Review article

OPTIMAL PERIOPERATIVE FLUID MANAGEMENT: WHAT IS THE STRATEGY?

Dragana Unić-Stojanović

¹School of Medicine, University of Belgrade, Serbia²Department of Anesthesiology, Cardiovascular Institute Dedinje Belgrade, Serbia

Perioperative Fluid Management

Abstract

Fluid therapy is a core concept in the management of perioperative patients for maintenance of intravascular volume and organ perfusion. The aim of perioperative fluid therapy is to keep patients at all times in the optimal volume loading, due to both hypovolemia and volume overload may cause organ dysfunction. Intravenous fluid is a drug and because of that, timing and dose is important. „Liberal“ or „restrictive“ strategies and crystalloid or colloid solutions are the unsolved controversies. The term „restriction“ is commonly interpreted to imply hypovolemia, whereas it may simply represent avoidance of the fluid excess seen in the „liberal“ group. The aim of goal-directed fluid therapy is to guide fluid and pharmacological (inotrope) therapy, by using flow-directed hemodynamic parameters, to maintain adequate tissue blood flow, circulating volume, and oxygen delivery. In order to minimize the complications related to fluid administration, preventive strategies and prompt treatments are of utmost importance.

Key words: surgery; fluid management; liberal; restrictive; crystalloid; colloid

Sažetak

Terapija tečnostima je osnova perioperativnog lečenja pacijenata i održavanja adekvatne organske perfuzije. Cilj perioperativne terapije tečnostima je održavanje optimalnog volumnog statusa bolesnika, s obzirom da i hipovolemija i hipervolemija mogu uzrokovati poremećaj funkcije organa. Intravenska tečnost je lek i zbog toga su od značaja vreme primene i primenjena doza. „Liberalna“ ili „restriktivna“ strategija, kristaloidni ili koloidni rastvori su i dalje kontroverzne teme. Termin „restrikcija“ se koristi za označavanje hipovolemije, mada jednostavno podrazumeva izbegavanje primene previše tečnosti koje se može videti u „liberalnom“ pristupu. U ciljano vođenoj terapiji (goal-directed therapy) u osnovi je da se terapija tečnostima i inotropnim lekovima primeni na osnovu volumetrijskih hemodinamskih parametara, kako bi se održali adekvatan krvni protok, cirkulišući volumen i isporuka kiseonika tkivima i organima. U cilju smanjenja komplikacija povezanih sa primenom tečnosti, od najvećeg značaja su primena preventivnih mera i promptna terapija nastalih poremećaja.

Ključne reči: hirurgija; nadoknada tečnosti; liberalni pristup; restriktivni pristup; kristaloidni rastvori; koloidni rastvori

Introduction

Optimal hemodynamic management is important to reduce the incidence and impact of complications, although the management of perioperative fluids has been a persistent controversy among anesthesiologists, surgeons, and intensivists.¹

Hypervolemia and hypovolemia

The aims of perioperative fluid therapy are to maintain an adequate circulating volume with adequate end-organ perfusion and oxygen delivery to the tissues.² Almost all clinicians agree that both, hypovolemia and volume overload cause organ

dysfunction due to inadequate oxygen delivery and increase the morbidity and mortality of patients.³ The relationship between risk and volume loading is a U-shaped curve (Fig. 1), with perioperative risk (on the y-axis) decreasing with increasing volume load (on the x-axis), up to a critical point.⁴ Beyond this point, further volume loading would result in a rapid increase in the risk of morbidity and mortality.⁴

Hypovolemia, because of an inadequate hydration, increases the risk of acute kidney injury (AKI), and organ dysfunction, associated with adverse outcomes.^{5,6}

Remarkably and perhaps not as readily acknowledged, fluid overload may be associated with

cerebral and intestinal edema, with resultant complications and the development of multiple organ dysfunction syndrome with adverse outcomes.⁷ Actually, fluid overload increases the release of natriuretic peptides, which may damage the endothelial glycocalyx, and this leads to a rapid shift of intravascular fluid into the interstitial space, leading to a marked increase in extra vascular lung water index (EVLW) and tissue edema.⁸ Also, volume overload can lead to acute cardiac decompensation, especially in patients with a preoperative reduced left ventricular function or postoperative myocardial stunning.⁹ Fluid overload may increase cardiac demands and pressure in the venous circulation with fluid redistribution from the intravascular space into the interstitial one.³

More importantly, the only reason for fluid administration in patients is to increase their stroke volume (SV); and if this does not happen, the fluid has no beneficial purpose and may be harmful¹⁰. It is interesting that only 50% of hemodynamically unstable patients (in the operating theatre (OT), intensive unit care (ICU), or emergency department (ED)) are volume responders¹¹. But, being a fluid responder is not equal to being hypovolemic. It is also important to emphasize that even if a patient is predicted to be fluid responsive, this does not imply a fluid bolus should necessarily be given. This decision should be weighed against markers of hypoperfusion and potential deleterious effects of the fluid itself¹².

