

At What Point Is the Accumulated Evidence Sufficient to Change Maintenance Intravenous Fluid Prescribing Practice in Children? How About Yesterday?

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It is intriguing and somewhat disturbing that despite intravenous fluids (IVFs) being the most commonly prescribed therapy in hospitalized children, there still seems to be such a wide variation in the approach to choosing what type of intravenous (IV) maintenance fluid to use^{1,2} and the required monitoring that goes along with it.

In this issue of *Hospital Pediatrics*, Rooholamini et al³ have attempted to address the discrepancy between evidence and practice through a quality improvement project using a standardized pathway to guide the choice of maintenance IVF. Their multidisciplinary approach included creating an evidence-based clinical pathway synthesizing the current consensus with regards to indications of when to start and discontinue IVFs and especially with regards to the optimal tonicity of the IVFs prescribed. They also included standardized monitoring for dysnatremia and signs of fluid overload. I would recommend readers electronically access the clinical pathway described by Romero et al⁴ because it is well designed with many good principles prominently highlighted (eg, “do not use 1/4 NS for maintenance fluids,” and “pay attention to weight fluctuations $\pm 3\%$ ”) and presents the latest evidence in a pragmatic, algorithmic fashion. Those with increased antidiuretic hormone (ADH) secretion risk factors are recommended to receive 0.9% saline, whereas the rest are given 0.45% saline. Some guidance on total IVF maintenance calculation is also given. In the section on monitoring, they have recommended that all children receiving $>75\%$ of their maintenance by IVF have their sodium (Na) checked within 24 hours of initiation, but only those on hypotonic fluids require routine daily checks if getting $\geq 75\%$ maintenance IVF. Their approach has tried to accommodate perceived gaps and areas of continuing controversy in the evidence (eg, potential adverse effects of isotonic fluids and frequency of Na monitoring). The most relevant and generalizable of their objectives were the following: Did the pathway implementation change the frequency of hypotonic fluid prescription, and were there any associated changes in the rate of severe dysnatremia? Did the pathway implantation improve appropriate clinical and laboratory monitoring for patients on maintenance IVF?

For almost 50 years, the standard practice was prescription of hypotonic IVF (0.2% saline) for maintenance requirements based on seminal work published by Holliday and Segar⁵ in 1957. At the turn of this century,

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increasing reports began to emerge of rare but serious adverse outcomes in hospitalized children related to acquired hyponatremia while on IV maintenance fluids and emerging evidence that this was at least in part related to the use of hypotonic IVFs.⁶ Before 2006, there were almost no randomized controlled trials in which researchers examined this issue, but in the last 10 years, there have been many, predominantly trials in which researchers looked at postoperative children and those cared for in the ICU. There are 2 recent meta-analyses and a Cochrane review on this topic.⁷⁻⁹ The findings are consistent: using hypotonic maintenance IVFs increases the risk of acute hyponatremia, whereas isotonic IVFs are associated with a lower risk of developing hyponatremia. There is also a gradual accumulation of evidence that the use of isotonic IV 0.9% saline for the purpose of providing maintenance fluid requirement does not appear to significantly increase the risk of hypernatremia or fluid retention in the population of children studied.⁹⁻¹¹

Although the decision of whether to use 0.45% saline versus 0.9% saline for the IV maintenance fluid requirement is still being debated and may continue to be for years,^{1,2} there are certain clinical circumstances of anticipated increased ADH secretion, for example, in ICU and postoperative patients as well as those with acute pulmonary or central nervous system disease,⁴ in which one would expect that practice would have changed to reflect the current evidence supporting the recommendation to use isotonic 0.9% saline. Yet in a recent article published earlier this year in this journal, Shein et al¹² reported that 96% of the almost 2000 orders for maintenance IVF in children with bronchiolitis were for hypotonic 0.2% or 0.45% saline, including 65% of those on mechanical ventilation receiving 0.2% saline. The practice of choosing hypotonic maintenance IVF in conditions associated with increased ADH secretion was also shown to be prevalent among 78% of surveyed pediatric residents in the United States.¹³ Why do so many clinicians still appear to be disregarding the evidence from trials and reviews over the last 10 years and continue to prescribe

hypotonic maintenance IVF in children at risk for increased ADH secretion? The answer is unclear, but we should salute the group in Seattle for trying to translate the growing evidence supporting a shift away from hypotonic toward isotonic fluids,¹⁴ particularly in children at risk for increased ADH secretion, to implementation into daily clinical practice and for producing the first report of a successful project in both medical and surgical pediatric patients in this regard.

