

How to Improve Maintenance Intravenous Fluid Prescribing Practices in Bronchiolitis

Michael L. Moritz, MD, FAAP,^a Juan C. Ayus, MD, FACP, FASN^{b,c,d}

Bronchiolitis is the most common reason for hospitalization in infants in the first year of life.¹ There are no proven therapies to treat this common condition, with the mainstay of therapy being supportive care with intravenous fluid (IVF) and supplemental oxygen when needed. Hyponatremia is often encountered in children with bronchiolitis and has been associated with more severe disease and worse outcomes, and neurologic complications have been reported.²⁻⁶ Explicit recommendations for IVF therapy in children with bronchiolitis are lacking in both consensus guidelines and authoritative reviews.⁷⁻⁹

The historical approach to providing maintenance fluids in children has been to administer hypotonic IVF with a sodium concentration similar to that found in breast and cow milk (30 mEq/L).¹⁰ In 2003, we began recommending 0.9% saline in 5% dextrose for the prevention of hospital-acquired hyponatremia, based on numerous reports of iatrogenic deaths related to hypotonic fluids and the incidence of syndrome of inappropriate secretion of antidiuretic hormone (SIADH)-like states in acutely ill children.¹¹ A 0.9% saline solution has a sodium concentration (154 mEq/L), which is isotonic to the aqueous phase of plasma water.¹² Since our initial recommendation, there have been >15 randomized, prospective trials involving >2000 children confirming that hypotonic maintenance fluids result in hospital-acquired hyponatremia and that isotonic fluids decrease the incidence of hyponatremia without associated complications.¹³⁻¹⁶ It would be reasonable to conclude that hypotonic fluids should be avoided in infants with bronchiolitis in favor of 0.9% saline, because bronchiolitis is associated with SIADH.^{2,17-20} However, surprisingly few studies have examined IVF prescribing practices in bronchiolitis or the impact of the sodium composition on the development of hyponatremia and how these fluids may affect outcome.²¹

In this issue of *Hospital Pediatrics*, Shein et al evaluated how the sodium composition of IVF may affect the development of hyponatremia and outcome in children with bronchiolitis.²² They evaluated a large retrospective cohort of >1500 children, comparing those who received maintenance IVF with a sodium concentration <70 mEq/L with those >70 mEq/L. They found that children with hyponatremia had an increased length of stay and higher need for mechanical ventilation. Those who received a more hypotonic fluid, <70 mEq/L, had both an increased length of stay and a significantly increased incidence of hyponatremia. These data demonstrated the deleterious effects that both hyponatremia and the administration of hypotonic IVF have on children with bronchiolitis. One area of this study that we would like to draw particular attention to is the ongoing pervasive practice of administering hypotonic maintenance IVF, even to the sickest children who are in the ICU on mechanical ventilation.

www.hospitalpediatrics.org

DOI:10.1542/hpeds.2017-0050

Copyright © 2017 by the American Academy of Pediatrics

Address correspondence to Michael L. Moritz, MD, Division of Nephrology, Children's Hospital of Pittsburgh of UPMC, One Children's Hospital Drive, 4401 Penn Ave, Pittsburgh, PA 15224. E-mail: moritzml@upmc.edu

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICTS OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

FREE

^aDepartment of Pediatrics, Children's Hospital of Pittsburgh of UPMC, The University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; ^bRenal Consultants of Houston, Houston, Texas; ^cHospital Italiano, Universidad Austral, Buenos Aires, Argentina; and ^dUniversity of California Irvine School of Medicine, Irvine, California

Ninety-six percent of the almost 2000 IVF orders that were written in this study were for either 0.2% or 0.45% saline, with only 2% for 0.9% saline. Sixty-five percent were receiving 0.2% saline at the time of mechanical ventilation. The incidence of hyponatremia increased throughout the study in patients where a sodium level was checked, from 19% to 66%. Ten patients developed severe hyponatremia, serum sodium <125 mEq/L, with 1 having a sodium level of 112 mEq/L. Neurologic complications due to hyponatremia were not reported in this study, but it is known that hyponatremia of this severity is potentially dangerous.^{2,25}

The administration of hypotonic maintenance IVF to children continues to be a pervasive practice, despite abundant evidence documenting that it causes hyponatremia.^{24,25} Our group and others have conducted surveys and observational studies of recent fluid prescribing practices in acutely ill children and have confirmed that the administration of hypotonic maintenance IVF continues to be a pervasive practice.^{26–28} The study by Shein et al suggests that 0.45% saline is superior to 0.2% saline, but neither is appropriate.²² Large prospective studies have already demonstrated that both 0.2% and 0.45% saline result in a high incidence of hyponatremia, whereas 0.9% saline does not.^{13,15,16} Neither 0.2% or 0.45% saline is appropriate maintenance IVF for the acutely ill child and certainly not a child needing mechanical ventilation. Acute respiratory illnesses are associated with elevated arginine vasopressin, and hyponatremia will be a predictable consequence of administering hypotonic fluids.^{18–20} Additional prospective studies including hypotonic fluids in a treatment arm in children with bronchiolitis are not needed and should be viewed as unethical, based on the extensive current literature. There is no advantage to administering hypotonic fluids, and it only subjects the patients to possible harm. The recent National Institute for Health Care Excellence guideline on intravenous fluid therapy in children and young people in the hospital recommends isotonic maintenance fluids.²⁹ The recent American Academy of Pediatrics

clinical practice guideline for bronchiolitis favors the use of isotonic maintenance fluids over hypotonic fluids in children.⁸

