TAJ December 2009; Volume 22 Number 2

ISSN 1019-8555
The Journal of
Teachers Association
RMC, Rajshahi

Original Article

Incidence of Hyponatraemia in Patients with Ischemic Stroke: Our Experience at RMCH

I Mahmood[1], MK Rahman[2], MMR Khan[2], MA Haque[2], MMH Chowdhury[2], A Iqbal[3], M H Rashid[4], M A Ahad[5], S M Kamal[6]

Abstract

Hyponatraemia is a common electrolyte disorder in central nervous system (CNS) disease and is often attributed to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). By contrast, there are patients with intracranial disease who develop hyponatraemia with similar characteristics, but differ in that there is clinical evidence of a contracted extracellular fluid (ECF) volume. This form of hyponatraemia is caused by excessive renal Na excretion, resulting from a centrally mediated process, and is termed cerebral salt wasting (CSW). Hyponatraemia, if acute that is developed within hours or days may cause confusion, coma restlessness or seizures.

72 patients with ischemic stroke admitted at RMCH were selected for this prospective cohort study. Among the subjects 34 (47.22%) cases were found to have hyponatraemia. The number was quite large and screening patients with stroke for electrolytes may be extremely helpful to reduce mortality and morbidity.

TAJ 2009; 22(2): 212-215

Introduction

Stroke is the 3rd most common cause of death in developed countries and major cause of disability. It is characterized by hemiparesis or hemiplegia with or without sensory or higher brain function deficit. Confusion may reflect brain damage, but may also be caused by other associated problems, like hyponatraemia. Any alteration in brain function like stroke may induce "Syndrome of Inappropriate Anti Diuretic Hormone" (SIADH) or "Cerebral Salt Wasting Syndrome (CSWS)" and cause hyponatraemia. Hyponatraemia, if acute that is developed within hours or days may cause confusion, coma restlessness or seizures. It may often be fatal. This study has been designed to look the extent or chance of developing hyponatraemia in patients with ischemic stroke especially within 72 hours of attack and justify why serum electrolyte should be measured in every patients with stroke.

Material and Methods

72 patients with ischemic stroke admitted at RMCH were selected for this prospective cohort study. Other pre-existing disease entities like Diarrhoea, Vomiting, Diabetes mellitus, Tuberculosis,

[1] Associate Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[2] Assistant Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[3] Indoor Medical Officer, Department of Medicine, Rajshahi Medical College, Rajshahi.
[4] Assistant Professor, Department of Hepatology, Rajshahi Medical College, Rajshahi.
[5] Associate Professor, Department of Gastroenterology, Khulna Medical College, Khulna.
[6] Associate Professor, Department of Medicine, Khulna Medical College, Khulna.

Pneumonia, Meningitis, Encephalitis, etc. were excluded. A careful drug history was obtained to exclude any drug that may cause SIADH. The study period was from September, 2009 to April, 2010. Among the patients 37 were females and 35 were males. Stroke was diagnosed by demonstrating infarcts on CT scan of brain reports. The subjects were investigated for serum electrolytes within 24 hours of their admission. As there were lack of diagnostic facilities of urinary sodium and urinary osmolality, SIADH could not be confirmed. Not many literatures were found as there are very few studies on this topic. The age range of the subjects was 45 years to 78 years, most of them being in between 55 to 75 years.

Results

Among the subjects 34 (47.22%) cases were found to have electrolyte imbalance (hyponatraemia). The details are shown in the tables.

Table 1: Age and Sex distribution of patients with hyponatraemia

Age (years)	Male		Female		Total	
	Subjects nM=35	With Hyponatraemia	Subjects nF=37	With Hyponatraemia	Subjects N=72	With Hyponatraemia
45-54	8 (22.86%)	2 (5.71%)	1 (2.7%)	-	9 (12.5%)	2 (2.78%)
55-64	14 (40%)	7 (20%)	19 (51.37%)	6 (16.22%)	33 (45.83%)	13 (18.06%)
65-74	6 (17.14%)	8 (22.86%)	15 (42.86%)	8 (21.62%)	21 (29.17%)	16 (22.22%)
75 +	7 (20%)	3 (8.57%)	2 (5.4%)	-	9 (12.5%)	3 (4.17%)

Table 2: Associated Symptoms (nHyp = 34)

Symptoms	Male	Female	Total
Anorexia	-	1(2.94%)	1 (2.94%)
Nausea & vomiting	2(5.88%)	-	2 (5.88%)
Lethargy	2(5.88%)	-	2 (5.88%)
Restlessness	7(20.59%)	6(17.65%)	13(38.24%)
Seizures	3(8.82%)	3(8.82%)	6 (17.65%)
Confusion	5(14.71%)	2(5.88%)	7 (20.59%)
Coma	1(2.94%)	2(5.88%)	3 (8.82%)

