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BURN RESUSCITATION: IS IT STRAIGHTFORWARD OR A CHALLENGE?

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SUMMARY. Burn shock resuscitation has been extensively studied over the past four decades. Many formulas exist and many parameters have been suggested to assess the adequacy of resuscitation. The most commonly used formula is the Parkland formula, the most commonly used fluids are crystalloids, and the most commonly used parameter is urine output. However, until now, no conclusive evidence has suggested that one formula is superior to another or that one parameter is a better predictor than another. In this article we will review the updated information about the subject and we will look into new advancements in this field. We will pose some questions at the end that will help researchers concentrate their future efforts to solve this important challenge in burn care.

Keywords: burn resuscitation, resuscitation fluids, resuscitation formulas, pathophysiology of burn shock, fluid creep

Introduction

The earliest documentation of interest in fluid shifts and resuscitation in burn injuries dates back to the early twentieth century.1 Underhill’s understanding of the relation between fluid shifts and burn shock during his experience in the Rialto Theater fire in 1921 and Moore’s suggestion that oedema occurring after burn contributes to the burn shock2 can be considered cornerstones in understanding the physiology of burn shock and the importance of adequate and timely burn resuscitation. This led to the Evans formula in 1952 and later to Moyer’s formula3 in 1965, which used body weight and burned body surface area as a reference for calculating the fluids to be given. Research in this field continued and, although the capillary leak syndrome was suggested by Arturson4 in 1979, it was Baxter and Shire who performed isotope studies indicating that the fluids leaking from the capillaries of burned patients had a similar protein content to serum, suggesting that proteins given during this period would leak out into the tissues.5 Then, in 1974, the same authors published their Parkland formula, which they developed after inflicting burns on dogs and giving them different amounts of fluids, finding that the animals that received 4 cc of crystalloids /kg/percentage burned body surface area were the ones that survived longest.6 Baxter recognized that this was a valid estimate of fluid requirements only in the first 24 h post-burn and that the best indicator for the adequacy of the resuscitation was urine output.7 His formula has remained the most commonly used until our own days.7

Around the time of Baxter’s work, the Brook formula developed by Pruitt and Moncrief in San Antonio, Texas, came out. This suggested the use of colloids at a rate of 2 cc/kg/percentage of burned body surface area.8 This was later modified to lactated Ringer’s solution instead of colloids. Alternatively, hypertonic saline was also explored for burn shock resuscitation.1 However, unlike the previous formulas utilizing colloids or crystalloids, studies on the use of hypertonic saline yielded conflicting results,9-13 even suggesting it might have adverse effects on the kidneys.14 Since the 1970s several other solutions have been suggested for use in burn shock resuscitation, including fresh frozen plasma, Dextran 40, Dextran 70, and many others.15-19 However, there is still no consensus on the best fluid resuscitation solution or volume.7

The pathophysiology of burn oedema

The development, extent, and resolution of oedema differ between superficial and deep-thickness burns.20 In partial-thickness burns there is increased blood flow to the injured area which pushes more fluids out of the capillaries, resulting in oedema.21 The oedema increases rapidly within the first few hours and then gradually desorbs over a period of 3-4 days.21 The rapid decrease in oedema is secondary to the preserved lymphatic channels under the burned area.22 In deep burns oedema increases at a slow-

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er rate and resolves over a longer period owing to the damage to the dermal vascular and lymphatic channels in these wounds. Demling reported that in deep burns tissue oedema peaked 18 h post-injury and that about 25% of the oedema fluid was present one week post-injury. Another difference is that in partial-thickness burns most of the excess fluid is in the dermis whereas in deep burns most of this fluid resides in the subcutaneous tissues. The accumulation of oedema fluid is due not only to the increase in the local blood flow in the injured area but also to the disturbance of many other factors. For example the perfusion coefficient increases two to three times after injury as a result of vasodilating factors, and this leads to increased capillary permeability. The capillary hydrostatic pressure also increases, especially after partial-thickness burns, and can reach values that are double the normal pressure. In contrast, the interstitial hydrostatic pressure becomes more negative; this may be due either to the breakdown of proteins into smaller more osmotically active molecules or to the coiling of the collagen and hyalouronic acid molecules creating a suctioning effect. Capillary vasodilation not only increases the flow but also alters the permeability of these vessels, making it possible for larger molecules to pass through their walls into the interstitial space. This will lead to a decrease in the intravascular plasma oncotic pressure and to an increase in the interstitial oncotic pressure. One should not forget the production of oxygen free radicals that occurs after burn injuries - this can contribute to tissue destruction and to increased capillary permeability.

