Review Article

Perioperative Fluid Management in Children

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Abstract

Fluid management in the perioperative period is of vital importance to both anaesthesiologists and surgeons to optimize the health and to prevent complications in children. It is similar to a drug prescription whose composition and volume must be tailored to patient's physiological status, the extent of surgical procedure with ongoing losses and fluid shifts and postoperative course of events. Recent literature and studies have challenged the perioperative routine use of hypotonic fluid and glucose supplementation due to their side effects. This review focuses the basics of perioperative fluid management in children and the limitations of previously used fluid guidelines and provides recent recommendations.

Key Words: Fluid resuscitation, Sepsis, Hemodynamic goals

Introduction

Fluid management in infants and children is of importance as they are sensitive to small degrees of dehydration. Before going ahead with the topic of fluid management it is important to discuss basic physiology of fluid composition in children and the various terminology used in this context. Adult human body comprises of 60% water out of which two third is intracellular and rest is extracellular. This is in contrast to term neonates in whom 80% of body weight is water. The majority of fluid is in extracellular compartment, contributing to 45% of body weight in term neonates and 30% by the age of 1 year[1]. The higher proportion of water in extracellular compartment makes them more susceptible to fluid loss intra operatively. The extracellular fluid comprises of intravascular plasma volume and interstitial volume. A physiologically non-functional "third space" or trans-cellular space is also a part of the extracellular space. It results from transudation of fluid from the cells and extracellular space. Recently the significance of intraoperative third space loss and its resuscitation with crystalloids has been questioned in adult patients.

Fluid requirement

The fluid requirement in children is based upon the calorie expenditure which is turn depends on body weight or surface area. For every one kilo calorie of energy consumed one ml of water is required. Holliday and Segar in 1957 published an article regarding prescription of intravenous fluids in children which still forms the basis of fluid administration all over the world. They described that the physiologic deficits from urine output and insensible loss from skin and respiratory tract amounts to 100ml per 100 kcal metabolized per day. Based upon the metabolic requirements of awake hospitalized children they proposed the following daily fluid intake depending upon body weight. For children weighing up to 10 kg it is 100ml/kg, in the 11-20 kg group 1000ml+50ml/kg for each kg in this range and for children above 20kg it is 1500ml+20ml/kg for each kilogram above 20 kg[2]. This can be easily translated into the 4-2-1 rule for hourly fluid requirement used today (Table 1).

Weight	Hourly fluid requirements	Daily fluid requirements
<10 kg	4ml/kg 40 ml+2 ml/	100 ml/kg
10-20 kg	kg above 10 kg	1000 ml+50ml/ kg above 10 kg
>20 kg	60 ml+1ml/ kg above 20 kg	1500 ml+25 ml/ kg above 20 kg

Table 1 - Hourly and daily maintenance fluids according to child's weight

The decrease in fluid demand with increasing age of the child is due to reduction in calorie expended for growth. The daily electrolyte requirements were depending upon the composition of human and cow's milk. The daily requirement for sodium was 3mEq/100kcal/day and 2 mEq/100kcal/day for potassium and these are met by the hypotonic fluids like 0.2% normal saline with 5% dextrose. These recommendations were meant only for maintenance needs and did not cover the deficits and abnormal loss of water[2]. Thus blind application of these formulas which are meant to treat the children in nonoperative settings may results iatrogenic injury to children undergoing surgery. Recent studies have found that usage of hypotonic crystalloids in perioperative period which is also associated with high levels of stress induced anti diuretic hormone (ADH) release can lead to hyponatremic encephalopathy, neurological deficits and even death[3,4,5]. Hyponatremia is often unrecognised and most common complication related to fluid therapy in children in post-operative period.

Perioperative Fluid Requirements

Routinely intraoperative fluids are administered to replace the preoperative deficits, meet the maintenance requirement and ongoing losses depending on the type of surgery[6]. The prolonged preoperative fasting as a traditional practice resulted in dehydration from insensible loss and urine output. In 1975, Furman et al proposed that preoperative deficits can be calculated by the hourly maintenance rate multiplied with numbers of hours the patient was kept nil per oral (NPO)[7]. They suggested to replace half of this deficit in first hour and rest of the deficit over next two hours of surgery. In 1986, Berry simplified the guidelines as per the age of child and the severity of surgical trauma (Table 2). The universal liberal preoperative fasting guidelines recommended by the American Society of Anesthesiologists (ASA) (Table 3) allows the intake of clear oral liquids upto 2 hours pre operatively.