Table 3: Distribution of Various Levels of Hyponatraemia (nHyp = 34)

Level of Sodium	Male	Female	Total
<110 meq/L	3(8.82%)	2(5.88%)	5 (14.71%)
110-115 meq/L	2(5.88%)	-	2 (5.88%)
116-120 meq/L	4(11.76%)	3(8.82%)	7 (20.59%)
121-125 meq/L	6(17.65%)	5(14.71%)	11(32.35%)
>125 meq/L	5(14.71%)	4(11.76%)	9 (26.47s%)

Table 4 : Symptom Manifestations in Various Level of Hyponatraemia (nHyp = 34)

Symptoms	<110 meq/L	110-115 meq/L	116-120 meq/L	121-125 meq/L	>125 meq/L	Total
Anorexia	-	-	-	-	1(2.94%)	1 (2.94%)
Nausea & vomiting	-	-	-	-	2(5.88%)	2 (5.88%)
Lethargy	-	-	-	-	2(5.88%)	2 (5.88%)
Restlessness	-	-	3(8.82%)	6(17.65%)	4(11.76%)	13(38.24%)
Seizures	2(5.88%)	1(2.94%)	1(2.94%)	2(5.88%)	-	6 (17.65%)
Confusion	1(2.94%)	-	3(8.82%)	3(8.82%)	-	7 (20.59%)
Coma	2(5.88%)	1(2.94%)	-	-	-	3 (8.82%)

Discussion

Hyponatraemia is a common electrolyte disorder in the setting of central nervous system (CNS) disease and is often attributed to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). This syndrome is characterized by hyponatraemia in the setting of an inappropriately concentrated urine, increased urine Na. concentration and evidence of normal or slightly increased intravascular volume. By contrast, there are patients with intracranial disease who develop hyponatraemia with similar characteristics, but differ in that there is clinical evidence of a contracted extracellular fluid (ECF) volume. This form of hyponatraemia is caused by excessive renal Na excretion, resulting from a centrally mediated process, and is termed cerebral salt wasting (CSW). In a study, hyponatraemia is seen in 10%-40% of the patients with subarachnoid hemorrhage (SAH) admitted to the neuro critical care unit (NCCU; Mayberg et al., 1994; Woo & Kale-Pradhan, 1997). But no specific study on hyponatraemia in ischemic stroke patients was found.

According to Palmer (2000), SIADH is an expansion of extracellular fluid volume resulting from the superfluous release of antidiuretic hormone (ADH) or increased renal sensitivity to ADH. SIADH is characterized by decreased serum osmolality with inappropriate urinary concentration (Larsen et al., 2003). ADH acts on the distal collecting duct tubules resulting in increased water reabsorption and increased intravascular volume (Albanese, Hindmarsh, & Stanhope, 2001; Andreoli et al., 2001). In response to the increased intravascular fluid volume, glomerular filtration rate and renal plasma flow increases, and proximal sodium reabsorption decreases in patients with SIADH. As a result, sodium excretion in the urine increases, resulting in low serum sodium values (Palmer, 2000). The release of ADH can be stimulated by pain, stress, increased intracranial pressure, and hypovolemic states (Diringer, 2001).

CSW has been proposed as a more immediate cause of hyponatremia in patients with brain injury. CSW is a transient phenomenon in which kidneys are unable to conserve sodium. CSW leads to serum hyponatremia and hypovolemia as a result of SAH or other intracranial disease (Harrigan, 2001). CSW was first described in 1950, after symptoms of volume contraction and decreased sodium in neurological patients were noted (Peters, Welt, Sims, Orloff, & Needham, 1950). Since that initial observation, clinical and experimental data suggest that patients with SAH and other intracranial diseases experience hypovolemia rather than the euvolemia or hypervolemia of SIADH. Derangements of sympathetic nervous system stimulation of kidneys, production of digoxin-like peptides, and excess natriuretic factors have all been implicated in CSW. A surge of sympathetic nervous system (SNS) hormones, norepinepherine and epinephrine, may cause renal sodium excretion. Stimulated by the stress response during brain injury, the SNS hormones stimulate both arterial and venous contraction, leading to increased preload, inotropy, and systemic blood pressure. The kidneys could respond to these cardiovascular changes with a pressure-induced natriuresis (Singh et al., 2002). This neural mechanism of hyponatremia is not the most likely scenario, though it may be a contributing factor. Although a pressure natriuresis is associated with an acute stress response, ongoing sodium excretion is less likely with sustained SNS stimulation in the presence of hypovolemia unless renal vasodilatation is also sustained. It may be that the initial brain injury and sympathetic response may, instead, contribute to the development of CSW.

