REVIEW ARTICLE

Fluid and Electrolyte Management of Very Low Birth Weight Infants

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Recent advances in medical knowledge and technology have markedly improved the survival rates of very low birth weight infants. Optimizing the neuro-developmental outcomes of these survivors has become an important priority in neonatal care, which includes appropriate management for achieving fluid and electrolyte balance. This review focuses on the principles of providing maintenance fluid to these infants, including careful assessment to avoid excessive fluid administration that may increase the risk of such neonatal morbidities as necrotizing enterocolitis, patent ductus arteriosus, and bronchopulmonary dysplasia (BPD). The review also describes the principles of fluid and electrolyte management of infants with BPD, which includes the strategy of providing adequate nutrition to promote normal growth.
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1. Introduction

The survival rate of very low birth weight (VLBW) infants has improved significantly during the past several decades.[1] This is a worldwide phenomenon resulting from improved antenatal and neonatal care. Unfortunately, the neuro-developmental outcomes of the survivors, particularly those who are of extremely low birth weight, have not improved, in part due to the persistence of acute neonatal morbidities such as necrotizing enterocolitis (NEC), late onset sepsis and bronchopulmonary dysplasia (BPD).[2] These morbidities have been shown to be associated with poor neuro-developmental outcomes.[3—5] Although the pathogenesis of these morbidities is multi-factorial, excess fluid and sodium intakes during the first week of life has been shown to impede normal contraction of extracellular fluid, leading to an increased risk of these morbidities.[6—8] Thus, in our quest to improve outcomes of these high-risk infants, appropriate fluid and electrolyte management is an essential component of overall management strategies. The

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focus of this review is to describe: (1) the physiologic basis for the provision of fluid and sodium to replace normal losses; (2) the universal physiologic contraction of extracellular fluid; (3) the consequences of not allowing this normal transition to occur; and (4) the physiologic basis for the fluid and electrolyte management of infants with BPD.

2. Maintenance Fluid Requirement

Calculation of maintenance fluid requirement in VLBW infants during the first week of life is essentially an exercise of estimating the amount of fluid needed to replace normal losses. These losses include insensible water loss (IWL), water loss via the kidney as urine, and, to some extent, water losses in the stool. In VLBW infants, during the first week of life, stool water loss is minimal and can be ignored in the calculation. In a growing infant, provision of fluid to maintain a positive fluid balance is essential for growth (each gram of new tissue requires 0.7 mL of positive water accretion). Since growth is not an issue during the first week, this allowance is also not needed in the calculation. Thus, the main items that need to be considered in calculating maintenance fluid requirement during the first week of life are IWL and renal water loss.

IWL is defined as water evaporated from the skin (2/3) and lung (1/3) not seen by the naked eye. Several environmental and clinical factors influence the amount of IWL: lower maturity,[9] less relative humidity,[10] ambient temperature exceeding the infant's neutral thermal environment,[11] abdominal skin defects such as omphalocele and gastroschisis, use of radiant warmer[12] and phototherapy [13-16] result in an increase in IWL. Increasing maturity, higher ambient and ventilator relative humidity, and postnatal age are associated with a decrease in IWL (Table 1). There are two reasons for the inverse relationship between maturity and IWL: a high surface-to-weight ratio[17] and a reduced skin epithelial barrier. As show in Figure 1, the skin surface-to-weight ratio in term and extremely low birth weight (ELBW) infants are 14 and two times greater, respectively, than in adults.[17,18] The immature skin epithelial development, as evidenced by the shiny skin appearance of ELBW infants, allows for greater water evaporation because there is less skin barrier. An ambient temperature exceeding 1°F results in an increase in IWL of 1 mL per hour. The reason for the increased IWl in infants with abdominal skin defects is obvious. The increase in IWL due to of the use of phototherapy and radiant warmer has been well documented. [12,13] The inverse relationship between skin and lung surface relative humidity and IWL is based on a simple principle of physics in that the evaporative water loss from a surface is
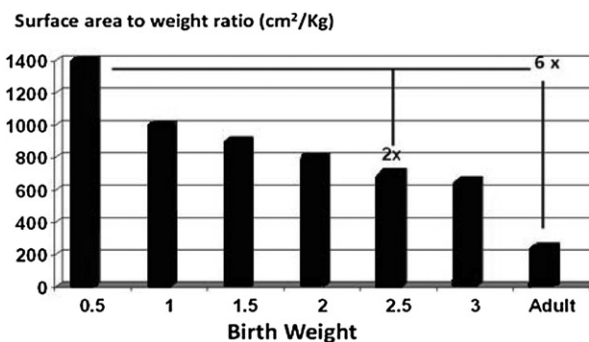
Table 1 Factors affecting insensible water loss.	
Increase	Decrease
Low maturity	Higher maturity
Low relative humidity	Increasing postnatal age
Ambient temperature exceeding neutral thermal environment	High environmental relative humidity
Skin defects (omphalocele, gastroschisis)	High ventilator relative humidity
Phototherapy and use of radiant warmer	

