Article published online: 2022-09-20

ORIGINAL ARTICLE

Impact of electrolyte imbalances on the outcome of aneurysmal subarachnoid hemorrhage: A prospective study

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ABSTRACT

Background: Electrolyte disturbances are frequently observed during the acute and subacute period after subarachnoid hemorrhage (SAH) and may potentially worsen therapeutic outcome. This study was conducted to determine the pattern of electrolyte disturbance in the acute and subacute phase after SAH and their effect on the long-term outcome of the patients.

Materials and Methods: Fifty-three patients were prospectively enrolled. The standards of care for all patients were uniformly performed. The serum levels of electrolytes (sodium, potassium and magnesium) were determined with measurements obtained on admission, 3–5 and 7–10 days after SAH. Radiographic intensity of hemorrhage (Fisher's scale), and the clinical grading (World Federation of Neurosurgical Societies grade) were documented in the first visit. The outcomes were evaluated using Glasgow outcome scale at 3 months after discharge.

Results: Hyponatremia was the most common electrolyte imbalance among the patients but did not worsen the outcome. Although less common, hypernatremia in the subacute phase was significantly associated with poor outcome. Both hypokalemia and hypomagnesemia were predictive of poor outcomes.

Conclusions: Because electrolyte abnormalities can adversely affect the outcome, the serum levels of electrolytes should be closely monitored with serial measurements and treated properly in patients with aneurysmal SAH.

Key words: Aneurysm, electrolyte imbalance, outcome, subarachnoid hemorrhage

Introduction

Nontraumatic Intracranial hemorrhages including subarachnoid, intraparenchymal and intraventricular hemorrhage, have remarkable mortalities.[1]

The incidence of subarachnoid hemorrhage (SAH) increases with advancing age and is more common among women above 50 years old. The mortality rate 1-month after aneurysmal SAH is about 45%[8] and if associated with ICH rises to 52%[4] and many of the survivors suffer from significant disabilities. Each year, among the 27,000 patients with SAH in the United States, about half of them die and only <25% have favorable outcomes.[2-4]

Although the main predictive factor of the outcome is the severity of neurologic morbidity, but nonneurologic complications can also affect the length of stay in Intensive Care Unit (ICU) and hospitalization and the final outcome the patients.[5]

Electrolyte disturbances are common in ICU-admitted patients. Intracranial disorders are associated with dysregulations of serum electrolyte levels. Thus, electrolyte abnormalities are of particular importance in neurosurgical ICU patients.

The studies on the pattern and importance of electrolyte disturbance in SAH patients, have reported conflicting results. Some of them have reported adverse effects of electrolyte abnormalities on the outcome of these patients,[6,7] while some others did not find such a relationship.[8,9]

Access this article online

Quick Response Code:

Website: www.asianjns.org

DOI: 10.4103/1793-5482.154978

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This study evaluates the pattern of electrolyte disturbances in patients with aneurysmal SAH and their impact on the outcome of these patients.

Materials and Methods

From March 2011 to May 2012, 53 consecutive patients with aneurysmal SAH, who were at least 18 years old, and did not have any of the exclusion criteria of the study were enrolled. The exclusion criteria of this study were: A history of chronic renal failure, cardiac disease and/or any other debilitative disease; prolonged use of diuretic drugs, angiotensin converting enzyme inhibitors and/or corticosteroids; history of endocrine dysregulations, history of moderate or severe traumatic brain injury.

All the patients were admitted to neurosurgical ICU and the standard care of SAH (including central venous catheter and central venous pressure monitoring, intake/output chart, and serial brain computed tomography and electrolyte measurements at the 1st, 3–5th and 7–10th day of admission) were performed for all of them. A brain digital subtraction angiography was performed for all of them during the first 48 h of admission and treatment of cerebral aneurysm, either microsurgical or endovascular, was done in the first 4 days of admission.

At the first visit, the clinical grading (World Federation of Neurosurgical Societies [WFNS] grade)[10] of the patients and the radiologic scaling (Fischer's grade)[9] were determined and documented. A uniform treatment protocol was applied to all of the patients.

