Cerebral Salt Wasting Is the Most Common Cause of Hyponatremia in Stroke

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Objective: The study aimed to evaluate the frequency, severity, and causes of hyponatremia in stroke and its influence on outcome. *Materials and Methods:* Consecutive computed tomography- or magnetic resonance imaging-proven stroke patients within 7 days of stroke were included. Severity of stroke was assessed using the National Institute of Health Stroke Scale and consciousness using the Glasgow Coma Scale. Hyponatremia was defined if 2 consecutive serum sodium levels were <135 mEq/L and hypernatremia if >145 mEq/L. Causes of hyponatremia, such as cerebral salt wasting (CSW) and syndrome of inappropriate secretion of antidiuretic hormone (SIADH), were based on predefined criteria. Patients with CSW were managed by salt supplementation and normal saline, and fludrocortisone was used in refractory cases. In SIADH, fluid was restricted. Outcome on discharge was defined using the modified Rankin Scale (mRS). *Results:* One hundred patients with stroke were included: 47% had ischemic stroke and 53% had intracerebral hemorrhage. Forty-three percent of the patients had hyponatremia, 6% had hypernatremia, and 4% had both. Hyponatremia was due to CSW in 19 (44.2%), SIADH in 3 (7%), miscellaneous causes in 14 (32.6%), and indeterminate in 7 (16.3%) patients. Duration of hospitalization was the independent predictor of hyponatremia and CSW. Fourteen patients died, whereas 15 had good outcome (mRS score of ≤2) and 71 had poor outcome (mRS score of 3-5). Hypernatremia was associated with high mortality compared with eunatremia and hyponatremia. *Conclusion:* Hyponatremia occurred in 43% of stroke patients. CSW was the most common cause of hyponatremia. Hyponatremia, however, was not related to death or disability.
Key Words: Stroke—hyponatremia—cerebral salt wasting—syndrome of inappropriate secretion of antidiuretic hormone—systemic inflammatory response syndrome—Glasgow Coma Scale.

Introduction

Stroke is the third most common cause of human mortality and morbidity after coronary artery disease and cancer.[1] Sodium homeostasis is critical for normal body functioning. Electrolyte disturbances are common in clinical practice and are attributed to comorbidities of stroke, such as diabetes mellitus, hypertension, heart failure, and iatrogenic causes. Hyponatremia occurs in subarachnoid hemorrhage,[2] ischemic stroke,[3] and spontaneous intracerebral hemorrhage (ICH).[4] Hyponatremia in acute stroke may increase the risk of seizures, thereby brain edema, mass effect, and death.[5] In stroke patients, vomiting, poor intake, use of osmotic agents, diuretics, and

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drugs may contribute to hyponatremia. Moreover, raised intracranial pressure and neurologic damage may also disturb sodium homeostasis, resulting in syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and cerebral salt wasting (CSW). In a Japanese study, SIADH was reported in 7.6% of stroke patients.[6] Hyponatremia may be evolving rather than preexistent and may reflect disease severity.[4] CSW and SIADH may have many common features, such as hyponatremia, low serum osmolality, high urinary sodium, and osmolality. Differentiation between CSW and SIADH is important because treatment of one may be hazardous to the other. SIADH is treated by fluid restriction, whereas CSW is treated by fluid replacement and sodium administration. In ICH, in-hospital mortality was doubled among hyponatremic patients,[4] but not among ischemic stroke patients.[3] Most of the studies on hyponatremia in stroke are based on retrospective analysis and chart review.[7-9] There is paucity of prospective studies that evaluate the frequency, severity, and cause of hyponatremia, and its outcome on stroke patients. The present study therefore reports the frequency, severity, and causes of hyponatremia in patients with stroke, and its effect on short-term outcome.

Subjects and Methods

Consecutive patients with computed tomography (CT)- or magnetic resonance imaging (MRI)-proven ischemic and hemorrhagic stroke between January 2014 and January 2016 admitted in the neurology service within 1 week of ictus were included. Their demographic information (age, gender, education, and residence) were noted, as well as their dietary habit, lifestyle, smoking, medication, alcohol, and tobacco consumption. Patients were considered hypertensive if their recorded blood pressure was >140/90 mm Hg after 1 week of stroke on 2 occasions 24 hours apart,[10] or if they were on antihypertensive drugs. Patients were considered diabetic if fasting blood sugar was more than 126 mg/dL, postprandial blood sugar was more than 200 mg/dL, or HbA1c was more than 6.5 gm/dL, or they were on insulin or oral hypoglycemic drugs.

Exclusion Criteria

Patients with preexisting renal or hepatic failure were excluded; however, those who developed hepatic or renal dysfunction during the treatment were not excluded.

Clinical Evaluation

Consciousness was assessed by the Glasgow Coma Scale (GCS), whereas the severity of stroke was assessed by the National Institute of Health Stroke Scale (NIHSS). Irregular heart rate, ictal blood pressure, systemic inflammatory response syndrome (SIRS), hyperventilation, and extensor posturing were noted. Cranial nerve palsy, pupillary asymmetry, and papilloedema were also recorded. Muscle power was graded into hemiplegia or hemiparesis. Sensations and cerebellar signs were tested in patients who could cooperate. Cardiovascular, chest, and abdominal examination findings were also noted.

Investigations

Blood counts, hemoglobin, erythrocyte sedimentation rate, blood sugar, blood urea nitrogen, and serum creatinine, albumin, transaminases, bilirubin, lactate dehydrogenase, sodium, and potassium were measured on admission. Arterial blood gas analysis, electrocardiogram, and chest radiography were done. Lipid profile was done on the next morning. Cranial CT scan was done within 1 hour of admission using a third-generation CT scanner. In patients with ischemic stroke, cranial MRI was done using a 3T MRI scanner (SIGNA GE Medical System, Madison, WI). Echocardiography was done in selected patients. The location of infarction (anterior versus posterior circulation, and cortical versus subcortical) and its size (large >½ of a lobe or multiple lobes, medium size <½ of a lobe, and small size—single or multiple lacunar infarcts) were noted. In patients with ICH, the location (lobar, putaminal, caudate, thalamic, pontine, and cerebellar) and size (large: >60 mL; medium: 30-60 mL; and small: <30 mL) of hematoma were noted. The presence of midline shift and brain herniation was also noted both in ischemic stroke and ICH. In patients with ICH, intraventricular and subarachnoid extension of blood was noted. The presence of SIRS on admission was also noted.[11]

Evaluation of Hyponatremia

Serum sodium was measured on alternate days for 14 days or until the patient was discharged, whichever earlier. Serum sodium level below 135 mEq/L was considered hyponatremia. The severity of hyponatremia was categorized as mild (130-134 mEq/L), moderate (120-129 mEq/L), and severe (<120 mEq/L).[12] In hyponatremic patients, further investigation was done to differentiate SIADH from CSW syndrome. Some baseline investigations, including hematocrit, blood urea and serum creatinine, uric acid, and albumin, were repeated as indicated. Extracellular fluid volume status was assessed by physical findings (tachycardia, dry mucous membranes, edema, tenting of the skin, capillary refill time). Central venous pressure (CVP) monitoring was done in selected patients, and a pressure of 6-10 cm of water was considered normal. Total fluid balance was calculated from a daily fluid intake and output chart.

CSW and SIADH were diagnosed as per the following criteria.[12]