Figure 1 Surface area-to-weight ratio infants compared with adults. (Calculated from formula in Haycock GB, Schwartz GJ, Wisotsky DH. *J Pediatr* 1978;93:62—6.[18] Figure adapted with permission from Sridhar S, Baumgart S. Water and electrolyte balance in newborn infants. In: Hay WW, Thureen PJ, editors. Neonatal nutrition and metabolism. 2nd ed. Cambridge, UK: Cambridge University Press; 2006.[17])

dependent on the relative vapor pressure gradient. If the ambient vapor pressure (product of ambient temperature and water content) is high and close to the vapor pressure of the skin (product of skin temperature and water content), the vapor pressure gradient will be small, with less IWL. A similar phenomenon occurs on the lung surface. If the ventilator is well humidified and warmed, the vapor pressure will be high and the gradient between inspired air and lung surface vapor pressure gradient will be less, resulting in decreased IWL.

It is apparent that a multitude of environmental and clinical factors affecting IWL will result in a large day-to-day variation of its value in individual infants. If accurate intake, output and weight data are collected over a specific time-frame (e.g. every 24 hours), the IWL of the individual infant can be calculated with a fairly high degree of precision by the following formula:

Intake − Output (mainly urine during the first week of life) − (Δ in weight)

For instance, a 1 kg infant, who receives 100 mL of fluid, passing 60 mL of urine and losing 20 g weight over a 24-hour period, would have an IWL of 60 mL/kg/24 hour. Using the data collected, and the formula above, one can calculate IWL for an infant on a daily basis that can be used to calculate the daily fluid requirement.

Renal water requirement is dependent on the solute load, which is endogenously derived or exogenously administered. During the first days of life, when nutrient energy intake is less than basal metabolic need, the infant will need to 'burn' his/her own tissue to meet the caloric requirement. The catabolic products amount to approximately 5 mOsm/kg, which will require approximately 20 mL/kg of free water for excretion. It should be emphasized, however, that, with recent data showing the beneficial effect of early parenteral amino acid administration,[19-21] the need for catabolic process to meet the caloric requirement is reduced, which lowers the endogenous solute load but increases the exogenous source of solute load. Beyond the first week of life, when the infant is receiving full enteral and parenteral intake, the exogenous solute load will be in the range of 20—25 mOsm/kg, requiring 60—75 mL/kg free water for its excretion.

Urine output exceeding the amount required for solute excretion is due to excess intake and excretion of isotonic fluid being removed from the extracellular fluid (ECF) compartment. The latter is a physiologic phenomenon and the amount excreted should not be replaced.

3. Contraction of Extracellular Fluid

During the first few days of life, all infants experience a contraction of extracellular fluid (ECF). The mechanism of this interesting physiologic phenomenon is unknown. The contraction of ECF is associated with an increase in urinary sodium excretion,[22] diuresis[23] and weight loss.[24–26] Figure 2 shows the high urinary sodium excretion in a group of VLBW infants during the first week of life, independent of respiratory status.[22,26] Bidiwala et al showed that diuresis begins in a large majority of VLBW infants at approximately 24–48 hours and ends at 72–96 hours of age.[23] These data suggest that natriuresis occurs in almost all VLBW infants independent of respiratory status during the first week, which coincides with the reduction of ECF.[22] These changes are also associated with weight loss due to the removal of ECF, and, to a lesser degree, the catabolic process. All infants, including the VLBW infants, experience a weight loss of 10–15% of birth weight during the first 5 days, with an inverse relationship between the magnitude of weight loss and birth weight.[25] The inverse relationship between maturity and postnatal weight loss is due to the difference in ECF volume, which is also inversely proportional to gestation.[27,28] The weight changes stabilize

Figure 2   Urinary sodium excretion in very low birth weight infants. (From Ross BS, Cowett RM, Oh W. *Pediatric Res* 1977;11:1162–4[22], with permission)

toward the end of the first week and begin to climb thereafter, reflecting anabolic state and growth.

