burn area with its peak occurring 24 h after the trauma. Edema formation exceeds the pretended beneficial effect activating the inflammatory response. Besides, the edema results in tissue hypoxia and an increase in tissue pressure, with the potential risk for circumferential lesions appearance [23, 24].

Fluid resuscitation

Excessive fluid resuscitation, surpassing the volume suggested by Baxter, has been a focus of discussion after the observation of the fluid creep phenomenon, described by Basil Pruitt as being the cause of morbidity and mortality increasing rates in burn patients [25]. The phenomenon is characterized by insidious edema in non-burned areas associated with pulmonary edema and cavitary effusions in patients submitted to excessive fluid resuscitation [19]. The author claims for more caution in fluid administration, stimulating a conservative infusion of fluids. Excessive resuscitation regarding the belief of "more is better" is controversial when applied to burn patients.

Chung et al. observed military burned patients and concluded that the initial resuscitation proposed initially with aggressive amount of fluids resulted in progressive demand of volume infusion followed by resuscitation. Excessive fluid amount can be threatening, as much as an insufficient infusion [26].

Current evidences suggest the fluid reposition formula is frequently inadequate. Mistakes are commonly observed regarding the diagnosis and classification of burn injuries (as extension and depth of lesions) during primary assistance, providing subsequent inappropriate volume for resuscitation. Patients may be admitted to specialized burn centers hours after the incident and they might have already being infused with a considerable amount of the 24 h volume need [27, 28].

A retrospective American multicenter cohort by Klein et al. observed 72 patients and demonstrated by linear regression that individuals that received 25% more fluids than that required for the BSA and weight in the resuscitation period, had more events as pneumonia, bloodstream infections, ARDS (acute respiratory distress syndrome), MODS (Multiple organ dysfunction syndrome) and death [29]. Besides, progressively higher doses of opioid administration 48 to 72 h after injury may worsen patients' hemodynamics, contributing to an increased fluid demand. This incident is determined by the authors as *opioid creep* [30]. Wibbenmeyer et al. in a replication of the previous study showed a strong and direct correlation between opioid administration in the first 24 h and liquid amount infused in the same period [31].

Even before the Parkland Formula, Baxter, besides recognizing that the formula was enough to successfully resuscitate the majority of burn patients, observed an important variability response among patients. He found that adjustments in the infusion rate based on different individual response were fundamental to improve the outcome. Baxter identified subgroups of patients that routinely required additional fluid. These were those with inhalatory and electric burns, and others whose resuscitation was substantially delayed [15].

Other studies equally demonstrated that airway burned patients needed increments between 35 and 65% of fluid amount compared to those who did not [32]. Patients with associated traumas, as well as alcohol and drug users were identified as potentially receivers of higher amounts of resuscitation fluid. Extensive burned patients have been shown to need significantly more fluids than those suggested by Baxter [33].

A rational explanation to this increment in fluid need is still unknown e may have more than one cause. This situation was first noticed when edema complications such as the abdominal compartment syndrome and others were recognized.

Ivy et al. reported that intra-abdominal pressure increase and the emergence of abdominal compartment syndrome frequently appeared in patients with lesions exceeding 20% of BSA and receiving large amounts of fluids infusion [34].

Fluid creep complications

Although reasons for the need of large amounts of fluid volume are unclear, edema related complications are well characterized. These include anasarca, airway edema (frequently leading to orotracheal intubation), pulmonary edema, pleural or pericardial effusion, swelling extremities (increasing the need of escharotomies and fasciotomies), prolonged mechanic pulmonary ventilation in patients without airway burns or facial burns and intraocular pressure increase (leading to orbital compartment syndrome) [25]. Studies report increased risk of pneumonia, bloodstream infection, SDRA, DMOS and death [29, 35, 36].

The most severe fluid creep complication is the abdominal hypertension that, when uncontrolled, may lead to abdominal compartment syndrome (vesical pressure higher than 25 mmHg, associated to pulmonary compliance reduction or oliguria and renal failure). The syndrome is considered secondary when no evident abdominal disorder is present and is typically fatal when left untreated. Intra-abdominal hypertension is common in extensive burned patients, frequently with more than 70% of BSA [37]. All of the aforementioned complications extend the length of stay in intensive care units though increasing treatment cost [33].

