

# Fluids' Safety in Children: Less Water or More Salt? Where does the truth lie?

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Now-a-days more children who come into the hospitals receive intravenous fluids than in the past. A standard formula is uniformly followed around the world by Paeditricians to calculate the maintenance fluid requirements (i.e, 100ml/kg for the first 10kg of body weight, 50ml/kg for the next 10kg and 20ml/kg for body weight exceeding 20kg).<sup>1,2</sup> This prescription of PMF is based on studies conducted in healthy children more than 50 years back by Holliday et al.<sup>3</sup> The primary basis for this recommendation is that the body needs 1ml of water/1 Cal spent. The Na and K requirement of 3 and 2 meq/100 Cals/day respectively reflects the electrolyte composition of breast and cow milk.<sup>3,4</sup> This formula resulted in almost the universal practice of using PDS as the paediatric standard maintenance fluid. Since its publication in 1957, the prescription has remained unchanged, although the safety of administering this hypotonic PMF has never been evaluated prospectively.<sup>4</sup> It is very important to remember that these recommendations are appropriate for a healthy child whose kidneys can handle significant variations in volume and composition of the fluid ingested.

There is a higher incidence of hospital acquired hyponatremia in children treated with traditional PMS often with devastating consequences.<sup>4-11</sup> Hyponatremia-definition-Plasma Na is less than 135meq/l.<sup>5,8</sup> International literature cites more than 50 cases of serious injury and 27 deaths of children resulting from hospital acquired hyponatremia as a result of receiving hypotonic PMF and another 4 deaths in the UK since 2000.<sup>5,8,9-11</sup> Although many researchers attribute this to the type of fluid used, after reviewing these studies, it was apparent that the volume of fluid infused was also an important contributing factor.

This report briefly discusses the altered water and electrolyte physiology in acute illnesses, the rationale for using a fluid with higher tonicity than PDS and WHAT should roughly be the right amount of maintenance fluid in a sick child.

Normal kidneys play a great role in maintaining extracellular fluid volume and tonicity by varying the amount of water and solutes they reabsorb and excrete. Most healthy children do not drink the water that is recommended each day, so their kidneys usually concentrate, or if they drink more, dilute the urine.<sup>12,13.</sup>

This is not the case for many children who come into the hospital with infections or for surgery. Antidiuresis during fever and sepsis has been known for over a century, especially in pneumonia and meningitis.<sup>14</sup>

Generally, two factors are required for Hyponatremia to develop. They are; excess electrolyte free water (EFW) and non-volumic, non-osmotic release of Anti diuretic hormone (ADH) to prevent the excretion of that water.<sup>5,8</sup> This non-osmotic release of ADH (SIADH) is stimulated by many abnormal physiological states commonly encountered during acute illnesses such as pain, anxiety, nausea, fever, illnesses affecting the lungs and brain and peri-operative states.<sup>4,14,15,16</sup> It is to be noted that this Syndrome of inappropriate ADH secretion(SIADH) thus occurs in most sick children and often aggravated by SIAD(syndrome of inappropriate dextrose infusion).<sup>17</sup> This phenomena of SIADH has clear evolutionary and physiological advantages in sickness.<sup>17</sup> The nature failed to anticipate an intravenous route of forceful fluid administration. In such situations of increased ADH release, hyponatremia does not develop because as PNa falls, thirst is suppressed and there is no longer any large intake of water. In contrast, in the hospital the physician rather than the patient determines the water intake.

Over 50% of children with PNa<125 meq/l develop hyponatremic encephalopathy of varying severity.<sup>8</sup> Thus children are more prone to acute encephalopathy because of the higher brain size compared to the skull size.<sup>18</sup> Children with CNS infections are prone to and deteriorate rapidly when they become hyponatremic, and there are suggestions to redefine the acceptable PNa values in such children to avoid even a mild fall in plasma Na.<sup>18,19</sup>

Acutely ill children who are not taking enteral feeds are at risk of hypoglycemia and should always have glucose in the maintenance fluid and the concentration recommended varies between 2.5 to 10%.<sup>9,14</sup>

People who still advocate the use of conventional fluid (PDS), widely quote two studies to augment their argument that there are other reasons for the hyponatremia. One of them is the Desalination theory.<sup>20</sup> Here Steele et al. argues that even patients given isotonic saline infusion developed Hyponatremia due to

natriuresis. Some degree of natriuresis develops in SIADH with the associated suppression of Aldosterone.<sup>14</sup> However, it is likely that their patient developed Hyponatremia not because of the type of fluid used but the amount of fluid infused (5l/day for an adult post-operative patient) resulting in acute expansion of extra cellular fluid volume and natriuresis. Another mechanism considered for the development of Hyponatremia is sick cell syndrome.<sup>16</sup> However, these mechanisms may not be relevant in most clinical situations.

