Reduced Volume Isotonic Saline (0.9%) as Maintenance Fluid in Children

ABDUL RAZAK
Motherhood Hospital, Bangalore, Karnataka, India.
razakmdpaed@gmail.com

The recent report by Shamim, *et al.* [1] brings out the most common and continued problem encountered in pediatric intensive care units. Research has proved that using isotonic fluids as maintenance fluids in sick children results in fewer hyponatremic episodes compared to hypotonic fluids [2,3]. However, there are few issues:

The statistics could have been extended to see how many children will be harmed if used hypotonic fluids compared to reduced volume isotonic fluids. The number needed to harm in this trial (to cause hyponatremia), if using hypotonic fluids, would be 1 in 4 at 24 hours (95% CI 1.9-15.2) and 48 hours (95% CI 1.9-11.8), which is higher compared to an earlier study [2]. The absolute risk increases by 30 percent if hypotonic fluids are used. However, the earlier trial used the same volume of fluids in both the participant groups which points towards a need of reduced volume rather than standard volume maintenance fluids apart from employing isotonic fluids, to reduce hyponatremia.

The participants in both groups received 1 mL of potassium chloride per 100 mL of intravenous fluids. The isotonic group compared to hypotonic group has received lesser potassium maintenance, as the volume was reduced to 60 percent in this group. However, there was no hypokalemia in the isotonic group. The potassium maintenance should have been adjusted so that the both groups received the same amount of potassium.

The study also had limitation of not measuring the urine osmolality. The basic principle to prevent hyponatremia in pediatric intensive care depends on the amount of free water given which further depends on the solute load (intravenous fluids) and urine osmolality. During the sickness the vasopressin levels would be high resulting in high urine osmolality. Hyponatremia can still occur in children given isotonic fluids at reduced volume which is also seen in this study.

It is very clear that the maintenance fluids used in sick children should be isotonic with reduced standard volume to prevent hyponatremia. How far and how much to reduce depends on the sickness of the child. If the child is very sick, the fluid reduction should be higher. In extreme sickness, the question to further reduce maintenance fluids or to increase the solute concentration in the maintenance fluids remains unanswered?

REFERENCES

1. Shamim A, Afzal k, Manzir AS. 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.
2. Montanana PA, Modesto AV, Ocon AP, Lopez PO, Lopez PJL, Toledo PJD. 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.
3. McNab S, Ware RS, Neville KA, Choong K, Coulthard MG, Duke TA, *et al*. Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children. Cochrane Database Syst Rev. 2014;12:CD009457.

Reduced Volume Isotonic Saline as Maintenance Fluids in Children: Author's reply

We thank the author for his interest and comments on our paper [1]. He has raised some very valid points. We had highlighted in our article that the risk of hyponatremia with use of hypotonic fluids was almost twice that with use of isotonic fluid (RR 0.48, 95% CI 0.27, 0.83; *P*= 0.01). The risk difference and the number-needed-to-harm (NNH) have been summarized in ***Table* I** [1]. As rightly pointed out, the NNH for hyponatremia was higher (1 in 4) compared to study by Montana, *et al*. [2] (1 in 7), possibly because their trial used same volume fluids in both groups. Similarly from the data of Kanan, *et al*. [3], figures for NNH would be 1 in 7 with isotonic fluid in standard volume and 1 in 9 when reduced volume hypotonic fluid is used. Higher figures of NNH in our study underline the additional benefit of reducing the volume of maintenance fluids apart from using isotonic solutions. Kanan, *et al*. [3] also showed that use of isotonic saline in 'standard volume' reduced the risk of hyponatremia by 12.6% compared to hypotonic fluid, whereas reducing the volume of hypotonic fluids also resulted in a risk difference of 10.5%. Our study demonstrated the cumulative effect of using isotonic fluid in reduced volume but there was no comparative 'standard volume' isotonic fluids group to demonstrate the benefit of either strategy.

We agree that same amount of potassium was not used in both arms of this study. If the same amount of

TABLE I RISK OF HYPONATREMIA WITH HYPOTONIC *VS* ISOTONIC MAINTENANCE FLUID

Time	*Fluid type**	*Hyponatremia (%)*	*Risk difference (95% CI)*	*NNH(95% CI)*	*P value*
At 24 h	IF	7 (23.3%)	30% (6.6% - 53.4%)	4 (1.9-15.2)	0.03
	HF	16 (53.3%)			
At 48 h	IF	4 (13.3%)	30% (8.5% - 51.5%)	4 (1.9-11.8)	0.02
	HF	13 (43.3%)			
Overall	IF	10 (33.3%)	36.7% (13.1% - 60.2%)	3 (1.7-7.6)	0.01
	HF	21 (70%)			

**IF, Isotonic fluid; HF, Hypotonic fluid; N =30 for each fluid type; NNH: number-needed-to-harm.*

potassium were to be used in both groups, the concentration of potassium would have been 60% higher in the isotonic fluids group (33.3 meq/L as against 20 meq/L). Moreover, this would have also increased the tonicity of the fluid by approximately 7.5%. For maintaining infusion concentration at 20 meq/L, potassium supplementation needed to be reduced.

We agree that urine osmolality should also have been measured to estimate free water clearance and could have explained hyponatremia despite using isotonic fluids.

***AHMAR SHAMIM AND KAMRAN AFZAL**
Department of Pediatrics, Jawaharlal Nehru Medical College, AMU, Aligarh, Uttar Pradesh, India.
**ahmar_shamim@yahoo.com*

REFERENCES

1. Shamim A, Afzal K, Manzir AS. 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.
2. Montanana PA, Modesto AV, Ocon AP, Lopez PO, Lopez PJL, Toledo PJD. 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.
3. 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.

Atypical Features of Severe Dengue: Probable Pathogenesis

Severe dengue typically consists of hypovolemic shock (dengue shock syndrome) and bleeding (dengue hemorrhagic fever) [1,2]. Two recent papers in Indian Pediatrics highlight "atypical" features of severe dengue, mainly as organ failure – liver, heart, lungs, kidneys, brain – in any combinations [1,2]. These are increasingly being recognized in recent years [1-3]. We suspect that these might be – at least partly – iatrogenic, associated with unwarranted platelet transfusions, a popular practice in recent years [4, 5].

Thrombocytopenia is characteristic of dengue fever and severe dengue. Hemophagocytosis and bone marrow suppression are the frequently described causes for thrombocytopenia [4]. We propose another pathway for platelet depletion, which has an important bearing on possible adverse effects of platelet transfusions [4].

We believe that platelets get sequestered on small vessel endothelial cells in dengue, similar to what happens in microangiopathy of thrombotic thrombocytopenic purpura (TTP) [4]. The adhesion ligand is von Willebrand factor (vWF). Increased vWF activation or decreased cleavage of vWF by protease ADAMTS 13 will result in increased adhesion and platelet microthrombi [4]. In severe dengue, the balance between vWF and ADAMTS 13 is deranged [4]. Deficiency of ADAMTS 13 will result in extremely adhesive, ultra-large vWF multimers, resulting in platelet microthrombi [4].

Microvascular plasma leakage causes hypovolemia in which low platelet counts seem not to be involved, at least directly. Small vessel bleeds do not get plugged by platelets as their numbers are grossly depleted, thus leading to uncontrolled bleeding at various sites. But, what is the pathogenesis of organ failure? We propose that platelet microthrombi obstruct perfusion resulting in organ hypoxemia and failure [4]. We suspect that multi-organ failure may be partly due to platelet transfusions