REVIEW ARTICLE

Intraoperative Fluid Therapy for Major Surgeries: A Narrative Review

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Intraoperative fluid equilibrium is a decisive matter in perioperative anesthesia management, because most of evaluation studies consider intraoperative fluid administration as a major participating agent in improving or worsening patient outcomes after surgery and it revolves within the responsibility of an anesthesiologist. The understanding of fluid physiology in the human body, clinical features of available intravenous fluid, and nature of surgery indeed will contribute to the success plan of management. Maintaining of patients' physiological milieu by preserving normal extracellular volume, adequate tissue perfusion, and a balanced acid base condition are the main goals of intraoperative fluid infusion. This review was conducted to overview fundamental basics of fluid therapy during the intraoperative period. Due to the dearth of supporting data for appropriate volume and the available definitions of restrictive and liberal are diffident, the polemic about which particular method of volume expansion still exists. Colloid versus crystalloid controversy in surgical patients is still going on and this would again be encouraged to be a topic for many clinical trials in the future. The current findings' trend prefers guided and restricted intraoperative fluid therapy with isotonic balanced crystalloids because such fluids are cost effective and have fewer side effects than other fluids.

keywords: major surgery; intraoperative fluid therapy; liberal vs restrictive; intravenous fluids

Typical fluid for intraoperative replacement is still a controversy between anesthesiologists and researchers in this field. There is increasing data which confirm that fluid therapy may influence outcomes negatively [1-2]. Technical assessment of patients' hydration may help in determining the appropriate amount of compensation during the surgery [3]. Maintaining of the patient physiological situation by preserving normal extracellular volume, adequate tissue perfusion, and a balanced acid base condition is intended from fluid therapy during intraoperative phase. Liberal infusion during surgery has been reported with a huge number of complications such as cardiopulmonary and gut problems [4-5]. In one hand, a restrictive strategy currently is more accepted because patient's outcomes have been reported to improve with guided restrictive infusion [6]. On the other hand, each strategy of fluid therapy has its own potential hazards. Reduced tissue perfusion and multi organ failure are the common complications related to restrictive approach [4,7]. Postoperative complications were not limited to the amount given to the patient during the procedure, but the fluid type also has the most prominent role in improving or worsening outcomes [8-9]. Fluid administration during intraoperative period completely revolves under the responsibility of the anesthesiologist [10]. This review was conducted to provide an overview of fundamental basics of fluid therapy during the intraoperative period. Fluid therapy historically extends from many years ago with many changes; from copious fluids that were given, now returning to a more restricted view, the perfect fluid is still not achieved as the narrative has still developed [2].

Intraoperative Fluid Therapy for Major Intra-Abdominal Procedures:

Dehydration is commonly correlated with most surgical procedures in the abdominal cavity. During long major surgeries, which are generally implemented with general anesthesia, the body loses fluids in different ways. Urination, bleeding, insensible loss, and the compensatory motion of fluid loss between compartments (third space loss); are the most common ways; in addition to preoperative fasting and anesthesia [2,10]. The duration of abdominal surgery affects both the fluid balance and fluid administration [11]. Special algorithm has been commonly used to run the current intraoperative fluid therapy, which is based on that the lost fluids must be substituted by crystalloid solutions in formula of "ml/ (kg /h)". Depending on this algorithm, the range of fluids to be administered is 10– 15 ml/ (kg h) for patients in major abdominal surgeries. According to recent dependent studies, the replacement in liberal approach includes pre-operative deficits, blood loss, and dilatation of vessels that are caused by anesthetics, third space redistribution, and physiological maintenance [12-14]. But the basis of this formula was flawed according to some findings such as that the fasting does not have any effect on