Resuscitation practices

Despite the large amount of research and data available in the field of resuscitation there is still no consensus on the right amount or the best solution for resuscitation. Many formulas exist and many end point parameters have been recommended but the commonest strategy is to use the Parkland formula to calculate the initial fluid amount and then to adjust the fluid rate according to the hourly urine output. In 2010 David Greenhalgh, publishing the results of a survey administered to directors of burn units, staff surgeons, and nurses from all the continents except Africa, reported the following:

1. The cut-off point for resuscitation was burns in 15% total body surface area
2. Most responders preferred peripheral intravenous catheters (70%); fewer used central lines (45.7%)
3. The most commonly used formula was the Parkland formula (69.3%)
4. The most commonly used solution was lactated Ringer’s (91.9%)
5. About 50% of the responders added colloids to their resuscitation regimen within the first 24 h
6. The most commonly used end point parameter to assess resuscitation adequacy was urine output (94.9%)
7. Although 88.8% of responders felt that their protocol was adequate, 55.1% believed they gave more than the amount recommended by the formula.

Greenhalgh concluded that no protocol was perfect and that there was a great need to develop randomized prospective trials to determine the best practice for choosing the right fluid at the right rate, adjusted with a better indicator for adequate resuscitation.

With the liberal use of fluids, burn care providers started to notice that patients frequently received larger amounts of fluids than required. The expression "fluid creep" was coined by Basil Pruitt in 2000 to define this phenomenon. Several publications appearing after Pruitt’s comments confirmed that the amount of fluid used for resuscitation exceeded the Parkland formula by an average of 4.8 to 6.7 cc/kg% burn surface area. Over-resuscitation is not benign and is associated with several morbidities that may lead to mortality. For example, it predisposes the patient to peripheral compartment syndromes, abdominal compartment syndrome, and pulmonary oedema. This phenomenon is not new and was recognized long ago by Baxter, who observed that fluids in excess of his formula were required in patients with inhalation injury, patients with electrical injury, and patients whose resuscitation was delayed. Other patients who may require additional fluid resuscitation include those with multiple trauma and those suffering from alcohol or drug addiction. Another important cause of over-resuscitation is physician-related: under- or over-estimation of burn depth or surface area will affect the amount of fluid given to the patient and may lead to under- or over-resuscitation. It is worth noting, however, that many recent reports have appeared describing over-resuscitation in patients who did not have any of the usual predisposing conditions. Possible contributors to this “fluid creep” phenomenon include:

1. The inaccuracy of the Parkland formula, especially in large surface area burns
2. The tendency of clinicians to be more inclined to increase the fluid rate liberally in the presence of low urine output than to decrease the fluid rate in the presence of high urine output
3. The more liberal use of opiates and narcotics for pain control, leading to peripheral vasodilation
4. The tendency of some centres to perform goal-directed resuscitation using lactic acid, base deficit, cardiac index, and oxygen delivery to assess the resuscitation achieved
5. The effect of excessive crystalloid infusion on the imbalance of oncotic pressures in the intravascular and interstitial compartments
End points of resuscitation

Until now, the end points used to guide fluid resuscitation in burn patients have been inaccurate. This was agreed upon during the State of Science meeting held in Washington DC in October 2006. In our humble opinion, all the end points studied so far occur after the event and do not predict the future. As such, these parameters will not tell us what will happen but rather reflect what happened. It is clear that all the formulas suggested in the course of time are just estimates and none is accurate, all of them needing to be adjusted according to certain parameters. Of these, urine output is the one most commonly used worldwide to assess the need to increase or decrease the fluid rate. Yet this is not the only parameter that is used or recommended, and the use of urine output as an indicator of resuscitation adequacy has in fact been challenged in several publications. However, other parameters that were studied as potential end points for resuscitation failed to show their superiority to urine output and were not cost effective. For example, invasive monitoring using central venous pressure and pulmonary artery catheterization failed to change mortality or morbidity in burn patients. A relatively newly developed method for monitoring the adequacy of resuscitation utilizes the shape or the arterial waveform to predict cardiac output and is termed “pulse contour analysis”. Information from this less invasive method might be useful in guiding resuscitation by monitoring cardiac output, intrathoracic blood volume, global end-diastolic volume, extravascular lung water, the pulmonary vascular permeability index, the cardiac function index, the global ejection fraction, pulse pressure variation, and stroke volume variation. Until now all the studies performed on this method have come from single centres, assessing a limited number of patients, and thus cannot be considered as gold standard until large prospective randomized trials are available to indicate their utilization and cost effectiveness. Other less used methods include transoesophageal echo cardiography, partial carbon dioxide rebreathing, and impedance electrocardiography. None of these methods have been validated in burn patients.

