

Hyponatremia in Children with Bronchiolitis Admitted to the Pediatric Intensive Care Unit Is Associated with Worse Outcomes

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Objective To characterize the relationship between hyponatremia (serum sodium <135 mEq/L) and clinical outcomes in children ages 1 month to 2 years admitted to the pediatric intensive care unit (PICU) with bronchiolitis.

Study design Single-center retrospective cohort study comprising children who were admitted to the PICU between January 2009 and April 2011. Serum sodium concentrations, collected within the first 2 hours after admission to the PICU, were recorded and associations with clinical outcomes were calculated. Quantitative data are presented as mean $\pm$ SD or percentage. Student *t*-test, Fisher exact test, and χ^2 analyses were performed as appropriate. Subjects were excluded if they were previously diagnosed with chronic disease that would affect initial serum sodium concentration.

Results Children with bronchiolitis were enrolled (*n* = 102; age = 10.7 $\pm$ 6.7 months). Twenty-three patients (22%) were diagnosed with hyponatremia within 2 hours of admission. Mortality (13% vs 0%; *P* = .011), ventilator time (8.41 $\pm$ 2 days vs 4.11 $\pm$ 2 days; *P* = .001), duration of stay in the PICU (10.63 $\pm$ 2.5 days vs 5.82 $\pm$ 2.09 days; *P* = .007), and noninvasive ventilator support (65% vs 24%; *P* = .007) were significantly different between subjects with hyponatremia vs those without. There were no differences in the number of patients with seizures, bronchodilator use, steroid use, intubation requirement, oxygen use at discharge, or hospital readmission.

Conclusions Pediatric patients diagnosed with bronchiolitis who present with a serum sodium concentration less than 135 mEq/L within 2 hours of admission to the PICU fare worse than their cohorts with normonatremia. A prospective study to evaluate the effects of hyponatremia appears justified. (*J Pediatr* 2013;163:1652-6).

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Hyponatremia has long been recognized in adult critical illness as an indicator of worse outcomes.^{1,2} The mechanism behind this phenomenon is not well understood, but may be attributable to the direct effects of low sodium concentrations leading to detrimental physiological responses such as inappropriate fluid shifts, or to low sodium acting as a biomarker of illness severity and overall fluid balance.³ The etiology of hyponatremia in these patients can range from syndrome of inappropriate antidiuretic hormone release observed, frequently in pulmonary diseases, to iatrogenic fluid overload occurring during resuscitation. Unlike adult data, little evidence has been found in pediatric patients to connect hyponatremia with clinical outcomes. Previous studies in general describe an association between an initial serum sodium of less than 130 mEq/L at the time of admission and increased mortality rate and hospital duration of stay in children.⁴

Bronchiolitis is a common pediatric disease of the lower respiratory tract that accounts for a high percentage of seasonal inpatient and pediatric intensive care unit (PICU) admissions. Some estimates suggest that 30% of all infants will be diagnosed with bronchiolitis, and 10% of those patients will require inpatient admission. Up to 15% of children admitted to the hospital for bronchiolitis will require admission to the PICU.⁵ In addition to its high prevalence, bronchiolitis in children is a disease with significant variability in terms of course, severity of illness, treatment regimens, and discharge status. In an attempt to standardize therapeutic approaches to bronchiolitis, the American Academy of Pediatrics (AAP) drafted clinical care guidelines in 2006.⁶ Despite these recommendations, treatment variation continues to exist, including the modes of invasive and noninvasive positive pressure ventilation.

The purpose of this study was to characterize the relationship between hyponatremia within 2 hours of admission to the intensive care unit, in the setting of bronchiolitis, and clinical outcomes including mortality, duration of PICU stay, intubation, mechanical ventilator time, seizures, bronchodilator use, steroid use, noninvasive support, oxygen support at discharge, and PICU readmission. We hypothesized that hyponatremia at the time of admission or hyponatremia that developed within 2 hours of admission in children with bronchiolitis is associated with worse outcomes compared with their normonatremic cohort.

AAP	American Academy of Pediatrics
PICU	Pediatric intensive care unit
PRISM III	Pediatric Risk of Mortality Scores III

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Methods

This was a retrospective medical chart review of all children admitted to the PICU with a diagnosis of bronchiolitis between January 1, 2009, and July 1, 2011. The PICU at Children's Hospital Colorado is a free-standing pediatric academic center that serves as the main referral center for pediatric critical illness in the multistate Rocky Mountain region.