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the blood volume, and the intraoperative replacement of third space loss has grown in controversy [13,15]. The definition of each strategy has not been agreed upon [16]. There is low evidence that the liberal approach improves outcomes after major abdominal procedures and increases oxygenation to tissues [17]. Holte et al. in their comparative study between two regimens (liberal versus restrictive), found that the intraoperative liberal administration of 3 L of balanced crystalloid will result in avoidance of postoperative hypovolemia, organ dysfunctions, and the risk of nausea and vomiting during the postoperative period [3,18]. In another hand, Holte and Kehlet in another study recommended that excess fluid administration should be avoided in the major elective abdominal procedures [19]. The liberal regimen (2-18 ml/ [kg hr]) is preferred in major procedures which is expected to require less than 3 hours [7,11]. In contrast to liberal, the restrictive regimen is more used currently and most of the current studies support restrictive infusion [3]. The restrictive regimen was defined in some studies as the amount of administered fluid less than 2 L; another study explained that the restrictive approach has incomplete replacement for some of fluid lost, such as preoperative deficits, intravascular expansion caused from anesthesia, and the third space replacement omitted in some trials [12-13,16,20-21]. Most of the clinical trials have a consensus that the restrictive approach has fewer complications in comparing with the liberal administration [2,16,22-24]. Nisanevich et al. and Holte et al. reported that the restrictive administration intraoperatively decreased postoperative mortality, the length of stay was less, and the pulmonary function had been improved [23,25]. The impaired organ function has been stated in some evidence as a secondary result to the induced hypovolemia by the restrictive approach [12,14]. Similar to the liberal, restrictive fluid infusion has its own complications in addition to hypovolemia, such as tachycardia, renal failure, and hypotension [26]. In the face of assortment of IV fluids available to use in major procedures, the perfect one is still vague. According to results from many studies, there was a correlation between some unwanted outcomes with different administered fluids [16]. Guidet and his colleagues in their study found that the use of balanced solutions of crystalloid has fewer effects in comparison with isotonic saline crystalloids [27]. Renal complications had been shown with using a large amount of 0.9% saline; these complications are presented by reduced blood flow and perfusion for the cortex [27-28]. Metabolic acidosis is associated with 0.9% saline administration as a result of hyperchloremia, also there is significant decrease in plasma ion with saline infusion [29-30]. Rapid crystalloid administration with high volume will result in pain, drowsiness, delayed micturition, and low mental capacity [31-32]. The isotonic saline crystalloids remain an acceptable option for plasma volume expansion for surgical patients with hypochloremic alkalosis, high gastric secretion, and nausea/vomiting [16,33]. Balanced crystalloids have been recommended for initial intraoperative replacement and maintenance by the British Guidelines on IV therapy in view to reduce the clinical implications of saline solutions [34]. Andrew Shaw, et al. reported in an observational study that the mortality with balanced solutions is less in comparison with using saline solutions in patients undergoing major abdominal surgery; also hemodialysis was less in comparing with saline use [35]. Colloids are preferred more from some anesthesiologists during the intraoperative period because the intravascular volume has been kept for a longer time by about 40 % more than the crystalloid effect, colloid solutions elevate the oncotic pressure in plasma and reduce as much as possible from the filtration to extravascular space [8,36-39]. Synthetic colloids (gelatin and hydroxyethyl starches) are commonly used in some area, but their administration has severe impression complications such as impaired hemostasis, anaphylaxis, nephrotoxic effect, renal injury, possibly impaired coagulation, and postoperative blood loss [2,8,9,39-41]. Limited availability of artificial colloids and their expensive costs are the most obstacles in using these fluids widely [13-42]. In specific indications such as anemia (Hemoglobin <6 g/dL, according to American Society of Anesthesiology guideline in 2006), the administration of blood products should be preferred [16,40,43]. In summary, guided intraoperative restrictive regimen has been recommended recently by many data for major abdominal surgeries. In spite of concerning hyperkalemia, the infusion of balanced crystalloids is convenient and recommended fluid therapy for replacement of fluid loss during intraoperative phase of perioperative anesthesia management in major abdominal procedures [2, 6,12,25,44-46].

