Clinical Guideline Highlights for the Hospitalist: Maintenance Intravenous Fluids in Infants and Children

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GUIDELINE TITLE: 2018 American Academy of Pediatrics (AAP) Clinical Practice Guideline: Maintenance Intravenous Fluids in Children

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PRIOR VERSION: Not Applicable

DEVELOPER: Multidisciplinary subcommittee of experts assembled by the AAP

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TARGET POPULATION: Patients 28 days to 18 years of age requiring maintenance intravenous fluids (IVFs).

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Hospitalized children with inadequate fluid intake are often administered maintenance intravenous fluids (IVFs) to support metabolic needs and sensible losses. Historically, hypotonic IVFs have been the standard, based on theoretical water and electrolyte requirements for estimated energy expenditure.[1] However, when combined with increased levels of arginine vasopressin (AVP) seen in acutely ill children which impairs free-water excretion,[2] hypotonic IVF can result in hyponatremia. The recently published guideline by the American Academy of Pediatrics (AAP)[3] is the first to provide an evidence-based recommendation on the use of maintenance IVF therapy in children.

KEY RECOMMENDATION FOR HOSPITALISTS

Patients between the ages of 28 days and 18 years should receive isotonic solutions with appropriate potassium chloride and dextrose for maintenance IVFs (evidence quality: high; recommendation strength: strong)

Isotonic fluids, such as 0.9% NaCl (normal saline), Hartmann solution and PlasmaLyte, contain a sodium concentration similar to that of plasma (135-144 mEq/L). Lactated Ringer solution (LR) is near-isotonic (sodium 130 mEq/L), but was not used in any of the reviewed studies and therefore not included in the recommendation. Excluded are patients with neurosurgical disorders, congenital or acquired cardiac disease, hepatic disease, cancer, renal dysfunction, diabetes insipidus, voluminous watery diarrhea, severe burns, or patients in the neonatal intensive care unit.

The primary benefit of the AAP recommendation is the reduced risk of iatrogenic hyponatremia and its associated sequelae, including complications or impact on cost of care. The number needed to treat with isotonic fluids was 7.5 to prevent any hyponatremia and 27.8 to prevent moderate hyponatremia (<130 mEq/L). Increases in readmission rates, length of stay, and cost of hospitalization have been reported in a recent meta-analysis reviewing the economic burden of hyponatremia in both adults and children.[4]

Potential harms from the use of isotonic fluids include hypernatremia, hyperchloremic metabolic acidosis, and fluid overload, although available data have not demonstrated an increased risk of these complications. In light of a recent normal saline (NS) shortage in the United States, limited availability is also a consideration. Plasmalyte is more costly than NS and is currently incompatible with the addition of dextrose.

CRITIQUE

Methods in Preparing Guideline

The guideline development committee included broad representation by pediatric experts in primary care, hospital medicine, emergency medicine, critical care medicine, nephrology, anesthesiology, surgery and quality improvement, as well as a guideline methodologist/informatician and epidemiologist.

Search strategies from recently published systematic reviews of clinical trials comparing isotonic with hypotonic maintenance IVFs were used to identify studies eligible for inclusion. A total of 17 studies with 2,455 total patients were initially identified and included. One additional study meeting inclusion criteria was found after the committee convened and excluded from the guideline.[5] Three reviewers from the subcommittee performed a structured critical appraisal of each article. The methods of each trial were assessed for risk-of-bias in multiple domains, including randomization, allocation concealment, performance, detection, attrition and reporting. Forest plots were generated using random-effects models and Mantel-Haenzel statistics with the outcome of hyponatremia.

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The guideline underwent review by various stakeholders including AAP councils, committees, and sections, and individuals considered experts in the field.

A strength of the guideline is the high quality of the evidence and the consistent findings. All of the included studies were randomized clinical trials and the number of included patients was large. Of the 17 included studies, 16 reported a risk ratio favoring isotonic fluids over hypotonic fluids in the prevention of developing hyponatremia; the results of the study that favored hypotonic fluids were not statistically significant on their own. A sensitivity analysis was performed to exclude one study with a 20% weight, determined by multiple factors such as sample size, confidence interval, and an unusually high rate of hyponatremia in the isotonic and hypotonic fluids groups (33.3 % and 70%, respectively).[6] After exclusion, there was no change in the overall estimated risk in hypotonic fluids leading to hyponatremia. Only one trial had two sources of high risk of bias (allocation concealment, attrition) and the remaining had only low or unclear risk of biases in the various domains.

The study that was excluded due to its late identification similarly shows increased risk of hyponatremia in groups administered hypotonic fluids (risk ratio 6.5-8.5), and would likely not affect the estimated risk.[5]

Despite differences in types of patients enrolled, rate of administered fluids, type of IVF, frequency of lab testing, and study duration, the I^2 (degree of heterogeneity) of the forest plot of all included studies remained low at 14% and the increased risk of hyponatremia from hypotonic fluids remained consistent.

Due to study design differences, a limitation of the guideline is that no recommendation is made regarding the type of isotonic fluids and the rate of IVF administration. Additionally, due to the low frequency of clinically significant sequelae of hyponatremia, such as hyponatremic encephalopathy, it remains uncertain how many patients would need to be treated with isotonic fluids to prevent a rare but potentially devastating event.

Sources of Potential Conflict of Interest or Bias

The guideline was developed and funded by the AAP. A formal conflict of interest management policy was followed, and subcommittee members had no conflicts of interests or financial relationships relevant to the guideline to disclose.

Generalizability

Given the large number of patients included in the studies and heterogeneity of the population included, the recommendation applies to most patients cared for by pediatric hospitalists. Several patient exclusions relevant to the pediatric hospitalist deserve mention: neonates, kidney disease, and voluminous diarrhea. Neonates under the age of 28 days, including febrile neonates, are excluded from the guideline because of the immature concentrating abilities of neonatal kidneys. Patients with renal impairment were excluded from the guideline recommendation because several studies excluded patients with kidney disease. Hospitalists often care for children who sustain prerenal acute kidney injury from severe dehydration. In this condition, the kidney conserves water through the release of AVP. While an excluded population, these patients would be even more susceptible to develop hyponatremia if administered hypotonic fluids. Patients with "voluminous diarrhea" are excluded from the guideline because those with gastroenteritis with ongoing losses may require IVFs at rates higher than maintenance, and are particularly vulnerable to electrolyte derangements. The guideline, however, does not define voluminous diarrhea, leaving it to the discretion of the treating clinician.

Finally, it is critical to mention that IVF should be considered a therapy to be judiciously used, and discontinued when possible. While the guideline addresses the choice of fluid composition, alternatives to orally or enterally hydrate a patient are always preferred.

AREAS IN NEED OF FUTURE STUDY

While the guideline strongly recommends isotonic fluids for maintenance therapy, the choice of isotonic fluid remains with the clinician. Most included studies used NS for their isotonic groups, but Hartmann's solution and Plasmalyte were represented in a few studies. LR, one of the more widely used balanced solutions, though slightly hypotonic (130 mEq/L), was not studied. The exclusion of LR from the included studies is unfortunate, as the benefit of balanced solutions compared to NS after significant fluid resuscitation has been shown in the setting of severe sepsis and shock.[7] Hyperchloremic metabolic acidosis after fluid resuscitation with NS has raised concern about continuing NS as maintenance fluid and possibly worsening acidosis or hyperchloremia and its adverse effects.[8] Further studies on the potential benefit of LR as maintenance fluid, or the potential harms of unbalanced solutions as maintenance fluids in the setting of significant resuscitation are needed.

Disclosures: The authors have nothing to disclose.

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