Hyponatremia in Traumatic Brain Injury: A Practical Management Protocol

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BACKGROUND: **Hyponatremia (defined as serum sodium <135 mEq/L) is the most common electrolyte abnormality in traumatic brain injury (TBI) and is also an independent predictor of poor neurologic outcome. The reported incidence of hyponatremia varies widely in literature reports, and there is continuing difficulty in clearly differentiating between the 2 common causes of hyponatremia with natriuresis: the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting (CSW). We encounter hyponatremia frequently in our practice, and we therefore decided to review data from our center to estimate the incidence of hyponatremia and the results of our management strategies, and attempt to formulate simple guidelines for the correction of hyponatremia in TBI.**

METHODS: **A retrospective analysis of 1500 consecutively admitted patients with TBI was performed by the use of electronic records and radiographic review. Hyponatremia was defined as serum sodium <135 mEq/L, and natriuresis as a urine spot sodium of more than >40 mEq/L. The incidence of TBI, its management, and the effect of fludrocortisone were evaluated.**

RESULTS: **The incidence of hyponatremia was 13.2%. Early therapy with fludrocortisone significantly reduced the duration of hospital stay ($P < 0.05$). Traumatic subarachnoid hemorrhage was the most common abnormality on the admission computed tomographic scan in patients who experienced hyponatremia.**

CONCLUSION: **Early initiation of fludrocortisone in the setting of hyponatremia with natriuresis decreases the hospital stay. This protocol is probably safer in a tropical country where fluid restriction might be harmful. It also eliminates the need to differentiate between SIADH and CSW.**

INTRODUCTION

Hyponatremia, defined as serum sodium <135 meq/L, is the most common electrolyte abnormality encountered in patients with traumatic brain injury (TBI).[1] The reported incidence of hyponatremia in TBI ranges from 9.6% to 51%,[2-6] and it is well established that hyponatremia is an independent predictor of poor neurologic outcome in patients with TBI.[7-9] Despite this, there are no practical management protocols, especially for use in areas where sophisticated laboratory investigations are unavailable and prolonged admission occupies precious hospital beds.

The common causes of hyponatremia in TBI are cerebral salt wasting syndrome (CSW), syndrome of inappropriate antidiuretic hormone secretion (SIADH), hypopituitarism, and inadequate dietary intake of salt.[1,10-16] Of those, inadequate salt intake can be diagnosed with reasonable certainty if the urine spot sodium is low (below 20–40 mEq/L), and hypopituitarism can be diagnosed by biochemical evaluation of pituitary hormones. After ruling out these 2 entities, the clinician is left with CSW and SIADH, both of which manifest as hyponatremia with natriuresis (urine spot sodium >40 mEq/L). The proportion of patients with hyponatremia caused by SIADH and CSW has been extensively debated in the medical literature without a definite consensus.[1,17-20] Further review of the literature takes the reader into the gray zone of differentiation between CSW and SIADH with panels of laboratory and clinical tests, none of which are conclusive.[17,19,21] Measurement of ADH levels is not available at most hospitals that manage head injury. Given that the fluid management strategies in these 2

Key words
- Fludrocortisone
- Hyponatremia
- Natriuresis
- Traumatic brain injury

Abbreviations and Acronyms
CSW: Cerebral salt wasting syndrome
GCS: Glasgow coma scale
SAH: Subarachnoid hemorrhage
SIADH: Syndrome of inappropriate antidiuretic hormone secretion
TBI: Traumatic brain injury

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conditions are completely divergent, the result is a serious clinical dilemma. Fluid restriction is a less than ideal option when the clinical consequences of dehydrating a TBI patient are considered, especially in a tropical climate.[8] Therefore, when serum sodium does not correct with dietary salt supplementation and hydration, though fluid restriction is possibly the appropriate treatment, the potential to cause harm must be kept in mind. Hyponatremia associated with TBI has been found to respond to salt-retaining therapy in the setting of natriuresis, the reasons for which have not been clearly explained.[2,16]

This retrospective analysis was undertaken to study the incidence of hyponatremia in patients with TBI and the results of different management strategies. We also describe a practical bedside management protocol for hyponatremia in TBI, with special mention of the early initiation of fludrocortisone.