Intraoperative Fluid Therapy in Major Neurosurgical Procedures

Neurosurgical patient has been considered as a difficult challenge during perioperative management for the neuro-anesthesiologist [42]. Hemodynamic stability, better brain oxygenation, and cerebral perfusion pressure are the main goals of neuro-anesthesia [47]. Intraoperative vasodilatation happens a lot due to the administration of inhaled anesthetics and intravascular volume depletion which results from blood loss. Patients undergoing neurosurgical procedures generally receive diuretics such as mannitol and furosemide; also those patients may need to be administered a high amount of IV fluids to rectify the preoperative dehydration and preserve the hemodynamic stability intraoperatively [48]. In fluid therapy for neurosurgical patients, appropriate serum osmolarity, and avoidance of both hypovolemia and elevated intracranial pressure (ICP) are the main principles and goals; in addition to maintaining a normal mean arterial pressure (MAP) [49]. Unfortunately, there were a few studies that had been conducted in the treatment and evaluation of water homeostasis disorders, and guided fluid therapy in neurosurgical patients [50]. Because the fear from liberal approach increases the risk of cerebral edema; the restrictive fluid regimen is the choice in neurosurgery; especially in patients with cerebral edema, mass lesions, and intracranial hypertension [48]. Shenkin and his colleagues in a human study demonstrated that the osmolality of plasma reduced gradually in patients receiving more than 2 L of fluids per day (standard maintenance) [51]. In another study, administration of 1 L or less of IV fluid for neurosurgical patients has been shown to cause dehydration and advanced increasing in serum osmolality [52]. Adequate replacement of insensible loss and urine output are the main rules in intraoperative period, lactated ringer and normal saline are commonly preferred over the period. Some evidence documented that the isotonic solutions are the choice for intraoperative maintenance and replacement of blood and insensible loss with dosing of >2ml/kg/h because theoretically, such fluids will cause a reduction in serum osmolarity and produce cerebral edema in high volume administration [53]. Furthermore, increased cerebral hydrostatic pressure should be avoided to decrease the risk of hypertension in the right heart and obviate excess administration. Generally, avoidance of free salt fluids (hypo-osmolar) administration has been recommended intraoperatively because this type of fluid causes a significant reduction in the serum osmolality and increases the water content in cerebral tissues [42,54]. The glucose level in neurosurgical patients should be maintained within 100-150 mg/dl [54-55]. Integrated administration of colloids and crystalloids is advisable in replacement of massive fluid loss [29,42,56]. High molecular colloids are more efficient in preserving intravascular volume because of the injured blood brain barrier still impermeable to high molecular weight solutes such as albumin, Penta-starch, and hetastarch [57]. The use of hetastarch solutions (HES) in neuro-anesthesia is recommended, but with caution and taking to account the recommended dose. The function of some coagulation factors (such as factor VIII) has been impaired with infusion of more than 1 L of high molecular weight hetastarch [58-59]. The smaller molecular weight of 6% HES (130/0.4) infusion is associated with fewer coagulation effects, renal complications, and low rate of mortality [60-61]. Administration of dextran (small molecular weight 40) is not preferred for patients with intracranial lesions because it is associated with elongated bleeding time by affecting the platelet functions and dextran can cause cerebral edema in abnormal BBB [48]. Khan and Tabatabai recommended that the packed red cells must be administered generally to patients when the hematocrit level comes down to less than 30% in neurosurgical practice [62]. In summary, preservation of plasma osmolarity within normality or little higher is the main goal during neurosurgery, so administration of fluids which lead to a significant reduction in the serum osmolarity should be excluded from replacement; in regarding to this statement; isovolumic patient status should be attained by using isotonic solutions (0.9% saline or balanced solutions) in restricted infusion [42,46,48,50].

