Modern trends in fluid therapy for burns

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Abstract

The majority of burn centres use the crystalloid-based Parkland formula to guide fluid therapy, but patients actually receive far more fluid than the formula predicts. Resuscitation with large volumes of crystalloid has numerous adverse consequences, including worsening of burn oedema, conversion of superficial into deep burns, and compartment syndromes. Resuscitation fluids influence the inflammatory response to burns in different ways and it may be possible, therefore, to affect this response using the appropriate fluid, at the appropriate time. Starches are effective volume expanders and early use of newer formulations may limit resuscitation requirements and burn oedema by reducing inflammation and capillary leak. Advanced endpoint monitoring may guide clinicians in when to ‘turn off’ aggressive fluid therapy and therefore avoid the problems of over-resuscitation.

Keywords:
Burn resuscitation
Fluid therapy
Modern trends

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1. Introduction

The goal of fluid therapy in the burn-injured patient is to maintain global tissue perfusion in the face of massive systemic inflammation, fluid extravasation and intravascular hypovolaemia. Early, aggressive treatment of burn shock has been the mainstay of burns resuscitation, but recently there have been growing concerns that burn-injured patients are being over fluid-resuscitated with excessive quantities of crystalloid, often with indistinct and inappropriate endpoint targets. The problems of this excess resuscitation have been well described, yet many centres still continue the practice. There have been efforts recently to address these concerns, particularly with the use of physiologically balanced fluids, advanced endpoint monitoring and therapies aimed at influencing the inflammatory response. It is still unclear how, or if these interventions can improve outcome. This review describes, and attempts to explain the recent trends in fluid therapy for burn-injured patients.

2. Pathophysiology of burn shock

An understanding of the pathophysiological mechanisms underlying burn injury is essential if clinicians are to resuscitate patients successfully.

2.1. Initial injury

Burn trauma results in an area of dead tissue, beneath which lies a zone of ischaemia that is potentially reversible [1]. This local injury results in release of inflammatory mediators (e.g. histamine, prostaglandins, thromboxane, nitric oxide) that increase capillary permeability and lead to localised burn wound oedema [2,3]. This occurs within minutes to hours of the injury and is followed by production of highly reactive oxygen species (ROS) during reperfusion of ischaemic tissues [2,4,5]. ROS are toxic cell metabolites that include oxygen free radicals and cause local cellular wall membrane dysfunction and propagate an immune response.

2.2. Systemic inflammatory response and burn oedema

If the burn is severe then circulating mediators (TNFα, interleukin-1,2,5,8, and interferon-γ) result in a systemic inflammatory response [5,6]. Increased microvascular permeability, vasodilatation, vascular stasis, decreased cardiac contractility, and reduced cardiac output, all impair tissue oxygen delivery. The widespread increase in microvascular permeability results in a massive leak of fluid, electrolytes and proteins from the intravascular space into the interstitial space, further impairing tissue perfusion [4,7]. The loss of proteins into the interstitial space rapidly decreases the intravascular colloid osmotic pressure, and results in a reversed osmotic gradient. Obstruction of lymph vessels by platelets, erythrocytes, or leukocytes, impairs tissue fluid drainage to the venous circulation. These factors, combined with the massive vasodilatory response drive the formation of further oedema as governed by Starling forces [8,9]. Although oedema formation is a natural protective response to inflammation, burn injury often results in a massive fluid leak that ceases to be beneficial to the patient. Oedema reaches a maximum at 24 h after-burn and begins to resolve after 1–2 days. The prevention and treatment of burn oedema represent a major challenge to clinicians treating burn-injured patients.

2.3. Burn shock

Loss of intravascular volume to the interstitium results in a unique phenomenon called burn shock, which is a combination of distributive, hypovolaemic and cardiogenic shock. Fluid is also lost through wound drainage and evaporation [8]. Plasma volume becomes insufficient to maintain adequate preload, cardiac output decreases and tissue hypoperfusion ensues. Failure to adequately resuscitate burn-injured patients can lead to significant organ injury from the systemic
inflammatory response syndrome (SIRS) or multi-organ dysfunction syndrome (MODS).

