REVIEWS

VIA MEDICA

An overview on fluid resuscitation and resuscitation endpoints in burns: Past, present and future. Part 1 — historical background, resuscitation fluid and adjunctive treatment

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Abstract

An improved understanding of burn shock pathophysiology and subsequent development of fluid resuscitation strategies has led to dramatic outcome improvements in burn care during the 20th century. While organ hypoperfusion caused by inadequate resuscitation has become rare in clinical practice, there is growing concern that increased morbidity and mortality related to over-resuscitation is occurring more frequently in burn care. In order to reduce complications related to this concept of "fluid creep", such as respiratory failure and compartment syndromes, efforts should be made to resuscitate with the least amount of fluid in order to provide adequate organ perfusion. In this first part of a concise review, historic and current evidence regarding the available fluids is discussed, as well as some adjunctive treatments modulating the inflammatory response. In the second part, special reference will be made to the role of abdominal hypertension in burn care and the endpoints used to guide fluid resuscitation will be discussed. Finally, as urine output has been recognized as a poor resuscitation target, a resuscitation protocol is suggested in part two which includes new targets and endpoints that can be obtained with modern, less invasive hemodynamic monitoring devices.

Key words: burns, fluid resuscitation, treatment, resuscitation endpoint/target, crystalloid, colloid, albumin, adjunctive treatments

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Following a severe burn injury, an overwhelming systemic inflammatory response with an associated capillary leak syndrome occurs. The result is a patient with profound hypovolemic shock which, at times, is accompanied by septic shock, due to fluid shifts that reach a maximum at 12 to 24 hours post injury. During this initial "ebb" phase, fluid resuscitation is of paramount importance and the amount of therapeutic fluid needs can be enormous due to plasma and proteins leaking into the extravascular compartment. This results in a positive (daily and cumulative) fluid balance associated with well-known complications [1]. As the systemic inflammatory response diminishes, a polyuric or "flow" phase is entered, where a negative fluid balance is seen, reflecting the loss of the initial resuscitation fluids [1].

Severe burn injury triggers a pathophysiologic chain of events, the loss of skin barrier; the loss of temperature control; the loss of fluid and protein from circulation, the creation of large open wounds; a systemic inflammatory response in case of a total burned surface area (TBSA) above 25%; an immediate inflammatory response (that can last up to 5 weeks), finally followed by a hypermetabolic response from day 5 that can last up to 24 months. Typically, a patient with burn shock suffers from a combination of hypovolemia and (systemic) inflammation. This will result in a drop in cardiac output, plasma volume and oliguria. Specific in burns is the edema formation that starts after 5 min — 1 hour in burned skin and, as stated previously, becomes maximal after 12 to 24 hours. This edema formation is related to

increased permeability so that all except red blood cells will leak from the capillaries. These volume shifts will lead to development of cellular edema while the real fluid losses remain limited. Gaps in endothelial cell junctions can occur as rapidly as 1 to 5 minutes after insult (substance P) [2]. Quantification of capillary leak with biomarkers is important in order to predict the natural course of the burn injury. The urine-albumin-over-creatinine ratio seems such a marker showing that endothelial dysfunction and capillary leak are present within 2 hours post-burn with the median duration being only 5 hours [3]. Other markers include the evolution of body weight, the evolution of (cumulative) fluid balance, serum osmolality, serum colloid oncotic pressure (COP), the presence of hemodilution vs hemoconcentration, or total protein and albumin levels. Some parameters that can be obtained via bio-electrical impedance analysis like extracellular and intracellular water (and their ratio) and quantification of volume excess also seem promising [4] together with the capillary leak index defined as the serum CRP over albumin ratio [5].

Although numerous articles regarding burn resuscitation have been published over recent decades, there is no universal consensus on the ideal resuscitation fluid nor on how to achieve adequate resuscitation whilst avoiding the adverse effects of excessive resuscitation. The objective of this first part is to review the past and present literature regarding fluid resuscitation and adjunctive treatments in burn care while an algorithm for future clinical use will be suggested in the second part.