Osmotherapy in neurosurgical patients

Humanitarian data conducted state that the osmotherapy is the first line in treatment of the cerebral edema with or without intracranial hypertension in patients undergoing neurosurgery [63-64]. The most effective osmotic agent is mannitol, and it has been used especially in intraoperative period for decades; but recently there were some RCTs and studies that recommended hypertonic saline (HS) solutions in osmotherapy because the mannitol can pass the blood brain barrier easier than HS [63-64], the ICP reduction can be accomplished with 0.25 g/kg of mannitol, but the larger doses more than 1 g/kg may be associated with uncomfortable effects such as acute kidney injury. The main goal of mannitol administration is to ameliorate the patient status during surgery [65-66]. In patients with herniation signs and surgical trauma without central access, mannitol will be effective for short term of hyper osmotherapy [63-64]. HES is recommended to be used in neurosurgical practice because these solutions had shown a positive effect; when used to resolve refractory ICP [52,63,67-68]. HS increases the osmotic gradients and colloid oncotic pressure, resulting in reduced water content in the brain tissue and decreases the ICP. Furthermore, administration of HS (such as 3% and 10%) recently has been preferred to mannitol by its advantages as a therapeutic accessory in treating intracranial hypertension and cerebral edema [52,69]. HS has fewer effects on blood coagulation than mannitol, and the administration of these fluids should be through the central line [63,70]. A potassium supplement is required with HS therapy because the hypokalemia is an associated problem with HS administration; while hyperkalemia is related to mannitol infusion [69,71].

Intraoperative Fluid Therapy for Cardiovascular Surgery

To improve the outcomes of patients undergoing cardiovascular surgery, convenient fluid therapy is necessary to prevent organ damage in the perioperative care. Electrolyte disorders and impaired renal function are the common problems during and after cardiovascular surgery. Polderman et al. in a prospective study in 500 patients with cardiopulmonary bypass (CPB), reported that there is a significant reduction in the electrolyte levels, in spite of all patients had been extradited cardioplegia solution and intraoperative supplementary infusion of potassium and magnesium [72]. The primed fluids of CPB, cardioplegia solutions, treated fluids for non-anticipated hypotension, and pre and intraoperative maintenance fluids caused plasma hemodilution and significant reduction about 20 -25 % in hematocrit level [73]. The using of liberal or restrictive fluid regimen in cardiac surgery is still in argument; because there are no comparative trials made to evaluate the outcomes of different fluid therapy regimens. Also, the available definitions of restrictive and liberal are diffident and considered as a stumbling block in the interpretation of those publications [74]. Massive fluid infusion in cardiac surgery may interfere and affect the action of cardiovascular drugs (such as inotropes), also the patients weaning from CPB will be affected. As a general recommendation, the liberal approach is logically unprofitable for patients with cardiac and renal morbidity [75]. Fluids that are used in intraoperative replacement and in priming CPB should be optimized as much as possible to avoid both increased cardiac muscle effort and related complications of hyper or hypovolemia [76]. The historic controversy has grown up to involve colloid-colloid in addition to typical fluid therapy approach and crystalloid-colloid [77]. Crystalloid infusion in cardiovascular patients is not suitable for restoring of intravascular volume when compared with colloids. A significant relationship between high mortality rates and infusion of large crystalloid volume had been reported [73,78]. In a comparative study of using crystalloids vs colloids in patients admitted to cardiovascular surgery, Ley et al. demonstrated that patients whom had received normal saline during surgery needed more time to stay in post-surgical care unit and increased necessity for administration fluid [79]. NaCl 0.9% is the commonist crystalloid solution, but increased volume administration of 0.9 % saline (>2L) rapidly, had been associated with reduced blood flux in kidney, furthermore metabolic acidosis [28,77]. Mannitol has been suggested as a priming solution in CPB because it can decrease the risk of crystalloid overload [75]. When crystalloids are favored to be infused, full electrolyte crystalloids (Ringers solutions, Plasmalyte, and Hartman's solutions) are preferable crystalloids for administration in cardiovascular procedures in many centers [80-81]. Unfortunately, there are no publications available in comparing balanced versus non-balanced crystalloids use in cardiac surgical patients [82]. In face of crystalloids, administration of different colloids begins to take up more space in the ongoing conflict, especially in cardiac surgery. Albumin (natural human derived solution) and hydroxyethyl starch (HES) are commonist colloids used in cardiac surgery [77]. Albumin can be infused in patients with cardiac output problems and more than 90% of infused albumin volume remains for more time in the intravascular space; for those reasons, albumin had been considered by some evidence as the golden choice in cardiac surgery [83-84]. Jacob et al. found that the formation of tissue edema is less or absent with albumin infusion when compared with synthetic colloids and crystalloids [85]. The requirement for transfusion of blood components was less in patients whom had received albumin in the operative room when compared with HES infusion in cardiac surgery [38]. Gelatins are the lower efficient colloids in plasma expansion because of short plasma half-life (2-3 hrs) and their use in cardiac surgery is considered safe with respect to coagulation systemic organ function [83,86]. HES have been used widely in rectifying hypovolemia. Knutson and colleagues reported that the postoperative bleeding and blood transfusion are associated more with intraoperative infusion of HES [87]. In a prospective randomized study of Linden and his associates it was found that infusion of the new generation of HES 130/0.4 is more effective in increasing the intravascular volume in patients undergoing cardiovascular procedures [86]. Robert et al. [84] and Ole Bayer et al. [88] documented that the administration of most synthetic colloids is considered harmful in cardiac surgical patients, and generally, it is associated with undesirable coagulation problems. All plasma components that are used in volume replacement during cardiovascular surgery are associated with adverse effects in coagulation factors [83]. In succinct words, crystalloids (balanced crystalloids) are more in priority for ongoing loss replacement, and colloids are more efficient in temporary losses; with regards to monitoring of intravascular volume during surgery by efficient invasive methods such as transesophageal echocardiogram [73-77,82,88].