3. Modern trends in fluid resuscitation volume

There is little doubt that the introduction of fluid resuscitation protocols in the 1960s and 1970s has helped to significantly reduce mortality from burns. Baxter and Shires devised the “Parkland Formula”, which calculates the amount of fluid required to resuscitate a patient based on percentage burn [10,11]. 4 ml/kg/% burn are given in the first 24 h, with half of this fluid given in the first 8 h. The Parkland Formula remains the most commonly used formula in the UK and US today [12,13]. Despite its almost universal acceptance as a tool for calculating the volume of fluid required to resuscitate the burn-injured patient, there is growing evidence that patients receive far more fluid than the Parkland formula predicts, a phenomenon that has been termed “fluid creep” [14].

3.1. Fluid creep

Baxter reported that 12% of patients would require more than 4.3 ml/kg/% burn in the first 24 h, and that adjustment of infusion rates according to urine output was essential [15]. However, a recent study of practice in six burn centres in the US found that 58% of patients exceeded the Parkland target [16]. This is confirmed by a Canadian group who found that the 24-h resuscitation volume was 6.7 ± 2.8 ml/kg/% burn, which was significantly greater than predicted and exceeded estimated volume in 84% of the patients [17]. This underestimate was found to be greatest after the first 8-h period, where the decrease in the rate of fluid infused recommended by the Parkland formula was not adhered to. Friedrich et al. [18] found that a group of burn-injured patients in 2000 received more than double the fluid received by a matched group in the 1970s, despite equal urine output. Groups of patients have been identified in whom resuscitation requirements are usually greater than the Parkland Formula predicts. These include patients with inhalational injuries [19], electrical burns, those with additional injuries, patients with high alcohol or drug intake, and those in whom resuscitation was delayed [11,20]. However, the patients included in the aforementioned studies were not confined to these groups.

3.2. Why does fluid creep occur?

The reasons why fluid creep occurs are not clear. Sullivan et al. [21] hypothesised that the growing trend to over-resuscitate burn-injured patients could be explained by the increased use of opioid agonists in the treatment of burn pain, a phenomenon they have termed “opioid creep”. Opioid agonists, particularly in higher doses are known to cause hypotension, which may increase the fluid requirements in the resuscitation period. They compared a group of patients admitted to the University of Washington Burn Centre with a major burn between 1975 and 1978, with a group of patients matched for age and percentage burn, admitted to the centre in 2000. The second group received significantly more fluid and significantly more opioid agonists than the first.

Saffle [22] recently suggested that as mortality from burns decreases and the success of aggressive fluid resuscitation is observed, clinicians are instinctively adopting a “more fluid is better” approach and applying this to smaller burns, with less stringent adherence to the formulae. Referring to a review by Cancio et al. [23], he suggests that modern clinicians are less likely to decrease infusion rates when presented with a high urine output. Saffle draws our attention to the influence of goal-directed therapy on resuscitation of burn-injured patients. It is undoubtedly common practice, particularly in critical care medicine with the advent of the Surviving Sepsis Campaign [24], to target fluid resuscitation towards lactate levels, base excess, central venous oxygen saturation and other indicators of tissue perfusion. Saffle suggests that burn clinicians, who often double as critical care physicians apply these practices to the care of their patients despite burn, often resulting in increased fluid infusions despite adequate urine output and vital signs. Holm et al. [25] recently showed an increased fluid requirement in burn patients resuscitated using a goal-directed approach when compared with patients resuscitated using the Parkland formula.

Modern burn care is often provided in specialist burn centres, and patients do not reach these centres for several hours. The early resuscitation phase is often therefore carried out in non-specialist centres where there is a tendency to over-resuscitate burn-injured patients [22,26].

Baxter recognised that crystalloid infusion alone would not adequately resuscitate the burned patient, and the original formula included a 4th 8-h period during which plasma was given. This was later abandoned leaving a purely crystalloid-based protocol. As will be discussed later, there is a growing trend towards the use of crystalloid throughout the resuscitation period and this trend has also been implicated as a major contributor towards fluid creep [22].

3.3. Consequences of fluid creep

There is growing concern that fluid creep is “feeding” burn oedema, the problems of which have been well described. Splanchnic oedema leads to an increase in gut permeability, bacterial translocation, and increased intraabdominal pressure [27]. Intraabdominal hypertension (IAH) is defined in the burn literature by intraabdominal pressures exceeding 25 mmHg, and has been associated with renal impairment, gut ischaemia, hepatic malperfusion, and cardiopulmonary dysfunction [28]. If severe or untreated, intraabdominal hypertension can progress to abdominal compartment syndrome (ACS) or death. There have been numerous reports in the literature of ACS occurring in burn patients [28–30]. Ivy et al. [28] found that the incidence of IAH during the resuscitation phase in a group of patients with large total body surface area (TBSA) burns was 70%, with progression to ACS requiring laparotomy occurring in 20%.