METHODS

A MEDLINE and Pubmed search was performed using the search terms "resuscitation", "burn(s)", "burn management", "resuscitation endpoint/target", "preload", "resuscitation fluids", "fluid creep", "cardiac output", "deresuscitation", "extravascular lung water", "abdominal pressure", "abdominal hypertension", "abdominal compartment syndrome". Selected articles and their bibliographies were used to supplement the authors' knowledge and to identify other relevant citations.

HISTORICAL BACKGROUND

Although burn wounds and burn-related deaths have been suffered throughout human history, fluid resuscitation management is relatively new and dates back less than a century.

In 1921, Frank Underhill performed landmark research following the New Haven Rialto Theater fire [9]. After observing the burn patients, he concluded that intravascular fluid loss rather than direct toxic effects causes burn shock. In subsequent years this concept would dramatically change the approach to burn patient management.

EARLY FORMULAS

A few years later, following the Coconut Grove fire in 1942, Cope and Moore described thermal injury, wound edema and fluid resuscitation. They attributed burn shock to edema and subsequently proposed a volume of fluid for resuscitation based on the patient's body weight and the severity of the burn (the so-called "body weight burn budget") [10]. In 1952, Evans postulated a formula for fluid volumes based on total burned surface area (TBSA) and also introduced colloids in burn resuscitation management [11]. This formula would be the standard until the 1960s [12].

THE PARKLAND FORMULA

During the 1960s, Baxter and Shires developed their historic formula at the Parkland Memorial Hospital, which would be used as the gold standard for fluid resuscitation in acute burn care across the world for decades [13]. The formula advocates 4 mL crystalloids per kg per percent of TBSA per 24 hours, of which half is given the first eight hours [13]. Resuscitation fluids are guided by urine output (1 mL kg^{-1} hour^{-1}) and increased with steps of 25% if deemed insufficient. During the second 24 hours of resuscitation, colloids are allowed and resuscitation volume is adapted according to urine output (with a gradual decrease if this is deemed adequate). Baxter and Shires also contributed to burn pathophysiology by describing intracellular edema, the importance of protein release and tissue edema.

After the introduction of these weight- and injury-based formulas, under-resuscitation had become rare in clinical practice. In short, one can say that fluid resuscitation revolutionized acute burn management, saved thousands of lives and reduced morbidity significantly during the last half a century. However, these initial formulas were guided by urine output, which is far from ideal as a resuscitation endpoint because it may not reflect end-organ or tissue hypoperfusion at a microvascular level.

FLUID CREEP

Over the last 15 years multiple centers have reported excess fluid administration during resuscitation [14–18]. This fluid excess often leads to "resuscitation morbidity", a group of complications linked to fluid overload such as pulmonary edema, delayed wound healing, delayed recovery of gastro-intestinal function (with ileus), limb compartment syndrome, orbital compartment syndrome, intra-abdominal hypertension (IAH), and abdominal compartment syndrome (ACS) leading to multiple organ failure [1, 8, 19–22].

A meta-analysis containing 23 clinical trials in the period 1980-2002 showed an average fluid resuscitation volume of 5.0 ± 1.2 mL kg^{-1} %TBSA^{-1}, well above the predicted volumes of the modified Brooke (2 mL kg^{-1} %TBSA^{-1}) and Parkland (4 mL kg^{-1} %TBSA^{-1}) formulas used in these clinical trials [17].

In 2004, Friedrich *et al.* [23] matched two cohorts of burn patients in a retrospective study and reported the fluid administration in his center had doubled between 1975 and 2000.

