

Isotonic Solutions Versus Hypotonic Solutions

Isotonic fluid has a sodium concentration similar to plasma (135–144 mEq/L). Plasma is approximately 93% aqueous and 7% anhydrous with a sodium concentration in the aqueous phase of plasma of 154 mEq/L and osmolality of 308 mOsm/L, similar to that of 0.9% sodium chloride (NaCl). Conversely, hypotonic fluid has a sodium concentration lower than that of the aqueous phase of plasma. In the studies evaluated in the formulation of these guidelines, there is some heterogeneity in both the isotonic and hypotonic fluids used. The sodium concentration of isotonic fluids ranged from 131 to 154 mEq/L. Hartmann solution (sodium concentration 131 mEq/L; osmolality 279 mOsm/L) was used in only 46 patients.^{48,49} PlasmaLyte (sodium concentration 140 mEq/L; osmolality 294 mOsm/L) was used in 346 patients.³⁵ Researchers in the majority of the studies used either 0.9% NaCl (sodium concentration 154 mEq/L; osmolality 308 mOsm/L) or a fluid of equivalent tonicity. Hypotonic fluids ranged from 30 to 100 mEq/L.³³ Lactated Ringer solution (sodium concentration 130 mEq/L; osmolality 273 mOsm/L), a slightly hypotonic solution, was not involved in any of the clinical trials. For the purposes of this guideline, isotonic solutions have a sodium concentration similar to PlasmaLyte, or 0.9% NaCl. Recommendations are not made regarding the safety of lactated Ringer solution. Researchers in the majority of studies added dextrose (2.5%–5%) to the intravenous (IV) solution.

The search revealed 17 randomized clinical trials^{20,31,32,35,48–60} that met the search criteria, including a total 2455 patients (2313 patients had primary outcome data for analysis in Supplemental Figs 2–4), to help evaluate the question

of whether isotonic or hypotonic fluids should be used in children who are hospitalized. Sixteen of the studies revealed that isotonic fluids were superior to hypotonic fluids in preventing hyponatremia. There have also been 7 systematic reviews over the past 11 years in which researchers have synthesized various combinations of the above RCTs.^{9,33,34,39–42} The number needed to treat with isotonic fluids to prevent hyponatremia (sodium <135 mEq/L) was 7.5 across all included studies and 27.8 for moderate hyponatremia (sodium <130 mEq/L).

Study appraisal for risk of bias (Supplemental Table 4) revealed the reviewed studies in total to be methodologically sound. Most types of bias were found to be of low risk in all but 2 studies. There was 1 study with 2 bias types of potentially high risk and 11 studies with 1 or more unclear bias areas.

Inclusion and Exclusion Criteria: Rationale for Specific Subgroups

Age

The specific age groups from which data are available from randomized clinical trials range from 1 day (1 trial) to 18 years. Given this broad age range, we specifically evaluated whether there was variability in the outcomes by age, particularly for the lower age range. McNab et al³³ examined this question in their systematic review and found 100 children studied at younger than 1 year of age, 243 children studied between the ages of 1 and 5 years, and 465 children studied at older than 5 years of age. They showed a significant benefit of isotonic IVFs in each age group stratum. There have been 7 additional studies in which researchers have also included children younger than 1 year old, although there are not specific outcome data reported for this age group.^{31,32,35,50,51,55,58}

Surgical (Postoperative Patients)

Surgical or postoperative patients have been specifically studied in 7 studies^{20,48,49,51,54,56,57} that included 529 patients. McNab³⁰ showed a pooled risk ratio of 0.48 (95% confidence interval [CI], 0.38–0.60) for the outcome of hyponatremia in favor of isotonic fluids.

Medical (Nonsurgical Patients)

Medical patients are defined here as children who are hospitalized in an acute-care setting with no indication for a surgical operation and no immediate history of a surgical operation. For these patients, there are 4 randomized clinical trials^{32,52,55,58} in which researchers enrolled only medical patients and 6 randomized clinical trials^{50,51,53,56,57,59} in which researchers enrolled both medical and surgical patients. Some of the mixed studies in which researchers looked at both medical and surgical patients include outcomes for only medical patients, whereas most include combined outcomes for both groups.

Varying Acuity (ICU Versus General Ward)

There are 6 randomized clinical trials^{31,49,50,53,56,59} in which researchers enrolled only ICU patients, and all but one⁵⁰ revealed a significant difference favoring isotonic IVFs for the prevention of hyponatremia. Researchers in 8 randomized clinical trials enrolled exclusively patients in a general ward setting,^{32,51,52,54,55,57,58,60} and those in all but 2^{32,57} found a significant reduction in hyponatremia among those receiving isotonic IVFs. McNab et al³⁵ enrolled patients in both the ICU and general surgical ward, and they were at similar risk for developing hyponatremia.

Exclusion of Specific Populations Not Studied

Patients with neurosurgical disorders, congenital or acquired cardiac disease, hepatic disease,