Adherence to this practice minimized preoperative dehydration in elective surgeries. None the less it is important to emphasize that preoperative deficits should be carefully assessed in emergency setting where ongoing fluid shifts or blood loss are significant. Estimation of degree of dehydration resulting from vomiting, diarrhoea or fever can be done using clinical signs and weight loss. The most important sign of normal hydration is kidney function[8] and therefore monitoring of urine output is essential for evaluating and treating any fluid deficit. The rate of fluid administration depends on the extent and rapidity of dehydration. In dehydrated paediatric patients needing resuscitation a bolus of Ringer Lactate 20ml/kg should be administered intravenously followed by repeat boluses in cases with severe dehydration[6]. It is important to replace fluid losses with normotonic and iso-osmolar fluids as the pathological fluid losses are always isotonic to plasma. Crystalloid solutions like Ringer lactate or normal saline are preferred and even colloids can be used. The goal of fluid resuscitation is to maintain cardiovascular stability, organ perfusion and adequate tissue oxygenation.

1)	First hour plus no 3 below Age 3 years and under – 25ml/kg Age 4 years and over – 15ml/kg
2)	All other hours (plus no 3) Maintenance +Trauma = basic hourly fluid Maintenance volume = 4ml/kg/hr Maintenance +mild trauma = 6ml/kg/hr Maintenance +moderate trauma = 8ml/kg/hr Maintenance +severe trauma =10ml/kg/hr
3)	Blood replacement 1:1with blood or colloid or 3:1 with crystalloids

Table 2 - Guidelines for fluid administration of balanced salt solution in children according to the age and to the severity of tissue trauma[47]

Ingested material	Minimum fasting period (hours)
Clear liquids	2
Breast milk	4
Infant formula	4(<3 month)-6 (>3 month)
Nonhuman milk	6
Light meal	6

Table 3 - Fasting guidelines for elective surgery[46]

Intraoperative Fluids

Intraoperative fluid requirement consists of hourly maintenance requirement, replacement of preoperative deficits and the surgical loss. The loss in surgical field can be in form of blood loss or as third space loss. Blood loss is replaced by three times the volume of crystalloid and in equal ratio with colloid. Third space loss refers to the sequestration of fluid to a non-functional extracellular space that is beyond osmotic equilibrium with the vascular space[9,10]. It is assumed to result from surgical trauma to cell membranes leading to hypoxic injury and loss of membrane integrity. In paediatrics it has been proposed to range from 1ml/kg/hr in minor surgical procedures to 50 ml/kg/hr in neonates undergoing surgery for necrotizing enterocolitis[6]. The concept of third space has been debated in adult population. A recent review of perioperative fluid therapy in adults concluded that the classic "third space" does not exist[11]. Overloading with crystalloid and iatrogenic deterioration of vascular barrier results in fluid accumulation in interstitial space[11]. In fact several studies in adults undergoing abdominal surgery have found improved outcomes with conservative fluid strategy in preoperative period[12,13,14]. In the paediatric population there is little evidence regarding this topic. There is a possibility that generous fluid supplementation for third space could be deleterious for patients. Goal directed administration of crystalloid or colloid to optimize flow related variables like stroke volume can alter the incidence of postoperative complications[15,16,17,18]. Similar studies in paediatric patients using esophageal doppler, pulse contour analysis, or mixed venous oxygen saturation to guide fluid management are lacking. Some important aspects which need attention are meticulous de airing of syringes and intravenous administration set, warming the intravenous fluids to body temperature and usage of burette set/paediatric drip set or infusion pumps for careful titration of fluids especially in young infants.

Perioperative Dextrose Requirement

Perioperative hypoglycaemia and hyperglycaemia can lead to complications in paediatric patients. Severe hypoglycaemia if not diagnosed and treated in time can cause permanent neurological impairment. Even mild hypoglycaemia (blood glucose < 45mg/dl) combined with mild hypoxia or ischemia can result in cerebral injury[19]. The incidence of hypoglycaemia in preoperative period has been shown to up to 2.5%. This incidence of hypoglycaemia is common after prolonged fasting periods, much beyond ASA recommendations on preoperative fasting. Strict adherence to ASA guidelines minimises the risk perioperative hypoglycaemia. In healthy children undergoing surgery, routine intraoperative supplementation of 5% dextrose is not recommended as the resulting hyperglycaemia itself can lead to various complications. Hyperglycaemia can result in osmotic diuresis leading to dehydration and electrolyte abnormalities[20,21]. It also has detrimental effect on nervous system especially in the presence of hypoxia when anaerobic metabolism of glucose causes accumulation of lactate, decrease in intracellular pH and compromised cellular function leading to cell death[22]. Nowadays growing consensus is to go for intraoperative selective supplementation of glucose in only those patients who are at greatest risk of hypoglycaemia and also to use fluid with lower dextrose concentrations of 1% or 2.5% with ringer lactate. The patient subset at high risk of hypoglycaemia are neonates, infants of diabetic mothers, malnourished children, children on parenteral nutrition and those with endocrinopathies in whom blood sugar should be monitored and rate of infusion also adjusted[21,6,23]. As dextrose gets metabolized by body it does not contribute to the tonicity of crystalloid and infusion of just dextrose containing fluids is practically similar to infusing water.

