Risk Factors and Outcomes in Patients With Hypernatremia and Sepsis

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ABSTRACT

Background: Hypernatremia is an uncommon but important electrolyte abnormality in intensive care unit patients. Sepsis is one of the most common causes of intensive care unit admission, but few studies about the role of hypernatremia in sepsis has been published yet. In this study, we aimed to explore the risk factors for developing hypernatremia in patients with sepsis, and the prognosis of patients with sepsis with or without hypernatremia was also assessed.

Materials and Methods: In this retrospective cohort study of 51 septic intensive care unit patients at a single center, we examined the risk factors for the development of hypernatremia and the association of hypernatremia with clinical outcomes using univariate and multivariable analyses. Clinical outcomes such as mortality and hospital duration of patients with or without hypernatremia were also compared.

Results: Acute Physiology and Chronic Health Evaluation II score (odds ratio = 1.15; 95% CI: 1.022-1.294) was found to be the only independent risk factor for hypernatremia in patients with sepsis. Moreover, patients developing hypernatremia during hospitalization showed significantly higher morbidity and mortality.

Conclusions: Acute Physiology and Chronic Health Evaluation II score may be an independent risk factor for hypernatremia in patients with sepsis. Moreover, hypernatremia is strongly associated with worse outcome in sepsis.

Key Indexing Terms: Hypernatremia; Sepsis; Risk factors; Prognosis. **[Am J Med Sci 2016;351(6):601–605.]**

INTRODUCTION

Acute disorders of blood sodium concentration, namely, dysnatremias (hyponatremia and hypernatremia) are commonly encountered in the intensive care unit (ICU) and have adverse effect on various organ systems mainly through alteration of effective plasma osmolality.[1,2] Definition of hyponatremia and hypernatremia varies in different studies, but mostly hyponatremia is defined as a plasma sodium level less than 136 mmol/L, whereas hypernatremia as greater than 145 mmol/L.

In the literature, hyponatremia was much better studied and its clinical effects including brain edema, increased intracranial pressure and gait disturbances were well described, although the mechanisms underlying its association with increased risk of death remain unclear.[3] In contrast, previous studies regarding the clinical relevance of hypernatremia were relatively limited.[4,5] Actually, on ICU admission, the prevalence of hypernatremia was reported to be between 2% and 9%[1] and Lindner et al[6] suggested that hypernatremia acquired during the ICU stay is an independent risk factor for death. However, although septic and septic shock patients are commonly seen in the ICUs worldwide, no study about the role of hypernatremia in patients with sepsis was published yet.

In the present study, we explored the risk factors for hypernatremia in sepsis and the relationship between hypernatremia and clinical outcomes. Moreover, we also compared the prognosis of patients with sepsis with or without hypernatremia to clarify the poor outcome of hypernatremia.

MATERIALS AND METHODS

Patients

Patients with a primary diagnosis of sepsis admitted to the ICU of the emergency department in Jiangsu Integrative Medicine Hospital within 48 hours after the onset of the disease were involved in this observational study. The study period extended from January 2012-January 2013. Inclusion criteria for sepsis were defined according to the Surviving Sepsis Campaign Guidelines 2012.[7] Hypernatremia was defined as $[Na^+] > 145$ mmol/L lasting for at least 48 hours to avoid laboratory error. In general, patients in the study ICU are treated in accordance with the Surviving Sepsis Campaign Guidelines from 2012[7,8] and were followed up until discharge from the hospital or hospital mortality.

Data Collection

The risk factors analyzed in the present investigation included demographic metrics like age, sex and clinical parameters such as Acute Physiology and Chronic Health Evaluation II (APACHE II) score, hyperglycemia occurrence, blood urea nitrogen levels, white blood

TABLE 1. General characteristics of the patients.

