Choice of Maintenance Fluids - Does it Hold Water?

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Maintenance intravenous fluids are an integral part of care in acutely ill hospitalized children, the main objective being to compensate for the renal and insensible losses.The fluid calculation is based on the five decade old Holliday and Segar formula derived from calorie expenditures of healthy children [1]. However, accumulating evidence over the years has challenged this traditional approach. The hypotonic formulae extrapolated from healthy children tend to overestimate fluid needs in sick children as their endogenous metabolism and calorie expenditure are reduced. Additionally, non-hemodynamic stimuli for Arginine Vasopressin (AVP) impairs the kidney's ability to excrete free water thus adding 'fuel to the fire, thereby increasing the risk of hyponatremia. It is believed that virtually every hospitalized patient requiring intravenous fluids has a potential stimulus for AVP excess and should be considered to be at risk for hyponatremia.

This physiological phenomenon has been amply supported by evidence that suggest that hypotonic fluids are the primary factor leading to hospital-acquired hyponatremia. A recent meta analysis [2] of 10 randomized controlled trials involving 855 subjects concluded that hypotonic intravenous fluids significantly increased the risk of hyponatremia in hospitalized children. In this issue of *Indian Pediatrics*, Shamim, *et al.* [3] have reported a randomized controlled trial comparing reduced maintenance volume (60%) isotonic *versus* standard maintenance volume hypotonic maintenance fluids, and concluded that the former resulted in fewer hyponatremic episodes during the first 48 hours of fluid therapy. The incidence of hyponatremia in the hypotonic *versus* isotonic saline group was 70% and 33.3%, respectively, thus echoing the previous observations on this issue. Also, the incidence was much higher than the previously reported range of 1.4% to 45% [4], possibly due to higher proportion of central nervous system and respiratory illnesses representing 71.6% of the total study population. It is well known that children with meningitis, encephalitis, bronchiolitis, gastroenteritis, and head injury are at an increased risk for hyponatremia [4]. However, what is intriguing is the higher incidence of hyponatremia in the isotonic group (33.3%). Most of the studies comparing the two regimens have reported incidence of hyponatremia in isotonic group to the tune of 1.7-16% [5-7]. This brings us to an important question – can hyponatremia be commonly seen even with isotonic maintenance fluids? The answer is yes, again throwing the spotlight on the role of kidneys in excreting hypertonic urine and generating electrolyte free water (EFW). Expansion of intravascular volume following isotonic fluids triggers partial secondary desalination resulting in hypertonic urine due to disproportionately more sodium than water loss. The excess EFW thus formed is retained in presence of non-osmotic AVP effect. The other mechanism to explain hyponatremia with isotonic fluids is the intracellular shift and redistribution of sodium due to increased membrane permeability known as translocational hyponatremia or sick cell hyponatremia [8]. This was the postulate put forward by authors of a prospective observational study where the fall in serum sodium levels in critically ill children could not be explained solely by EFW excess or natriuresis [9]. The above findings suggest that hyponatremia in this study cohort was possibly multifactorial. Alternative mechanisms of secondary desalination and trans-locational hyponatremia may need further exploration. Urine output measurements, urinary electrolytes, and AVP estimation would have been invaluable and thrown more light on this issue.

The other question the current study raises but does not answer is that of rate of administration *versus* tonicity of fluids. This debate has been addressed by a few investigators. The opponents of isotonic fluid use argue that if the most important determinant of hyponatremia is excess EFW then why not counter it with restricted fluids rather than increased salt? This argument finds favor in the observations reported in susceptible euvolemic patients, in whom both isotonic and hypotonic maintenance fluids resulted in net sodium increase when fluid restriction countered the AVP-induced 'secondary desalination' [10]. On the contrary, Yung, *et al.* [11] in their double-blind randomized controlled trial concluded

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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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