Both this, and a more recent study [31] demonstrated a correlation between the volume of resuscitation fluid infused and intraabdominal pressure. In two recent studies by Oda et al. [32,33], the critical volume associated with development of intraabdominal hypertension was approximately 300 ml/kg over a 24-h period. Close monitoring of intraabdominal pressure...
is recommended in any burn patient who has received 0.25 l/kg or more of fluid resuscitation [28].

Several other complications of fluid resuscitation in burn patients have been described, including pulmonary oedema requiring prolonged ventilatory support [34], the need for fasciotomies in unburned limbs [22], the conversion of superficial into deep burns [35], and elevated intraocular pressure requiring lateral canthotomy [36].

4. Modern trends in choice of fluid

The ideal burn resuscitation fluid is one that effectively restores plasma volume, with no adverse effects [37]. The extensive choice of fluids available to resuscitate burn-injured patients has fuelled research efforts aimed at determining which fluid is best. None of them are ideal, and no valid study exists that implicates the superiority of a specific solution. Much of the evidence available to guide burn clinicians in choosing the right fluid has been pooled into meta-analyses. These often combine multiple fluid types, multiple patient groups, and multiple outcomes and so may not be helpful instruments in this respect. The longstanding crystalloid or colloid debate is not confined to trauma and intensive care disciplines, and extends to burn care also.

4.1. Isotonic crystalloids

Isotonic crystalloids have been the fluid of choice for many years for initial burn resuscitation. They are readily available and cheaper than some alternatives (Table 1). High volume administration of normal saline has been shown to produce a temporary hyperchloraemic acidosis [38], and Hartmann’s solution is favoured as it is a physiologically balanced crystalloid solution that is more isotonic with plasma.

Isotonic crystalloids distribute evenly between the intravascular and interstitial space. After 30 min only 16% of the infused crystalloid volume remains in the intravascular space [39]. This is undesirable, particularly in burn-injured patients where this may worsen tissue oedema and increase the diffusion distance within tissues, thus compromising tissue perfusion. There is also convincing evidence that crystalloids have a substantial influence on coagulation. Three recent studies [40–42] have shown that in vivo dilution with crystalloids resulted in a hypercoaguable state, and one further study has shown that this is independent from the type of crystalloid used [43]. As will be discussed later, there are also concerns regarding the influence isotonic crystalloids have on the immunological response to burns.

Despite the concerns regarding the use of isotonic crystalloids, a recent survey of practice in the UK and Ireland reported that 76% of adult burns units use Hartmann’s solution to resuscitate their burns patients [12]. Ringer’s Lactate, which is similar in composition to Hartmann’s solution is the predominant burn resuscitation fluid in the US [13].

4.2. Hypertonic solutions

Hypertonic saline has several properties that make it theoretically attractive for burn resuscitation. Rapid infusion of hypertonic saline results in an increased plasma osmolality that potentially limits burn oedema, and may actually mobilize fluid from the interstitial space by osmotic action. A recent study by Oda et al. [33] compared outcomes in patients resuscitated with hypertonic lactated saline and lactated Ringer’s. Patients in the hypertonic group required significantly less fluid in the first 24 h to achieve the target urine output than those in the lactated Ringers group, and demonstrated a decreased risk of abdominal compartment syndrome. However, the serum sodium concentration in the hypertonic group increased to a peak of 150.7 ± 10 mequiv./l 24 h after injury compared with a range of 136–138 mequiv./l in the lactated Ringers group. Earlier studies by Shimazaki et al. [44] found that when plasma sodium levels reached 160 mequiv./l during hypertonic saline resuscitation, urine output fell precipitously, forcing a change in resuscitation fluid. Huang et al. [45] also achieved resuscitation endpoints with significantly less fluid in the first 24 h using hypertonic saline compared with lactated Ringer’s solution, but after 48 h cumulative fluid loads were similar. In addition, patients resuscitated with hypertonic saline had a fourfold increase in renal failure and twice the mortality of the lactated Ringer’s group. The interest in hypertonic saline resuscitation is growing, but therapy needs to be closely monitored in view of the risk of hypernatraemia and renal failure.