Two additional molecular factors have been implicated in the onset of hyponatraemia. One potential factor causing CSW is a digoxin-like peptide that has been found in the plasma of a series of patients with SAH. How this peptide causes renal sodium excretion has yet to be to be elucidated, but it was determined that infusing digoxin-specific antibodies directly into the ventricles of the rat brain, blocks the central nervous system response to natriuresis (Wijdicks, Vermulean, van Brummelen, den Boer, & van Gijn, 1987).

A second molecular factor is endogenous natriuretics. Both atrial and brain (or b-type) natriuretic factors have been linked to CSW. Both factors lead to natriuresis or excretion of sodium with subsequent serum hyponatraemia. Renal sodium excretion, in turn, leads to a concurrent fluid diuresis and hypovolemia.

However, whatever the cause may be, hyponatraemia warrants immediate attention and appropriate management. Our study has been designed to see the extent of hyponatraemia in patients with ischemic stroke. In our study we have found that among the 72 subjects 34 that is 47.22% developed hyponatraemia. The tendency to develop such condition was more pronounced in males (57.14%) than in females (37.83%). 20(58.82%) out of 34 patients with hyponatraemia had their sodium levels above 121 m eq/L. While 14 (41.17%) were under that level. The presentations with hyponatraemic patients included anorexia, nausea, vomiting, lethargy, restlessness, seizures, confusion and coma. We found that restlessness (38.24%) is the most common feature, while confusion (20.59%) and seizure (17.65%) is also not very uncommon. Profound clinical features (Restlessness, confusion, seizures, coma) tend to develop below the level of 121 meq/ L. However, most patients (58.82%) did not go under that level.

Conclusion

Ischemic stroke itself is a grave condition. It becomes worse when it is complicated by situations like hyponatraemia which are quite often treatable. So screening patients with stroke for electrolytes may be extremely helpful to reduce mortality and morbidity.

References

1. Hyponatraemia in patients with central nervous system disease: SIADH versus CSW Biff F. Palmer Division of Nephrology, Department of Internal Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75235, USA1 Peters, J.P. et al. (1950) A salt-wasting syndrome associated with cerebral disease. Trans. Assoc. Am. Physicians 63, 57–64
2. Welt, L.G. et al. (1952) Role of the central nervous system in metabolism of electrolytes and water. Arch. Intern. Med. 90, 355–378
3. Cort, J.H. (1954) Cerebral salt wasting. Lancet 1, 752–754
4. Schwartz, W.B. et al. (1957) A syndrome of renal sodium loss and hyponatremia probably resulting from inappropriate secretion of antidiuretic hormone. Am. J. Med. 13, 529–542
5. Coenraad, M.J. et al. (2001) Hyponatremia in intracranial disorders. Neth. J. Med. 58, 123–127
6. Betjes, M. (2002) Hyponatremia in acute brain disease: the cerebral salt wasting syndrome. Eur. J. Intern. Med. 13, 9–14
7. Leaf, A. et al. (1953) Evidence in man that urinary electrolyte loss induced by pitressin is a function of water retention. J. Clin. Invest. 32, 878–886
8. Nolph, K.D. and Schrier, R.W. (1970) Sodium, potassium and water metabolism in the syndrome of inappropriate antidiuretic hormone secretion. Am.
9. Nelson, P.B. et al. (1981) Hyponatremia in intracranial disease: perhaps not the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). J. Neurosurg. 55, 938–941
10. Nelson, P.B. et al. (1984) Hyponatremia and natriuresis following subarachnoid hemorrhage in a monkey model. J. Neurosurg. 60, 233–237
11. Wijdicks, E. et al. (1985) Volume depletion and natriuresis in patients with a ruptured intracranial aneurysm. Ann. Neurol. 18, 211–216
12. Levine, J.P. et al. (2001) Hyponatremia in the postoperative craniofacial pediatric patient population: a connection to cerebral salt wasting syndrome and management of the disorder. Plast. Reconstr. Surg. 108, 1501–1508
13. Sivakumar, V. et al. (1994)Management of neurosurgical patientswith hyponatremia and natriuresis. Neurosurgery 34, 269–274
14. Filippella, M. et al. (2002) Very delayed hyponatremia after surgery and radiotherapy for a pituitarymacroadenoma. J. Endocrinol. Invest. 25, 163–168
15. Sengupta, K. et al. (2002) Cerebral salt wasting. Indian atr. 39, 488–491
16. Ti, L. et al. (1998) Acute hyponatremia secondary to cerebral salt wasting syndrome in a patient with tuberculous meningitis. Anaesth. Intensive Care 26, 420–423
17. Peters, J.P. et al. (1950) A salt-wasting syndrome associated with cerebral disease. Trans. Assoc. Am. Physicians 63, 57–64
18. www.turner-white.com Hospital Physician April 2007 33 The syndrome of inappropriate antidiuretic hormone secretion (SIADH)

All correspondence to:
I Mahmood
Associate Professor
Department of Medicine
Rajshahi Medical College, Rajshahi