Pharmacological modulation of resuscitation

Despite the fact that mediators such as histamine, serotonin, prostaglandin, and many others have been found to be active in burn shock, the exact pathophysiology of this process has not yet been well delineated. Blockers of these vasoactive substances have been used to try to reverse the processes that occur in burn shock but the results were not very encouraging, apart from some minor effects that decreased the extent of the process. Recently, Matsuda and Tanaka used high-dose vitamin C (L-ascorbic acid) in the early post-burn period and reported a significant decrease in the volume of resuscitation in both animals and humans, together with a significantly decreased rate of compartment syndromes in the extremities and abdomen. Although promising, vitamin C administration needs to be studied further in multicentre trials in order to delineate the extent of reversal of the burn shock and to uncover any side effects that might arise from giving such a high dose of vitamin C.

Plasmapheresis and exchange transfusions have also been tried and have shown promising results probably by removing the mediators from the circulation. Both treatments require considerable personnel and equipment and are associated with significant risks, thus being reserved for patients not responding to regular resuscitation methods.

Future endeavours

Looking back over the past three decades one can easily see that there has been very little advancement in resuscitation since the development of resuscitation formulas. Vitamin C is a promising area in our opinion and should be further explored to delineate its advantages and disadvantages. Another new advancement is the development of a computerized system that will predict the volume of fluids for the next hour based on the urine output for the previous hour. This is a valuable instrument, especially in combat areas where burn specialists are far away and most casualties are treated by undertrained personnel. In our opinion, although this system still utilizes urine output (which is an after-effect), it can surpass human calculation by normalizing the data and helping the system to become a better predictor every time new data are fed into the equation. Other areas that are still waiting for clear answers include: what is the best solution, or combination of solutions, to be used in burn shock resuscitation? How can we improve on oral resuscitation formulas and can we extend their use to moderate burn injuries, especially if we are able to reverse the capillary leak syndrome? Is urine output the best indicator of resuscitation adequacy or can we develop a predictor of resuscitation fluid requirements? Is there a way to reverse burn shock pharmacologically without major adverse events? All these questions should be considered in our future research endeavours to serve our patients in the best way we can.

Conclusion

In conclusion, the resuscitation of patients suffering from burn shock is a challenging process that for many decades has attracted the attention of physicians and researchers. Much has been discovered, yet much still needs to be done in order to answer all the questions posted above; hence the challenge.
RÉSUMÉ. La réanimation des patients atteints du choc des brûlés a été largement étudiée au cours des quatre dernières décennies. On peut utiliser de nombreuses formules et de nombreux paramètres pour évaluer l'opportunité de l'une ou l'autre méthode de réanimation. La formule la plus couramment utilisée est la formule de Parkland, les fluides les plus couramment utilisés sont les cristalloïdes, et le paramètre le plus fréquemment utilisé est la production d’urine. Cependant, jusqu’ici, aucune preuve n’a démontré en manière irréfutable la supériorité d’une formule par rapport à une autre ni la capacité d’un paramètre de permettre de prédire les résultats en manière plus efficace que les autres. Nous nous sommes proposés de passer en revue les informations à jour sur le sujet et nous allons examiner les progrès les plus récents dans ce domaine. Nous allons poser en conclusion quelques questions qui devraient aider les chercheurs à concentrer leurs efforts futurs sur la solution de ce grand problème qui intéresse tous les brûlologues.

Mots-clés : réanimation des patients brûlés, fluides pour la réanimation, pathophysiologie du choc des brûlés, déplacement des fluides

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