4.3. Colloids

The role of colloids in burn resuscitation is controversial. Colloids remain in the intravascular space longer than crystalloids, but the evidence demonstrating the translation of this into clinical outcome benefit is sparse, particularly in situations where capillary integrity is impaired. Baxter’s early work showed that capillary leak may persist for up to 24 h post burn [11], and that plasma expansion during this period was independent of the type of fluid given [10]. Other studies have shown that colloids provide little clinical benefit when given in the first 24 h post burn, and may have detrimental effects on pulmonary function [46,47]. In addition, the notable Cochrane reviews [48,49] concluded that there was no survival benefit with the use of colloids for resuscitation. Consequently, many burn clinicians avoid the use of colloids in the early post-burn period.

This approach may be unjustified. Vlachou et al. [50] recently showed that endothelial dysfunction and capillary leak are present within 2 h of burn injury and last for a median

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<th>Table 1 – Costs of intravenous fluids.</th>
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<tr>
<td>0.9% saline 500 ml</td>
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<td>Hartmann’s 500 ml</td>
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<tr>
<td>Human albumin solution 4.5% 400 ml</td>
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<tr>
<td>Gelofusine® 500 ml (4% gelatin, MW 30,000 Da)</td>
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<tr>
<td>Hetastarch 500 ml (6% HES, MW 450,000 Da, MS 0.7)</td>
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<td>Voluven® 500 ml (6% HES, MW 130,000 Da, MS 0.4)</td>
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of 5 h, much shorter than previously described. The Cochrane reviews have been criticised for the wide confidence intervals used, and the heterogeneity of the included studies. Only three papers in the Cochrane review specifically targeted burns patients, all of which were relatively small studies and only one of which showed a worse outcome with albumin use. Since then, the SAFE study has showed similar survival rates in critically ill patients resuscitated with saline versus albumin [51], and Cochran et al. [52] have demonstrated decreased mortality in patients who received albumin. In addition, some burn clinicians have reported successful resuscitation with colloids in the early post-burn period; Du et al. [53] found that early use of plasma lead to improved cardiac parameters, decreased volume requirements, and lower weight gain, compared with pure crystalloid resuscitation. O’Mara et al. demonstrated decreased fluid requirements and lower intraabdominal pressures with use of plasma in the first 48 h following large TBSA (>50%) burns [31].

4.4. Starches

A number of studies using high molecular weight hydroxyethylstarch (HES) preparations as volume expanders in the early post-burn period have demonstrated decreased oedema formation and improved haemodynamics [54,55], yet concerns regarding the adverse effects of starches, particularly on coagulation, have limited their use. Waxman et al. [55] found that plasma expansion with as little as 500 ml of pentastarch towards the end of the first 24-h post-burn period, whilst facilitating improved haemodynamics and oxygen delivery, also caused measurable coagulation impairments. Many of the adverse effects of starches, however, are limited to these older, larger molecular weight and highly substituted solutions. All artificial colloids are potentially associated with an increased bleeding tendency after infusion of very large volumes [56], but balanced smaller molecular weight, lower molar substituted HES preparations appear to impair coagulation the least [57]. Third generation HES preparations have also been shown to improve tissue oxygenation and renal function in patients undergoing major abdominal surgery [58,59]. These newer starches have a significantly longer volume expansion effect than both gelatins and albumin, and interest in their use early on in burn resuscitation when capillary leak is maximal is likely to grow in the near future.

4.5. Blood

Blood loss in burned patients is multifactorial, but is most closely related to the total burn area excised [60]. A restricted blood transfusion protocol is associated with lower mortality and infectious episodes in patients with major burns [61,62]. A recent study in children with major burns and concomitant inhalation injury showed that they are more likely to develop sepsis if they are given large amounts of blood products [63].