Intraoperative Fluid Therapy for Major Thoracic Surgery (Noncardiac)

Major thoracic procedures are associated with higher rate of mortality than other major surgeries because the function of the lung will be adversely affected by many of perioperative related factors [89-90]. As a response result of surgical trauma and induced stress by some thoracic disease, the permeability of capillary endothelium and secretion of inflammatory mediators are strikingly increased; these factors will facilitate the passage of plasma proteins into the interstitial space and fluid will be shifted out of intravascular space. Massive fluid accumulation in the interstitium will be more in intra and postoperative period [90-92]. Pulmonary edema is a familiar complication with major prolonged procedures, but in patients undergoing major thoracic surgery, the incidence rate of edema in lung tissue will be higher [93]. The surfactant and endothelial cells of alveoli are adversely affected by many anesthetics ("mechanical ventilation and rapid fluid infusion) and non-anesthetic (preoperative chemotherapy, surgical trauma and dissection, ischemia reperfusion, exposure to blood products and microbes, hyperglycemia") related factors during thoracic surgery resulting in undesirable respiratory complications such as acute lung injuries [92,94]. In the same line with neurosurgical and cardiovascular procedures, the fluid therapy in thoracic surgery is a more continuous debatable question, and this is due to the scarcity in available trials which compare different fluid regimens and evaluate their advantages and adverse effects [94]. Restricted fluid regimen has seemed more compatible with thoracic surgery; but perfusion of vital organs may be affected [7,95-96]. Excess intraoperative infusion of fluids has been linked in many data as one of many factors which predispose undesirable cardiorespiratory impacts after major thoracic surgery [93,96-97]. Licker and his colleagues in a retrospective study, reported that the massive fluid administration (>3L) is a potential cause for postoperative acute lung injury (ALI) [98]. Zeldin and his collagenous in their famous landmark study of 10 admitted patients for pneumonectomy, found that the incidence of pulmonary edema was significantly high in patients given approximately > 4L in the intraoperative period [99]. Fluid overload in pulmonary surgery has been associated with hypoxemia and tissue edema especially in the dependent lung during lateral position [96-97]. The incidence of ALI and ARDS was reported in many studies with an infusion of high fluid dose > 7ml/kg/h during the intraoperative period [97]. Intraoperative infusion of high fluid amounts in esophageal procedures has been reported to be associated with respiratory and cardiac complications [96,100]. Restricted intraoperative fluid is necessary for thoracic procedures to improve patient outcomes; but massive restriction may be associated with arrhythmia, hypotension renal troubles and decreased in organ perfusion because of intravascular hypovolemia [97,100]. Gut perfusion will be exacerbated by correction of epidural hypotension with the massive fluid administration [90]. Early ablactation from mechanical ventilation and minimizing weight gain is the most common advantages of restricted fluids in major thoracic procedures [94]. Type of fluid (Crystalloids or colloids) is more disputable topic in thoracic surgery, and this is due to the paucity of data regarding the associated outcomes for both colloids and crystalloids in major thoracic surgeries [95,97]. Many of crystalloids' features such as easy availability, lower renal risks than colloids, and inexpensiveness make it more to be used; but pulmonary edema is formed with a massive infusion of crystalloids. Infusion of crystalloid in high volumes had been reported a hazardous by increasing fluid retention and significant weight gain in postoperative care [101-102]. In another hand, decreased pulmonary edema, efficient intravascular volume, and hemodynamic stability can be realized with an infusion of low colloid volume [95,97]. But using of synthetic colloids is associated with high mortality rate because the most common systematic adverse effects of colloid infusion represent in AKI and coagulopathy [97,102-103]. Perioperative transfusion in thoracic surgery is associated with adverse outcomes, and some evidence recommended that the transfusion during surgery should be avoided or minimized [104]. In opposite direction for most noncardiac chest surgeries, the immunological condition may be ameliorated by blood transfusion during transplant surgery of lung [105]. Regrettably, there is no available guided data in a blood transfusion during thoracic surgery [97]. In summary, the commonly recommended basics of intraoperative fluid administration in major thoracic procedures are summarized by:

1-Restricted fluid infusion is more convenient to avoid correlated overloads problems.

2-The preferably use of colloids is to recompense blood loss.

3-Intraoperative maintenance rate should be preserved <6ml/kg/hr (not to exceed >2 L of crystalloids).

4-Avoiding of third space replacement is recently recommended.

5- Advanced and effective monitor is necessary for combination therapy of vasopressors and fluid infusion. The controversy of preferred fluid in chest surgeries has not yet been resolved. Further trials are needed to guide fluid management in thoracic surgery [89,96].

Intraoperative Fluid Therapy in Major Orthopedic Procedures

The challenges faced by anesthesiologist are many and sometimes serious in orthopedic surgical patients; because the majority of this population is from the elderly with increased morbidity. Fluid shifting between different body water compartments, massive loss of blood and massive transfusion of blood components are the common concerns which may induce post-surgical complications such as ischemia in cardiac muscle, and elevation in both blood pressure and oxygen conception [106-107]. Hypovolemia is common in elderly patients due to many reasons. Anxiety from incontinence may increase patients' reluctance to drink fluids before surgery. Demented patient status and limited mobilization before surgery decrease fluid intake in preoperative phase. Also some patients have concomitant medications such as diuretics. All of these factors contribute in exacerbating the dehydration of the patient and mysterious hypovolemia on admission to hospital [108]. Since 20 years ago, application of regional anesthesia has been increased by more than 50% in orthopedics procedures to avoid related impacts of general anesthesia [109]. For that reason, there is significant paucity in guided data for intraoperative fluid therapy in major orthopedic processes. Orthopedic patients should be considered as a high risk patient and optimal hemodynamic status during surgery is required to improve the outcomes [110]. Risk of cardiac resuscitation in perioperative period is high in this population because frailty, advanced age, and cardiac morbidity are frequently seen. Anesthesiologists generally avoid massive administration of fluid in such patients because it will contribute to left heart failure [108,110-111]. This was a limitation in many RCTs to evaluate different regimens of fluid therapy. Volume therapy in high risk patients aims to avoid related risks of hypervolemia and decrease the incidence of hypoperfusion by preventing hypovolemia [20]. Well tissue oxygenation during surgery can participate in better and short recovery. Crystalloid infusion negatively affects the concentration of proteins in plasma. Crystalloid infusion in large amounts is known with adverse complications, the most common one is formation of edema in different tissues [112]. Contrary to crystalloids, colloids are considered as the choice for plasma expansion in massive decreased blood volume; because it has a longer staying time than crystalloids inside vessels [113]. Recently, hydroxyethyl starches' solutions are the common colloids used in most of developed countries. Requirement for renal replacement therapy and kidney injury are the most common complications with HES infusion [114]. There is congruence between clinical researchers about the correlated hemostasis effects for colloid infusion [115]. In most orthopedic procedures, transfusion of blood components is required because of the increased perioperative loss of blood [116]. The goal of perioperative transfusion is to correct decreased hemoglobin and hematocrit levels which result from surgical blood loss. During surgery, transfusion is not necessary when the hemoglobin level decreases to less than 7g/dl in normal surgical patients. Generally transfusion has associated problems may increase mortality rate after surgery; the common problems are impairment of immune system, bacterial contamination, and allergic reaction [116-117]. In summary, the available data recommended that the intraoperative fluids should be optimized in orthopedic patients by using advanced techniques in cardiac output monitoring. Appropriate coagulation function can be preserved by avoiding large volume infusion of synthetic colloids especially HES; but gelatins have minimal coagulation effects than HES. Optimal amounts of balanced crystalloids are more suggested to infuse in this surgical population. If combined infusion is required, colloids with minimum coagulation effects are recommended to administer during orthopedic surgery. Initial hemoglobin monitoring and accuracy in estimation of blood loss are important to minimize transfusion and related complications [20,110-112,116-117].