Some fluid creep studies reveal that large volumes of crystalloid solution are provided even in patients without any complications. Even excluding inhalation injury patients, the fluid volume remains high, above 6.2 ml/kg/%BSA. Friedrich et al. reported, in 2004, results of an investigation showing that patients in their burn center received twice the volume (8 ml/kg/%BSA) than that previously used (25 years ago). Some likely causes for this change of behavior may be a more invasive monitorization, how the Parkland Formula is interpreted and prescribed, changes in the type of burn injuries, and the increase in opioids use for patients' analgesia [36].

Engrav et al. observed fluid creep in 58% of the patients they studied, and Cartotto, Ivy e Kaups found respectively even higher rates: 84%, 90%, and 100%, in fluid creep occurrence [33, 38].

Monitoring

Ideal clinical and hemodynamic parameters are fundamental tasks in burn patients and are the second most difficult challenge in burn resuscitation. Urine output (UO), heart rate, and blood pressure are primary indicators in burn patients monitorization. Conscience level and peripheral perfusion are additional clinical markers of organ perfusion [17].

The UO range (the most important role in burn patient monitorization, a paradox considering the sophisticated monitoring devices available in high standard intensive care units nowadays) recommendation of the American

Burn Association resuscitation guidelines for burn shock is between 0.5 and 1 ml/kg/h for adults and 1 and 1.5 ml/kg/h for children under 30 kg. Apart from being the best clinical parameter of resuscitation, UO is an important clinical marker of disease improvement, due to the allowance of fluid infusion adjustment over time, based on patients' individual feedback [39].

Monitorization of intravesical pressure to observe the presence of intra-abdominal hypertension must be performed in extensive burned patients that demand a large amount of fluid for resuscitation [34].

Pulmonary artery pressure and central venous pressure are not appropriate indicators of preload in burn patients and are not recommended. However, they may be occasionally indicated in special situations, as severe airway burn or inadequate response to the selected treatment protocol [39].

There are no associated benefits for supra levels of volemia. If the signs of adequate tissue perfusion are normal, the attempt to normalize central venous pressure and pulmonary artery pressure must be avoided. Excessive efforts to stabilize these parameters may cause fluid creep [21].

Abnormal admission values of lactate and base excess are correlated to burn magnitude and delay in normalization of these parameters are mortality predictors. There are no studies to support the use of these parameters to guide fluid resuscitation in burn patients. Due to the burn shock pathophysiology, that creates a prolonged hypovolemic state, attempts to rapidly clear anaerobic metabolism sub-products with aggressive volemic reposition may be threatening and may exacerbate edema development. Increased hematocrit (55 to 60%) is commonly observed in the initial period after burn; however, this variable also must not be used to monitor fluid resuscitation [21].

Kelly et al. recently described a method to calculate the rate of fluid influx and UO of each resuscitation hour [40]. Fewer complications and better results were found in burn adult patients. Because individual physiological responses to resuscitation vary substantially, one viable approach would be to calculate the I/O ratio of total fluid infusion (ml/kg/BSA)/UO (ml/kg/h), in a routinely manner and use it to quickly apply albumin therapy in some patients [41]. This study was reproduced in children, obtaining similar results [42••].

Fluid creep control

Some centers have demonstrated that selection of more strict protocols of fluid resuscitation, rigorous urine output control, moderate use of opioids, early and regular use of albumin are correlated to positive outcomes and thus may attenuate fluid creep [17, 43].

Currently, permissive hypovolemia has been also proposed as a safe approach to reduce fluid offer to these patients. Permissive hypovolemia, characterized as fluid administration in lower amounts than preconized by the Parkland Formula, has been shown to effectively reduce organ and systems dysfunction induced by edema during conventional fluid resuscitation, when applied a rigorous control of patient diuresis [44].

Infusion of extremely large amounts of crystalloids certainly determines the occurrence of fluid creep, and adequate titration of resuscitation fluids is probably the first step in order to prevent this complication. An important and clear circumstance with the use of large amounts of crystalloids may be the inadequate titration of fluid infusion. Clinical practice shows expertise regarding increasing the amount of fluid infusion rate when patients exhibit inadequate low urine output; however, a restrictive effort is not the rule when patient shows a UO exceeding its' limit range, and indicating that fluid infusion must be reduced [21].

Fluid infusion regulation is essential, as early as possible. Precise liquid infusion balance to reach an adequate UO avoiding hypoperfusion and fluid creep is challenging and relies on appropriate professional experience. When the desired urine output is achieved together with stable clinical parameters, crystalloid infusion reduction is mandatory. UO control and infusion rate titration must be performed hourly during the entire resuscitation. When the UO remains stable, a reduction of the intravenous liquid infusion rate is recommended [28].

