PAEDIATRIC FLUID UPDATE

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'Probably the proper use of water and electrolyte solution is responsible for saving more lives of seriously ill patients than the use of any other substance'. D C Darrow, E L Pratt. Yale University 1950

1. Introduction:

Perioperative fluid therapy should be viewed as a prescription. The volume and composition of the fluid administered should be tailored to the specific needs of the patient concerned. The aim of fluid therapy is to provide maintenance requirements, correcting any fluid deficits and replace ongoing losses. Meticulous fluid management is required in paediatric patients because of an extremely limited margin for error.

2. Body composition and basic fluid physiology:

The total body water (TBW) of a newborn is 75 – 80 %. TBW decreases gradually as fat and muscle content increase with age to the adult level of approximately 60%. The distribution of this TBW also differs for the paediatric population. The extra cellular fluid (ECF) fluid represents 45% of body weight in term neonates, 30% by the age of one year compared with 20% in adults. The blood volume too of the paediatric population differs from that of adults as will be discussed later.

In order to understand the exchange of fluid between the various compartments (i.e. intravascular, intracellular and interstitial), basic understanding of fluid physiology is required.

Some definitions:

Osmolality : The number of osmoles per kilogram of solvent.

Osmolarity : The number of osmoles per litre solution.

Tonicity : The term used to describe the osmolality of a solution relative to plasma.

Movement of fluid across a capillary is determined by Starling's law:

$$Q = k\,A\,[(Pc - Pi) - \sigma\,(\pi c - \pi i)]$$

Q = Net flow of fluid
k = Hydraulic conductivity coefficient (Index of pore size)
A = Area of the membrane concerned
Pc = Capillary hydrostatic pressure
Pi = Interstitial hydrostatic pressure
σ = Protein reflectance coefficient
πc = Capillary oncotic pressure
πi = Interstitial oncotic pressure

σ defines the capacity of the capillary membrane to prevent translocation of proteins. If $\sigma = 1$, the membrane is totally impermeable and proteins are able to exert their full oncotic effect. If $\sigma = 0$, the membrane permits protein to pass without impedance. σ is approximately 1 in the brain.

Oncotic pressure vs. osmotic pressure:

The tight junction of the blood-brain-barrier (BBB) render movement of free water dependent more on the ionic concentrations than the oncotic effect of proteins (as compared to other areas in the body). The oncotic pressure is that component of the osmotic pressure determined by particles with a molecular weight above an arbitrary limit of 30 000 Daltons. The total osmotic pressure exerted by all the plasma proteins (the oncotic pressure), adds up to less than 1% of the plasma osmotic pressure of 285 mmol/L. Thus for the BBB, the last part of the Starling equation should have the *oncotic* pressure substituted with the *osmotic* pressure. The importance of this concept of osmotic pressure and the brain will become apparent when considering hyponatraemic encephalopathy.

3. '4 – 2 – 1'

The '4:2:1' rule frequently quoted for maintenance fluid prescription is derived from the work carried out by Holliday and Segar in 1957. Maintenance requirement for water was determined by calorific expenditure, approximately 1ml/cal spent. Thus, in the awake child, calorie and water consumption are considered equal. In the same study, electrolyte requirements were determined from the amount delivered by the same volume of human milk. Daily sodium and potassium requirements are 3 mmol/kg and 2 mmol/kg respectively. Thus the combination of maintenance fluid requirements and electrolyte requirements resulted in the use of a hypotonic solution. For many decades the fluid given to children by paediatricians was one fourth - to one third – strength saline. However work by Lindahl found that energy expenditure during anaesthesia was 50 % lower than that calculated by Holliday and Segar and was close to basal metabolic rate. This would suggest that the '4-2-1 rule' *overestimates* maintenance fluid requirements.

4. **Hyponatraemia & cerebral oedema:**

In the United Kingdom, there have been more than 50 case reports of serious morbidity or death in previously healthy children with the administration of i.v. fluids and hospital acquired hyponatraemia. The most devastating complication of hyponatraemia is cerebral oedema. If there is an acute drop in plasma tonicity, brain water accumulates leading to cerebral oedema. If the increase in brain volume exceeds 5 – 7 % of its initial volume, there is a risk of brain herniation and death. Children are at a higher risk for hyponatraemic encephalopathy than adults because the number of brain cells decreases with age and children have a larger brain to intracranial volume ratio compared with that of adults. In addition, there is evidence to suggest that pre-pubertal patients have a limited cerebral Na^+-K^+-ATPase system, reflecting a limited ability to extrude sodium from the brain. This explains why hyponatraemic encephalopathy occurs sooner in children than in adults. The average sodium concentration in children with hyponatraemic encephalopathy is 120 mmol/l, while the concentration in adults is 111mmol/l.

