that fluid type rather than rate had a greater effect on sodium concentration even though the pre-admission fluids received by the patients were not recorded. Kannan, *et al.* [5], in their randomized controlled trial demonstrated that incidence of hyponatremia was reduced in the group receiving 0.9% saline in 5% dextrose at standard maintenance volume. Similar observations were reported by Coulthard, *et al.* [12], where post operative administration of one-third normal saline at two-thirds of standard rate caused hyponatremia in 37% of patients.

As of now, the body of evidence is largely tilted in favor of isotonic maintenance fluids in sick children. However before a 'one size fits all' strategy becomes applicable across the board, we need more answers on alternative mechanisms for hyponatremia. To put the fluid type *versus* rate debate to rest, further robust studies with multiple arms for different fluid tonicity and volumes along with measurement of urinary electrolytes, osmolality and plasma AVP levels are needed. Until then we need to tailor individual fluid needs, based on clinical scenario and strict serum sodium monitoring.

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REFERENCES

1. Holliday M, Segar W. The maintenance need for water in parenteral fluid therapy. Pediatrics. 1957;19:823-32.
2. Wang J, Xu E, Xiao Y. Isotonic versus hypotonic fluids in hospitalized children: A Meta-Analysis. Pediatrics. 2014;133:2013-41.
3. Shamim A, Afzal K, Ali M. Safety and efficacy of isotonic (0.9%) *vs.* hypotonic (0.18%) saline as maintenance intravenous fluids in children. A randomized controlled trial. Indian Pediatr. 2014;51:969-74.
4. Moritz M, Ayus JC. New aspects in the pathogenesis, prevention, and treatment of hyponatremic encephalopathy in children. Pediatr Nephrol. 2010;25:1225-38.
5. Kannan L, Lodha R, Vivekanandhan S, Bagga A, Kabra SK, Kabra M. Intravenous fluid regimen and hyponatremia among children: A randomized controlled trial. Pediatr Nephrol. 2010;25:2303-9.
6. Montanana PA, Modesto I Alapont V, Ocon AP, López PO, López Prats JL, *et al*. The use of isotonic fluid as maintenance therapy prevents iatrogenic hyponatremia in pediatrics: A randomized, controlled open study. Pediatr Crit Care Med. 2008;9:589-97.
7. Neville KA, Sandeman DJ, Rubinstein A, Henry G, McGlynn M, Walker JL. Prevention of hyponatremia during maintenance intravenous fluid administration: A prospective randomized study of fluid type versus fluid rate. J Pediatr. 2010;156:313-9.
8. Guglielminotti J, Tao S, Maury E, Fierobe L, Mantz J, Desmonts JM. Hyponatremia after hip arthroplasty may be related to a translocational rather than to a dilutional mechanism. Crit Care Med. 2003;31:442-8.
9. Singhi S, Jayashree M. Free water excess is not the main cause for hyponatremia in critically ill children receiving conventional maintenance fluids. Indian Pediatr. 2009;46:577-83.
10. Taylor D, Durward A. Pouring salt on troubled waters. Arch Dis Child. 2004;89:411-4.
11. Yung M, Keeley S. Randomised controlled trial of intravenous maintenance fluids. J Pediatr Child Health. 2009;45:9-14.
12. Coulthard MG, Cheater LS, Long DA. Perioperative fluid therapy in children. Br J Anaesth. 2007;98:146-7.

Isn't it Time to Stop Using 0.18% Saline in Dextrose Solutions for Intravenous Maintenance Fluid Therapy in Children?

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Maintenance intravenous fluids are integral in management of sick children in whom enteral administration of fluids, electrolytes and energy needs is not possible or feasible. This maintenance fluid requirement has commonly been calculated on the basis of Holliday and Segar formula [1], based on healthy children's energy expenditure needs. This estimation may not be applicable for sick children as they have alterations in fluid balance, renal sodium and water handling. There are non-osmotic stimulants to vasopressin release in sick children resulting in a tendency to free water retention by kidney [2]. These factors predispose sick children to hyponatremia and fluid overload when given maintenance fluids and electrolytes using the Holliday and Segar formula.