Why is the administration of hypotonic fluids still so pervasive in pediatrics, and what can be done to change this practice? We suspect that pediatricians feel uncomfortable using 0.9% saline in 5% dextrose because they may have had no previous experience with it as a maintenance fluid. They may have concerns that 0.9% saline will result in untoward complications such as hypertension. These complications have all been evaluated in prospective studies in children and adults, and they do not occur.^{12,30} We also suspect that pediatricians do not really consider mild hyponatremia, sodium 130 to 135 mEq/L, to be a significant health concern. Many physicians may be unaware of dangers of hypotonic IVF and are unfamiliar with the literature on this topic. The data from this study, and other data, particularly in adults, demonstrate the length of stay, hospital cost, and mortality increase when hyponatremia is present.^{31,32}

There is a great opportunity to improve the health care in children with bronchiolitis by administering 0.9% saline in favor of hypotonic saline in maintenance IVF. It would be a valuable quality improvement project for hospitals to assess the IVF prescribing practices in their hospital and set goals to increase the use of 0.9% saline. Hospital electronic medical records could carry an alert if hypotonic IVF is administered to a child with bronchiolitis. Guidelines on bronchiolitis should make explicit recommendations to administer 0.9% saline in 5% dextrose when IVF is indicated. More data demonstrating the safety of administering 0.9% saline in children with bronchiolitis would be of value, because it would encourage others to use 0.9% saline, but no more studies evaluating hypotonic fluids are indicated, because they have proven to be unsafe and there is no physiologic rationale for administering them.

REFERENCES

1. Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA Jr. Trends in bronchiolitis hospitalizations in the

United States, 2000–2009. *Pediatrics*. 2013;132(1):28–36

2. Hanna S, Tibby SM, Durward A, Murdoch IA. Incidence of hyponatraemia and hyponatraemic seizures in severe respiratory syncytial virus bronchiolitis. *Acta Paediatr*. 2003;92(4):430–434
3. Van Steensel-Moll HA, Van der Voort E, Bos AP, Rothbarth PH, Neijens HJ. Respiratory syncytial virus infections in children admitted to the intensive care unit. *Pediatr*. 1989;44(7):583–588
4. Luu R, DeWitt PE, Reiter PD, Dobyns EL, Kaufman J. Hyponatremia in children with bronchiolitis admitted to the pediatric intensive care unit is associated with worse outcomes. *J Pediatr*. 2013;163(6):1652–1656.e1
5. Eisenhut M. Extrapulmonary manifestations of severe respiratory syncytial virus infection: a systematic review. *Crit Care*. 2006;10(4):R107
6. Kanai H, Sato Y, Ichihashi K. Hyponatremia in patients with respiratory syncytial virus bronchiolitis. *Pediatr Health Med Ther*. 2012;3:39–43
7. Meissner HC. Viral bronchiolitis in children. *N Engl J Med*. 2016;374(1):62–72
8. Ralston SL, Lieberthal AS, Meissner HC, et al; American Academy of Pediatrics. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. *Pediatrics*. 2014;134(5). Available at: www.pediatrics.org/cgi/content/full/134/5/e1474
9. Ricci V, Delgado Nunes V, Murphy MS, Cunningham S; Guideline Development Group and Technical Team. Bronchiolitis in children: summary of NICE guidance. *BMJ*. 2015;350:h2305
10. Holliday MA, Segar WE. The maintenance need for water in parenteral fluid therapy. *Pediatrics*. 1957;19(5):823–832
11. Moritz ML, Ayus JC. Prevention of hospital-acquired hyponatremia: a case for using isotonic saline. *Pediatrics*. 2003;111(2):227–230
12. Moritz ML, Ayus JC. Maintenance intravenous fluids in acutely ill patients. *N Engl J Med*. 2015;373(14):1350–1360