Mechanisms of hyponatraeimia:

The mechanism of hyponatraemia in the paediatric surgery population is complex and multifactorial and is not limited to the inappropriate administration of hypotonic fluids. Antidiuretic hormone (ADH) also plays an important role. The most important physiological trigger for the release of ADH under normal conditions is increased plasma osmolality. In disease states there are multiple non-osmotic triggers for ADH release. These include stress, haemorrhage, opiates, pain and nausea. This ADH release results in increased water reabsorption from the renal collecting ducts resulting in a dilutional hyponatraemia. The inappropriate addition of high concentrations of dextrose to solutions is an important and often under-recognised cause of hyponatraemia. Take for example 0,18% NaCl with 4% glucose. This is *isomolar* compared to plasma, with an osmolality of 284. However the glucose component is an ineffective solute which readily enters the cells and is metabolized. Thus the effective *tonicity* of the solution is dependent on the effects of the NaCl content, in this case 31 + 31 meq/l = 62 meq/l, making the solution *hypotonic.* Other rare causes of hyponatraemia include adrenal insufficiency, SIADH and the cerebral salt wasting syndrome.

5. Glucose:

Should dextrose be administered during surgery? If so, how much?

Neonates have low glycogen stores that predispose them to hypoglycaemia. They are at greatest risk if premature or small for gestational age. In the past 20 years there has been there has been a complete re-evaluation of the place of glucose in routine intraoperative solutions. As mentioned previously, energy requirements during anaesthesia are close to basal metabolic rate. In the past, dextrose was routinely added to perioperative solutions to avoid hypoglycaemia which may be difficult to diagnose in the anaesthetised child. Hypoglycaemia is known to cause brain damage, especially in the neonate. However, the risk of hypoglycaemia has been demonstrated to be low in normal healthy infants (1 – 2%), despite prolonged fasting periods.

The risks of *hyper*glycaemia are significant. High serum glucose levels can induce osmotic diuresis leading to dehydration and electrolyte disturbances. Studies have shown than hyperglycaemia increases the risk of hypoxic-ischaemic brain damage. In infants subjected to profound hypothermic circulatory arrest for cardiac surgery, high pre-arrest blood glucose levels are associated with postoperative neurological deficits. Among the mechanisms involved in this damage are both glucose aerobic metabolism and the production of intracellular acidosis.

Intraoperative administration of glucose-free isotonic hydrating solutions should be standard for healthy children over 4 -5 years of age. In infants and younger children 5% dextrose should be *avoided*, but 1 – 2% dextrose in Ringer's lactate is appropriate. Glucose infusion at a rate of 120 – 300 mg/kg/hour is sufficient to maintain acceptable blood glucose levels and prevent lipid mobilisation.

6. Fasting:

Preoperative fasting is a prerequisite for elective surgery. However, recent work has shown that prolonged fasting does not reduce the risk for aspiration during anaesthesia. There is now convincing evidence that free intake of clear fluids up to two hours preoperatively does not affect the gastric pH or volume. Current guidelines for preoperative fasting for elective surgery are as follows:

Clear liquids	2 hours
Breast milk	4 hours
Infant formula	4 hours (< 3 months) 6 hours(>3 months)
Non human milk	6 hours

7. PRACTICAL APPROACH TO THE MANAGEMENT OF FLUID IN THE PERIOPERATIVE PERIOD:

The cardinal questions which need answering when considering perioperative fluids are:

i) What type of fluid?
ii) What volume of fluid?
iii) What rate of administration?

Unfortunately answers to these questions are not always easy and the regimen needs to be tailored to the patient concerned considering variables such as the preoperative state of the patient, the nature of the surgery and any co-morbidity.

7.1. Preoperative assessment : Resuscitation and estimation of fluid deficit

Patients presenting for elective minor surgery will have no or slowly developing fluid deficits. In contrast, the severely traumatised patient has dynamic fluid shifts in blood and interstitial volume and in whom the fluid balance is more difficult to evaluate.