Hyponatremia is the most common dyselectrolytemia in sick children; it can cause encephalopathy, death and

permanent neurological sequelae. Holiday and Segar's formula suggests adding 3 mEq of sodium per 100 mL of water for infants; this is equivalent to administering 0.18% normal saline, which is a hypotonic fluid and predisposes to development of iatrogenic hyponatremia. However, many pediatricians use the same fluid for older children as well, which is inappropriate even by the Holiday and Segar's formula. There is increasing evidence showing the risk of hyponatremia with administration of hypotonic maintenance fluids in hospitalized children [3,4], but hypotonic fluids still remain the most commonly prescribed fluids for admitted children [5]. While administration of hypotonic fluids alone cannot explain hyponatremia [6], administration of isotonic maintenance fluid is associated with reduced incidence of hyponatremia amongst admitted children [7]. It is noteworthy that hyponatremia is related more significantly to the tonicity of administered fluid rather that volume [7]. Concerns regarding possibility of excessive sodium load and volume overload with administration of isotonic maintenance fluid have been allayed in various studies [7,8].

Fluid overload is associated with increased morbidity and mortality amongst sick children, independent of abnormalities in serum sodium levels [9]. Maintenance fluid volume calculated using the Holliday and Segar formula is based on normal urine output and energy expenditure in children. It does not take into account the effect of increased vasopressin level, reduced insensible fluid losses, reduced energy expenditures and increased tendency to fluid retention in a sick child. The formula consequently over-estimates the maintenance requirements. This may predispose children to harmful effects of iatrogenic fluid overload, especially in circumstances such as Acute respiratory distress syndrome. The maintenance fluid requirement should be individualized based on energy expenditures, input-output balance and hemodynamic status.

In this issue of *Indian Pediatrics*, Shamin, *et al.* [10] provide further evidence of increased incidence of hyponatremia associated with commonly practiced method to calculate daily maintenance fluid requirement in hospitalized children. In a randomized controlled trial, the authors compared administration of hypotonic fluid at volume calculated using the Holliday-Segar formula with administration of isotonic fluid at 60% of the calculated volume. They also found that children in hypotonic fluid group had a weight gain as compared to isotonic fluid group who had weight loss, thus indicating a fluid overload state.

The reason to highlight the above points is to emphasize that the general approach to intravenous maintenance fluids is now being questioned. The method of calculation of volume and composition of maintenance fluids that has been used over half a century is now being considered inappropriate for sick children. The concept of a single formulation of fluid for all may be inappropriate, as each child is different. Intravenous fluids should be tailored according to child's need and condition. The intravenous fluid prescriptions should be reviewed, based on electrolytes, fluid balance, hemodynamic status and weight monitoring at frequent intervals. The National Patient Safety Agency for England and Wales (UK) in 2007 published guidelines recommending the use of 0.45% NaCl or 0.9% NaCl as maintenance intravenous fluids, and to avoid 0.18% NaCl [11]. Despite this recommendation and growing evidence against use of hypotonic fluids, practice has not changed much.

To conclude, hyponatremia and fluid overload are common amongst hospitalized children and are associated with increased morbidity and mortality. There is enough evidence supporting the prevention of hyponatremia by use of isotonic maintenance fluids. It is time that we stopped using hypotonic fluids, especially 0.18% saline in 5% dextrose for maintenance intravenous fluid therapy in children in general pediatric care; the availability should be limited to critical care units and specialist wards, for use in limited numbers of scenarios. This information should be disseminated by the Academy; the professionals involved in care of sick children also need to be informed and trained adequately. At present, isotonic fluids are considered safe for maintenance fluid therapy and the use of hypotonic fluid should be completely curtailed, except in special circumstances where there is a need to administer extra free water.

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REFERENCES

1. Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. Pediatrics. 1957;19:823-32.
2. Gerigk M, Gnehm HE, Rascher W. Arginine vasopressin and renin in acutely ill children: Implication for fluid therapy. Acta Paediatr. 1996;85:550-3.
3. Wang J, Xu E, Xiao Y. Isotonic versus hypotonic maintenance IV fluids in hospitalized children: A meta-analysis. Pediatrics. 2014;133:105-13.
4. Foster BA, Tom D, Hill V. Hypotonic versus isotonic fluids in hospitalized children: A systematic review and meta-analysis. J Pediatr. 2014;165:163-9.
5. Freeman MA, Ayus JC, Moritz ML. Maintenance intravenous fluid prescribing practices among paediatric residents. Acta Paediatr. 2012;101:e465-8.
6. Singhi S, Jayashree M. Free water excess is not the main cause for hyponatremia in critically ill children receiving conventional maintenance fluids. Indian Pediatr. 2009;46:577-83.

