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WHEN IN DOUBT, GIVE FLUIDS AND KILL YOUR PATIENT

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ABSTRACT The art of giving the correct amount of intravenous fluids is a very important part of anesthetic management. Intraoperative liberal fluid management during surgery, particularly during major abdominal surgery, has been the golden standard until the beginning of the 21st century. Recent studies and insights have shifted our fluid management towards a more conservative regimen. However, due to conflicting conclusions, heterogeneous studies and a variety of existing fluids, there is still no consensus about the optimal amount and composition to administer. This editorial will give a historical overview on fluid therapy in major abdominal surgery and the currently available evidence. The daily practice, of course, raises a number of questions, and the important ones out of these will be discussed.

KEYWORDS : Fluid therapy; Abdominal surgery; Cardiac output, Non-invasive; Crystalloids; Colloids

Many of us have been trained in the last part of the twentieth century with the idea of liberal fluid therapy. Patients needed to be hyperhydrated to maintain hemodynamic stability. Wet and exudative intestines were considered a sign of a well-hydrated patient and were considered good practice. Other dogmas and paradigms at that time were to impose long fasting hours from after midnight preoperative up to six hours postoperatively. Preoperative enemas were common and were leading to electrolytes depletion. Fasting hours were compensated with fluids up to 2 ml/kg/h of fasting, usually given within the first hours of surgery. The use of this regimen was supposed to reduce the symptoms related to the dehydration and improve patient outcome.

At the induction of anesthesia, it was a custom to give even more fluids, mostly colloids, to prevent hypotension. During open abdominal surgery, golden standard was a liberal fluid management: up to 12 milliliters per kilograms per hour to compensate the evaporation of fluid from the exposed organs. The goal was supra-optimization of our patients, without thinking of the consequences. Studies at the time concluded that a liberal fluid management with both colloids and crystalloids was safe and that a postoperative fluid overloading did not cause a significant problem.[1]

From the early 90's, with the widespread use of propofol as a hypnotic induction agent, the systematic use of ephedrine or phenylephrine to prevent or treat hypotension post induction was becoming more and more common. The extended perioperative use of epidural analgesia during major abdominal surgery was also a contributing factor leading to hypotension, which of course, at that time, had to be compensated with more fluids to prevent the use of vasopressors.[2] The concepts of volume therapy were based on the relationship of preload and cardiac output described by the Frank Starling law, and the use of clinical parameters like blood pressure, heart rate and urine output. At that time, a small number of articles tried to alert us about the eventual devastating effects of fluid replacement overload. Only a few physicians were recognizing the iatrogenic threat of replacement of body fluids that were being based solely on the concepts of volumetric and caloric need.[3]

When we look at volumetric needs for the patient we have to go back to our basic physiology and its concepts like cardiac output (CO), stroke volume (SV), oxygen delivery (DO_2) and arterial oxygen content (CaO_2) and of course the Franck Starling's law. The latter made us understand that intravenous fluid administration with the goal to improve stroke volume will only be effective up to a certain point. When the non-responsive part of the curve is reached, more fluid administration will not contribute to a higher stroke volume but will increase the venous return and the end diastolic pressure until a point at which it can have negative effects on the hemodynamic stability and will bring the patient in danger. With basic monitoring, we only measure pressures without any precise idea of the flow. More state of the art monitoring systems can give us an idea of flow by calculating stroke volumes or a cardiac index; however, whether we should base our fluid management solely on this new measurement remains to be determined. We do not know yet which endpoints to target and what exact goals we want to achieve.

Twenty-five years later, we have dramatically changed the way on how we think about the subject. After so many pro's and con's debates about intravenous fluid therapy, more knowledge is now available. Surgeons became aware that fluid overload prolonged recovery time and gave more surgical complications. It resulted in several trials and clinical approaches for intravenous fluid management during abdominal surgery. These trials compared liberal versus restrictive fluid therapy and tried to investigate the value of available clinical parameters. One of these parameters was measurement of pulse variations as a method of non-invasive cardiac output and stroke volume measurements. It is important to distinguish fluid responsiveness from optimal fluid resuscitation; the latter of course being optimized tissue oxygenation. A healthy human being is fluid responsive without needing fluids: could this be the foundation of liberal fluid therapy?

In 2001 the first step towards goal directed fluid therapy (GFDT) was set with the study Early Goal-Directed Therapy (EGDT) in septic patients.[4] The results were disappointing as compared to usual modern care and did not appear to improve outcomes but resulted in greater expense. It was abandoned in 2015.[5] The most important thing at this point was a new concept and an increasing interest for fluid management during surgery. Plenty of studies would follow trying to optimize the perioperative fluid administration to ameliorate patient outcome: Goal Directed Fluid Therapy (GDFT). The target is not the intravascular volume, but tissue oxygen requirements and cardiac performance. GDFT in elective abdominal surgery is a method to evaluate whether the patient is still responsive to the administered fluids. If the patient is unresponsive to fluid, adding inotropes or vasopressor agents might be appropriate. The general conclusions of these GFDT trials were that measuring flow, to optimize cardiac output and oxygen delivery, should be the best way to manage perioperative fluid therapy.[6]

Do we really have to forget arterial blood pressure and central venous pressure and let us only be guided by cardiac output and systemic vascular resistances? Will a non-negligible marketing aspect influence our thoughts? We are indeed giving less and less fluid, but this restrictive fluid administration results in continuous infusions of vasopressors (noradrenaline, phenylephrine) with dramatically increasing dosages. We were practicing the opposite of our fluid therapy in the eighties and nineties: from a “ultra-wet” to a “ultra-dry” one. Is noninvasive cardiac output monitor the best way to determine fluid regimen during major abdominal surgery?