An important common factor in many reported cases of hospital acquired hyponatremia is excess volume of the fluid infused.<sup>5,6,14,21</sup> The RR(relative risk) of death or severe neurological sequel when facial oedema (a sign of fluid overload) was present was 2.5 (95% CI 1.4-4.8) despite the absence of differences in serum Na.<sup>14</sup> This shows that fluid overload without hyponatremia is equally dangerous and can contribute to adverse neurological events.

Current weight based fluid calculation overestimates the maintenance intravenous fluid requirement in children. The requirements are based on the supposition that energy expenditure is based on body weight, and for every 100 Cals consumed, there is a loss of 100 ml of water.<sup>3</sup> In actual fact, resting energy expenditure is related to fat free mass (25% children are obese in industrialized nations). Almost half of calorie intake (hence water) suggested by Holliday and Segar is designated for growth.<sup>3</sup> An unrealistic goal in acute illness, and the energy expenditure in sick children is significantly lower than in healthy children, as low as 40-50Cal/kg/day.<sup>22,23,24</sup>

Hence, in sick children in whom renal clearance of free water is reduced by more than 50%, a further 30% reduction of insensible water loss can be expected if the child is on a ventilator.<sup>18,23</sup> Therefore, the actual fluid requirement may amount to approximately half that suggested by Holliday and Segar- roughly 50ml/kg/day for a sick child who has no hypovolemia and adequate organ perfusion.<sup>7,22,23,24</sup> Most authors agree that in children with Pneumonia and CNS injury, fluid should be restricted to half to two thirds of the maintenance.<sup>15,17</sup>

Post-operative states need special emphasis. The most frequent clinical setting for acute hyponatremia is after elective surgery.<sup>5,6,10</sup> The problem mainly arises when appropriate adjustments (restrictions) are not made in the volume of fluid, in addition to the hypotonicity of the fluid.<sup>20</sup> Up to 7.5% of patients develop significant hyponatremia in the first post-operative week and sometimes, this may lead to life threatening complications such as encephalopathy.<sup>25-27</sup>

It seems that the rationale for changing the conventional PMS is very clear from these studies since there is overwhelming

evidence of a greater level of risk of hospital acquired hyponatremia associated with the use of hypotonic solutions.<sup>4-11,14,18,19,21,28</sup> The National Patient safety Agency (NPSA) alerts that with the range of hypotonic fluids available, the use of NaCl 0.18% with glucose 4%(PDS) presents an even greater risk and all the deaths cited in UK literature since 2000 were all associated with PDS infusion.<sup>9</sup>

NPSA in their patient safety alert dated September 2007, recommended changing the standard paediatric maintenance fluid from 0.18%(PDS) to 0.45% saline(1/2 Normal saline), to prevent children from developing serious Hyponatremia.<sup>9</sup> In 2003, the Royal College of Anaesthetist issued a statement advising against the use of traditional PDS and this statement was supported by The Royal College of Paediatrics and Child Health, although a subsequent survey showed that action had not been implemented in some institutions.<sup>9,29</sup> There are many studies and review articles in Paediatric literature strongly arguing in favor of using Normal saline (with added glucose) as a safe maintenance solution both peri-operatively and in the acute phase of most childhood illnesses requiring hospitalization along with a moderate degree of fluid restriction (50-60%).<sup>7,14</sup>

Overall, the original guidelines for maintenance fluid and volume may not be applicable now. The development of Hyponatremia is unacceptably high in hospitalized children and there is already substantial experience of harm from hypotonic solutions especially less than 0.3% saline at the conventional prescribed volume. Although most of the recommendations are in favor of replacing PDS with isotonic saline, there are some who still find it difficult to change and shed the traditional practice and argue in favor of the PDS.

Here it has been postulated that the "truth lies somewhere in between" and that 0.45 % ( half normal saline) with added glucose could be the PMS of choice. Fluid restriction is also an equally important child safety practice during illnesses and in the absence of hypovolemia, and with adequate organ perfusion, limiting fluid intake to 50-60%of previous recommendations would be in the best interest of the Child.

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