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CLINICAL PERSPECTIVE

Intraoperative fluid therapy in neonates

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The evidence base for the administration of intraoperative fluids in neonates is poor and extrapolated from adults and children. Differences from adults and children in physiology and anatomy of neonates inform our practice.

Keywords: fluid responsiveness, fluid therapy, intraoperative, neonates

Introduction

Fluid therapy should ensure adequate organ perfusion but not cause electrolyte abnormalities, increase in lung water or tissue oedema.[1] Any intraoperative fluid plan includes maintenance therapy, replacement for blood loss and for insensible and sensible water loss due to surgery and anaesthesia.

Maintenance fluid

Factors that determine maintenance fluid volumes during surgery

Adjustment of maintenance fluid volume during surgery needs an appreciation of the factors that determine how maintenance fluid volumes are calculated.

The most common way maintenance fluid volumes are calculated is based on energy expenditure indexed to bodyweight.[2] Energy expenditure is much lower during surgery than in a healthy active child. Intraoperative maintenance fluid volumes calculated on energy expenditure will overestimate volumes required.[3]

Insensible and sensible losses are altered by surgery, and so estimations of these made on the ward may not be relevant. Insensible losses in neonates vary with gestational age.[4] Premature neonates lose water through their skin, which is fragile and poorly keratinised.[5]

The effect of radiant heaters on transepidermal water loss has been well characterised.[6] Transepidermal water loss due to convector heaters is less well characterised in infants below 1 month.[7]

Water lost from the respiratory tract is affected by the respiratory rate. It can be minimised by the use of circle systems and heat and moisture exchangers.[8]

Renal losses make up for the majority of sensible water loss and are determined by the plasma levels of antidiuretic hormone (ADH) and atrial natriuretic hormone (ANP) and renal maturation.[9] On the first day of birth, levels of ADH are high and so renal losses are low. As lung function improves, pulmonary vascular resistance decreases; there is an increase in the blood flowing back into the left atrium with a subsequent release of ANP.[10] Diuresis occurs in term neonates from day 2–3 and from a week in the premature neonate. This cardiorespiratory adaptation is responsible for the weight loss in the first few days after birth.[9]

The volume of maintenance fluid given during surgery should reflect the stage of cardiorespiratory adaptation: maintenance fluid volumes should be much lower immediately after birth and only be increased when adaptation has taken place at around day 3.[8,11]

ADH rises when intravascular volume falls by 10%, which is common in neonatal surgery and so surgery is accompanied by a decrease in urine volume.[12] The neonate often presents to surgery with inadequate intravascular volume due to early cord clamping and repeated blood sampling on the neonatal intensive care unit (NICU).[13]

ADH may also be raised inappropriately (syndrome of inappropriate ADH secretion [SIADH]). SIADH is a raised level of ADH in the absence of osmotic and baroreceptor stimulation; although this is rare it does occur during surgery. SIADH can occur in neonates with sepsis and respiratory failure.[14,15]

Urinary losses are also determined by the maturity of the neonatal renal system. Both term and preterm infants can vary their urine volumes over variable fluid loads once cardiorespiratory adaptation has occurred.[16,17] The neonate is not able to concentrate the urine in the face of dehydration.[8] This is not related only to insensitivity of the collecting ducts to ADH but also to an inability to produce a hypertonic environment around the collecting tubules and may be related to reduced protein intake in the diet.[18] The low concentrating ability of neonates means that very conservative fluid regimes in neonates may lead to dehydration.

Decreases in cardiac output caused by ventilation and intravascular volume depletion will not only affect ADH levels but also decrease the glomerular filtration rate in neonates and so reduce urine volumes.

Should maintenance fluids be hypotonic or isotonic?