One study compared fluid resuscitation using the Parkland formula and the modified Brooke formula in military burn casualties. This showed how patients in the Parkland group required significantly more fluid than the patients using the modified Brooke formula (5.9 vs 3.8 mL kg^{-1} %TBSA^{-1}, $P < 0.0001$). From these data, it would appear that the starting fluid rate affects the total volume given and can possibly lead to resuscitation morbidity (24). The percentage of patients exceeding the Ivy index, defined as resuscitation fluid > 250 mL kg^{-1} during the first 24 h [25], was significantly greater in the Parkland group while in multivariate logistic regression, exceeding the Ivy index was an independent predictor of death [24].

This discrepancy between the predicted and the administered fluid is known as "fluid creep". This term was coined by Basil Pruitt [20]. There are different hypotheses regarding the phenomenon of fluid creep, although its cause remains uncertain [14–16, 26].

In 2007, Saffle [16] stated that there was considerable evidence showing excessive administration of crystalloid, together with the abandonment of colloid replenishment, and that these could be major contributors to fluid creep. In addition, early goal-directed therapy has led to more aggressive fluid resuscitation [27, 28], as shown in a study conducted in 2004 where the goal-directed therapy led to significantly increased fluid volumes in comparison to the Parkland formula [29]. Permissive hypovolemia has been studied afterwards and seems to have benefits regarding outcomes, without the associated adverse effects [30, 31].

An interesting hypothesis is that of "opioid creep", a term introduced by Sullivan *et al.* [32]. When comparing two cohorts of burn patients, one from the 1970s and the other from 2000, there was, together with an increase in the amount of opioids used, an increase in fluid administration [32]. The association may be explained by the concomitant drop in blood pressure experienced when large doses of opioids are administered (related to peripheral vasodilatation) and thus contribute to greater resuscitation fluid requirements.

In 2004, a study looking at the factors for predicting increased fluid requirements in burn patients noted that physicians were significantly less likely to titrate infusion rates down than to titrate infusions up in response to an adequate or inadequate urine output [33]. Inaccurate assessment of TBSA involved in the injury may also contribute to inappropriate fluid volumes during resuscitation. A recent study in a pediatric burn hospital noted significant discrepancies between the TBSA estimation of the referring hospitals and the tertiary center where 59% of study patients were administered more fluid at the referring hospital than would have been expected by the burn size calculated at the pediatric burn hospital [34].

Over the last fifteen years, significant attention has been paid to the phenomenon of fluid creep while the awareness of morbidity caused by inappropriate fluid resuscitation has improved. However, currently there is no evidence supported by large prospective clinical trials identifying the best resuscitation protocol associated with the least adverse outcomes and avoiding over- or under-resuscitation. Efforts should therefore be made to avoid "futile loading" with excessive amounts of crystalloids along with identifying ways to measure appropriate peripheral perfusion. Moreover, the role of colloids in early resuscitation needs further investigation [26].

TYPES OF RESUSCITATION FLUID

The ideal fluid in burn resuscitation is one that predictably maintains the intravascular volume without producing adverse systemic and metabolic effects, thus reducing the complications of both under- and over-resuscitation. Currently, although no such ideal resuscitation fluid exists, a wide variety of both fluids and strategies provides for ongoing debate and discussion.

Classically, the two major types of resuscitation fluids, crystalloids and colloids, have been discussed for decades, not only in burn patients but also in virtually every medical discipline and situation. It is unusual in modern medicine to still find a lack of consensus after decades of research and study, and what follows is a summary. Recommendations regarding fluid resuscitation are listed in Table 1.

CRYSTALLOIDS

Crystalloids are aqueous solutions consisting of mineral salts that are freely permeable through membranes. The main ions determining tonicity are sodium and chlorine. The first reported use of intravenous fluid therapy, except anecdotal attempts with regard to blood transfusions, was performed by Thomas Latta in 1832 where he used a saline solution to resuscitate a cholera patient [35].

In 1882, a saline solution, very similar to what today is known as "normal saline" (NaCl 0.9%, 154 mEq L^{-1}), was developed by Hamburger, believing it to be the sodium concentration of the plasma, thus avoiding hemolysis in his laboratory experiments. However, despite its non-physiological concentrations of sodium and chloride, it remains probably the most widely administered crystalloid solution globally [36]. Several adverse associations have been linked to 0.9% saline solutions, contributed to by the development of hyperchloremic metabolic acidosis after large volume infusions [37].

