Fluid Resuscitation

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Learning Objectives

In this chapter we will analyse different aspects of fluid resuscitation in order to inform decision-making. This will include an analysis of the rationale for fluid resuscitation, assessing different types of fluid compounds, and provide an applicable approach to fluid therapy based on available evidence.

31.1 Introduction

Fluid resuscitation is a very frequent intervention in critical care and has been used for almost two centuries. Fluid resuscitation lacks a uniformly recognized definition but may be defined as intravenous fluid administration with the aim of improving the circulation in the case of shock. Most intravenous fluid compounds are cheap and readily available.

The main mechanism by which intravenous fluid may improve the circulation is by increasing stroke volume through increased preload and, in turn, cardiac output. However, intravenous fluid administration also carries potential adverse effects, including electrolyte derangements and organ and peripheral oedema that may lead to impaired ventilation, kidney function and circulation. The balance between benefits and harms is presently not fully elucidated, and clinicians must, thereby, base their decisions concerning fluid resuscitation mostly on patient history and pathophysiology and lower quality of evidence.

31.2 Physiological Rationale for Intravenous Fluid Resuscitation

The first documented use of intravenous fluid resuscitation was performed in 1832 when Dr. Thomas Latta treated severely dehydrated cholera patients with large amounts of saline fluids intravenously [1]. Fluid administration was somewhat paradigm challenging since the predominant treatments at the time were laxatives, emetics and venesection [2]; since then, few have questioned the administration of fluids in replacement of severe losses. The concept of administering intravenous fluids beyond replacement of losses is based on the findings of early twentieth-century physiologists Ernest Starling and Otto frank, who gave name to the "frank-Starling mechanism" that states when all other variables are constant, a larger end-diastolic volume increases the stroke volume until a certain point where the heart becomes over-distended and the stroke volume decreases. Thus, the idea of fluid resuscitation is to increase the venous return and preload and in turn increasing stroke volume and cardiac output.

31.2.1 Fluid Responsiveness

The term "fluid responder" is rooted in the frank-Starling mechanism and is used when a patient responds to a fluid challenge with an increase in stroke volume and/or cardiac output – Usually a 10–15% increase. Conversely, if the stroke volume/cardiac output does not increase, the term "nonresponder" is used. The fluid challenge can either be performed by administering a fixed amount of intravenous fluid or by mobilizing venous blood by a passive leg raising test [3]. Numerous invasive and noninvasive techniques have been proposed to assess stroke volume/cardiac output. Importantly, regardless of the validity of

the technique used, a "positive" fluid response does not necessarily infer that the patient will benefit from fluid administration – Only that the stroke volume/cardiac output will increase.

31.2.2 Adverse Effects

All medical interventions are associated with potential beneficial effects and potential adverse effects; intravenous fluids are no exception. Increased fluid balance has been associated with worse outcome in several observational studies [4–6]. Organ oedema impeding diffusion of oxygen into the tissue including – but not restricted to – the lungs are likely to contribute to these findings. High fluid input also increases the risk of electrolyte derangements, especially in case of acute kidney injury (AKI) with impaired excretion. Hypernatraemia is not uncommon following high-volume fluid administration, and restoring plasma sodium to acceptable values in presence of AKI represents a substantial challenge for clinicians. Despite the long history of using intravenous fluids, there may also be potential adverse effects that are not yet fully understood. The FEAST randomized clinical trial was stopped early due to increased mortality in febrile children with impaired circulation receiving either a saline bolus or an albumin bolus as compared with those receiving no fluid bolus [7]. A subsequent analysis of the observed increase in mortality suggested cardiovascular collapse rather than respiratory failure to be the driving cause of death indicating that the physiology of fluid resuscitation is not yet fully understood by the medical community [8].

31.3 When to Administer Fluids?

The decision on whether to administer intravenous fluids is a perpetual challenge for clinicians and is still a matter of discussion. Unfortunately, the available evidence do not allow for clear and easy-to-apply recommendations. Two seemingly simple clinical questions are important to answer to inform decision-making.

1. Do we have to intervene?
2. If so, is fluid likely beneficial?

■ Do we have to intervene?