13. Foster BA, Tom D, Hill V. Hypotonic versus isotonic fluids in hospitalized children: a systematic review and meta-analysis. *J Pediatr*. 2014;165(1):163–169.e2
14. Friedman JN, Beck CE, DeGroot J, Geary DF, Sklansky DJ, Freedman SB. Comparison of isotonic and hypotonic intravenous maintenance fluids: a randomized clinical trial. *JAMA Pediatr*. 2015;169(5):445–451
15. McNab S, Duke T, South M, et al. 140 mmol/L of sodium versus 77 mmol/L of sodium in maintenance intravenous fluid therapy for children in hospital (PIMS): a randomised controlled double-blind trial. *Lancet*. 2015;385(9974):1190–1197
16. McNab S, Ware RS, Neville KA, et al. Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children. *Cochrane Database Syst Rev*. 2014;(12):CD009457
17. Ashraf A, Albert A. Bronchiolitis with hyponatremia. *Clin Pediatr (Phila)*. 2006;45(1):101–102
18. Gozal D, Colin AA, Jaffe M, Hochberg Z. Water, electrolyte, and endocrine homeostasis in infants with bronchiolitis. *Pediatr Res*. 1990;27(2):204–209
19. Poddar U, Singhi S, Ganguli NK, Sialy R. Water electrolyte homeostasis in acute bronchiolitis. *Indian Pediatr*. 1995;32(1):59–65
20. Rivers RP, Forsling ML, Olver RP. Inappropriate secretion of antidiuretic hormone in infants with respiratory infections. *Arch Dis Child*. 1981;56(5):358–363
21. Rodrigues RM, Schwartsman BG, Farhat SC, Schwartsman C. Hypotonic solution decreases serum sodium in infants with moderate bronchiolitis. *Acta Paediatr*. 2014;103(3):e111–e115
22. Shein S, Slain K, Martinez Schlurmann N, Speicher R, Rotta A. Hyponatremia and Hypotonic Intravenous Fluids are Associated with Unfavorable Outcomes of Bronchiolitis Admissions. *Hospital Pediatrics*. 2017;7(5)
23. Albinski M, Gämperli L, Regamey N, Stettler J, Tomaske M. Hyponatraemia in paediatric bronchiolitis: a harmful complication not to be ignored. *Klin Padiatr*. 2016;228(5):275–276
24. Moritz ML, Ayus JC. Preventing neurological complications from dysnatremias in children. *Pediatr Nephrol*. 2005;20(12):1687–1700
25. Moritz ML, Ayus JC. New aspects in the pathogenesis, prevention, and treatment of hyponatremic encephalopathy in children. *Pediatr Nephrol*. 2010;25(7):1225–1238
26. Freeman MA, Ayus JC, Moritz ML. Maintenance intravenous fluid prescribing practices among paediatric residents. *Acta Paediatr*. 2012;101(10):e465–e468
27. Shukla S, Basu S, Moritz ML. Use of hypotonic maintenance intravenous fluids and hospital-acquired hyponatremia remain common in children admitted to a general pediatric ward. *Front Pediatr*. 2016;4:90
28. Carandang F, Anglemeyer A, Longhurst CA, et al. Association between maintenance fluid tonicity and hospital-acquired hyponatremia. *J Pediatr*. 2013;163(6):1646–1651
29. NCGC (UK). *IV Fluids in Children: Intravenous Fluid Therapy in Children and Young People in Hospital*. London, UK: National Institute for Health and Care Excellence; 2015
30. Young P, Bailey M, Beasley R, et al; SPLIT Investigators; ANZICS CTG. Effect of a buffered crystalloid solution vs saline on acute kidney injury among patients in the intensive care unit: the SPLIT randomized clinical trial. *JAMA*. 2015;314(16):1701–1710
31. Corona G, Giuliani C, Parenti G, et al. Moderate hyponatremia is associated with increased risk of mortality: evidence from a meta-analysis. *PLoS One*. 2013;8(12):e80451
32. Wald R, Jaber BL, Price LL, Upadhyay A, Madias NE. Impact of hospital-associated hyponatremia on selected outcomes. *Arch Intern Med*. 2010;170(3):294–302

How to Improve Maintenance Intravenous Fluid Prescribing Practices in Bronchiolitis

Michael L. Moritz and Juan C. Ayus

Hospital Pediatrics 2017;7;300

DOI: 10.1542/hpeds.2017-0050 originally published online April 13, 2017;

Updated Information & Services	including high resolution figures, can be found at: http://hosppeds.aappublications.org/content/7/5/300
Supplementary Material	Supplementary material can be found at:
References	This article cites 28 articles, 5 of which you can access for free at: http://hosppeds.aappublications.org/content/7/5/300#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Hospital Medicine http://www.hosppeds.aappublications.org/cgi/collection/hospital_medicine_sub Nephrology http://www.hosppeds.aappublications.org/cgi/collection/nephrology_sub Patient Education/Patient Safety/Public Education http://www.hosppeds.aappublications.org/cgi/collection/patient_education:patient_safety:public_education_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.hosppeds.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://www.hosppeds.aappublications.org/site/misc/reprints.xhtml

Hospital Pediatrics®

AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

How to Improve Maintenance Intravenous Fluid Prescribing Practices in Bronchiolitis

Michael L. Moritz and Juan C. Ayus

Hospital Pediatrics 2017;7;300

DOI: 10.1542/hpeds.2017-0050 originally published online April 13, 2017;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://hosppeds.aappublications.org/content/7/5/300>

Hospital Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Hospital Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