4.6. Immunological and microcirculatory effects of fluid resuscitation

The ability of different fluids to resuscitate burn-injured patients is not simply related to their effects on intravascular volume. There is growing interest in the immunological and microcirculatory effects of various fluids, and the impact this has on the resuscitation process. Both crystalloids and colloids have been shown to cause neutrophil activation following haemorrhagic shock [64,65]. Recent reports have suggested that lactated Ringers solution contains both L- and D-lactate isomers [66]. The D-lactate isomer has been found to increase cellular apoptosis. The L-lactate form does not have this toxicity and thus might have better resuscitation properties. There has also been recent interest in Ringer’s ethyl pyruvate solution, which has been shown to possess anti-inflammatory and antioxidant properties [67].

Hyperonotic saline and HES solutions have been shown to be immunosuppressive, and may also improve microcirculatory haemodynamics [68,69]. In addition, animal models have demonstrated specific benefit of certain starches in retaining fluid within the capillaries, probably by physically plugging endothelial pores, in situations where capillary leak occurs [70]. There is the potential, therefore to modulate the inflammatory response to burn shock using the appropriate fluid, at the appropriate time.

5. Modern trends in fluid protocols

With such a wide variety of fluids available to resuscitate burn-injured patients, it is imperative that each individual burn unit has a well-defined fluid resuscitation protocol. With a lack of evidence-based literature supporting one protocol over another, modern burn resuscitation is often guided by local tradition of treating units.

5.1. UK and US protocols

Baker et al. [12] recently conducted a survey of 26 burns units in the UK and Ireland. The majority of units commence fluid resuscitation at 10% TBSA burns in children and 15% TBSA in adults. Seventy-six percent of units use the Parkland formula to calculate resuscitation volumes. Eleven percent of units use the Muir and Barclay formula and the remainder use both, using the Muir and Barclay formula for patients with very large burns. This was considerably different from previous surveys of practice in the UK and Ireland and correlates well with trends in the US [13]. The survey also revealed that only 51% of UK units routinely alter the type of fluid used after 24 h. In the US, 78% of units routinely alter the type of fluid used after 24 h [13]. With the emergence of compartment syndromes there has been a recent move away from the Parkland formula and a move towards formulae that predict lower fluid volume requirements in the first 24 h post burn. This is particularly evident in the US where more and more burn surgeons are using 2 ml/kg/% burn as a starting point.

5.2. The Haifa formula

A group in Israel recently described their experiences with a unique formula that combines plasma and crystalloid [71]. In the first 24 h after injury they administer 1.5 ml/kg/% burn of fresh frozen plasma, plus 1 ml/kg/% burn Ringer’s lactate. Half of the amount is given during the first 8 h and half in the next
16 h. Ringer’s lactate is added if urine output is less than 0.5 ml/kg/h. Over a 15-year period they treated 356 patients with major burns using this ‘Haifa’ formula. Twenty-seven deaths were recorded during this period and 19 had third degree burns involving more than 80% TBSA.

5.3. Operation Iraqi Freedom

Chung et al. recently described their experiences of burn resuscitation in Operation Iraqi Freedom [72]. At the start of the conflict, under-resuscitation appeared to be the main concern, but as the problems of fluid creep became more apparent, fears of over-resuscitation set in. They termed the effects of over-resuscitation as “resuscitation morbidity” which encompasses the complications previously described. Military unit medical personnel often only carry colloid in an attempt to reduce the weight of intravenous fluid transported. They developed an impressive protocol for the difficult fluid resuscitation that uses albumin if projected 24-h resuscitation requirements exceed 6 ml/kg/% burn. Bladder pressures are measured frequently to detect raised intraabdominal pressures, and resuscitation is guided by urine output, pulmonary capillary wedge pressure, central venous pressure and mixed venous oxygen saturation. Since the implementation of these guidelines, the percentage of patients with TBSA burns greater than 20% requiring decompressive laparotomies for abdominal compartment syndrome has fallen from 13 to 0.

6. Modern trends in endpoint monitoring

Arguably, more important than the choice of burn resuscitation fluid is the determination of the success, or otherwise of the resuscitation. Each patient will react differently to burn injury and may require varying amounts of fluid support. A myriad of factors will affect the patient’s response to resuscitation such as age, depth of burn, concurrent inhalation injury, and pre-existing disease [73]. If burn clinicians used an endpoint of resuscitation that reliably and accurately measures the adequacy of cellular perfusion, then they would know when to “turn off” aggressive fluid therapy and potentially avoid the problems of over-resuscitation. Unfortunately, no such measure currently exists.