Isotonic fluids are now used routinely for intraoperative maintenance in children.[19–21] In the neonate, there has been reluctance to switch to isotonic solutions due to concerns regarding the ability of the neonate to handle salt solutions.[22] This is despite a risk of hyponatremia, particularly in the premature infant.[23]

Premature neonates have a reduced ability to reabsorb sodium with consequential negative sodium balance and risk of hyponatraemia.[24,25] Renal absorption of sodium increases at a gestational age of 33 weeks and the risk of hyponatraemia in term neonates is thus much less than in the premature neonate.[24]

There is a paucity of studies demonstrating the neonate's ability to handle sodium loads. In low birth weight neonates, those that received higher fluid and sodium intakes between days 3 and 10 did not undergo the normal contraction of extracellular fluid associated with postnatal diuresis but were still at greater risk of hyponatraemia than of hypernatraemia.[26]

A total of 34 newborn infants undergoing surgery were observed for incidence of postoperative hyponatraemia. All neonates were on glucose containing maintenance fluids in the preoperative period. Intraoperative fluid consisted of a maintenance rate of glucose 5% at 4 ml/kg/h plus compensation for other surgical losses: insensible water loss (ISWL), third space loss and blood loss, with glucose 5% at a rate of between 4 and 20 ml/kg/h. Hartmann's solution was given after induction, and if increases in heart rate and/or drops in blood pressure of greater than 20% occurred. Three subjects were hyponatraemic before surgery (less than 135 mmol/l), all of whom corrected with surgery. Four neonates were found to be hyponatraemic after surgery. There was a relationship between hypontraemia and the free water administered intraoperatively. A change in sodium concentration of greater than 4 mM was statistically associated with increases in intraoperative free water volumes.[27]

Lonnqvist suggests that isotonic solutions for maintenance in neonates should be considered.[28] A novel isotonic balanced salt solution BS-G1 has been used recently in 66 neonates in a multicentre trial from Germany. The fluid was started at a rate of 10 ml/kg/h and adjusted in accordance with blood glucose levels. There were no episodes of hyponatraemia or hypernatraemia in this cohort.[29]

Should maintenance fluid contain glucose?

Intraoperative glucose is no longer required in the maintenance fluid for the majority of children[1,19,30] The one group where there is uncertainty is the neonate.

The dangers of hypoglycaemia in the neonate are well recognised.[31–33] In one study there were radiological abnormalities in 94% of term neonates with hypoglycaemia (blood glucose levels < 2.6 mmol/l).[34,35]

In 30 neonates exposed to a balanced salt solution with or without glucose, it was found that the blood glucose was low in the group given only a balanced salt solution if a preoperative glucose infusion was interrupted at the start of anaesthesia. Hypoglycaemia occurred in 3/15 in the group given only a balanced salt solution and 1/15 in the group with glucose and balanced salt solution. Hypoglycaemia was found only in those neonates less than 48 h old.[36]

The worries concerning neonatal hypoglycaemia have tended to inform practice, so that glucose-containing solutions are used for maintenance in neonates, particularly when the neonate has an infusion of glucose or parenteral nutrition in the immediate preoperative period.[30]

The normal glucose infusions used have concentrations ranging from 5% to 10%. These solutions may produce hyperglycaemia, which concern some. The differences in the ability of the neonate to metabolise ketone bodies, free fatty acids and lactate for energy means that hyperglycaemia may indeed protect the neonatal brain from ischaemic injury, which is in sharp contrast to the adult brain.[37] In 171 neonates having cardiac surgery, it was discovered that those with high glucose levels did not have a worse neurological outcome. This study was conducted on neonates undergoing cardiac operations that involved periods of low flow and cardiac arrest; caution should thus be used to extrapolate this to neonates having non-cardiac surgery.[38]

The risk of neonates developing osmotic diuresis is rare below a glucose concentration of 12 mmol/l because the neonate's relatively low glomerular filtration rate limits the filtered load of glucose.[39]

A recent study on 66 neonates with a 1% glucose solution in an isotonic balanced solution has shown no evidence of hypoglycaemia or hyperglycaemia during surgery.[40] The authors suggest that a lower concentration of glucose solutions should be administered to neonates.

In view of the catastrophic consequences of hypoglycaemia against the minimal impact of hyperglycaemia in the neonate, reducing the glucose concentrations of maintenance solutions for neonates should be done cautiously and accompanied by regular monitoring.

Replacement for losses during surgery

Does a third space exist in neonates?