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„Liberal“ and „restrictive“ fluid management

Recent study results suggest that fluids should be viewed as drugs that should be prescribed carefully, with attention to type, dose, and toxicity in order to maximize efficacy and minimize toxicity^{13,14}. Fluid optimization is of paramount importance during the first postoperative hours.¹⁵ The application of the right kind of fluid therapy at the right time in the right amount is needed for optimal patient outcome¹⁶. Late circulatory optimization after the establishment of organ failure is probably ineffective and may be harmful¹⁷.

In the past, the concept of the intraoperative

„third space“ fluid loss, insensible perspiration, urinary output, leads to aggressive „liberal“ fluid replacement of the insensible loss, with infusion of a large volume of fluids¹⁸. But, there is evidence that shows improved outcomes with the application of „restrictive“ fluid administration¹⁹. It is important that making comparison between restrictive or liberal fluid administration in the surgical population is difficult, because there is no clear definition of restrictive or liberal fluid management. Then, what is regarded restrictive at one center is often considered liberal at another²⁰. Bundgaard-Nielsen et al¹⁹. published a review, including seven randomized trials, of restrictive vs. liberal fluid therapy, and its effect on postoperative outcome. Outcomes were different among studies, with controversial results¹⁹.

In the cardiac surgery patients, the use of cardiopulmonary bypass (CPB) is associated with hemodilution and increasing in capillary permeability, that should be taken into account when one considers the amount of fluid administration^{5,6}. Vretzakis et al²¹. conducted randomized study (restrictive or liberal fluid regimen) that included 172 cardiac surgery patients and showed that fluid restriction was associated with a lower risk of blood transfusion (62 vs. 82%, $P < 0.04$)²¹. Another study, which included 1280 consecutive patients underwent cardiac surgery (CABG), observed the increased blood transfusion and length of hospital stay in patients with intraoperative volume overload²².

Although, most studies found that a positive fluid balance was a risk factor, in patients with acute respiratory distress syndrome and septic shock, higher initial intravenous fluid volumes followed by a negative fluid balance for 2 consecutive days within the first 7 days of shock resulted in a lower mortality rate²³. Because of that, it is more important to focus on timing and the precise volume of fluid administration based on targets for correcting hypovolemia, rather than relying on „liberal“ or „restrictive“ terms.

Goal-directed fluid therapy (GDT)

GDT in the perioperative period involves measurement of an individual patient's oxygen flux or reliable surrogates and interventions directed to augment flow. The key component in activating the systemic inflammatory response in postsurgical patients is a tissue hypoxia that may not mani-

fest clinically for days. The aim of GDT is to guide fluid and pharmacological (inotrope) therapy, by using flow-directed hemodynamic parameters, to maintain adequate tissue blood flow, circulating volume, and oxygen delivery. This is an individualized approach to fluid management²⁴⁻²⁷, offering additional parameters to determine optimal level of venous return related to individual heart requires. Goal-directed therapy (GDT) in the perioperative period has been demonstrated to save lives, decrease complications, and save costs^{28,29}. However, despite overwhelming evidence to support the practice, its adoption by the anesthesia/perioperative care community is generally poor.

Shoemaker et al. first published the positive effect of GDT based on pulmonary artery catheter (PAC)-derived hemodynamic goals on outcome in noncardiac high-risk patients undergoing surgery²⁴.

There are several studies to date that specifically address the effectiveness of GDT in cardiac surgery. Polonen and al²⁵. included 403 elective cardiac surgical patients presenting for coronary revascularization randomized in two groups: mixed venous oxygen saturation SvO₂-guided therapy group (aims are central venous oxygen saturation ScvO₂ > 70% and Lactate ≤ 2 mmol/litre up to 8 h) and standard care group. They published that SvO₂-guided therapy in these patients\ improves outcome in regard to morbidity and hospital length of stay. This study showed that mortality between the groups was similar, however there was a trend towards a reduction in the protocol patients at 28 days²⁵. It is interesting to note that only about half the protocol patients (57.1%) in this study achieved the predetermined goals. But, despite a lack of directed therapy in the control group, significant number of these patients (42.1%) achieved the same goals. Patients in whom targets were achieved had better outcomes. Also, patients who achieved these goals in both groups tended to be younger, had a better ejection fraction (EF), and rarely had diabetes.