6.1. Traditional endpoints

Traditional markers of resuscitation success such as blood pressure and pulse may be normal in states of compensated shock and may not detect occult cellular hypoperfusion. Non-invasive blood pressure measurement may be difficult in the presence of tissue oedema. Tachycardia can be the result of pain and anxiety, which is common in burn-injured patients and is therefore an unreliable marker of hypovolaemia. Traditionally, urine output has been used to guide resuscitation. Urine output closely reflects renal perfusion, which is sensitive to decreasing cardiac output and hypovolaemic states [73]. The American Burn Association suggest that the fluid infusion rate should be titrated to a urine output of 0.5–1.0 ml/kg/h in adults [74], although with the emergence of compartment syndromes the most experienced burn clinicians are beginning to accept lower urine outputs as a resuscitation endpoint. However, there are no studies demonstrating which value of hourly urine output indicates adequate perfusion. In addition, there are numerous studies highlighting the failure of urine output to assess adequate global perfusion [75–77]. The limitations of these traditional guides to resuscitation have led to interest in more advanced methods of endpoint monitoring.

6.2. Advanced haemodynamic monitoring

In 1996, a survey of the use of invasive cardiovascular monitoring in patients with burns greater than 30% TBSA showed that 55% of burns units in the UK, USA, Canada, Australia and New Zealand used central venous pressure (CVP) monitoring in more than half of their patients [78]. Only 8% of the units used pulmonary artery catheters in over half of their patients, and this number may well have declined further since then. Pulmonary artery catheters have been associated with a number of complications, and pulmonary artery occlusion pressure (PAOP) has been shown to be an unreliable marker of preload [79]. However, a reliable and accurate marker of cardiac preload would appear to be an attractive tool to guide resuscitation in burns patients.

Intrathoracic blood volume (ITBV) is the total combined volume of the right heart, left heart, and pulmonary blood volumes measured at end-diastole. ITBV has been shown to be closely correlated to cardiac output, and that this correlation is not simply a mathematical coupling [80]. Holm et al. [25] recently investigated the effects of invasive monitoring of ITBV on burn shock resuscitation. Haemodynamic measurements were made using the COLD system (Pulsion Medical Systems), which utilises a standard central venous catheter and a thermistor-tipped fibreoptic catheter inserted into the femoral artery. Patients who received ITBV guided resuscitation received significantly more fluid in the first 24 h after-burn than those who were resuscitated according to the Parkland formula. There was no significant difference in ITBV, cardiac output, serum lactate levels, mortality or morbidity between the groups. Sixty percent of patients failed to reach the ITBV goal (~800 ml/m²), which was independent of the choice of resuscitation treatment, indicating that the additional fluid received in the treatment group did not confer haemodynamic advantages. Measurements of plasma protein concentration indicated that, as expected, this additional fluid was lost from the intravascular space. As reported in previous studies, Holm et al. demonstrated that despite aggressive fluid therapy, occult hypoperfusion still exists. In contrast, Arlati et al. [81] achieved resuscitation targets with less fluid administered, less oedema formation, and lower organ dysfunction scores using an intrathoracic blood volume-guided and cardiac output-guided approach compared with a Parkland approach.

Oesophageal Doppler monitoring provides a relatively non-invasive estimate of cardiac preload by measuring the aortic blood flow in the descending thoracic aorta. The corrected flow time (FTc), if used appropriately can assess cardiovascular response to a fluid challenge [82–86]. Stroke volume variation (SVV) is the change in left-ventricular stroke volume induced by cyclic positive pressure breathing in mechanically ventilated patients, and has also been shown to be a reliable predictor of fluid responsiveness [85,87]. The use of oesopha-
geal Doppler in the perioperative period to guide fluid management has led to improved outcome and decreased hospital stay in patients undergoing major surgery [88,89]. Yamamoto et al. [90] recently evaluated the use of oesophageal Doppler in four patients with extensive burns, and found that cardiac index measurements by oesophageal Doppler correlated well with those obtained from a pulmonary artery catheter. The placement of central venous catheters can be technically difficult in burn-injured patients due to oedema and burn damage, and oesophageal Doppler has particular advantages in these situations. Studies demonstrating improved outcome with use of oesophageal Doppler in burns patients are lacking.