Intraoperative Fluid Therapy in Major Pediatric Surgeries

The fluid proportion in the pediatric body is different from that in an adult person. Water is the largest component in neonates and it is more than 75% of total body weight. Recent evidence recommended that the fasting term from oral intakes is two hours before surgery for clear fluids, and 4-6 hours for breast milk, formulated milk, and solids. In very young infants these times may lead the patient to be uncomforted and associate with the rapid incidence of dehydration and hypotension when anesthesia induction is predisposed. Some evidence found that the fasting in pediatrics for more than six hours will not be beneficial in regards to gastric PH and volume [118]. Intraoperative fluid compensation is calculated by using a special formula based on body weight. As we know perioperative replacement involves compensation for four purposes: deficit before the operation, blood and insensible losses, maintenance requirements, and fluid given to correct hypovolemia. In pediatrics, the infusion in the operating room includes one of the four purposes mentioned earlier. Related weight rule of 4-2-1 has become recently most dependent in calculating of given intraoperative fluids in both pediatrics and adults [16,40,119]. Evaluation of intraoperative liberal or restrictive effects on patient outcomes in pediatric population had been reported in few data. The liberal administration has been used widely overall the world in replacing of fluid loss in major pediatric procedures. Third space replacement in adults has been reconsidered recently, but in major surgery for pediatric it is still dependent on perioperative management. Third space replacement ranges between 10-20 ml/kg/h in pediatrics undergoing major surgical interventions in the abdominal cavity [40,120]. In case of high amount of fluid being administered, the incomplete renal function in infants and neonates should be considered [40,121]. Fluid infusion liberally is associated with high rate of brain edema and intracranial bleeding [122]. Whereas restricted fluid infusion is preferred over liberal because patient outcomes are significantly improved, also restrictive regimen may contribute in influencing outcomes in case of precipitating hypovolemia resulting in reduced organ perfusion and systemic dysfunction [120,122-124). Due to the dearth of supporting data for typical fluid, the polemic of crystalloids or crystalloids still exists. The first choice of fluids for most anesthesiologist in intraoperative management is crystalloid solutions for initial replacements [40]. Occurrence of perioperative hyperglycemia, hyponatremia, and lipolysis has been reported highest with hypotonic infusion. Both hyponatremia and hyperglycemia lead to increase water content in brain cells resulting in cerebral edema, adverse neurological outcomes, and death [40,120,123,125]. In cases of decreased blood glucose being expected during surgery; regular infusion of 0.45% hypotonic saline containing 5% dextrose is preferred with the necessity to monitor glucose level [120]. Recent findings trend recommend infusion of isotonic fluids with low glucose content (<2%) for intraoperative replacement in pediatrics [125-128]. Due to plasma analog content of electrolytes and osmolarity; balanced solutions are preferable from 0.9% saline for perioperative use [8,129]. Colloids, in one hand, are known with its prolonged intravascular volume expansion in massive blood loss and severe hypovolemia; but on the other hand, colloid related adverse reactions make its infusion difficult to decide. There is a significant variation between colloid products in their