Whether or not to intervene on circulatory comprise is in some cases obvious (e.g. septic shock with mean arterial pressure (MAP) 40 mmHg, heart rate 150 beats/min, lactate 10 mmol/l) but in many cases less clear (e.g. sepsis with MAP 62 mmHg, heart rate 110 beats/min, lactate 1,9 mmol/l). To inform the decision on whether to intervene, doing a thorough clinical exam and gathering available haemodynamic measurements are needed (◘ Fig. 31.1). Markers of hypoperfusion such as lactate and mottling are likely to be superior to surrogate markers such as heart rate, blood pressure and, especially in sepsis, urinary output, because they are suggestive of a circulation unable to fulfil the supply/demand of the organs. Advanced invasive haemodynamic monitoring using pulmonary artery catheter (PAC) has not suggested benefit compared to less invasive monitoring [9]. Accordingly, observational studies have shown that the majority of clinicians use simple markers rather than advanced haemodynamic measurements when assessing indication for fluid resuscitation – the most frequent being hypotension/high-dose vasopressor, oli-

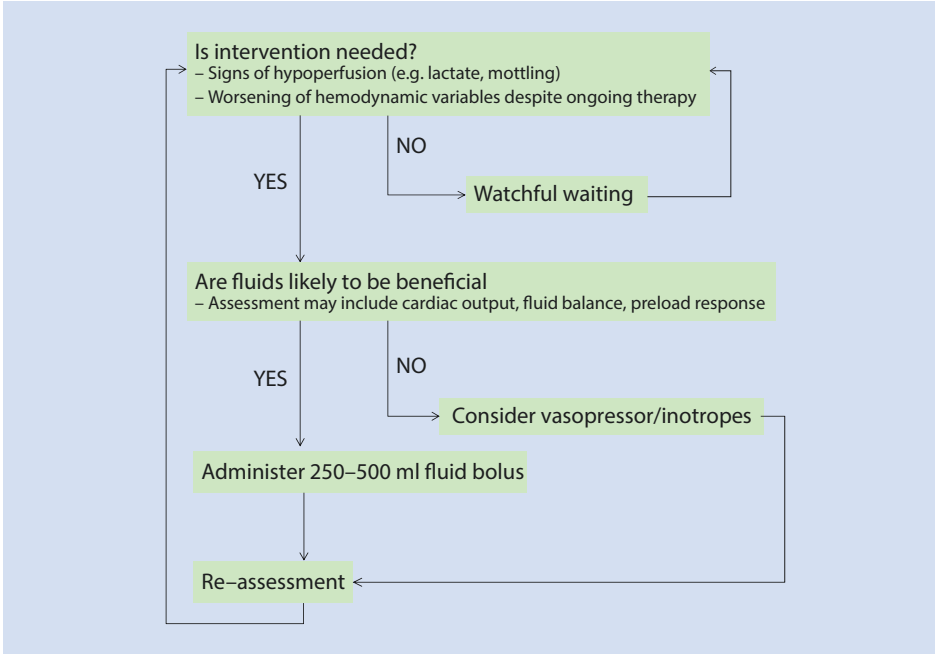

Fig. 31.1 Flow chart for clinicians assessing patients with haemodynamic compromise

guria and high plasma lactate [10, 11]. Also, simple clinical exam findings such as mottling and capillary refill time have been associated with increased mortality [12, 13]; however, association with worse outcome does not infer that intervening will benefit patients, and trials assessing benefit vs. harm with interventions on these markers of haemodynamic compromise are lacking.

If so, is fluid likely beneficial?

Facing a patient with haemodynamic compromise, clinicians are basically presented with three options: fluid administration, vasopressor/inotropic therapy or watchful waiting. If watchful waiting is not deemed pertinent (see above), then an assessment of whether fluid is likely to be beneficial is needed (Fig. 31.1). Since the potential benefit of fluid resuscitation is to increase cardiac output, first clinicians must estimate whether cardiac output/stroke volume is insufficient. The clinical gold standard for measuring cardiac output is using invasive thermodilution, but the routine use of this technique has not been shown to improve outcome [14, 15]. Less invasive markers of cardiac output have been suggested, including pulse contour analysis and echocardiography [16, 17], none of which have been sufficiently validated in shocked patients. Simple markers such as central venous oxygen saturation [18], temperature gradients on the extremities or temperature of the great toe may be easy and readily available alternatives [19].