6.3. Subcutaneous tissue gas tensions

Venkatesh et al. [75] recently measured subcutaneous tissue gas tensions in burn-injured patients using silastic tubing inserted into the subcutaneous tissue of both burned and unburned skin. Despite normal indices of both systemic circulation and oxygenation throughout the resuscitation period, subcutaneous tissue gas tensions in both burned and unburned skin deteriorated significantly, indicating significant impairment of tissue oxygenation. The authors attributed the changes in gas tensions to the worsening tissue oedema that develops in burn and unburned skin that is exacerbated by fluid administration. Subcutaneous tissue monitors may have a role in early detection of burn oedema and in guiding fluid resuscitation in burn patients in the future.

6.4. Optically based devices

Optically based tissue monitoring devices have been used in severely injured trauma patients to show that despite adequate tissue oxygen delivery, a derangement in cellular use of oxygen persists [91]. Tissue oxygen saturation measured using near-infrared spectroscopy (NIRS) has been shown to as good as base excess in identifying trauma patients at risk of developing MODS [92]. These are potentially extremely useful endpoint monitoring devices but further research into their use in burn-injured patients is needed.

7. Alternative approaches and adjuncts to fluid resuscitation

As we have seen, it may be impossible to restore normovolaemia during the early post-burn period using pure crystalloid resuscitation, and even despite adequate oxygen delivery tissue hypoxia still persists. This suggests that modern burn research should be focussed on developing methods to correct microcapillary leak and improve microcirculatory perfusion and cellular oxygen utilisation, and strategies aimed at reducing resuscitation volumes need to be pursued.

7.1. Modifying the inflammatory response

Early burn wound excision has been shown to modulate the inflammatory response to burn injury by reducing levels of pro-inflammatory mediators [93], and is widely accepted. Continuous venovenous haemofiltration has been shown to reduce serum cytokine levels in patients with septic shock and renal failure when high ultrafiltration rates are used [94]. Current filtration methods are not specific enough for pro-inflammatory mediators but this technique has a promising future in the treatment of burn shock. The effect of different fluids on endothelial leakage and inflammation has already been discussed and is likely be an active area of burn research in the future.

7.2. Vitamin C

Following burn injury, due to the ensuing oxidative stress, there is an increased requirement for vitamin C as indicated by the reduced serum vitamin C levels seen in such patients [95]. Tanaka et al. [96] demonstrated that high dose vitamin C reduces the amount of fluid required to resuscitate burn-injured patients and leads to a significant decrease in burn oedema and length of time on mechanical ventilation. Mortality during the study period was not significantly different. The optimum dose of vitamin C has yet to be defined and further research using large multi-centre randomised-controlled trials is needed.

7.3. Enteral resuscitation

Resuscitation of burn-injured patients using the oral route has been well described. Even in developed countries, many centres resuscitate patients with smaller burns (less than 20% in adults, less than 15% in children) using oral fluids only [97,98]. Uncertainty exists regarding the nature of the ideal enteral resuscitation fluid, and there are concerns regarding delayed gastric emptying and intestinal absorption in shock states [99]. However, a recent study by Kramer et al. [100] showed that gastric emptying and subsequent intestinal absorption can deliver significant resuscitation volumes in hypovolaemic anaesthetised swine. They also found that increases in cardiac output and plasma volume were similar using intravenous and rectal infusions (“proctoclysis”) of resuscitation fluid in anaesthetised swine that had been subjected to 40% TBSA full-thickness burns. Oral or rectal routes of fluid administration may well be favoured in certain situations, i.e. in the treatment of burns victims in the third world and remote locations where supplies of intravenous fluids are often very limited, and in major disasters where supplies of intravenous fluids may not meet demand. Patients receiving enteral resuscitation should be closely monitored in view of the risk of vomiting and aspiration, and it should be avoided in patients with impaired conscious level, and in patients with gastro-intestinal injury. Further research is needed to define the ideal nature and timing of oral and rectal resuscitation fluid and to determine their effectiveness in humans.

7.4. Permissive hypovolaemia

Arlati et al. [81] recently investigated a “permissive hypovolaemia” approach to resuscitation after severe burns. They compared the outcome of 12 patients resuscitated according
to the Parkland formula, with that of 12 patients resuscitated using the permissive hypovolaemic approach. Permissive hypovolaemia allowed for less volume infusion in the first 24 h (3.2 ± 0.7 ml/kg/% burn versus 4.6 ± 0.3 ml/kg/% burn; P < 0.001) and significantly lower multiple-organ dysfunction scores than the Parkland formula. Haemodynamic variables and blood lactate levels were comparable between the groups throughout the resuscitation period.