Table 1. Recommendations regarding fluid resuscitation and adjunctive treatment in severe burns patients

Fluids	
1. Normal saline	Given the fact that fluid resuscitation in burn management requires large volumes, the use of saline cannot be recommended in a burn resuscitation protocol
2. Balanced crystalloid	Based on the available evidence, balanced crystalloid solutions are a pragmatic initial resuscitation fluid in the majority of acutely ill (and burn) patients
3. Semi-synthetic colloids	Given the recent data concerning the use of semi-synthetic colloids (and starches in particular), their use in critically ill patients, including burn patients cannot be recommended
4. Albumin	Based on the available evidence, the use of albumin 20% can be recommended in severe burns, especially in the de-resuscitation phase guided by indices of capillary leak, body weight, (cumulative) fluid balance, fluid overload, extravascular lung water, and intra-abdominal pressure
5. Hypertonic solutions	To this day, there is insufficient evidence to reach consensus regarding the safety of hypertonic saline in burn resuscitation. Whenever using hypertonic saline in clinical practice however, close monitoring of sodium levels is highly advised
Adjunctive therapy	
6. Vitamin C	Given the available evidence, the benefit of adjunctive high dose ascorbic acid treatment may be strongly suspected to be the limiting of fluid intake and prevention of secondary abdominal hypertension; while, equally important, no adverse effects have been reported
7. Plasmapheresis	The benefit of plasmapheresis on outcomes in burn patients still needs to be validated in large prospective, randomized trials. As such, its use cannot be recommended
8. Intravenous immunoglobulins (IVIG)	The use of IVIG should be limited to cases of toxic epidermal necrolysis

Recommendation: *Given the fact that fluid resuscitation in burn management requires large volumes, the use of saline cannot be recommended as the first-line choice in a burn resuscitation protocol* [28].

The more "balanced" or "physiological" solutions, such as lactated Ringer's or Hartmann's solutions, replace the anion bicarbonate in the form of lactate, acetate or gluconate. This provides a strong ion difference that is physiologically better from an acid-base perspective. These often-hypotonic solutions contain additional minerals such as potassium, magnesium or calcium. Adverse effects following infusion of large quantities of "balanced" crystalloid solutions are still possible and include hypotonicity and metabolic alkalosis [38–40]. Hyperlactatemia can also occur, but usually only in patients with impaired liver function.

Throughout the history of burn resuscitation protocols, most formulas advocate the use of balanced crystalloid solutions. There are unfortunately no sufficiently large randomized controlled trials to determine the best choice for an isotonic crystalloid resuscitation fluid. One observational study reported lower Sequential Organ Failure Assessment scores in severely burned patients resuscitated with Ringer's acetate, however, this is an isolated study [41].

The general concern with isotonic crystalloids is rapid redistribution to the extravascular fluid compartment (interstitium), requiring further intravenous fluids to maintain volume in the intravascular compartment. Furthermore, a decrease in plasma oncotic pressure, a consequence of hemodilution, further promotes extravascular leak and edema formation [42, 43]. It has been the concern about this movement of crystalloid fluid therapy that has fuelled the crystalloid-colloid controversy.

Recommendation: *Based on the available evidence, we conclude that balanced crystalloid solutions are a pragmatic initial resuscitation fluid in the majority of acutely ill (and burn) patients.*

COLLOIDS

Colloid fluids contain large molecules in a carrier solution (most often isotonic crystalloids). These high molecular weight molecules are less likely to leak into the extravascular compartment and will increase the plasma oncotic pressure while in the intravascular compartment. This theoretically enhances intravascular volume expansion, which has been considered an advantage over crystalloid fluids. Traditional teaching has described a crystalloid: colloid ratio of 1: 3 in order to achieve a similar intravascular effect. However, virtually every fluid study since 2004 has shown that this ratio is closer to 1: 1.5 (range 1: 1.1–1.7) [44].