It is important to formulate the fluid and electrolyte intakes to allow for the occurrence of this physiologic transition. Lack of these will contribute to the development of neonatal morbidities such as symptomatic patent ductus arteriosus (PDA),[7] necrotizing enterocolitis (NEC)[6] and bronchopulmonary dysplasia (BPD).[29,30] In a randomized controlled trial, Bell et al [6,7] have shown that giving a high fluid load to VLBW infants resulted in an increased incidence of PDA and NEC. Using the inulin dilution technique to measure ECF changes in a subset of the study patients, Stonestreet et al[24] showed that the high fluid load (mean = 160/kg/day) resulted in no change in ECF between day of life 2 and 8, in contrast to a reduction of ECF between the same time interval when the infants were given a low fluid load (mean = 120/kg/day). The mechanism of this finding is unclear. The speculation is that, when the VLBW infant is given too much fluid and the relatively immature kidney cannot compensate for the excess, a retention (rather than contraction) of ECF occurs. The latter may result in an increased level of prostaglandin E_2 that results in PDA with left-to-right shunt with decreased systemic blood flow (aortic steal) and reduced mesenteric perfusion, with ischemia that enables the development of NEC.

Retrospective studies have established the association between high fluid intake during the first week and lack of appropriate postnatal weight loss and bronchopulmonary dysplasia (BPD) in VLBW infants.[29,30] This association is probably due to a lack of ECF contraction, with increased interstitial fluid content, including within the lungs. The latter results in reduced lung compliance, necessitating more oxygen and ventilatory support, leading to BPD. Excess sodium intake during the first week is also associated with increased risk of at 1 month and at 36 weeks completed postmenstrual age, although, due to small sample size, the difference is not statistically significantly in the latter.[31] The speculation for this observation is that excess sodium intake results in expansion of ECF, leading to similar changes in lung fluid retention as occur with excess fluid intake, with increased needs for oxygen and ventilatory support While these data are strongly suggestive of the association between excess fluid intake during the first week with PDA, NEC and BPD in VLBW infants, a large clinical trial to make conservative fluid and sodium administration a standard practice to confirm this association is essential.
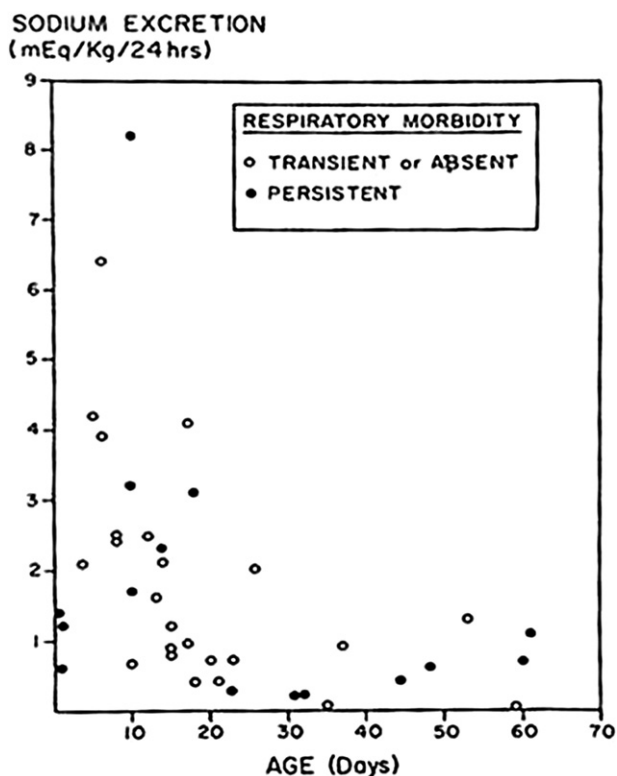
4. Fluid and Electrolyte Management of Infants with BPD