Thus the first step is to recognise the patient requiring *resuscitation*. Restoration of an adequate vascular fluid volume is essential to maintain cardiovascular stability and organ perfusion. In the acute clinical situation the weight loss of the child is usually a good indication of water loss.

The degree of dehydration will determine the volume and rate of administration of fluid:

MODERATE DEHYDRATION (5 – 10%)	SEVERE DEHYDRATION (> 10%)
Irritable Sunken eyes Thirst Decreased skin turgor. (Abdominal skin pinch goes back in < 2 seconds)	Apathetic or unconscious Sunken fontanelle Capillary refill > 4 seconds Decreased skin turgor. (Abdominal skin pinch goes back in > 2 seconds)

In the dehydrated paediatric patient requiring resuscitation, a bolus of Ringer's lactate (20 ml/kg) should be administered intravenously as soon as possible. This bolus may need to be repeated in cases of more severe dehydration.

Colloids can also be used during the initial resuscitation period. In the case of hydroxyethyl starch (HES), limited clinical data on the perioperative period is available. In a study of 41 children including neonates and infants, a mean dose of 7.5 – 16 ml/kg of Voluven® was administered safely and well tolerated for stabilisation of haemodynamics. In another study HES starch was compared with 5 % albumin during general surgery in infants and children. Results found that HES was as effective as albumin and no undesirable side effects were reported.

Gelatins have been used for many years in children and early infancy to treat intravascular fluid deficits. Safety in the neonatal population is less clear and there is some evidence that gelatin usage, especially in the premature neonate, may increase the risk of NEC. Currently the package insert for Gelofusine® (a succinylated gelatin), states that the product is contraindicated in children below 1 year of age.

7.2 Intraoperative fluid management

Intraoperative fluid therapy is aimed at providing basal metabolic requirements (maintenance fluids), compensating for preoperative fasting deficit and at replacing losses from the surgical field.

If the new NPO guidelines are followed as described above, fasting fluid deficit is expected to be minimal. Unfortunately this is often not the case and prolonged periods of fasting still occur. Fasting deficit is calculated by multiplying the hourly maintenance fluid requirement by the number of hours of restriction. In 1975, Furman *et. al.* proposed to replace 50% of the fasting deficit in the first hour, 25% of the deficit in the second hour and 25 % of the deficit in the third hour. Conversely, Holliday and Segar have changed their recommendations for maintenance fluid therapy, especially for surgical patients. They recommend to correct first fluid deficit with 20 – 40 ml/kg, then to give HALF of the average maintenance for the first 24 hours and to monitor daily sodium plasma concentrations. This fluid deficit is typically replaced using an isotonic solution such as Ringer's lactate. In infants and young children who have been starved for excessive periods, addition of 1% or 2% Dextrose to the Ringer's lactate is appropriate.

In summary there has been a trend to administer LESS fluid volume to correct fluid deficit as calculated by the original '4-2-1 rule' described by Holliday and Segar.

Arbitrary modifications of this rule have seen practitioners administering 60% of the volume calculated by the original formula.

7.2. <u>Postoperative fluid therapy</u>

In the postoperative period, maintenance fluids are required to replace insensible losses, urinary losses and provide a source of dextrose when oral intake is not possible. Oral fluid intake is usually allowed within 3 hours postop in most paediatric patients undergoing minor surgery. If oral intake should be delayed (e.g. after abdominal surgery), fluid therapy should be administered intravenously. In addition, isotonic replacement may be required for ongoing or abnormal losses (eg. gastrointestinal losses).

There is great debate to the volume and composition of maintenance fluid required in the first 24 hours postoperatively. As previously mentioned, ADH secretion from non-osmotic triggers such as pain, nausea, opiates etc. will decrease the volume of fluid required in the post op period. Energy expenditure is often reduced in children in the ICU, particularly those who are breathing warmed humidified air through a ventilator circuit. 5 % Dextrose is usually adequate to provide energy needs in the early *postoperative* period.