The diagnosis of bronchiolitis was made by the primary critical care physician at time of admission on the basis of clinical signs of tachypnea, hypoxia, rhinorrhea, cough, wheeze, subcostal or intercostal retractions, nasal flaring, and grunting. Dependent upon physician preference, a direct viral nasal stain via direct fluorescent antibody was collected to confirm infection. Patients were categorized into 2 main groups, those with hyponatremia (serum sodium <135 mEq/L) and those with normonatremia according to current hospital laboratory standards.

This study was reviewed and approved by the Colorado Multiple Institutional Review Board, and informed parent/patient consent was waived. Chart review was performed using a combination of the Virtual PICU database, which was used to identify patients with a diagnosis of bronchiolitis and the electronic medical record (Epic Hyperspace [Epic Rx] Systems Corporation, Verona, Wisconsin) to retrieve sodium concentrations within 2 hours of admission and clinical outcomes. The Virtual PICU database is an ongoing record of all patients admitted to the Children's Hospital Colorado PICU that identifies age, chart number, and corresponding primary diagnosis and is used primarily for research purposes.

Serum sodium concentrations collected from enrolled patients within 2 hours of admission to the PICU were reviewed. By collecting serum sodium values within 2 hours of admission to the PICU, the possible effect of fluid management on sodium concentrations was minimized. Hyponatremia was further characterized as mild (130-134 mEq/L), moderate (125-129 mEq/L), or severe (<125 mEq/L). Because of low number of observations regarding severe hyponatremia, data comparison occurred primarily between normonatremia (>134 mEq/L) subjects and hyponatremia (<134 mEq/L) subjects, which included subjects with severe hyponatremia. To eliminate the effects of chronic diseases affecting sodium concentrations, subjects were excluded if they carried a diagnosis of cystic fibrosis, hypothyroidism, pan-hypopituitarism, renal failure, metabolic disease, chromosomal disorder, genetic disorder, or any recent surgery. Any child with a previous diagnosis of syndrome of inappropriate antidiuretic hormone syndrome also was excluded because hyponatremia has an increased prevalence in this group and fluid therapy needs to be directed towards treatment.⁷

Outcome measures studied included hospital mortality, duration of hospital stay, intubation requirement, duration of intubation, incidence of seizures, and readmission to the hospital within 5 days of hospital discharge. Associated

Table I. Characteristics of study population

	Whole population	Hyponatremia	Normonatremia	P value
Number of patients	102	23	79	
Age in months (SD)	10.7 (6.7)	11.2 (7)	10.6 (6.6)	.730
Sex, male, n (%)	55 (54)	5 (22)	50 (64)	.0008
PRISM score, mean (range)	4.39 (1-24)	4.41 (1-24)	4.30 (1-20)	.3680

uses of therapies were also examined and these included noninvasive ventilation, steroids, bronchodilators, and oxygen requirement at the time of hospital discharge. Steroids administered were either intravenous methylprednisolone, or oral prednisone. Initial Pediatric Risk of Mortality Scores III (PRISM III) were calculated at 24 hours and recorded for all patients. The PRISM III score uses multiple physiologic variables at time of admission and is used as a predictor of mortality.⁸ Infectious comorbidities are known to increase the severity of illness; therefore, the presence of confirmed or suspected viral or bacterial coinfections (indicated by cultures or antibiotic use) were recorded.⁹

The data set was collected and transcribed into a Microsoft Excel Workbook (Microsoft Corp, Redmond, Washington) and then read into R version 2.14.1 (www.r-project.org) for analysis.¹⁰ Simple tests to determine whether there is a difference in any of the noted variables between the hyponatremic statuses were conducted. These methods include Student *t*-test for the difference in means and χ^2 or Fisher exact tests for the differences in proportions. χ^2 tests are used preferentially over Fisher exact tests when the observed data supported the asymptotic assumptions of the χ^2 test. Duration of stay in the PICU and duration of ventilator dependence were log transformed before analysis to correct for the skewness in the observed data. Geometric means are reported for these 2 metrics. Statistical significance was set at $P < .05$.

Results

A total of 102 subjects with bronchiolitis were admitted during the study period. Twenty-three (22%) were found to have hyponatremia (Table I). There was no significant difference in PRISM III scores between patients admitted with normonatremia and those with hyponatremia at time of admission. There was a significant difference in sex, with a larger percentage of male patients having normonatremia at time of admission. Infectious etiologies of bronchiolitis are shown in Table II (available at www.jpeds.com). Respiratory syncytial virus accounted for more than one-half of the cases, with enterovirus, adenovirus, and rhinovirus accounting for approximately one-third of the cases of bronchiolitis. Stratification of the 23 subjects based on hyponatremia severity is depicted in Table III; only 1 exhibited severe hyponatremia defined as serum sodium <125 mEq/L.

Comparative variables for normal serum sodium and subjects with hyponatremia are shown in Table IV. Mortality did

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