The concept of a third space was introduced into adult anaesthesia on the basis of Shire's study of 13 patients undergoing elective major surgery.[41] Fluid was supposedly sequestered in a space that did not communicate with the extracellular space. This led to an era of liberal fluid administration to compensate for these losses. In recent times a more restrictive approach has been taken in adult anaesthesia.[42] This change in practice has resulted not only from an understanding of the shortcomings of the early tracer studies, but also from outcome studies that have favoured the use of restrictive therapy in colorectal and thoracic surgery.[43]

In neonatal surgery, liberal fluids are still encouraged.[44] Evidence for the deleterious effects of fluid were shown in a retrospective study on 407 neonates having gastroschisis repair. In total, 162 neonates received no fluid before surgery whilst 200 received a mean of 21.49 ml/kg of fluid. Multivariate analysis demonstrated a direct relation between the amount of fluid and days of ventilation after surgery. Every 17 ml/kg increased the ventilation by a day.[45]

A Cochrane review based on five studies comparing a restrictive versus a liberal fluid regime in premature infants on the NICU showed that a restrictive regime reduced weight gain, and the risks of a patent ductus arteriosus and necrotising enterocolitis.[46]

A recent small paediatric study in children aged under 3 showed no difference in outcome between a restrictive and a liberal intraoperative regime.[47] The size of this study makes it difficult to draw any conclusions for the management of neonates.

Fluid responsiveness in the neonate

Adult perioperative fluid management has evolved so that replacement for intravascular fluid loss is tailored to each patient's requirement using goal-directed therapy.[48]

Whereas the technology for the measurement of stroke volume and cardiac output is well advanced in adults, there is a long way to go in neonates.

Fluid responsiveness is the ability of stroke volume to be increased by a fluid bolus. Fluid is usually given until the increase in stroke volume is less than 15%; the patient is then regarded as fluid unresponsive.[49]

Half of fluid boluses given by clinicians are inappropriate (i.e. given when the patient is not fluid responsive).[49]

Despite the dogma that stroke volume is fixed in the neonate, and that the cardiac output is totally heart-rate dependent, the neonatal myocardium is preload dependent.[50] In neonatal sheep, increases in heart rate induced by pacing do not increase cardiac output unless accompanied by increases in the filling time of the left and right atrium.[51] Neonates receiving fluid boluses in the intensive care unit increase their cardiac output with no increase in heart rate.[52]

Fluid requirements in neonates are determined by surrogate measurements: drops in blood pressure, increases in heart rate, increasing capillary refill time, widening of core–peripheral temperature gradients and increasing base deficits. These do not predict fluid responsiveness reliably.[53,54] Measurement of central venous pressure and pulmonary artery wedge pressure also do not predict fluid responsiveness.[53]

A parameter that has been shown to predict fluid responsiveness in the neonate is stroke volume index (iSV) measured using a transoesophageal Doppler.

The reliability of classical parameters and iSV was investigated using receiver operator curves in 50 neonates. Heart rate and mean arterial blood pressure did not predict fluid responsiveness, but stroke volume index (iSV) did.[55]

Dynamic parameters – any use in neonates?

Neonates have poor cardiac compliance and a very narrow window that separates adequate cardiac filling and overfilling.[56] The philosophy of challenging the heart with a fluid load until it no longer responds with a rise in stroke volume risks fluid overload and increased lung water.[49]

Dynamic parameters have been used in the adult literature to predict fluid responsiveness without the need to give fluid.[49] These include the cardiovascular response to straight leg raising and to positive pressure ventilation.

There is limited evidence of the predictive value of dynamic monitors in neonates and much has been extrapolated from small children and infants.

The most useful parameter that predicts fluid responsiveness in neonates is the ventilation-induced variation in aortic flow velocity as measured by the transthoracic or oesophageal echocardiogram. Of the five studies that have been conducted in children on this parameter all have been positive. There is enormous variability in the threshold value of aortic flow velocity variation that distinguishes fluid responders from non-responders; it ranges from 7% to 20%.[57–61]

Dynamic parameters based on arterial pressure waveform analysis and arterial waveform contour analysis are not predictive in small infants and neonates.[53] The reason that the success of these modalities in adults is not emulated in the neonate could be because of the difference in the compliance of the neonatal vascular system.[62] The younger child has a much more distensible vascular system and so changes in blood pressure induced by ventilation are much smaller. Other factors such as reduced cardiac compliance and higher chest wall and lung compliances may also alter the respiratory–cardiovascular relationship and so alter the usefulness of dynamic parameters based on the arterial waveform.[53]

The reliability of the variation in the pulse oximeter waveform (plethysmograph variability index (PVI)) with ventilation, to predict fluid responsiveness, is equivocal in children. PVI measured in stable conditions is predictive whilst those where major fluid shifts are present are less predictive.[63,64] The difficulties of getting reliable oximetry tracing in neonates may preclude this as a reliable monitor for fluid responsiveness in neonates.

