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Water, water everywhere and not a drop to drink: Choosing maintenance IV fluid tonicity

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DEFINITION/EPIDEMIOLOGY

The use of salt solutions to expand the vascular volume has been utilized for almost one hundred years[2]. During this time the methods, techniques and indications for expanding vascular volume has increased. The original method of infusing salt water into the peritoneal space was eventually supplanted by intraveneous fluid administration.[2] Hypotonic fluid administration for pediatric patients has been advocated for the past 50 years.[2-4] The rationale for hypotonic fluid resuscitation is rooted in the idea that the ideal fluid is human breast or cow's milk.[4,5] It was thought that because people had evolved to digest this fluid, it would contain the correct calorie to electrolyte ratio, even though milk is given enterally and metabolized through digestion.[4,5] This assumption was central to determining the amount of maintenance electrolytes required for parenteral therapy.[4] Since Holiday and Segar's landmark paper, which focused on water requirements, clinicians have widely followed their maintenance fluid suggestions, partly due to the new ease in calculating fluid requirements of variously sized children compared to previous calorie dependent methods.[2] However, there is an evolving concern that using hypotonic fluids, for maintenance fluid, can cause hyponatremia. Therefore, some clinicians now advocate that isotonic fluids, are safer and should be the standard of care, for both acute resuscitation and maintenance fluid therapy.[2,5-12]

PHYSIOLOGY

The central argument for transitioning to isotonic fluids is the concern for iatrogenic induced hyponatremia from excess free water administration with hypotonic solutions.[5,13] Vasopressin (antidiuretic hormone, ADH) helps regulate osmolality of body fluids by manipulating water excretion.[14] Although vasopressin is thought to be primarily regulated by

osmolality other factors can stimulate secretion from the posterior pituitary including, a decrease in circulating blood volume and blood pressure, stress, pain, hypoglycemia, temperature increase, and angiotensin II.[14] There is a greater appreciation of the many physiologic situations that induce vasopressin release in the normal, euvolemic patient independent of osmolality, particularly patients under stress or in pain.[2] This increase in vasopressin release independent of osmolality or intravascular volume depletion plays an important role in iatrogenic induced hyponatremia because vasopressin limits/inhibits free water excretion.[14]

CLINICAL QUESTION

The incidence of iatrogenic induced hyponatremia has been reported to occur in 9%-24% of hospitalized children on IV fluids.[5] Studies show that iatrogenic induced hyponatremia can cause significant morbidity and even death.[7] This prompted some clinicians to advocate for normal saline use as maintenance fluids.[7] However, there was concern that children could not excrete the increased sodium load in isotonic saline and therefore use of normal saline may cause hypernatremia and edema. These concerns (hyponatremia from hypotonic fluids versus hypernatremia from isotonic fluids) spawned a debate and increased interest in collecting data to support the selection of a preferred maintenance fluid[3,8].

Numerous centers from around the world, with various patient populations have performed retrospective[13], prospective[10,11,15] and randomized controlled trials[9] to determine the risk of hyponatremia when treated with hypotonic saline versus isotonic saline. Some of the essential risk factors associated with iatrogenic hyponatremia include the tonicity of the fluid and the amount of maintenance fluid given.[6,10,11,13,15-17] Both are important variables, since the argument is that reducing free water administration can be remedied by either increasing tonicity or by lowering the total amount of hypotonic solution given.[10,11,15]

TREATMENT

Multiple studies find an increased risk of hyponatremia in children treated with hypotonic fluids for maintenance therapy when compared to isotonic maintenance fluids.[9-11,13,15] Changing the rate of hypotonic fluid did not appear to have an effect as predicted on hyponatremia. In two separate studies changing the rate of hypotonic fluids did not impact incidence of hyponatremia.[10,18] Instead, the most important predictor of hyponatremia was the fluid tonicity, with hypotonic fluids more likely to cause hyponatremia.[18] Two meta-analysis of several fluid trials show a decreased risk of hyponatremia if isotonic saline is used as maintenance therapy[16,17]. The meta-analysis by Foster et al. reported that the relative risk of hyponatremia (sodium < 135mmol/L) was 2.37 (95% CI, 1.72-3.26) when comparing hypotonic versus isotonic saline.[17] In a population at low risk for hyponatremia, this corresponds to a number needed to harm of 15 (95% CI, 9-28), while in a high risk population for hyponatremia the number needed to harm is only 4 (95% CI, 3-7).[17] This is concerning due to the large number of children placed on maintenance IV fluid therapy.

Many clinicians espouse that changing to isotonic maintenance fluids would be just as dangerous as using hypotonic fluids because of the risk of hypernatremia from the increased sodium load.[2,3] However, the meta-analysis by Foster et al. of 10 randomized controlled trials (n = 893) did not show an increased risk of hypernatremia as previously feared. The relative risk of hypernatremia when using isotonic versus hypotonic saline was 0.81 (95% CI, 0.32-2.04).[17] Furthermore, there was no difference in frequency of edema or hypertension between the patients receiving isotonic versus hypotonic saline.[17] Subgroup analysis also favored treatment with isotonic fluids when compared to hypotonic fluids for maintenance therapy in the ICU and surgical settings.[17]

CONCLUSION

In summary, there is a risk of iatrogenic induced hyponatremia in children treated with hypotonic IV fluids, particularly if they are in a stressed state that promotes vasopressin release. Clinicians can reduce the rate of iatrogenic hyponatremia by using isotonic fluids. Reducing the

rate of administration when using hypotonic fluids does not have a risk reduction effect compared to treatment with isotonic fluids.[10,17,18] Increasing tonicity of maintenance fluids does not increase the risk for hypernatremia, edema or swelling.[17] These studies were performed in children outside of the neonatal period and should not be extrapolated to neonates or very young patients. The clinician still must use their judgment in deciding how to best treat each patient and tailor their plan and management accordingly, but numerous studies show that isotonic saline should be the default fluid prescribed rather than the exception in the management of the hospitalized child in need of maintenance fluids.

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