chemical structure and mechanism of action [8]. During recent period, there is increasing demand for use of synthetic colloid solution because they are less expensive than albumin. Gelatin administration is considered as more safe and efficacious than albumin, but anaphylactic reaction occurred repeatedly with gelatin [8]. Short term of gelatin for infants without pre-existing morbidity has been shown with no adverse outcomes. In children with coagulation disorders, gelatin solutions should be avoided [130]. In a randomized study, Paul et al. documented that the hemoglobin level significantly reduced with an infusion of low molecular weight HES [131]. The common complications of HES solution are coagulation impairment, acute renal failure and electrolyte troubles [40]. Infusion of HES in high doses is harmful and may cause severe hemodilution problems, and iatrogenic hypervolemia [8]. In general, colloids are associated with impairment of respiratory function in low body weight infants [120]. Transfusion for pediatrics seems similar to that for adult patients. Recommended hemoglobin threshold in stable child for transfusion is 7-8g/dl. Preoperative investigations should be done to evaluate hemoglobin level and avoid perioperative severe anemia. In anemic pediatrics, surgery should be postponed if the hemoglobin level is < 9g/dl. Unnecessary transfusion may have adverse patient outcomes and increase mortality [40,132]. In summary, liberal or restrictive intraoperative fluids is still in debate for the pediatric majority because of scarcity of supporting data for each regimen, and the necessity for more studies still exists. The calculated amount of pre-operative deficit is recommended to infuse during intraoperative period. Isotonic Ringer and plasma-lyte solutions with low glucose contents are more preferred during the intraoperative period. If hypoglycemia is expected, dextrose infusion is recommended under glucose level monitoring. Using infusion techniques such as electrical syringe during surgery is necessary to avoid related complications of accidental overload [8,40,118-120,123,125-129].

Conclusion

Intraoperative fluid equilibrium is a decisive matter in perioperative anesthesia management because most of the evaluation studies considered intraoperative fluid administration as a major participating agent in improving or worsening patient outcomes after surgery. A successful intraoperative fluid therapy plan depends mainly on understanding both of the body fluid physiology and clinical features of obtainable IV fluids and their hemodynamic and electrolyte effects. Well planned strategy for replacement may contribute to enhance systemic perfusion and reduce postoperative morbidity. Generally, over fluid administration should be avoided for intraoperative replacements. Restricted fluid therapy has been reported with fewer complications after major surgical procedures. In some patients with cardiopulmonary morbidity, traditional monitoring methods are not considered to be efficient in reflecting the responsiveness for fluid administration. Colloid or crystalloid infusion for surgical patients is an ongoing controversy of perioperative fluid therapy. Crystalloids should be used initially for replacement and maintenance, and the total amount should not be exceeding 2L. Balanced crystalloids have several advantages which make it preferable to be infused in the intraoperative period; these advantages include maintenance of renal blood flow, less hemodilution effects and avoidance of metabolic acidosis. Blood loss replacements should be limited to colloids in a 1:1 ratio.

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