In burn resuscitation, the use of synthetic colloids in the first 24 hours of resuscitation has been controversial ever since it was theorized that the existing capillary leak would allow large molecules to leak in the extravascular space and exert an osmotic pull, thus increasing the formation of edema. This concern was based mainly on the early work of Baxter [45]. However, the capillary leak in question may be much shorter in duration than initially thought. In 2006, a study concluded that endothelial dysfunction and capillary leak are present within 2 hours post-burn with the median duration being only 5 hours [3].

Previously, colloids had been omitted from many resuscitation formulas. During the last fifteen years, however, there has been renewed interest in colloids, fuelled by the awareness of morbidity related to inappropriate resuscitation volumes and fluid creep.

These colloid solutions may be categorized as natural (derived from blood, for example, albumin or fresh frozen plasma) or semi-synthetic. The major limitation to natural colloids is cost. This has resulted in the promotion and development of semi-synthetic colloids. These have gained popularity because of their relatively low cost, long shelf life and stability, as well as their availability. The major subclasses are hydroxylethyl starches (HES), gelatins and dextrans, with HES solutions being the most commonly used [38].

HES molecules are metabolized slowly, resulting in a prolonged intravascular volume expansion, but with the potential to accumulate in reticulo-endothelial tissues such as skin, liver and kidneys [46]. Additional concerns include their associations with altered blood coagulation. This effect is greatest with high molecular weight molecules [47]. These high molecular weight HES molecules have also been associated with a higher mortality rate and higher incidence of acute renal failure and renal replacement therapy when compared to other fluids [48].

Until recently, low molecular weight HES solutions were widely used as a resuscitation fluid in critically ill, surgical and burn patients. However, recently published trials such as CHEST, 6S and CRYSTMAS have raised alarming conclusions regarding their safety. Increased mortality in some trials, and a higher rate of renal replacement therapy were consistent among these trials [49–52]. Importantly, no statistically significant benefit was evident when using HES solutions in such trials. This led to recommendations from the Pharmacovigilance Risk Assessment Committee (PRAC) against the use of HES solutions in patients with sepsis, burn injuries or critically ill patients because of the increased risk of acute kidney injury and possibly mortality [53]. These recommendations were endorsed by the Coordination Group for Mutual Recognition and Decentralised Procedures — human (CMDh) in October 2013. Despite these data, controversy and disagreement still remain [53]. Today, HES solutions are primarily only indicated in acute hypovolemic shock, where their benefit was apparent in the 2013 CRISTAL study [54].

The safety of other semi-synthetic colloid solutions, such as gelatin solutions, remains unclear. The older gelatin solutions are associated with a higher risk of anaphylaxis and, in a systematic review of randomized controlled trials, their safety and efficacy could not be ascertained [55].

Recommendation: *Given the recent data concerning the use of semi-synthetic colloids and especially HES molecules, their use in critically ill patients, including burn patients cannot be recommended.*

ALBUMIN

Albumin is a natural plasma protein that contributes significantly to intravascular oncotic pressure. The most common solution is 4 or 5% albumin in a saline solution. It is a relatively expensive fluid and its availability is limited in some countries. As with other colloids, questions concerning the safety and efficacy of albumin have been ongoing.

A meta-analysis published in 1998 raised concerns about safety [56]. Albumin was compared with other crystalloid solutions in patients with hypovolemia, burns or hypoalbuminemia. The conclusion was an increased mortality in the groups receiving albumin. However, this meta-analysis had severe limitations, especially the limited size of the studies included.

A few years after this alarming meta-analysis, the SAFE study was conducted. This randomized controlled trial, which included 7,000 critically ill patients, compared saline and 4% albumin. Although it showed no significant difference in mortality or new organ failure, it did not include burn patients [57].