Aiming to reduce volume titration dependency to clinical decisions, some centers implemented clinical protocols standardized with algorithms based on UO to guide liquid infusion rate reduction. There are established algorithms that may be used by the nursing team that allow a decreasing titration of fluid volume in presence of elevated UO, reinforcing the reduction of infusion rates when the urine output remains adequate along the resuscitation [41, 42••, 45•, 46•].

With the purpose to minimize even more the human misunderstandings, some centers use computer-oriented resuscitation algorithms. The computerized support system to burn resuscitation is based in an algorithm that defines an answer (fluid administration) for a certain data input (UO) being the foundation of a modernized and promising concept of closed circuit approach to burned patients that have been resuscitated in a traditional method [47].

Currently, many centers advocate for the use of colloid in the first 24 h after the trauma. The rising interest in reviewing resuscitation strategies, attempting to reduce the emergence of fluid creep, suggests the reintroduction of colloids in the management of these patients. There is still no consensus regarding colloid use, neither concerning which is the best moment where they would be most useful to be infused, especially in the acute resuscitation phase.

Literature evidence suggests that the early use of colloids may help to limit the total requirement of fluids, and there may also be a role for an earlier and ordinary use of albumin [35, 48].

The control of excessive liquid infusion including colloids in the burn patient resuscitation strategy has been repetitively shown. Hence, earlier colloid administration may reduce the total requirement of fluids in the resuscitation period. Reducing the fluid loss to the interstitial compartment as well as glycocalyx restoration may decrease fluid creep complications [43].

Goodwin et al. demonstrated that the use of colloid reduces fluid administration during resuscitation [49]. Additionally, O'Mara et al. observed that the administration of colloid in plasma form is associated with a reduction of fluid requirements and lower intra-abdominal pressure ranges [37].

Some authors advocate for colloid infusion 12 h after the burn accident when the liquid requirement exceeds 120% of the expected volume or when the resuscitation exceeds 6 ml/kg/h close to 12 h after the accident [12••].

A recent study has demonstrated that earlier albumin infusion, between 8 and 12 h after injury, in pediatric patients with burns greater than 15–45% TBSA reduces the need for crystalloid fluid infusion during resuscitation. Furthermore, significantly fewer cases of fluid creep and shorter hospitalization were observed in this group of patients [50].

The Galveston protocol includes albumin administration starting at 8 h after the accident. The patient is considered eligible for a colloid replacement solution in presence of serum albumin lower than or equal to 2.5 g/dl [51].

In addition to the attempt of avoiding edema to prevent clinical complications due to liquid extravasations, it is necessary to prevent the deepening of burn lesions. This prevention reduces the number of surgery procedures, accelerates tissue recovery and allows earlier hospital discharge, limiting morbidity and reducing treatment cost.

Refinement of existing protocols may help to reduce the excess in crystalloid administration. High doses of vitamin C may also reduce fluid requirements and have been studied as a promising adjuvant treatment [33].

There is no consensus about resuscitation of severely burned patients presenting important comorbidities. This specific group of patients with significant comorbidities requires a differential approach, and highly individualized resuscitation management [52].

Conclusion

Decisions regarding fluid resuscitation constitute a cornerstone of initial burn management. However, besides the development of formulas and guidelines for fluid administration, there are still important controversies regarding volume resuscitation. In the past, there was a tendency to use higher volumes of fluid in the resuscitation period. This seems to be now a potentially negative practice.

The current success of resuscitation relies on the administration of smaller volumes of fluid and the use of colloid solutions considered essential components for severely burned patients in this period. This practice promptly restores volemia and avoids the emergence of fluid creep and other related complications.

Despite trying to avoid tissue edema, in order to prevent the clinical complications resulting from the fluid leakage process, it is necessary to avoid the deepening of the burned lesions, reducing the number of surgical procedures to be performed. This accelerates scars recovery, limiting morbidity, reducing patient's length of stay and consequently treatment costs.

In the future, the potential of individual genomic responses will need to be considered for an individual approach in the complications' development and outcomes regarding burn-related injuries. Understanding the role of genetic factors related to thermal trauma, as well as in sepsis [53], may work as a connection to therapeutic discoveries, as well as an approach to evaluate the fluid requirements, diminishing the risks for complications.

Compliance with Ethical Standards

Conflict of Interest
Maria Helena Müller Dittrich declares that she has no conflict of interest. Nicole Dittrich Hosni declares that she has no conflict of interest. Werther Brunow de Carvalho declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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