If an increase in cardiac output is deemed indicated, an assessment whether fluid resuscitation is likely to do so is needed. Several advanced techniques of assessing fluid responsiveness have been proposed with and without administering fluids, but both precise and accurate less invasive methods that may be used in the majority of patients have

Table 31.1 Ranking of clinical variables favouring and opposing fluid resuscitation, respectively

	Favours fluid resuscitation	Oppose fluid resuscitation
Strong	Documented fluid loss	Pulmonary oedema
		No effect by a previous fluid bolus
Moderate	Mottling	
	Low $ScvO_2$/SvO_2	Peripheral oedemas
	Low cardiac output	Known cardiac failure
	Elongated capillary refill time	Negative preload response
	High plasma lactate, e.g. >4 mmol/l	Established AKI with low urinary output
	Temperature gradients on arms and legs	
Weak	Low CVP	High CVP
	Low MAP	
	High heart rate	
	Low urinary output	
	Higher vasopressor dose	
	Positive preload response	

Abbreviations: *$ScvO_2$* central venous oxygen saturation, *SvO_2* mixed venous oxygen saturation, *CVP* central venous pressure, *MAP* mean arterial pressure

not yet been found. The passive leg raising test has shown promising predictive values for fluid response but needs an estimate of changes in stroke volume to assess fluid response [20]. A meticulous fluid balance history with in- and outputs may provide important information along a clinical examination. A high positive fluid balance, considerable peripheral oedemas and established AKI with low urinary output should be cause for concern for further fluid input (Table 31.1). On the other hand, a low fluid balance and documented fluid losses from gut or drains should advocate fluid administration. Fluid resuscitation aimed at increasing central venous pressure (CVP) has previously been promoted by international guidelines [21], but the predictive value of CVP for fluid response is low, and fluid administration aiming at increasing CVP should no longer be used as standard practice [22].

If a decision to administer fluid is taken, it is of paramount importance to reassess the patient after the administration. In order to allow a meaningful reassessment, the fluid administration can be performed with a fixed amount (e.g. 250–500 ml) bolus administration. The most important observations in this regard are the values/observations that led to the fluid administration, but signs of adverse effects such as worsening respiratory function should be assessed and plasma electrolyte concentrations monitored regularly.

31.4 Effects of Fluid Resuscitation

Knowledge on the balance between benefits and harms with a medical intervention is necessary in order to provide recommendation for its use. Patient-important outcomes such as survival and quality of life are of special interest, because they inherently assess the balance between beneficial effects and harmful effects. Results from randomized trials on fluid volumes are presently limited. A recent meta-analysis of fluid volumes in ARDS and sepsis included only 11 trials, and the results were therefore imprecise due to the limited sample [23]. Although the point estimate for mortality favoured fluid restriction, the results were not statistically significant. Fluid restriction was associated with reduced use of mechanical ventilation, but this result was largely driven by the FACTT trial done in patients with acute lung injury [14]. Other potential harm has been suggested. Fluid bolus in African children with impaired perfusion was associated with increased mortality compared with no bolus [7], and in a small trial of patients with septic shock, a restrictive fluid resuscitation strategy was associated with less AKI compared to standard care [24].

In case of fluid resuscitation, the haemodynamic effects are often measured immediately following administration, but the adverse effects may accumulate during a longer period of time. Traditionally, the term fluid responder is used when the patient has an immediate response to fluids (<30 min), but the sustained effect is less studied, and suggestions on a transient effect have been reported in fluid responders where the initial increase in cardiac output following a fluid bolus returned to baseline within 90 minutes [25]. In concordance with this, in a post hoc analysis of the CLASSIC randomized trial, no apparent effects of increased fluid resuscitation volume were observed on urinary output, vasopressor dose or plasma lactate levels in patients with septic shock [24]. Thus, sustained haemodynamic effects have not been established, and repeated episodes of fluid resuscitation following a "positive" fluid challenge may carry the risk of longer-term adverse effects.

31.4.1 Fluid Resuscitation and AKI

Low urinary output is one of the most frequently reported indications for fluid resuscitation, but there are limited data to support this practice. The rationale for this practice is likely that low urinary output is interpreted as prerenal AKI caused by decreased blood flow to the kidneys. This notion may be an oversimplification, especially in case of sepsis where AKI has been associated with increased renal blood flow [26–28]. Albeit not strong evidence, there are data to suggest that fluid resuscitation may aggravate rather mitigate AKI [23, 24, 29]. If fluid resuscitation is administered due to low urinary output, special vigilance to the response is pertinent. In the case of a modest response in urinary output to fluid resuscitation, it may take several days to excrete the additional fluid without further interventions.

31.5 Choosing Type of Fluid

Choosing type of fluid is another intensely discussed topic when it comes to fluid resuscitation. Basically the choice stands between crystalloids, either saline or buffered salt solutions, and colloids, either human albumin or synthetic colloids. Synthetic colloids,

with hydroxyethyl starches being the most studied, have been associated with increased mortality and use of renal replacement therapy and should not be used [30–32]. Human albumin solutions appear safe and have a potential volume-reducing effect of around a factor 1.3 compared to crystalloids, but firm evidence of benefit has not been shown, and albumin is an expensive and limited resource [33, 34].