Patient outcomes were measured using Glasgow outcome scale (GOS) 3 months after discharge. In this study, the normal range of serum Na, K, and mg levels was considered 135–145 mEq/L, 3–4.5 mEq/L, 1.5–3 mEq/L, respectively.

Statistical analysis was done using SPSS Version 19.00 (SPSS, Inc., Chicago, IL). The Chi-square and the Kruskal-Wallis nonparametric tests were used for statistical comparison and $P < 0.05$ were considered as statistically significant in this study.

Results

The mean age of patients was 49 (range of 36-64). Twenty-one (39.6%) patients were male and 32 (60.4%) were female.

Fifteen patients (28.3%) had Fischer Grade I, 17 (34%) Grade II, 15 (28.3%) Grade III and 5 (9.4%) had Fischer Grade IV.

According to WFNS grading, 7 patients (13.2%) were Grade I, 17 (34%) Grade II, 17 (34%) Grade III, 10 (18.9%) Grade IV and 2 patients (3.7%) were Grade V.

Twenty-one patients (39.6%) had a final GOS I (good recovery), 19 had GOS II (moderate disability), 7 (13.7%) had GOS III (severe disability), 2 patients (3.7%) were discharged in persistent vegetative state (GOS IV), and there were 4 (7.5%) mortalities among the cases (GOS V) [Figure 1].

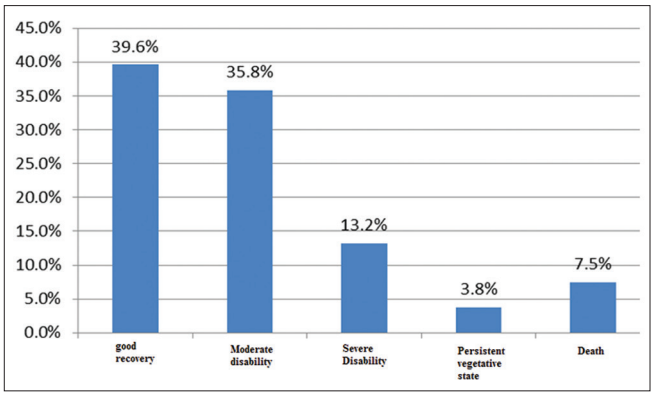

Figure 1: Patient outcome according to Glasgow outcome scale

The treatment method was microsurgical in 43 (81.1%), endovascular in 6 (11.3%) and no treatment of aneurysm in 4 (7.5%) of the patients. 9 patients (17%) had one episode of rebleeding and 3 (5.7%) had multiple episodes. 15 patients (28.3%) had clinical vasospasm.

Hyponatremia was seen in 8 patients (15.1%) at the 1st day, 12 (22.6%) in 3–5th day and 15 (28.3%) in 7–10th day. Hypernatremia was present in 2 patients (3.8%) at the 1st day, 10 (18.9%) in 3–5th day and 15 (28.3%) in 7–10th day.

At the 1st day, 1 patient (1.9%) was hypokalemic, and 11 (20.8%) were hyperkalemic. Hyerkalemia was seen in 12 (22.6%) at 3–5th day and in 12 (22.6%) in 7–10th day. Hypokalemia was absent in the 3–5th day and present in 18 (33%) at 7–10th day. Hypomagnesemia was absent at the 1st day and seen in 2 (3.8%) at 3– 5th day and 18 (34%) at 7–10th day.

The relative prevalence of electrolyte imbalances according to radiographic grading of the patients (Fisher's grade) is seen in Table 1. In the 3–5th and 7–10th day (subacute phase) hypernatremia and hyponatremia were associated with higher and lower Fisher grades, respectively. In all of the three checkpoints, hyperkalemia and hypokalemia were associated with higher and lower Fisher grades, respectively. Hypomagnesemia at 7–10th day was associated with higher radiographic grades. The relative prevalence of electrolyte imbalances according to clinical severity of SAH (WFNS grade) is seen in Table 2. Potassium levels did not have a significant difference between different WFNS grades. In the subacute phase, hypernatremia and hyponatremia were associated with higher and lower WFNS grades, respectively. Hypomagnesemia at 7–10th day was significantly more prevalent in patients with higher WFNS grades.

