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EDITORIAL COMMENTARY

Maintenance fluid therapy: what it is and what it is not

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Abstract Fifty years after the publication of a prescription for maintenance fluid therapy, concerns have been raised about the use of hypotonic fluids in hospitalized children. We discuss what maintenance fluid therapy is or what it is not; where maintenance fluid therapy has been misused. We also discuss concerns with the immediate adoption of isotonic fluid as maintenance fluid without careful consideration and testing.

Keywords Maintenance fluid therapy · Isotonic fluids · Hypotonic fluids · Hyponatremia

In a seminal article published in 1957 Holliday and Segar provided a prescription for the maintenance need for water and electrolytes in parenteral fluid therapy for children [1]. This prescription was rapidly adopted throughout the world as the way to prescribe fluids and electrolytes to hospitalized children [2, 3]. Recently, some authors have recommended a very different prescription for maintenance fluid therapy. Because of the recent flurry of interest in maintenance fluid therapy, we think it is appropriate to focus on what maintenance fluid therapy was designed to do, how it has evolved, in some instances incorrectly, and to re-establish the concepts of maintenance fluid therapy apart from restoration fluid therapy (rehydration).

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Maintenance fluid therapy as defined by Holliday and Segar is a water and electrolyte prescription designed to replace anticipated water and electrolyte losses over the ensuing 24-hour period in primarily euvolemic children [4]. The average physiologic, that is to say insensible plus urinary, water losses per day come to approximately 100 ml/100 kcal expended per day. This calculation, derived from direct observation, followed from the development of empiric equations that estimated the changing relationship between the average daily metabolic rate and body weight (reviewed in a recent publication) [4]. The prescription—the water, sodium, potassium and chloride—delivered to a child as maintenance fluid therapy results in the delivery of a hypo-osmolar (compared to extracellular fluid) solution.

This prescription was designed with the average hospitalized patient in the mid-1950s as the patients to be treated. It was designed with certain assumptions/caveats to be considered. For example, patients who were consistently febrile would lose more water through evaporative and/or respiratory losses than accounted for by the formula. Higher water intake would be needed. The formula assumes normal renal function and normal concentrating ability. Thus, maintenance needs for a child with oliguric renal failure on the one hand, or diabetes insipidus on the other hand, required alteration of the standard maintenance water calculation.

What, if anything, has changed? Since its introduction, maintenance fluid therapy has been used as designed, namely as fluid therapy to provide for anticipated insensible and urinary losses, but it has also evolved, inappropriately, into fluid therapy for restoration of losses (diarrhea, vomiting, burns, etc.) and expansion of extracellular and blood volume (i.e. chemotherapy protocols).

The average hospitalized patient today is very different. A greater percentage of patients are in intensive care units,

on ventilators, undergoing operative procedures with shortened lengths of stay for perioperative care.

Also, our understanding of body fluid physiology has changed. In particular, let us consider the pathophysiology of the contraction in volume of extracellular fluid and then the use of intravenously administered fluids to restore normal fluid volume. In clinical situations, extracellular fluid volume (including blood volume) is reduced, due to losses from conditions such as diarrhea, vomiting, and burns, and the pathophysiologic response to this hypovolemia can be understood, at least in part, if we understand the relationship between extracellular fluid volume and, in particular, arterial circulation [5]. Extracellular fluid is in three compartments: (1) plasma and lymph; (2) cellular interstitial fluid—the solution through which solute exchanges occur between capillaries and cells; (3) extracellular fluid in the large reservoir found in skin and connective tissue, which can serve as a source of plasma fluid when plasma volume is reduced. In sepsis, fluid may not leave the body, but reduced vascular tone and/or capillary leak syndrome results in decreased effective circulating volume and increased interstitial fluid.

A number of mechanisms influence arterial circulation, such as the autonomic nervous system, cardiac function and circulating hormones. Of particular interest to a discussion of fluid therapy for hypovolemia is antidiuretic hormone (arginine vasopressin). Antidiuretic hormone in high concentrations has a pressor effect, which could increase arterial pressure. It also has the effect of increasing water reabsorption by the kidneys' collecting ducts. Hypovolemia results in the ongoing release of antidiuretic hormone. This non-osmotic release of antidiuretic hormone is well documented in a variety of clinical and experimental situations [6]. Other non-osmotic stimuli to antidiuretic hormone release include: medications and anesthetics, and nausea and vomiting. Regardless of the cause, the hallmark consequences of antidiuretic hormone release are lower urine volume and the production of concentrated urine.