As with so many things in medicine, there is a bit of fine print. Only patients who were deemed euvoletic, did not have severe dysnatremia, and did not have various organ involvement were eligible for the pathway. Nevertheless, in the 2 years in which the study occurred, with pathway implementation in the middle, they were able to study over 10 000 children. The groups pre- and post-implementation were similar, and the use of isotonic maintenance IVF increased from 9% to 51%, with a decrease in hypotonic fluids from 94% to 56%. They did see significant increases in both recommended serum Na testing as well as daily weight measurement.

There are a number of lessons to be learned as well as additional questions that arise from this project.³ The widespread adoption of electronic medical records is a facilitator for this type of work, enabling the recommended practice to be embedded into order sets, as in this case. For those clinical leaders wanting to change ordering behavior, making it easy for prescribers to do the “right” thing by incorporating the recommended practice into all order sets (ie, hard coding changes) is an effective way of impacting practice change. A similar example would be their success in changing the ordering behavior of their emergency department clinicians to include potassium in their IVF prescription by changing the types of bags supplied in the emergency department automated dispensing cabinet, which, again, is making it harder for clinicians to do the “wrong” thing. Just in case we complacently believe that these projects are easy, even in this “freestanding tertiary care children’s hospital with a culture of patient safety and standard

pathways,” this pathway was only used in 62% of eligible children.³ How would this extrapolate to more community-level hospitals with less academic-focused clinicians?

A Web-based training module was also developed as part of their project. Although the awareness and education component of teaching the recommended practice change is essential, it is labor and time intensive and, especially in the teaching hospital with frequently rotating staff, logistically challenging. Hard coding changes may be easier to develop and implement and may prove more effective in achieving the desired behavior change. I was interested to see that the Web-based training was “not required” for surgical and medical residents, which seemed like a lost opportunity because these clinicians will go out into practice and may continue to inappropriately prescribe hypotonic maintenance IVF with inadequate monitoring.

In the case of regular monitoring of serum Na in patients on maintenance IVF, the exact consensus of who requires a needle poke and how often is much less clear. This is reflected in the observation that pre-implementation, only 18% of eligible patients in their study had their Na level checked, and even post-implementation, this percentage only increased to 30%. This means that 70% of eligible patients did not have their Na checked despite this being recommended in many standard IVF guidelines.¹⁴ It was disappointing, but perhaps not surprising, for those of us in hospitalist practice that the percent of days on which the children were weighed only edged up from 48% to 56%, suggesting that even post-implementation, children were only being weighed approximately half the time it was required. An accurate weight and, in particular, the change in weight over 24 hours should be an essential part of the daily assessment of fluid status for young children requiring maintenance IVF.

One of the difficulties of trials in which researchers study different types of IVF practices is the rarity of the outcome of severe adverse events from dysnatremia.⁷⁻⁹ Although potentially devastating and often

unpredictable, these events are still rare and no trials to date have been sufficiently powered so that researchers could actually address the true difference in risk of adverse events. Therefore, it is hard to interpret the increase from 2 to 4 cases of severe dysnatremia post-implementation. The number of cases of severe hyponatremia (2) actually stayed the same, but 2 additional cases of severe hypernatremia were noted. The knee-jerk assumption that this may be related to increased use of 0.9% saline is likely erroneous because 1 of the patients was actually treated with hypotonic fluids, and the second patient had a serum Na of 149 mEq/L before starting 0.9% saline, after which the level was measured marginally higher at 152 mEq/L. With the almost doubling in Na monitoring, greater detection post-implementation is another factor to consider. Additionally, not all hypotonic fluids should be lumped together; the use of 0.2% saline is thought to be more inappropriate and fortunately was only used in 4% of patients pre-implementation and down to 0.3% of patients post-implementation. Finally, the total fluid intake, including any oral component, will, of course, have an impact on Na levels, and this was not discussed in any detail in this article.

Considering that so many of the >2 million children hospitalized per year in the United States require IVF, it is troubling that we seem to have made so little impact in improving practice variability with regards to both the type of fluid required as well as the frequency and protocol for monitoring. In their article, Rooholamini et al³ provide good ideas for nudging clinicians in the right direction, and their clinical pathway could be adapted and used to improve the current practice in many hospitals. Although we may not be able to convince all clinicians on the exact details of which settings to use 0.45% versus 0.9% saline or exactly how frequently to check the Na level of patients, the need to implement a more standardized (and long overdue) algorithmic approach

that carefully monitors all the parameters and strives for continuous improvement in quality and safety of care cannot be denied.

While we wait for hospital electronic medical record clinical pathways to be updated to reflect current evidence (and frankly even after this has happened), the safest principle is to consider the prescription of IVF in the same way as any medication: approaching the indication, type of fluid, rate of infusion, monitoring parameters, and frequency on an individual, case-by-case fashion, at least daily while in hospital. We will continue to need to use clinical judgment and careful, individualized reevaluation in conjunction with algorithms, like the one studied here, to continue to improve the safety of the care we provide.

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