7.5. Closed-loop resuscitation

“Closed-loop” resuscitation of burn-injured patients has recently been described [100,101]. This utilises a computer-controlled resuscitation system to titrate fluid therapy to a target urine output, and was shown to be at least as effective as human monitors. Such systems may help to avoid over-resuscitation, as they may well be better at responding to high urine outputs than humans. Trials of closed-loop resuscitation are in progress.

7.6. Vasopressin

Arginine vasopressin is an important stress hormone that has both vasoactive and antidiuretic properties. It has recently been discovered that there is a deficiency of vasopressin in septic shock and that infusion of relatively low doses of vasopressin improves responsiveness to noradrenaline and increases blood pressure and urine output [102,103]. Cartotto et al. [104] recently reviewed the use of vasopressin in 30 burn patients with sepsis. They found that there was a significant increase in mean arterial pressure, a significant decrease in heart rate, and a trend towards increased urine output following initiation of vasopressin. When vasopressin was added to an existing infusion of noradrenaline, there was a significant noradrenaline sparing effect. Despite these beneficial haemodynamic effects, the effect of vasopressin on mortality remains unclear. The recent VASST study concluded that there was no survival benefit in patients treated with low-dose vasopressin (0.03 U/min) compared with norepinephrine among patients with septic shock [105].

The use of vasopressin is not without risks. In Cartotto’s study [104] vasopressin was implicated in the death of one patient who developed diffuse gastrointestinal necrosis while on vasopressin. The detrimental effects of vasopressin on gastrointestinal perfusion was confirmed by van Haren et al. [106]. They investigated the effect of low-dose vasopressin infusion (0.04 U/min) on gastric perfusion in a small group of patients who remained hypotensive despite norepinephrine infusion. They found that vasopressin infusion lead to an immediate increase in the difference between gastric and arterial CO2 partial pressure (P(g-a)CO2 gap). The P(g-a)CO2 gap is a reliable measure of gastrointestinal hypoperfusion, and is easily measured using gastric tonometry. They also found a strong correlation between median plasma levels of vasopressin and the median P(g-a)CO2 gap, suggesting a dose-dependent effect. Gastrointestinal hypoperfusion can be reversed by infusion of vasodilating agents such as prostacyclin [107], although all patients in van Haren’s study received low-dose vasodilator therapy.

The optimum dose and duration of vasopressin therapy remains unclear and until further evidence is available, vasopressin should be used with caution. Its use should be limited to low-dose infusions, and should be accompanied by careful monitoring of gastric perfusion.

8. Conclusion

There is little doubt that excessive fluid therapy may worsen the burn injury, and the trend to over-resuscitate burn-injured patients is a worrying one, particularly in the light of increasing number of publications describing the adverse consequences of “fluid creep.” Any fluid regimen must, in the first instance do as little harm to the patient as possible. The use of colloids and hypertonic solutions have been shown to result in decreased fluid requirements and lower intraabdominal pressures compared with isotonic crystalloid resuscitation, but the majority of units continue to resuscitate their burn-injured patients using crystalloid-based protocols. Adjuncts such as vitamin C and vasopressin may also help to reduce fluid requirements in burn resuscitation.

Invasive cardiac preload monitors are a useful resuscitation guide, but they have been shown to result in the administration of more fluid as well as less. How best to use this information, and what impact it may have on patient outcome is yet to be defined. There is great interest in endpoint monitors that allow the clinician to direct fluid resuscitation to cellular metabolic conditions, and this needs to be explored further.

There is growing evidence to suggest that different fluids affect the inflammatory response to shock in different ways, and this could be utilised in burn resuscitation. It seems likely that the best fluid resuscitation protocol is one that delivers a variety of fluids with different immunological and microcirculatory properties, tailored to suit the individual patient and timed to mirror the dynamic pathophysiological processes underlying burn shock. The ability of HES solutions to modify capillary leak and inflammation is promising, and use of modern preparations in the first few hours post-burn, when capillary leak is maximal, needs to be investigated.

Conflict of interest

None declared.

REFERENCES