Although albumin resuscitation has been used with some reservations, especially in the acute phase of burn resuscitation, trials provide promising data regarding its use as an adjunctive therapy. In 2007, a case-controlled study reported decreased mortality on a multivariate analysis in burn patients receiving albumin during resuscitation [58]. In 2010, Lawrence *et al.* found that the addition of albumin to the Parkland formula resuscitation rapidly reduced hourly fluid requirements, restored normal resuscitation ratios, and ameliorated fluid creep [26].

There is even less evidence for the use of fresh frozen plasma as a resuscitation fluid in burns. However, a prospective randomized trial did show plasma-resuscitated patients maintained an intra-abdominal pressure (IAP) below the threshold of IAH which appeared to be a direct result of the decreased volume required [59]. An older study, comparing fresh frozen plasma with crystalloids and hypertonic saline for resuscitation of severely burned patients, noted minimal weight gain and minimal edema in the fresh frozen plasma group [60, 61]. There is some evidence on the beneficial effects of hypertonic albumin 20% in the later stages of the disease in a subgroup of patients with sepsis and capillary leak [5, 6, 62].

Recommendation: *Based on the available evidence, the use of albumin 20% may be recommended in severe burns, especially in the de-resuscitation phase (after 24 hours) when guided by indices of capillary leak, body weight, (cumulative) fluid balance, fluid overload, extravascular lung water, and intra-abdominal pressure* [1].

HYPERTONIC SALINE

Hypertonic saline has been used for decades in burn resuscitation. It theoretically expands the circulating vol-

ume by way of an intravascular water shift [43]. Proponents suggest that this may decrease tissue edema and lower the rate of complications. In the 1970s, studies concluded that hypertonic saline did indeed reduce the volume required for burn resuscitation [63, 64]. However, when infusing large quantities of hypertonic saline, the risk of severe hypernatremia, and associated renal failure and acute cerebral fluid shifts, still exists [65].

In 1995, Huang *et al.* published a large retrospective historical cohort study, comparing burn patients who received hypertonic saline versus controls who had a crystalloid resuscitation [66]. Patients who received hypertonic saline had significantly higher acute renal failure (40% vs 10.1%, $P < 0.001$) and mortality rates (53.3% vs 26.6%, $P < 0.001$) [66]. A study performed in 2006, however, showed a significantly reduced risk of secondary abdominal compartment syndrome in patients receiving hypertonic saline, most likely linked to the lower fluid volumes required for resuscitation (67).

Recommendation: *Currently there is insufficient evidence to reach a consensus regarding the safe use of hypertonic saline in burn resuscitation. Whenever using hypertonic saline in clinical practice, close monitoring of sodium levels is highly advised.*

ADJUNCTIVE THERAPY
VITAMIN C

Research has revealed that oxidative stress is a major part of burn pathophysiology. After the resultant hypoperfusion of tissues in the initial phase of burn shock, restoration of oxygen delivery to tissues can exacerbate the production of deleterious free radicals such as hydrogen peroxide and superoxide. At the same time, antioxidant mechanisms such as glutathione and ascorbic acid are decreased due to burn-mediated changes in the liver [68–70].

In the 1990s, Matsuda *et al.* were able to reduce fluid requirements and edema formation during burn resuscitation in dogs and guinea pigs by using high-dose ascorbic acid therapy [71, 72]. A few years later they reproduced the beneficial effects of high dose ascorbic acid in humans in a prospective, randomized study [73]. During the first 24 hours, resuscitation fluid volume requirements were significantly reduced (3.0 vs 5.5 mL kg^{-1} %$TBSA^{-1}$, $P < 0.01$) as well as body weight gain, wound edema and the severity of respiratory dysfunction. Ascorbic acid has an apparent (osmotic) diuretic effect that may lead to hypovolemia. The decreased insensible fluid losses may also lead to a reduced inflammatory response and earlier mobilization of fluid. Although a retrospective review in 2011 found significantly lower fluid requirements and higher urinary output in burn patients treated with high dose ascorbic acid, no difference

in outcome was found [74]. The available data indicates ascorbic acid should be infused at 66 mL kg^{-1} $hour^{-1}$ for the initial 24 hours of burn resuscitation (25 grams of ascorbic acid in 1000 mL of Plasma-Lyte® solution covered with a black bag to prevent light-induced auto-oxidation).