7. Kannan L, Lodha R, Vivekanandhan S, Bagga A, Kabra SK, Kabra M. Intravenous fluid regimen and hyponatraemia among children: A randomized controlled trial. Pediatr Nephrol. 2010;25:2303-9.
8. Neville KA, Sandeman DJ, Rubinstein A, Henry GM, McGlynn M, Walker JL. Prevention of hyponatremia during maintenance intravenous fluid administration: A prospective randomized study of fluid type versus fluid rate. J Pediatr. 2010;156:313-9.
9. Arikan AA, Zappitelli M, Goldstein SL, Naipaul A, Jefferson LS, Loftis LL. Fluid overload is associated with impaired oxygenation and morbidity in critically ill children. Pediatr Crit Care Med J. 2012;13:253-8.
10. Shamin A, Afzal K, Ali SM. Safety and efficacy of isotonic (0.9%) *vs.* hypotonic (0.18%) saline as maintenance intravenous fluids in children: A randomized controlled trial. Indian Pediatr. 2014:51:969-74.
11. National Patient Safety Agency. Reducing the risk of hyponatraemia when administering intravenous infusions to children. 28 March 2007. Available from: http://www.nrls.npsa.nhs.uk/resources/?entryid45=59809. Accessed November 7, 20014.

Changes in Preterm Breast Milk Composition with Advancing Infant Age

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Breast milk has a dynamic and a variable composition during a single feed, diurnally, and differs in composition according to gestation, chronological age of the infant, and health status of the mother. The timing of expression of milk and storage can also alter this composition [1]. The difference between preterm and term milk has been studied in great detail by researchers; a few studies have focused on the changes that occur in these two kinds of milk over a longitudinal period of time. A recent systematic review of these studies did not find any study on preterm milk composition beyond two months of chronological age [2]. The pilot study by Dutta, *et al.* [3], in this issue of *Indian Pediatrics,* explores an important area that has not been evaluated well in previous studies, i.e. change in composition of breast milk as the chronologic age advances and the other feeds are added. The study provides some more information regarding composition at 90 and 180 days [3]. The duration of exclusive breastfeeding in preterm infants is likely to be foreshortened due to delay in initiation of breastfeeding, intensive care in neonatal period and prolonged hospitalization. These infants are more likely to have complementary feeding introduced before 6 months of corrected age and hence are likely to be bereft of benefits of exclusive breastfeeding. In this study, analysis of serial breast milk samples reveals that as the chronologic age advances, there is an increase in the triglyceride and sodium levels and progressive decline in the protein content. However, to suggest that there is a possible cause-effect relationship in sodium and triglycerides between exclusive breastfeeding mothers compared to those who have introduced mixed feeding is a speculation, because of low numbers and some methodology related issues. Limitations of the study include sample collection time as fat content beyond three minutes is expected to be more, and with increasing age the lipid concentration in the initial milk is higher due to efficient breast emptying. The information related to milk volume and other components of milk such as trace elements, bioactive proteins, or anti-inflammatory substances have not been collected. Future studies would benefit from tracking caloric intake of infants, breastfeeding frequency in mothers, and anthropometric data of infants. These parameters would inform us about infant health and other important modifiers in addition to changes in breast milk composition over a period of time. Authors speculate on the pathophysiology behind differences in composition as the chronologic age advances, such as involution of mammary gland or changes in the cellular permeability. Although this is possible theoretically, one cannot make a strong case for these physiologic attributes, unless there are data on milk volumes, secretory rates, and the concentration of components measured and analyzed using regression analysis. Human milk is species-specific and it is uniquely superior for infant feeding [4]. This basic understanding raises the question whether the compositional changes that occur over time are nature's way of adapting the milk constituents to suit the infant needs. The compositional changes in term infants during weaning have been reported earlier in other studies [5-7], but the pathophysiologic mechanisms that lead to these changes have not been