In 2014, the results of the POEMAS Study (Peri Operative goal-directed thErapy in Major Abdominal Surgery) were published: “a perioperative hemodynamic protocol guided by a noninvasive cardiac output monitor was not associated with a decrease in the incidence of overall complications or length of stay in major abdominal surgery.”[7] The comments in the same journal “Goal-directed therapy, time to move on?”[8] would mark the first step to new considerations about fluid

administration during abdominal surgery. The meta-analysis published by Pearse et al. in JAMA in 2014 found a positive effect of goal-directed fluid therapy, but the compared trials were so different that their conclusions are debatable due to heterogeneity of the included studies.[9]

In 2015 a major study about the association of fluid administration variability and outcome concluded that "high fluid utilization was associated with increased presence of postoperative ileus in both rectal and colon surgery patients. Low fluid utilization was also associated with worse outcomes."[10]

The arrival of ERAS (Enhanced Recovery After Surgery) protocols has been linked to a new view on fluid therapy. The goals of ERAS programs are to improve the outcomes of surgical patients using multimodal perioperative pathways and evidenced-based practices. The aim is to reduce surgical stress, to maintain postoperative physiological function, and to enhance mobilization after surgery. Is goal-directed fluid therapy compatible with ERAS? We are actually not so sure about this.[11] More studies may be needed to conclude.

The correlation between Surgical Site Infections (SSI) and fluid administration during abdominal surgery is also a major issue. Yuan et al. found a reduction of SSI's of 26% and patients went home 1.16 days earlier. Myles et al., in randomized trial including 3000 patients, found an increased rate of complications. The rates of surgical-site infection (16.5% vs. 13.6%, P=0.02) were higher in the restrictive fluid group, but the between-group difference was not significant after adjustment for multiple testing.[12,13]

Recently two important articles demonstrated the difficult balance between liberal and restrictive fluid therapy. Shin et al. analyzed a large database from 2007 – 2014 on fluid therapy in 92.094 patients undergoing non-cardiac surgery. They observed a U-shaped correlation with an increased rate of complications in patients receiving liberal or restrictive fluid therapy compared to moderate fluid therapy: "intraoperative fluid dosing at both the liberal and restrictive margins of observed practice is associated with increased morbidity, mortality, cost, and length of stay. "[14]Myles et al. in a large international trial including 3000 patients concluded: "Among patients that are at increased risk for complications during major abdominal surgery, a restrictive fluid regiment was not associated with a higher rate of disability-free survival than a liberal fluid regiment and was associated with a higher rate of acute kidney injury". [13]

In conclusion, we have been given during many years too much fluid to our patients, mixing crystalloids and colloids. At the beginning of the 21st century, we entered a period of fluid restriction with positive effects on patient outcome. Fluid restriction went extreme with use of increasing dosages of inotropes and vasopressors, with a certainly worse outcome. "Normovolemia seems to be the best with a modestly liberal fluid administration. Both hypovolemia and oliguria must be recognized and treated with fluids." The time has come for "finding the right balance".[15]

Concerning the types of fluids we administer, we should realize it still is a long never-ending debate. Until now, nobody has the right answer. Ideally, we would like to administrate fluids, which have a predictable and sustained effect, which are totally metabolized, their composition has to be close to the extra-cellular fluid, they can increase the intravascular volume, but not in the least, they have to be widely available and cheap.

We are replacing singular fluids and these fluids should not be seen as water but as IV drugs. Fluid replacement has to be in accordance to the patient needs: maintenance, replacement or resuscitation.

Crystalloids are considered as basic fluids. The supra physiological level of chloride in 0.9% NaCl (154 mmol/L compared to round 100 mmol/L in plasma) is associated with hyperchloremic acidosis and reduction of renal blood flow. Balanced solutions, with a lower osmolality, a lower chloride level and lower pH are preferred.

The choice colloids or crystalloids depends on the goal we want to reach. Known is that colloids are effective plasma expanders; they remain intravascular longer compared to crystalloids, which may result in increased edema formation.

In terms of morbidity or mortality, can we find any differences between colloids and crystalloids? The last Cochrane analysis concluded: "using colloids compared to crystalloids for fluid replacement probably makes little or no difference to the number of critically ill people who die. It may make little or no difference to the number of people who die if gelatins or crystalloids are used for fluid replacement."[16]

Within the colloids, there are gelatins, albumin and Hydroxyl-Ethyl Starch (HES) solutions. The prescription of HES is restricted to several specific situations and the list of contra-indication is long. The European Medicines Agency and the American Food and Drugs Administration give strict regulations regarding the use of HES solutions.[17,18]

Because Albumin is not meant for daily volume therapy, only gelatins are available as volume expander or plasma alternative. Gelatins should be actually only indicated in case of hemorrhagic shock or possibly to replace reasonable blood loss. Albumin is certainly interesting in septic shock and in elderly patients.

When blood transfusion is needed, trigger thresholds have to be respected. In 2018, patients should not receive blood transfusion based on a low hemoglobin due to iatrogenic dilutional anemia.

In conclusion, we have to admit that we still have not found the Holy Grail in the administration of intravenous fluids during major abdominal surgery. It is difficult to find the guide we need for our daily practice in all the diverse, sometimes contradictory publications. General advice is to individualize your therapy. Do not give fluids without analyzing the underlying problem. Try to find a balance between an optimal fluid therapy in combination with low dose vasopressor if needed. Although most of us will use physical parameters like blood pressure, heart rate, urine output and ventilation-induced plethysmographic variations, we have to realize that these are derived data and may not reflect volume status or fluid responsiveness. More studies are needed to give answers on all our questions.

Conflict of interest: Nil

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