Recommendation: *Given the available evidence, the beneficial effect of adjunctive high dose ascorbic acid treatment is possible with no adverse effects having been reported, thus pushing the risk-benefit in favor of using ascorbic acid.*

PLASMAPHERESIS

Plasmapheresis or plasma exchange has previously been described as a rescue therapy in burn resuscitation. In burn shock, a humorally mediated systemic inflammation is initiated and the beneficial effect of plasmapheresis is attributed to the mechanical removal of these inflammatory mediators. When using this strategy, part of the patient's plasma is removed and replaced with either albumin or fresh frozen plasma.

In the 1980s, a retrospective study described plasmapheresis treatment in patients who failed to respond to conventional therapy. The therapeutic response was characterized by a sharp decrease in fluid requirements, with a mean volume of 260% above the predicted hourly volume dropping to within the calculated requirements within 2.3 hours of the plasma exchange [75].

More recent retrospective studies have confirmed the benefits of plasmapheresis as a salvage therapy. In the early resuscitation period, this was associated with decreased fluid administration, as well as increased urine output. Indeed, groups studied by Klein and Neff found a 28.3% and 25% respective decrease in hourly fluid administration after therapeutic plasmapheresis [76, 78].

Recommendation: *The benefit of plasmapheresis on outcomes in burn patients still needs to be validated in large prospective, randomized trials. Its use cannot be currently recommended.*

INTRAVENOUS IMMUNOGLOBULINS

Recent reviews and meta-analyses have concluded that the administration of polyvalent immunoglobulins has a significant beneficial effect on mortality (on average a 25% reduction) in patients with severe sepsis and septic shock (compared to those without organ dysfunction), favouring the administration of IgG or a combination of IgG, IgA and IgM [79–81]. However, in burn patients no beneficial effects have been observed, except in cases of toxic epidermal necrolysis (TEN) and then in combination with steroids [82, 83].

Recommendations: *The use of intravenous immunoglobulins (IVIG) should be limited to cases of TEN.*

CONCLUSIONS

During recent decades, burn resuscitation has kept evolving and new trends have appeared. Over the last fifteen years, much attention has been given to avoiding over-resuscitation and subsequent morbidity and mortality. Fluid creep is recognized by nearly all physicians involved in burn care and the pathophysiology behind it is probably multi-factorial (urine output as a weak endpoint, over-estimation of TBSA, opioid creep, etc.).

As common sense must prevail, fluids should be seen as drugs and, as such, coming with indications and contra-indications and possible adverse effects. Thus, it is all about the type of fluid, dose, timing, infusion rate and the duration. Fluid requirements are dynamic and change over time while the resuscitation approach should be targeted and protocol driven. Although balanced solutions are a pragmatic first choice resuscitation fluid in the majority of burns cases, efforts should be made to avoid excess crystalloid administration by revising resuscitation protocols. Physicians need to be aware of the harm caused by fluid overload during resuscitation. They should therefore actively aim to avoid fluid accumulation, as this can be at least as harmful, if not more so, than under-resuscitation. While the evidence suggests that the addition of a colloid, such as albumin 20%, may decrease fluid requirements and may potentially reduce resuscitation-related morbidity, the use of colloids in burn resuscitation continues to be a great source of controversy and discussion. Ascorbic acid, as an adjunctive therapy, has shown promising results and without presenting adverse effects. Its use should be considered in patients at risk of fluid overload or secondary IAH and ACS. The endpoints of burn resuscitation should therefore be redefined. These issues will be discussed in the second part of this concise review.

ACKNOWLEDGEMENTS

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