Choice of crystalloids

Crystalloids are the fluids commonly preferred to treat absolute or relative blood volume deficits observed during surgery in children. The low cost, lack of effect on coagulation or risk of anaphylaxis and transmission of infectious agents are the advantages crystalloids have over colloids. Most commonly used crystalloids are normal saline or ringer lactate as they have an osmolarity near to the physiological range (Table 4).

Fluids	Glucose (gm/100ml)	Na mEq/L	K mEq/L	Cl mEq/L	Lactate mEq/L	Acetate mEq/L	Ca mEq/L	Other mEq/L	Osmolality	Tonicity
Lactated ringer		130	4	109	28		3		273	Slightly hypotonic
Normal saline		154		154					308	Isotonic
D5	5								252	Hypotonic
D5 ¼ NS	5	34		34					329	Hypotonic
Isolyte P in D5%	5	23	20	29		23		Mg = 3, Phosphate= 3	330	Hypotonic
Plasmalyte A		140	5	98		27		Mg=3	295	Isotonic

Table 4 - Common crystalloids and their composition

It is recommended that the fluid used intraoperatively in children should be iso-osmolar to plasma to avoid hyponatremia and also include metabolic anions (acetate, lactate or malate) as bicarbonate precursors to prevent hyperchloremic acidosis especially in neonates[24,25]. If the requirement of crystalloids exceeds the amount of 30-50ml/kg body weight, a colloid solution may be indicated to maintain intravascular oncotic pressure[26]. A recent practice guideline from the Dutch paediatric society concluded that in view of limited number and quality of paediatric research studies the recommendations for volume expansion should be made based on side effect, mechanism of action and cost of intravenous fluids. Thus isotonic saline was recommended as safe, effective and 100 times less expensive than albumin[27].

Colloids use in children

Colloids can be either natural protein colloids like albumin or synthetic colloids like hydroxyethyl starch, dextran and gelatins. Depending upon their chemical and pharmacokinetic properties they have different impact on hemodynamic parameters. Albumin is the naturally found colloid and is considered as the colloid "gold standard"[28]. It has a molecular weight of 69 kDa and is available in 5% and 25% solution. Albumin causesvolume expansion by translocation of fluid from interstitial space to intravascular space such that 5% albumin solution is osmotically equal to similar volume of plasma. But in patients with sepsis, critical illness, trauma and burns who have increased vascular permeability, the leakage of colloids into interstitial space may worsen oedema. Side effects include weak anticoagulant effect resulting from inhibition of platelet aggregation or heparin like effect on antithrombin III if volume replacement exceeds more than 25% of blood volume and risk of allergic reactions[29,30]. Data in support of using albumin for fluid resuscitation in children are lacking and it has found to be harmful in those with traumatic brain injury[31]. In certain subgroup of patients like neonates and children undergoing cardiac surgery it has been found to be useful[32,33].

Hyrdoxyethyl starch are a class of non-protein synthetic colloid derived from modified natural polysaccharides. The substitution of hydroxyl group at carbon position C2, C3 and C6 by hydroxyethyl group makes them resistant to hydrolysis by circulating amylases. They are classified depending on their concentration, weighted average mean molecular weight in kilo Dalton and also by their molar substitution (MS) and C2:C6 ratio. The incidence of side effects and degree of volume expansion are in proportion to molecular weight and molar substitution ratio. Coagulation abnormalities due to interference with Von Willibrand factor, factor VIII and platelets, renal injury due to renal tubular swelling and pruritus resulting from accumulation in the skin are the side effects more often observed with older generation HES[34,35,32]. Newer generation HES have low molecular weight and molar substitution ratio to reduce side effects and high C2:C6 hydroxylation ratio to prolong the duration of action (4-6 hours). A European prospective multicentre, observational, post authorization safety study to evaluate safety of HES (130/0.42) for perioperative replacement in children found no serious drug adverse drug reactions when infused with mean volumes of 11±4.8ml/kg[36]. The side effects noted were decrease in the anion gap as well as increase in the chloride concentration. This could mask a high anion gap acidosis signifying acute renal failure or sepsis during surgery[37].