In a randomized controlled trial that included 174 postoperative cardiothoracic patients, McKendry et al²⁷. showed that GDT protocol guided by esophageal Doppler flowmetry with maintaining stroke index (SVI) more than 35 ml/m² (with optimizing the SVI by infusion of 200 mL colloid boluses and, if this is unsuccessful, vasodilator or inotropic therapy was used) significantly reduces hospital stay (from a median of 9 to a median of 7 days) in comparison to conventional fluid man-

agement. There was also a trend towards a reduction in ICU length of stay (LOS) and a reduction in major complications (17% versus 26%). Similar to the previous study, achieving the goals in GDT was difficult and only in 61% of protocol patients, the target – SVI > 35 ml/m² was achieved²⁷.

Meta-analysis of 5 randomized trials with 694 cardiac surgery patients, showed significantly reduced incidence of the cardiac and noncardiac complications with the use of GDT, without any improvement in mortality with GDT³⁰. This may be related to the relatively low mortality in cardiac surgery despite the high-risk nature of the procedures and the severity of illness, and to the relatively small number of studies and patients included in this meta-analysis³⁰.

The study targeted global end-diastolic volume index (GEDVI) above 640 mL/m², CI above 2.5 L/min/m², and mean arterial pressure (MAP) above 70 mmHg showed that guiding therapy by GEDVI leads to reduced need for vasopressors, catecholamines, ICU therapy and shorter mechanical ventilation in patients undergoing cardiac surgery²⁶. GDT is associated with decreased morbidity although there is no reduction in postoperative mortality in cardiac patients. This fact is enough to justify applying algorithms to optimize flow and/or oxygen delivery in major surgery patients. Also, GDT simply may be a method of choice, on basis of using flow-and/or oxygen delivery data, to determine the safe limits of fluid restriction.

Actually, „blind“ fluid restriction approach is associated with risk of tissue hypoperfusion, even in patients with poor cardiac function. There is no single Frank-Starling curve that describes how cardiac output (CO) varies in relation to preload, on which a ventricle operates. (Fig. 2) Also, the contractile state of the heart can vary hour to hour. Although the Starling curve in heart failure is flatter, it is still a curve. Even volume may improve contraction of the compromised myocardium. Hypo- or hypervolemia is difficult to be predicted from conventional parameters and cannot be assumed based on preoperative fasting, theoretic „third-spacing“, or estimated blood loss³¹. Because of that, besides the extra fluid associated with CPB, these patients may be hypovolemic. According to the Frank-Starling mechanism, the heart increases its force of contraction in response to increases in preload, up to a point. After this point, additional fluid does not enhance SV. Heart failure is associated with „flattening“ of the Starling curve,

causing the point of potential complications to be reached at a lower preload³². For this reason, as well as extra fluid associated with CPB, there is a trend toward restrict fluids in these cardiac surgical patients. The using a flow-based parameter to determine the hemodynamic status in cardiac surgical patients allows restriction background fluids administration and volume resuscitation based on flow-related parameters, with reduced incidence of postoperative complications.

Importance of fluid types

A paradigm exists that four times as much crystalloid compared to colloid is needed for the same volume effect³³. It is, also, shown that the duration of distribution phase of isotonic or near-isotonic crystalloids is about 25–30 minutes and increase in plasma volume after 30 min of infusion is 50–75%³³. A relatively long period of time is required for crystalloid fluids to distribute, so slow infusions are more effective than bolus administration³⁴. Comparison of fluid therapy with different solutions: a balanced salt solution vs. normal saline, showed significantly lower mortality and complications with using of balanced salt solution in observational clinical study³⁵. A significant decrease in the incidence of acute kidney injury (AKI) and the need for renal replacement therapy (RRT) were observed, when hyperchloremic solutions including normal saline (NS) were avoided³⁶.

There were widespread clinical application of semisynthetic colloids in anesthesiology and critical care³⁷. But, there are serious concerns about the clinical safety and efficacy of semisynthetic colloids (HES) solutions in comparison to crystalloid alternatives such as normal saline or Ringer's lactate. Two large trials (CHEST and 6S) examining the use of hydroxyethyl starch (HES) in the ICU have shown no benefit from the use of the more expensive colloids solutions in the ICU and that HES is associated with harm^{38,39}. The Scandinavian Starch for Severe Sepsis/Septic Shock (6S) trial, RCT involving 800 patients with severe sepsis and septic shock, showed that the use of 6% HES (130/0.42), compared with acetated Ringer's solution, is associated with increased incidence of AKI, increased need for renal replacement therapy (RRT), increased overall mortality at 30 days (by 8%) and significantly increased mortality at 90 days³⁸. The CHEST trial (Crystalloid versus Hydroxy-Ethyl Starch Trial), an RCT involving 7000