The relative prevalence of electrolyte imbalances according to the final outcome (GOS) of the patients is seen in Table 3.

Table 1: Prevalence of the electrolyte disturbances according to Fischer grades of the patients

Electrolyte status	Fischer grade (%)				*P*
	I	II	III	IV	
Sodium (1st day)					
Hyponatremia	3 (20)	3 (16.7)	1 (6.7)	1 (20)	0.408
Hypernatremia	0 (0)	0 (0)	2 (13.3)	0 (0)	
Normal	12 (80)	15 (83.3)	12 (80)	4 (80)	
Sodium (3rd-5th day)					
Hyponatremia	5 (33.3)	4 (22.2)	3 (20)	0 (0)	0.0001
Hypernatremia	0 (0)	0 (0)	6 (40)	4 (80)	
Normal	10 (66.7)	14 (77.8)	6 (40)	1 (20)	
Sodium (7-10th day)					
Hyponatremia	6 (40)	5 (27.8)	4 (26.7)	0 (0)	0.0001
Hypernatremia	0 (0)	2 (11.1)	8 (53.3)	5 (100)	
Normal	9 (60)	11 (61.1)	3 (20)	0 (0)	
Potassium (1st day)					
Hypokalemia	0 (0)	0 (0)	1 (6.7)	0 (0)	0.105
Hyperkalemia	5 (33.3)	6 (33.3)	0 (0)	0 (0)	
Normal	10 (66.7)	12 (66.7)	14 (93.3)	5 (100)	
Potassium (3rd-5th day)					
Hypokalemia	0 (0)	0 (0)	0 (0)	0 (0)	0.023
Hyperkalemia	5 (33.3)	7 (38.9)	0 (0)	0 (0)	
Normal	10 (66.7)	11 (61.1)	15 (100)	5 (100)	
Potassium (7-10th day)					
Hypokalemia	2 (13.3)	5 (27.7)	7 (47)	4 (80)	0.001
Hyperkalemia	5 (33.3)	7 (39)	0 (0)	0 (0)	
Normal	8 (53.4)	6 (33.3)	8 (53)	1 (20)	
Magnesium (3rd-5th day)					
Hypomagnesemia	0 (0)	0 (0)	1 (6.7)	1 (20)	0.153
Hypermagnesemia	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	15 (100)	18 (100)	14 (93.3)	4 (80)	
Magnesium (7-10th day)					
Hypomagnesemia	4 (26.7)	3 (16.7)	7 (46.7)	4 (80)	0.036
Hypermagnesemia	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	11 (73.3)	15 (83.3)	8 (53.3)	1 (20)	

Table 2: Prevalence of electrolyte disturbances according to different WFNS grades

Electrolyte status	WFNS grade* (%)					*P*
	I	II	III	IV	V	
Sodium (1st day)						
Hyponatremia	1 (14.3)	3 (16.7)	2 (13.3)	2 (20)	0 (0)	0.233
hypernatremia	0 (0)	0 (0)	0 (0)	1 (10)	1 (33.3)	
Normal	6 (85.7)	15 (83.3)	13 (86.7)	7 (70)	2 (66.7)	
Sodium (3rd-5th day)						
Hyponatremia	0 (0)	4 (22.2)	7 (46.7)	1 (10)	0 (0)	0.0001
hypernatremia	0 (0)	0 (0)	1 (6.7)	7 (70)	2 (66.7)	
Normal	7 (100)	14 (77.8)	7 (46.7)	2 (20)	1 (33.3)	
Sodium (7-10th day)						
Hyponatremia	1 (14.3)	5 (27.8)	8 (53.3)	1 (10)	0 (0)	0.0001
Hypernatremia	0 (0)	0 (0)	4 (26.7)	9 (90)	2 (66.7)	
Normal	6 (85.7)	13 (72.2)	3 (20)	0 (0)	1 (33.3)	
Magnesium (3rd-5th day)						
Hypomagnesemia	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0.063
Hypermagnesemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	7 (100)	18 (100)	15 (100)	8 (80)	3 (100)	
Magnesium (7-10th day)						
Hypomagnesemia	2 (28.6)	3 (16.7)	3 (20)	7 (70)	3 (100)	0.004
Hypermagnesemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	5 (71.4)	15 (83.3)	12 (80)	3 (30)	0 (0)	