Characteristic	Total ($n = 51$)	Hypernatremia ($n = 24$)	Nonhypernatremia ($n = 27$)	*P* Value
Age, years (range)	74 (66-80)	76.5 (68.25-82.25)	72 (48-80)	0.05
Sex, M/F	39/12	21/3	20/7	
APACHE II score	18 (14-23)	22 (18.5-30)	16 (14-19)	<0.001
Glasgow score	10 (7-14)	7.5 (7-10)	14 (11-14)	<0.001
Hyperglycemia	10 (19.6%)	4 (16.6%)	6 (22.2%)	0.09
Severity of sepsis				
Sepsis	27 (52.9%)	10 (41.6%)	17 (62.9%)	0.13
Severe sepsis	14 (27.5%)	7 (29.2%)	7 (25.9%)	0.8
Septic shock	10 (19.6%)	7 (29.2%)	3 (11.1%)	0.11
BUN levels (mmol/L)	9.9 (6.7-18.3)	11.95 (8.2-22.3)	8.1 (6.1-12.2)	0.03
Creatinine levels (μmol/L)	131.5 (68.4-175.3)	159.3 (80.1-191.3)	112.0 (64.8-145.4)	0.04
Sodiun levels (mmol/L)	142 (138-149)	143 (137-149.5)	139 (137-142)	<0.001
Chloride levels (mmol/L)	105 (101-111)	109 (103.5-117.8)	103 (100-106)	<0.001
Bicarbonate (mmol/L)	19.3 (17.5-23.4)	18.1 (16.4-21.1)	21 (19.1-24.2)	0.05
WBC levels ($\times 10^9$/L)	14.82 (8.8-19.4)	15.42 (12.37-20.93)	10.85 (6.08-21.1)	0.475
CRP levels (mg/dL)	147 (53-160)	130.5 (40.3-160)	160 (55-160)	0.761
D-D (mg/L)	1.03 (0.63-3.49)	0.97 (0.65-4.01)	1.03 (0.62-2.44)	0.425
Albumin (g/L)	29.1 (27-33.4)	29.55 (28.2-33.3)	29 (25-34.3)	0.556
RDH	3/51	2/24	1/72	0.493
Underlying infections				0.264
Pneumonia		21	18	
Urinary tract infection		1	2	
Intrabdominal infection		1	6	
Bloodstream infection		1	1	

APACHE, Acute Physiology and Chronic Health Evaluation; BUN, blood urea nitrogen; CRP, c-reactive protein; D-D, d-dimer; RDH, renal disease history; WBC, white blood cells.

cells levels, C-reactive protein level, D-dimer, albumin levels and renal disease history at admission. All the laboratory results were studied at the Central Laboratory of Jiangsu Integrative Medicine Hospital. Moreover, clinical characteristics for each patient such as need of mechanical ventilation, ICU duration of stay, rate of complications including multiple organ dysfunction syndrome, infection and mortality were recorded to compare the prognosis of patients with or without hypernatremia. Infection was confirmed after the culture results. Hyperglycemia was defined serum glucose concentrations greater than 12 mmol/L (215 mg/dL). All data were collected by 2 research nurses and they were blinded to the patients' clinical treatment. This study was approved by the ethic committee of Jiangsu Province Hospital on Integration of Chinese and Western Medicine with fast track process (for observational studies).

Statistical Analysis

Results were expressed as the median (interquartile range) unless mentioned otherwise. Categorical variables were described in absolute numbers and in percentages. Continuous variables were compared using the Mann-Whitney *U* test, and categorical data were analyzed with the chi-square test. To identify risk factors for hypernatremia, several series of univariate logistics regression analyses using the 16 indices mentioned above were performed. Variables that showed statistical significance were tested in further multiple logistic regression analyses with the stepwise method. All statistical tests were 2-tailed, and the significance level was set at $P < 0.05$. Data were analyzed with SPSS 17.0 for Windows (SPSS Inc., Chicago, IL).

RESULTS

Of the 51 patients with sepsis, 24 patients (47.1%) developed hypernatremia during the study period. Table 1 shows the demographic and clinical characteristics of these patients.

Taking these significant variables together into the multiple logistic regression model, only 1 variable (APACHE II score) is proved to be an independent risk factor for the development of hypernatremia (Table 2).

Table 3 shows a variety of clinical variables with regard to the clinical outcomes. Of all 51 patients, 15 patients died during hospitalization and 11 of which were in the hypernatremia group. The median ICU duration was 19 days and 10 days in patient with or without hypernatremia, respectively. Patients with hypernatremia were more critically ill, as evidenced by higher rates of organ failure and higher in-hospital mortality.

In the present study, most patients did not receive specific treatment to lower blood sodium level except