4.1. Maintenance fluid therapy

By definition, infants who develop BPD are at least 36 weeks postmenstrual age. Their organ maturity, including the skin, has approached the level of a term infant. Thus, their IWL is close to the value of a term infant (20–25 mL/kg/day)[32] because their body surface-to-weight ratio and skin epithelial development are close to that of a term infant Most infants with BPD have attained full

nutritional intake either enterally and/or parenterally. The solute load is generally in the range of 25—30 mOsm/kg, which requires approximately 60—75 mL/kg of free renal water for its excretion. Unlike an infant during the first week of life, an infant with BPD will have significant water loss via the stools (10—15 mL/kg); this water loss should be replaced. The water requirement for growth is approximately 10—15 mL/kg/day to meet the net water accretion of new tissue (approximately 20 g/kg/day) as a function of growth. Thus, a growing infant with BPD should have a total fluid intake of 120/mL/kg/day. If the intake is all through the enteral route, given a known net gastrointestinal absorption of approximately 70%, the enterally fed infant should have a gross intake of approximately 140—150 mL/kg/day to ensure a positive water balance.

4.2. Diuretic therapy

Studies have demonstrated short-term improvement in lung mechanics when diuretics are administered to preterm infants who are at risk of or who have already developed BPD.[33,34] However, in a recent meta-analysis, the authors concluded that "there is no strong evidence for routine chronic use of tubular diuretics in preterm infants with chronic lung disease".[35] Despite this statement, many clinicians use chronic diuretics therapy (loop or thiazide diuretics) in infants with BPD. This use results in increased renal excretion of sodium, potassium, and calcium, which need to be replaced to avoid the complications of hyponatremia, hypokalemia, and hypocalcemia. Based on the carefully measured urinary excretion of these electrolytes,[36] the average amount of replacement of these elements is 2—3 mEq /kg/day if diuretics are used daily. Other potential complications of chronic diuretics therapy include ototoxicity, transient nephrocalcinosis, and hypokalemic metabolic alkalosis.

4.3. Growth promotion

Achieving a normal somatic growth is an important goal in the management of preterm infants with BPD. A study by Ehrenkranz et al, which used a large cohort of ELBW infants admitted to the Neonatal Research Network, showed that poor weight gain is significantly associated with neurodevelopmental impairment.[37] Optimal growth requires adequate caloric, nutrient, and water intake in the presence of normal growth factors and other genetic elements for growth. The basal metabolic rate in infants with BPD is approximately 25% higher than in infants without BPD because of increased work involved in breathing,[38] (Figure 3) necessitating a corresponding increase in caloric intake to ensure adequate energy for growth. From the fluid therapy standpoint, if the caloric density of the nutrient is maximal, increased fluid intake may be necessary to provide the required caloric intake. Another important consideration is that the net gastrointestinal absorption of enterally administered nutrients is only 70%. This adjustment needs to be considered in calculating the nutrient intake to ensure adequate caloric and nutrient intake essential for optimal growth.
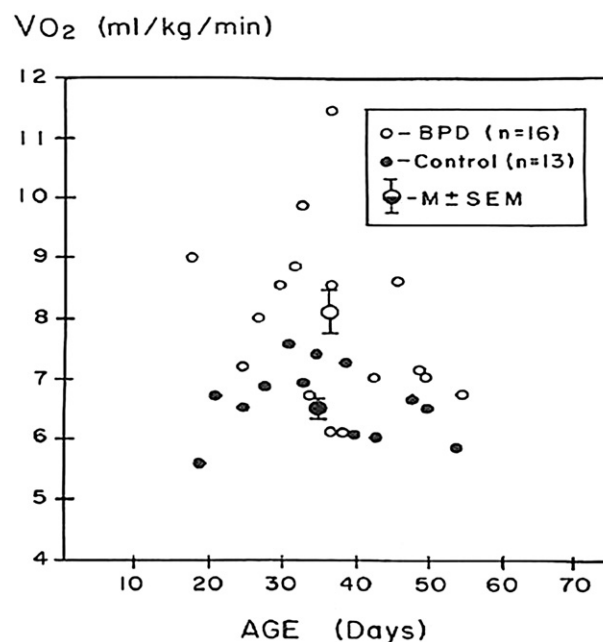

Figure 3 Basal oxygen consumption in very low birth weight infants with and without bronchopulmonary dysplasia. (From Weinstein MR, Oh, W. *J Pediatr* 1981;99:958—61[38], with permission)

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