Gelatins are polypeptides produced by degradation of bovine collagen. Their molecular weight is approximately 30-3500 Da which is lower compared to other colloids. The resulting increase in blood volume is less than the volume infused due to rapid but transient passage into interstitial space, rapid glomerular filtration and susceptibility to cleavage by proteases. This results in need of repeated infusions, fortunately there is lack of gelatin dose limitation. Gelatins have also been found to effect TEG values and should be used with caution in patients with bleeding tendencies[38]. In a Cochrane review of early volume expansion in preterm infants, use of gelatin or no treatment was associated with an increased risk of developing necrotizing enterocolitis when compared with FFP[39].

Dextran is a water soluble glucose polymer synthesized by specific bacteria from sucrose. The current formulations are 10% dextran 40 and 6% dextran70. The number denotes molecular weight in kilo daltons. The higher molecular weight results in delayed renal excretion and accounts for longer duration of volume expansion. They result in dose dependent Von Willibrand syndrome and enhanced fibrinolysis more with higher molecular weight dextrans. Other side effects include ARF in patients with acute ischemic stroke and anaphylactoid reactions as a result of dextran reactive antibodies[40,41]. The current recommendation is to limit the use of dextran to 20ml/kg/day in children.

Postoperative Fluid Therapy

Oral intake is usually allowed in first three postoperative hours in most paediatric patients undergoing minor surgeries. In cases where oral intake is delayed intravenous fluid therapy should be administered to provide for basic metabolic requirements and also compensate for losses through nasogastric tube, drains and additional loses (e.g. fever). Hyponatremia is the most frequent electrolyte disorder in the postoperative period. Severe hyponatremia (<120-125 mmol/l) may result in transient or permanent brain damage[42,43].

This hyponatremia results primarily due to extra renal loss of electrolytes, the elevated levels of antidiuretic hormone (ADH) activity and administration of hypotonic fluids. Hyponatremia causes osmotic movement of free water across cell membranes from extracellular to intracellular compartment and most seriously affects brain. All children are more susceptible to cerebral oedema due to the differences in ratio of intracranial capacity to brain size, cerebrospinal fluid volume and brain water and electrolyte content. The early symptoms like lethargy, headache and nausea vomiting are vague in nature and are commonly seen in postoperative period. A respiratory arrest may be the event pointing towards identification and treatment of hyponatremia. In a meta-analysis comparing hypotonic versus isotonic fluids in all hospitalized patients, hyponatremia was 17 times more commonly seen in patients receiving hypotonic versus isotonic fluids[43]. In 2007, the national safety agency of the United Kingdom issued an alert recommending removal of 4% dextrose with 0.18% saline from general use in children[44]. They recommended usage of isotonic fluids with monitoring electrolytes and urea and /or creatinine at baseline and once daily in any child who receives intravenous fluids.

Conclusions

Isotonic fluids are essential to maintain homeostasis intra operatively. Routine dextrose supplementation is no longer needed except in neonates and certain other patients who also need monitoring of blood glucose. More studies are needed in paediatric population to define optimal fluid management especially in major abdominal surgeries. Similarly the safety and outcomes of synthetic colloid usage in children needs to be studied. A rational, goal directed combination of both crystalloid and colloid therapy similar to that in adults is the need of hour. The routine use of hypotonic fluids in postoperative period should be strictly avoided and more awareness needs to be created regarding the early detection of hyponatremia and its treatment and prevention.

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Uterine Transplantation

Uterine factor infertility is an irreversible condition that affects between 3 and 5 % women globally. Until now, surrogacy offered the only hope for such women. All that has changed in the last decade. First successful uterine transplantation was carried out in Sweden. Since then 11 transplants have been performed globally. This has led to five pregnancies and four successful deliveries. The latest country to join the band wagon is US. In Cleveland Clinic, the first uterine transplant in US was successfully carried out during a nine hour long surgery. The recipient is apparently doing very well. (http://my.clevelandclinic.org/about-cleveland-clinic/newsroom/r eleases-videos-newsletters/2016-2-25-cleveland-clinic-performs-nations- first-uterus-transplan)

- Dr. K. Ramesh Rao

Active life means long life

In a study conducted by Centers for Disease Control and Prevention (CDC), 3000 subjects were fitted with ultrasensitive accelerometers to record the body movement for 7 days. The activity data collected during this period was correlated with mortality among the study subjects over the next 8 years. Five times more deaths were recorded among the least active when compared with the most active subjects. Even extra 10 minutes of light activity such as walking around or washing dishes or sweeping the floor appeared to make a significant difference. If you want to live long, it makes a lot of sense to lead a physically active life. But if you like everything short and sweet, munching popcorn while watching a soap-opera on TV will do. Results of the study are published in the latest edition of the journal "Medicine & Science in Sports & Exercise".

- Dr. K. Ramesh Rao