*WFNS – World Federation of Neurosurgical Societies

Hypernatremia and hyponatremia in the subacute phase were associated with worse and better outcomes, respectively. Hypokalemia and hypomagnesemia in the subacute phase were significantly more prevalent among the poor outcome patients and hyperkalemia in this period was associated with more favorable outcomes.

Discussion

Saccular aneurysms are the most common causes of nontraumatic SAH, causing about 80% of cases of SAH. About 6–8% of strokes result from rupture of cerebral aneurysms.[11] SAH is responsible for death and disability of about 18,000 North American people each year.[1,3,12,13] Although the prevalence of stroke has declined over the last decades, but the incidence of SAH has not decreased yet.[14]

Causes of mortality and morbidity after aneurysmal SAH could be divided into two groups: Neurologic and nonneurologic. The most important neurologic causes are rebleeding, vasospasm and hydrocephalus and electrolyte imbalance, aspiration pneumonia, and venous thromboembolism are the most important nonneurologic causes. The mortality and morbidity rate increase with advancing age and more than one-third of the survivors have major neurologic affections.

In the study of Qureshi *et al*.,[8] it was shown that hyponatremia is more common that hypernatremia (30% vs. 19%) after aneurysmal SAH. None of them was associated with symptomatic vasospasm. Hypernatremia was significantly associated with poor outcome, and a positive correlation was detected between higher serum sodium levels and poor GOS at 3 months after the ictus. Chandy *et al*. found that hyponatremia was associated with increased risk of cerebral vasospasm after aneurysmal SAH.[15]

Sherlock *et al*., in a retrospective study on 316 patients with aneurysmal SAH found that hyponatremia was a common electrolyte imbalance among their patients (56% overall prevalence) that caused longer hospital stay but did not affect the mortality rate. They observed that in a significant group of the hyponatremic patients (21.4–31.8%, according to the treatment modality), this may develop more than 7 days following SAH.[16]

McGirt *et al*. showed that a rise in the serum levels of brain natriuretic peptide (BNP) was independently associated with hyponatremia, and the incidence of hyponatremia increases