Non-osmotic release of antidiuretic hormone should influence our thinking about fluid therapy. If such a release of antidiuretic hormone is often seen in children with acute illness and especially those with volume depletion, then restoration of extracellular fluid is the proper therapy to provide. The rapid expansion of extracellular fluid with isotonic saline solution or lactated Ringer's solution has been demonstrated to restore extracellular fluid volume and decrease circulating antidiuretic hormone [7, 8]. The maintenance fluid prescription described by Holliday and Segar is not isotonic and is not appropriate for the restoration (replenishment) of extracellular fluid volume. Once extracellular fluid volume has been restored, then oral or intravenous (i.v.) therapy with maintenance fluid is safe, tailored to urine output and urine concentration. If urine concentration is high [evidence of elevated circulating antidiuretic hormone (ADH)], which is often associated with low urine volume, half the maintenance volume should be prescribed. The provision of half the maintenance allowance in situations of reduced urine output was recommended before we appreciated non-osmotic stimulation of antidiuretic hormone release. This recommendation was published in 1972 [9]. It was known then that delivering water to patients when they were excreting concentrated urine would result in dilution of the extracellular space (hyponatremia).

Recently, some authors have recommended a change to isotonic saline solution as the electrolyte composition of maintenance fluids [2, 3, 10, 11]. The argument for the use of isotonic saline solution as a maintenance fluid centers on two issues: physiology and safety ("prophylaxis against hyponatremia").

The volume of intravenously given fluid recommended for maintenance therapy is generally agreed upon. The Holliday/Segar formula of 100 ml/kg body weight (BW) for the first 10 kg; 1,000 ml plus 50 ml/kg BW for each kilogram between 11 kg and 20 kg, and 1,500 ml plus 20 ml/kg BW for each kilogram above 20 kg, or another commonly used formula of 1,600 ml/m^2 body surface area per day, is used throughout the world. Routinely forgotten from the Holliday and Segar publication are the following: first, the sodium (chloride) and potassium prescription is based on 100 ml of fluid to be infused, and not on kilograms of body weight. Second, in the 1957 publication is this quote, "...it should be emphasized that these figures provide only maintenance needs of water. It is beyond the scope of this paper to consider repair of deficit and replacement of continuing abnormal losses. These must be considered separately." As maintenance fluid therapy was defined 50 years ago, as a prescription for the anticipated sensible and insensible losses of the average inpatient, isotonic saline solution is not that prescription. However, this raises the questions: Is the patient population so different, and, therefore, is isotonic saline solution a safer solution?

As noted above, the hospitalized child of today is different from that of 50 years ago. Second, our understanding of salt and water homeostatic controls is more advanced, including our understanding of non-osmotic ADH release or the influence of volume expansion on heart rate, blood pressure, cardiac before- and after-load, and the synthesis/release of ADH [12]. Also, our understanding of cell volume regulation is substantially greater than it was 50 years ago [13]. Recently, the proponents of isotonic saline solution as a "maintenance" fluid have begun to describe this usage of isotonic saline as "prophylaxis against hyponatremia" [11].

Physicians are all too aware that therapies they employ have the potential to heal and/or to harm. This is true of

medications or, as in the situation discussed here, fluid therapy, which can result in injury or death. Intravenous treatment with solutions with hypo-osmotic sodium concentration (hypotonic) has been given to children with ongoing non-osmotic antidiuretic hormone release, and children have suffered injury or died as a result. What have we learned from these reported cases [10, 11]? First, some of the reported cases involved children who were being treated for extracellular volume depletion with the Holliday/Segar maintenance solutions, often with volume prescriptions greater than the recommended maintenance volume. This is the wrong solution, the wrong volume, and is clearly inappropriate fluid management. Other patients described were postoperative patients, or patients with central nervous system conditions (including encephalitis)—both recognized as causing non-osmotic ADH release. Those patients received a hypo-osmotic sodium solution ranging from 5% dextrose in water to 5% dextrose 0.45 NaCl. What is not cited in the reviews is the volume provided to these patients. Would the outcomes have been different if the purpose of maintenance therapy had been understood and the isotonic saline solution needed to correct extracellular volume contraction had been employed? Would the outcome have been different if the maintenance fluid prescription took into account the recommendation to reduce the maintenance volume provided because of a concentrated urine and low urine volume? Did some of the patients have cerebral salt wasting, where even isotonic solutions may not have provided sufficient NaCl?