METHODS

A retrospective analysis of 1500 patients admitted with a diagnosis of TBI between May 2013 and December 2015 was undertaken from the hospital electronic patient records and from radiologic data obtained from the institutional picture archiving and communicating system (GE PACS version 3.0). The severity of the head injury was graded on the basis of the Glasgow coma score (GCS) as mild (GCS 13–15), moderate (GCS 9–12), and severe (GCS 3–8).[22] The clinical determinations recorded were GCS at admission, age, pupillary status, blood pressure at admission, presence of other significant injuries, and need for surgical intervention. Radiologic factors recorded included the presence of hematomas, subarachnoid hemorrhage (SAH), and diffuse cerebral edema.

Hyponatremia was defined as serum sodium <135 meq/L and was further classified as mild (serum sodium 130–134 mEq/L), moderate (serum sodium 125–129 mEq/L), and severe (serum sodium <125 mEq/L). Patients with acute kidney injury or chronic renal failure were excluded from the study. The cause of hyponatremia was broadly dichotomized into nonnatriuretic (urine spot sodium <40 mEq/L) and natriuretic (urine spot sodium >40 mEq/L). Patients with nonnatriuretic hyponatremia were treated with additional dietary salt. Patients with natriuresis were treated with either hydration or fluid restriction according to the clinical suspicion of CSW or SIADH based on a daily review of intake/output chart and hydration status. Hypertonic (3%) saline was used for severe or symptomatic hyponatremia. Some patients with natriuretic hyponatremia were treated with fludrocortisone, but at that time we did not follow a definite protocol, and the decision was made by the treating physician. The total duration of fludrocortisone therapy was obtained from a review of the brain injury clinic follow-up data.

This study was approved by the institutional review board (IRB No: 10299 dt 21/09/2016).

Statistical Analysis

Means and standard deviations were used to summarize all continuous variables; categoric variables were summarized by the use of frequencies with percentages. Association between hyponatremia and other risk factors were assessed with χ^2 tests. The results are presented as odds ratios with 95% confidence intervals (CI). All analyses were done with Stata 11.0 (StataCorp, College Station, Texas, USA).

Table 1. Patient Characteristics and Duration of Stay

Factor	Number	%
Hyponatremia	198/1500	13.2
Number of men	170	87.85
Mean age at presentation (years)	39.2	
Head injury		
Mild	52	26.26
Moderate	115	58
Severe	31	15.6
Hyponatremia		
Mild	56	28.28
Moderate	98	49.49
Severe	44	21.71
Hyponatremia with natriuresis	195	98.5
Mean duration of stay in patients (in days)		
With hyponatremia	12.74	
Without hyponatremia	7.19	
Number of patients who received fludrocortisone	72	36.36
Duration of stay (days)		
Patients who received fludrocortisone	10.89	$P < 0.05$
Patients who did not receive fludrocortisone	15.84	

RESULTS

A total of 1500 patients were admitted with a diagnosis of TBI at our center during the review period, in whom hyponatremia developed in 198 (13.2%); 170 were men (85.85%), and the mean age was 39.2 years. Thirty-one patients had severe, 115 moderate, and 52 mild head injuries. The incidence of mild, moderate, and severe hyponatremia was 28.28%, 49.49%, and 21.71%, respectively. Hyponatremia was associated with natriuresis in 195 of 198 patients (98.5%). The presence of SAH on the admission CT scan of the brain was the most common finding in these patients.

The mean duration of stay for patients with hyponatremia was 12.74 days as opposed to 7.19 days for those without hyponatremia. Thirty-six percent (72/198) of patients with hyponatremia received fludrocortisone for salt retention (Table 1). Patients receiving fludrocortisone had significantly reduced hospital stay (10.89 days vs. 15.84 days, $P < 0.05$) (Figure 1) Fludrocortisone was initiated at a dose of 50 μg daily and escalated to a maximum dose of 150 μg daily based on the response. Among the 72 patients who received fludrocortisone, the drug was discontinued within 1 month in 33 (45.8%) and within 2 months in another 16 (23.6%) patients. We did not observe any side effects of fludrocortisone therapy such as cardiac failure or hypokalemia.