Table 3: Patient outcomes according to the serum electrolyte status

Electrolyte status	GOS					*P*
	I (good recovery)	II (moderate disability)	III (severe disability)	IV (persistent vegetative state)	V (death)	
Sodium (1st day)						
Hyponatremia	3 (14.3)	2 (10.5)	2 (28.6)	1 (50)	0 (0)	0.122
Hypernatremia	0 (0)	0 (0)	1 (14.3)	0 (0)	1 (25)	
Normal	18 (85.7)	17 (89.5)	4 (57.1)	1 (50)	3 (75)	
Sodium (3rd-5th day)						
Hyponatremia	4 (19)	6 (31.6)	2 (28.6)	0 (0)	0 (0)	0.002
Hypernatremia	0 (0)	2 (10.5)	4 (57.1)	1 (50)	3 (75)	
Normal	17 (81)	11 (57.9)	1 (14.3)	1 (50)	1 (25)	
Sodium (7-10th day)						
Hyponatremia	6 (28.6)	7 (36.8)	2 (28.6)	0 (0)	0 (0)	0.001
Hypernatremia	0 (0)	5 (26.3)	5 (71.4)	2 (100)	3 (75)	
Normal	15 (71.4)	7 (36.8)	0 (0)	0 (0)	1 (25)	
Potassium (1st day)						
Hypokalemia	0 (0)	1 (5.3)	0 (0)	0 (0)	0 (0)	0.587
Hyperkalemia	6 (28.6)	5 (26.3)	0 (0)	0 (0)	0 (0)	
Normal	15 (71.4)	13 (68.4)	7 (100)	2 (100)	4 (100)	
Potassium (3rd-5th day)						
Hypokalemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0.256
Hyperkalemia	7 (33.3)	5 (26.3)	0 (0)	0 (0)	0 (0)	
Normal	14 (66.7)	14 (73.7)	7 (100)	2 (100)	4 (100)	
Potassium (7-10th day)						
Hypokalemia	4 (19)	5 (26.3)	4 (57.1)	1 (50)	4 (100)	0.016
Hyperkalemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	17 (81)	14 (73.7)	3 (42.9)	1 (50)	0 (0)	
Magnesium (3rd-5th day)						
Hypomagnesemia	0 (0)	0 (0)	1 (14.3)	0 (0)	1 (25)	0.068
Hypermagnesemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	21 (100)	19 (100)	6 (85.7)	2 (100)	3 (75)	
Magnesium (7-10th day)						
Hypomagnesemia	4 (19)	5 (26.3)	4 (57.1)	1 (50)	4 (100)	0.016
Hypermagnesemia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Normal	17 (81)	14 (73.7)	3 (42.9)	1 (50)	0 (0)	

GOS – Glasgow outcome scale

significantly within 24 h after the onset of delayed ischemic neurologic deficits.[17]

Van den Bergh *et al*. reported that hypomagnesemia is frequently seen between the 2nd and 12th day after SAH and is related to the severity of hemorrhage.[18] The study of Collignon *et al*. failed to show a correlation between hypomagnesemia and vasospasm and the outcome of SAH patients.[19]

In the current study, there was not a correlation between serum electrolytes levels in the acute phase and patient outcome 3 months after SAH. In the subacute phase, hyponatremia was associated with better clinical grades, less radiographic severity, and more favorable outcome, but hypernatremia was associated with worse clinical grades, more radiographic severity and less favorable outcome.

Hypokalemia in the subacute phase correlated with poor outcomes. Hyperkalemia in this phase was significantly associated with less radiographic severity. Hypomagnesemia in the subacute phase was associated with more radiographic severity, worse clinical grades (especially Grade V) and poor outcome. This study in line with several others indicates that hyponatremia is more common but does not predict the outcome while hypernatremia is less common but more predictive of long-term clinical outcome.

To our knowledge, this is the first study that provides information on the relationship between dysnatremias and other electrolyte disturbances in immediate, acute and subacute phase with Fisher scale and WFNS grade and clinical outcome of the patients with aneurysmal SAH. The results of this study propose that the time course of development of such abnormalities may also be important on their eventual impact on the outcome.

Conclusions

The results of this study show that electrolyte imbalance is a major nonneurologic source of mortality and morbidity after aneurysmal SAH. This study in concert with many others emphasizes the impact of hypernatremia in the acute and subacute phase on the long-term outcome of patients with aneurysmal SAH, and also as well as the few other studies available in the literature highlights the negative effect of hypomagnesemia in the subacute phase on their outcome. These results elucidate that the timely and appropriate management of these abnormalities may further improve the treatment results of aneurysmal SAH. The efficacy of different therapeutic modalities in improving the outcome is an issue that remains to be determined yet. We recommend future studies to evaluate the impact of these treatment regimens and to monitor serum levels of biomarkers such as BNP as well.

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How to cite this article: Alimohamadi M, Saghafinia M, Alikhani F, Danial Z, Shirani M, Amirjamshidi A. Impact of electrolyte imbalances on the outcome of aneurysmal subarachnoid hemorrhage: A prospective study. Asian J Neurosurg 2016;11:29-33.

Source of Support: Nil, **Conflict of Interest:** None declared.