8. <u>Other practical tips:</u>

Beside the volume and composition if fluid administered, here are a few other practical things to consider:

i) Always get rid of air bubbles in the intravenous administration set. (Risk of paradoxical air embolism via patent cardiac shunts)
ii) Use ‘flush’ syringe to negate dead space when administering intravenous drugs.
iii) Warm intravenous fluids where possible.
iv) Hidden fluid administration such as used to dilute antibiotics or analgesics should be taken into account, especially in neonatal anaesthesia where margin for error is miniscule.
v) Always administer calculated volumes accurately using a buretrol or syringe driver.

9. Blood products … In brief

As mentioned previously, the blood volume of the paediatric population differs markedly from that of the adult population. An initial Hct. of 55% in the healthy full term neonate gradually falls to as low as 30% in the 3 month old infant before rising to 35% by 6 months. Blood loss is typically replaced with a crystalloid (3ml crystalloid : 1ml blood loss) or colloid (1 ml colloid : 1ml blood loss) until the haematocrit reaches a predetermined lower limit. Various formulae exist to calculate the allowable blood loss. These should only be used as a guide:

Allowable Blood Loss (ABL)*

$$\frac{EBV \times (H_i - H_f)}{H_i} = ABL$$

H_i = initial Hct
H_f = final lowest acceptable Hct

Estimated Blood Volume (EBV)

EBV = weight (kg) x average blood volume

Average blood volumes

Age	*Blood volume*
Premature Neonates	100 mL/kg
Full Term Neonates	85 mL/kg
Infants	80 mL/kg
Adult Men	75 mL/kg
Adult Women	65 mL/kg

The volume of blood transfused can be estimated using the formula:

Desired Hb (g/dl) – Current Hb (g/dl) × weight (kg) × 3 = Approximate volume to transfuse.

(This typically works out to be approximately 10 – 15 ml /kg of packed cells)

What about leucocyte depletion, washed cells and irradiation of blood products?

9.1. Leucocyte depeletion:

These products are prepared by filtration of red cell concentrates. Leucocyte depleted components contain fewer than 5×10^{6} leucocytes per red cell unit (99.9% leucocyte removal).
Some countries in the developed world have recommended universal pre-storage leucocyte depletion of cellular concentrates. This is however very costly and not practiced in developing countries. According to the South African National Blood Service (SANBS) guidelines, the indications for leucocyte depleted components are as follows:

i) Recurrent febrile non haemolytic transfusion reactions.
ii) Patients with severe aplastic anemia who are potential stem cell transplant recipients.
iii) Leucocyte depletion of blood components is an effective alternative to the use of CMV seronegative blood components for prevention of transfusion transmitted CMV infection to at risk patients.
iv) Leucocyte depleted blood components should be used for intra-uterine transfusions and are recommended for *all infants under 1 year of age*.

9.2. Washed Red cells:

These products are prepared by washing red cell concentrate. This ensures 80% leucocyte removal as well as absolute plasma removal. Of interest is that the SANBS recommends washed red cells for, amongst others, transfusion of neonates with T-cell activation due to NEC.

9.3. Irradiated Blood Products:

These products are used for prevention of graft-vs-host disease in:

i) Immune suppressed patients
ii) Pre- and post bone marrow transplant patients.
iii) Patients receiving blood from blood relatives.
iv) Intrauterine transfusions.
v) Neonates; exchange transfusions only.

10. Summary:

- Identify and treat hypovolemia rapidly.
- After major surgery in patients at risk of high ADH secretion, daily maintenance fluids are to be reduced by 1/3 for the first postoperative day, provided the child is normovolemic.
- Plasma sodium and glucose concentrations should be measured at least daily in patients who are acutely ill.

11. Conclusion:

While there is still some debate on the ideal maintenance therapy for children, all caregivers agree that there is a need to individualise fluid therapy and to monitor sodium concentration in children receiving an infusion. There is also strong evidence to limit the average fluid maintenance volume to approximately half to two thirds that of the classical '4-2-1 rule'. Isotonic fluids such as Ringer's lactate are more appropriate intraopertively than hypotonic solution.

Fasting guidelines allowing clear fluids up till 2 hours preoperatively are widely accepted and if applied, should in negate the need for complex calculations of large fluid deficits as well as reduce the risk of perioperative hypoglycaemia.

Recently the dangers of hyperglycaemia from inappropriate administration of high concentrations of dextrose have been realised. The danger of perioperative hyponatraemia from administration of hypotonic fluids combined with the increased non-osmotic secretion of ADH has recently been recognized as a risk factor for cerebral oedema.