Advocates for isotonic saline solution as maintenance and as prophylaxis against hyponatremia argue that using one-half the recommended maintenance volume of a hypo-osmolar for sodium solution is not appropriate because: (1) clinicians may not appreciate extracellular volume contraction leading to non-osmotic ADH release. This argument conflates the purpose of maintenance therapy with restoration therapy. (2) Even reduced volumes of a hypo-osmolar for sodium solution can lead to hyponatremia. The study cited to prove number (2) is by Coulthard et al. in which a very hypotonic solution 3% dextrose plus one-third isotonic saline solution at two-thirds maintenance was compared with a 5% dextrose plus nearly isotonic saline solution (Hartmann's) in postoperative spinal instrumentation children [14]. The authors found that 37% (11 of 30) of the patients in the 3%, one-third isotonic saline group and 17% (five of 29) of the patients in the 5% dextrose Hartmann's solution group had a serum sodium level at follow-up of <135 mEq/l. Follow-up time was not provided. The authors' final paragraph states "However, in our 2-year study there were no patients in either cohort with clinically significant hyponatremia. We are not aware of good quality clinical trials to guide the management of pediatrics postoperative fluid therapy." The authors do not state why they chose a two-thirds maintenance volume for the 3%, one-third maintenance solution rather than the one-half maintenance as was recommended by Holliday. They also point out that each group received bolus fluid therapy at the discretion of the treating doctor. No difference in the mean total volume of the fluid bolus (milliliters per kilogram) was noted, and the bolus solution was not described.

Previous publications by Moritz and Ayus have reviewed the literature regarding the use of isotonic saline solutions in the perioperative period and state, "several prospective studies in children and adults have shown that administration of 0.9% NaCl is effective prophylaxis against the development of hyponatremia [11]." The studies cited pertain mostly to the perioperative (especially intra- or post-operative) periods. The prevention of hyponatremia in hospitalized patients is important [15]. However, a recommendation to replace lower sodium-containing maintenance solutions with isotonic saline solutions requires a very careful analysis of the safety of this approach, not only in the peri-operative, but for all hospitalized, patients. What does happen to serum sodium in a wide range of inpatients intravenously treated with "maintenance" volumes of isotonic saline solution? What about such issues as the development of edema or the use of diuretics with isotonic saline as "maintenance"? Even in the peri-operative period, should isotonic saline solution be used for the first 12 hours after surgery? Twenty-four hours? Until discharge? As patients move from no oral intake of fluid to fluid intake even in the peri-operative period, does this not mean that the patient's fluid intake is effectively hypo-osmotic with respect to sodium? Does the oral route protect patients, at least to some degree, from clinically significant hyponatremia? Is isotonic saline solution associated with metabolic acidosis [16]?

How do we proceed? Intravenous fluid therapy should be viewed as a prescription requiring careful thought and measurement of intake, output, vital signs and even serum electrolytes. No one formula, either hypotonic or isotonic, will be optimal for all hospitalized patients receiving intravenous administration of fluids. No one formula does, in fact, provide for the anticipated upcoming needs of all hospitalized children (maintenance therapy). Holliday and Segar, in 1957 stated, "As with any method, and understanding the limitations of and exceptions to the system is required. Even more essential is the clinical judgment to modify the system as circumstances dictate." We feel it is important to understand what maintenance fluid was designed to do—what it is and is not.

- Today's hospitalized patient is different from that of 50 years ago.
- Our understanding of the hormonal control of water and electrolyte homeostasis has advanced. Even 40 years ago, we knew that giving water in excess

to patients with release of ADH would lead to hyponatremia.

- Hyponatremia, especially very low serum sodium concentrations or a rapid decline in serum sodium, is dangerous and is associated with morbidity and mortality in hospitalized patients.
- Reports of low-sodium-containing solutions given erroneously to treat extracellular volume depletion or given in high volume peri-operatively make up the bulk of published studies regarding morbidity or mortality related to hyponatremia.
- For those patients described in previous reports, isotonic saline solution may have been prophylactic against the morbidity or mortality associated with the intravenous administration of low-sodium-containing solutions. Would one-half maintenance volumes also have prevented morbidity or mortality?
- Prophylaxis against hyponatremia is a desired and laudable goal, but so is assuring that the use of isotonic saline solution as a maintenance fluid for a broad range of patients does not result in other adverse outcomes—hypertension, hypernatremia, edema, metabolic acidosis.
- We recommended in the past that isotonic saline solution be the intravenous therapy of choice in the peri-operative period [17]. We do not know for how long, post-operatively, isotonic saline solution should be administered, but, certainly, a minimum of 12–24 hours is necessary if intravenous fluid therapy is needed. This seems prudent, especially if one recognizes the high potential for bolus infusions in the peri-operative period.
- We fully agree with Moritz and Ayus that "Further prospective studies are needed to assess the safety and efficacy of 0.9% NaCl in a variety of disease states in children, adults, and the elderly [11]." We also agree with Choong et al., who state in a systemic review of i. v. fluid regimens, "Our current responsibility however, is to refrain from adopting a 'new standard of care' until rigorous clinical trials comparing the safety and effectiveness of different IV fluid regimens in children have been completed [18]."

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