Stroke volume variability measured by a bioreactance monitor (NICOM, Cheetah Medical, Wilmington, DE, USA) has had conflicting results. In children under 5 having cardiac surgery it was even less predictive than the CVP, although in an earlier study in smaller children having cardiac surgery it was nearly as useful as the ventilation-induced variability of peak aortic flow velocity.[65,66]

Ventilation-induced cardiovascular changes occur in the neonate only if he/she is ventilated with a tidal volume of at least 10 ml/kg.[53] Lung-sparing ventilation techniques favour the use of low tidal volumes and high PEEP.[67] This limits the practicability of dynamic parameters.

Whilst optimising the stroke volume in neonates is important for tissue perfusion, blood pressure also determines perfusion to the brain and other vital organs. There is no consensus on the definition of hypotension in the neonate and this has been extensively reviewed recently.[68] Blood pressure is a poor surrogate for systemic flow in neonates. Studies in infants and neonates have shown that fluid responders did not have an associated rise in blood pressure.[65,69–72]

Monitors of end organ perfusion have been used to titrate fluid therapy. Near infrared spectroscopy (NIRS) has shown that a systolic blood pressure fall of 37% from baseline is associated with significant cerebral desaturation. Fluids not only raised blood pressure but improved cerebral desaturation.[73]

Efforts to find suitable monitors of tissue perfusion in neonates need to be pursued.[74]

Replacement for blood loss before reaching the transfusion trigger: colloids or crystalloid?

Transfusion triggers and neonatal blood and blood product administration is beyond the scope of this review but has been reviewed recently.[75–77]

There is controversy about what fluid to give before blood is transfused in neonates. In a survey to members of the Association

of Paediatric Anaesthetists (APA) and the French-language Society of Paediatric Anaesthesiologists (ADARPEF), a majority of both the APA (90%) and ADARPEF (81%) preferred the use of albumin for the replacement of perioperative fluid losses in premature and term neonates.[78]

It is difficult to understand why this is. A randomised controlled trial in premature infants suggests that saline is as effective as 5% albumin for treating hypotension in preterm infants and reduces fluid retention in the first 48 h.[79]

Colloid infusions in very low birthweight infants (VLBW) are associated with impaired lung function and increased oxygen dependency.[80]

Recent studies on the glycocalyx endothelium barrier (EGL) have shown it is a major determinant of vascular permeability. Inflammatory mediators released during sepsis and trauma as well as mechanical injury from lung stretching may damage the EGL.[81,82]

Surgery in septic neonates present conditions that may compromise normal EGL integrity and so enhance extravasation of albumin and other colloids into the interstitial space. This will compromise lung function and wound healing.

The EGL develops early in gestation although there are some differences between the developing and the adult EGL. These differences may favour albumin loss into interstitial spaces.[83]

Conclusions: what do I do?

The neonatal intraoperative fluid regime needs replacement of fluid for maintenance, to replace losses associated with surgery and replacement for blood loss. [68] I continue maintenance fluid at the same rate as that of the immediate preoperative period. I use dextrose solutions with additives of sodium and potassium adjusted to the phase in which the neonate is in its cardiorespiratory adaptation.

I make an estimation of insensible loss from the skin, viscera, respiratory tract and urine. I replace this loss with a balanced salt solution. I use Hartmann's solution (there is no evidence of the benefits of acetate-based balanced salt solutions in neonates).[84] I do not compensate for third space losses.

I set a transfusion trigger based on respiratory and cardiac comorbidity and then before I start giving blood I will transfuse 2 ml of Hartmann's for every 1 ml of blood lost.

I use a combination of classical parameters and the transoesophageal Doppler (in neonates above 2.5 kg) to guide fluid therapy; I use the response of stroke volume index (iSV) to 10 ml/kg of Hartmann's. A modality that has shown promise is ventilation-induced variability in peak aortic flow velocity, a function that is now available on the transoesophageal Doppler monitor (Cardio QP, Deltex Medical, Chichester UK).

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