patients with severe sepsis showed that the use of 6% HES (130/0.4), compared with NS, was associated with lower incidence of AKI, and was not associated with a significant difference in mortality at 90 days³⁹. However, this trial found that use of HES was associated with increased levels of serum creatinine in patients with higher risk for AKI. Both the 6S trial and the CHEST trial found a significant increase in the need for RRT associated with HES administration, and no significant difference in short term hemodynamic resuscitation targets between HES and crystalloids^{38,39}. Possible criticisms of the both studies, the 6S and CHEST trials, are following: these studies are not optimally designed to assess fluid resuscitation, because patients were included after admission to the ICU, when the requirements for fluid resuscitation are often less than those for patients in the operating room or the emergency department⁴⁰. Also, in the 6S trial, there was the lack of hemodynamic monitoring and goal-directed therapy in the protocol design, leading to potential volume overload, or hemodi-

Figure 1. Fluid load versus complications. The aim is to keep patients at all times in the optimal zone. (Modified according to Reference 4)

lution and the association with blood transfusion of patients thus affecting outcomes⁴⁰.

Large meta-analysis showed that HES for resuscitation in critically ill patients significantly increased incidence of mortality, renal failure and risk of renal replacement therapy⁴¹.

A prospective observational cohort study of 6478 cardiac surgery patients with using CPB tested different fluid therapy approaches (colloid vs. crystalloid vs. gelatin). The fluid intake was higher in the crystalloid group during the first 20h only. More importantly, perioperative administration of colloids was associated with a high risk of RRT, and

was no more effective than crystalloid regimen⁴².

Navickis et al⁴³, recently published a meta-analysis, investigating the coagulation effects of HES solutions, that its use increased bleeding, reoperation for

Figure 1. Frank-Starling curves of ventricular contractility

bleeding and blood product use after CPB, and these effects were similar between solutions of various molecular weights and molar substitutions⁴³.

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) concluded that, until further evidence is available, because of the risk of AKI and mortality, the benefits of HES solutions no longer outweighed their risks and HES must no longer be used in patients with critical illness, burn injuries or sepsis^{44,45}. HES is contra-indicated for use in and patients with renal impairment or needing RRT, and patients with severe coagulopathy, use of HES must be discontinued at the first sign of coagulopathy or AKI. HES should only be used for rapid volume replacement due to acute blood loss, guided by continuous hemodynamic monitoring, at the lowest effective dose for the shortest period of time, when crystalloids alone are not considered sufficient³⁴.

The United States Food and Drug Administration (FDA) and Health Canada did not withdraw HES solutions completely but recommended they should not be used in patients with pre-existing renal failure and in critically ill patients⁴⁶. This decision was influenced by several studies including metaanalysis published by Gillies, that reported no difference between two groups of 6% HES and alternative intravenous fluids in hospital mortality, the requirement for RRT or AKI in patients un-

dergoing surgery⁴⁷. Systematic review, showed no association between tetrastarch use and blood loss, increased incidence of renal impairment or failure, or mortality if administered during and/or immediately before surgery⁴⁸. Also, Martin et al. showed there is no association between the administration of HES and the incidence of AKI in patients undergoing surgery⁴⁹.

Human albumin 4–5% in saline is a natural colloid for volume resuscitation. The Saline vs Albumin Fluid Evaluation (SAFE) study showed no significant benefits in terms of mortality rate at 28 days or development of new organ failure⁵⁰, but in patients with severe sepsis, there was an association between decreased mortality rate at 28 days and albumin administration⁵¹. In 2013, a Cochrane review found no evidence that colloid resuscitation (including albumin) reduces the risk of morbidity or mortality compared with crystalloid resuscitation in heterogeneous critically ill patients⁵². Also, there is no clear benefit of albumin solution in specific subgroups such as patients with severe sepsis although it was shown equivalent hemodynamic effects and clinical outcomes of albumin and crystalloid⁵³.

Conclusion

The management of fluid therapy significantly may impact organs' functions and postoperative outcomes and because of that it is important to achieve the optimal balance between hypovolemia and fluid overload in these patients. Fluid management strategy has to be tailored according to cardiac disease, dependent on cardio-vascular compliance and guided by appropriate monitoring. Intravenous fluid is a drug and because of that, timing and dose is important. Also, it should be only given when its administration is expected to produce some benefit. Goal-directed therapy can optimize perioperative fluid resuscitation, and perhaps limit excessive fluid administration, which has a benefit in morbidity but no proven benefit in mortality.

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