Isotonic saline has been used for decades but has been increasingly replaced by buffered salt solutions such as Ringer's lactate/acetate [35]. Use of chloride-rich solutions such as saline has been associated with AKI [36], but firm evidence on causality is lacking. Buffered salt solutions, the euphemism "balanced crystalloids" often used, are crystalloids which are buffered with anions like lactate, acetate, gluconate and/or malate to lower the chloride content as compared to saline. The effects of these nonphysiological concentrations of anions are currently unknown. Of note, the buffered salt solutions often contain lower concentrations of sodium (around 130 mmol/l), which may reduce patient sodium levels compared to saline [37]. On the other hand, there is still a risk of hypernatraemia with the buffered solutions if the renal excretion of sodium is lower than the infused quantity. The best available evidence on saline vs. buffered salt solutions is the results of the SPLIT trial. In this cluster randomized trial, ICU patients with relatively low illness severity were allocated to either saline or a buffered salt solution. No differences were observed between the two groups in the main outcomes including marker of AKI and mortality [38]. Large randomized trials comparing buffered salt solutions and saline are currently ongoing; until the results of these are reported, both saline and buffered salt solutions are viable choices. Changes in plasma sodium and base excess should, however, be observed during the care because of risks of dysnatremia and hyperchloremic acidosis with buffered solutions and saline, respectively [37].

Conclusions

Fluid resuscitation has been one of the most frequent interventions performed in critical care for decades, and most types of fluids are cheap and readily available, but the effects including haemodynamic effects beyond an initial response are not yet fully understood. Moreover, harm has been suggested with higher fluid inputs within the range of standard practice. Initiation and especially continued fluid resuscitation should be based on thorough clinical exam and assessment of available haemodynamic values and vigilant monitoring of signs of adverse effects to fluids.

Take-Home Messages

- Fluids are drugs, and administration of fluids is only indicated when the potential beneficial effects are judged to outweigh the potential harmful effects. In order to make this assessment a careful medical history, clinical exam and evaluation of available haemodynamic variables are needed.
- In case of haemodynamic compromise, two clinical questions should be answered [1]. Is any intervention needed? And [2] if yes, are fluids likely to be beneficial?
- Following fluid administration, a reassessment is pivotal in order to assess the potential need for further fluid administration.

31.6 Questions

1. A test finding a patient to be a fluid responder tells us that the patient needs fluids.
2. Buffered crystalloid solutions may lower plasma sodium levels.
3. The first documented use of intravenous fluid administration was aimed at maximizing cardiac output.
4. The frank-Starling mechanism states that a larger end-diastolic volume increases the stroke volume until a certain point.
5. The most commonly used indication for fluid administration is a low cardiac output measurement.
6. Organ failure due to increased diffusion path due to organ oedema is a potential risk with higher fluid balance.
7. Fluid resuscitation based on advanced haemodynamic monitoring has been shown to benefit intensive care patients compared to simple haemodynamic variables.
8. The temperature gradient on the extremities may be used as a surrogate for cardiac output.
9. Central venous pressure has high predicted value for fluid response.
10. Slow continuous fluid administration will improve the ability to assess the haemodynamic effects compared to bolus therapy.
11. Infusion of large volumes of buffered salt solutions with a sodium content of 130 mmol/l may cause hypernatraemia (plasma sodium >145 mmol/litre).
12. Infusion of 1 litre of colloid solution has the same potency as 3 litres of crystalloids.
13. Increased mean arterial pressure following a passive leg raising test is a strong predictor of fluid responsiveness.
14. Buffered salt solutions such as Ringer's solutions contain bicarbonate anions mimicking plasma values.
15. A plasma lactate >4 mmol/L suggests impaired perfusion.
16. Pulse contour analysis is the gold standard for measuring cardiac output.
17. Reassessment following fluid resuscitation is important.
18. Low urinary output is always due to decreased renal blood flow.

19. Watchful waiting can be a valid choice instead of intervening with fluids and/or vasopressors.

20. Synthetic colloids may cause kidney failure.

31.7 Answers

1. N
2. Y
3. N
4. Y
5. N
6. Y
7. N
8. Y
9. N
10. N
11. Y
12. N
13. N
14. N
15. Y
16. N
17. Y
18. N
19. Y
20. Y

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