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Study on Electrolyte Abnormality and Quality Outcomes in the Management of Stroke

Sriram S[1], Asokan K[2], Suruthi Priyaa J.M[3], Tharani C[4], Arthy L[5], Cleyliya N.A[6]

[1]College of Pharmacy, Sri Ramakrishna Institute of Paramedical Sciences, Coimbatore, India

[2]Head, Department of Neurology, Sri Ramakrishna Hospital, Coimbatore, India

[3, 4, 5, 6]Pharm D Interns, College of Pharmacy, SRIPMS, Coimbatore, India

Abstract: ***Objectives: The objectives of the study is to find out the electrolyte disturbance in first-ever stroke by comparing serum sodium, potassium, chloride and bicarbonate levels and the outcomes using Glasgow Outcome Scale (GOS). Methods: First ever stroke patients were enrolled and to determine the subtype of stroke, clinical examination followed by CT / MRI scan of brain taken was used. Total serum sodium, potassium, chloride and bicarbonate levels were determined using serum samples. The patients were followed up for outcome up to 2 weeks during their stay in hospital and before discharge using GOS. Key findings: A total of 105 patients were included in the present study. Normal serum sodium was seen in 32 patients (30.5%), hyponatremia was present in 72 patients (68.6%) and hypernatremia in 1 patient (1%). 71 patients (67.6%) had normal serum potassium, 31 patients (29.5%) had hypokalaemia and 3 patients (2.9%) had hyperkalaemia. The outcome of the patient was assessed using Glasgow Outcome Scale (GOS), which revealed that 8 patients (8%) had a score of 3 which indicates severe disability, 43 patients (41%) had a score of 4 which indicates moderate disability and 54 patients (51%) had a score of 5 which indicates good recovery. Conclusion: The results of the present study demonstrated that electrolyte disturbances especially hyponatremia and hypokalaemia were highly prevalent in CVA patients. Thus, early assessment of electrolyte disturbance is essential to prevent morbidity and mortality and for better prognosis.***

Keywords: Stroke, electrolyte abnormality, GOS, hyponatremia, hypokalaemia

1. Introduction

Stroke is the fifth leading cause of death worldwide. In almost all neurological disorders, electrolyte disturbances were prominent. Electrolyte disturbance are commonly found in acute stroke setting. Hypernatremia, hyponatremia and hypokalaemia was the commonest type of disturbance. Recent researches with electrolyte disturbances are not only focusing on the neuroendocrine mechanism but also on its prevalence, risk factors and association with other medical condition.

The study reported here sought to identify the common electrolyte disturbance in acute phase of different type of stroke patients & their association with some common clinical presentation & outcome.

Stroke, according to the American Heart Association (AHA) definition, is a sudden loss of brain function due to disturbance in the cerebral blood supply with symptoms lasting at least 24 hours or leading to death. Stroke is defined as an acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of signs and symptoms [1]. Stroke is the rapid loss of brain function due to a disturbance in the blood supply to the brain.

The two main types of stroke are ischemic and haemorrhagic, accounting for approximately 85% and 15%, respectively. A third type of stroke, called as transient ischemic attack or TIA is a minor stroke that serves as a warning sign that a more serve stroke may occur. Haemorrhagic stroke includes spontaneous intracerebral haemorrhage and subarachnoid haemorrhage due to leakage or rupture of an artery [2,3,4]

The three main pathology of ischemic strokes are: Thrombosis, Embolism and Global ischemia (hypotensive) stroke.

Stroke is dominantly occurred at the middle age group or above and is commonly found in male than female and most of the patients are above 60 year age group [5].Hypertension is a well-documented risk factor for both IS and HS. Hypertension and diabetes favoured IS and high alcohol intake favoured HS. Smoking damages blood vessels. This can lead to blockages within those blood vessels, causing a stroke. High cholesterol increases the risk of blocked arteries. If an artery leading to the brain becomes blocked, a stroke can result. Being inactive, obese, or both, can increase your risk of heart disease and stroke. A carotid artery damaged by a fatty build-up of plaque inside the artery wall may become blocked by a blood clot. This causes a stroke. Sickle cell anaemia increases stroke risk because the “sickled” cells stick to blood vessel walls and may block arteries. Drugs including cocaine, ecstasy amphetamines, and heroin are associated with an increased risk of stroke. Sleep disordered breathing contributes to risk of stroke[6].

Therapy with clot-busting drugs must start within 4.5 hours if they are given into the vein — and the sooner, the better. Quick treatment not only improves your chances of survival but also may reduce complications. Injection of recombinant tissue Plasminogen Activator (tPA), also called alteplase, is considered the gold standard treatment for ischemic stroke. Other drugs include antiplatelet agents, statins, ACE inhibitors, ARBs, etc. Emergency treatment of haemorrhagic stroke focuses on controlling the bleeding and reducing pressure in the brain. One might also need surgery to help reduce future risk.

Electrolyte disturbance are commonly found in acute stroke setting. Recently, research with electrolyte disturbances is not only focusing on the neuroendocrine mechanism but also on its prevalence, risk factors and association with other medical condition [5].

In addition to regulating fluids, electrolytes have many functions. These include:

- Transmitting nerve signals from the heart, muscles, and nerve cells to other cells
- Building new tissue
- Supporting blood clotting
- Keeping your heart beating by electrically stimulating muscle contractions
- Maintaining the blood's pH level
- Regulating the fluid level in blood plasma [7]

Even though there are some data about large number of electrolyte disturbances in acute stroke setting, reports on the association between electrolyte imbalance and severity of acute stroke are still in limited number. There is a lack of data about this association especially from developing countries [5].

Intracerebral haemorrhage can be associated with raised ICT and cause headache and vomiting further leading to dyselectrolytemia in acute phage of stroke.

Development of hyponatraemia can causes further altered sensorium in stroke patients and when occur abruptly causes convulsions and aggravate cerebral oedema leading to cerebral ischemia causing further brain damage and leads to deaths.

Electrolyte disturbances are common at the time of presentation of patients with acute stroke associated with increased morbidity and mortality irrespective of types, location, and size of strokes and associated co- morbidities [8].

2. Methods

During the study period of March 2019 to August 2019, a total of 105 cases of stroke (as per the WHO definition) were included in the studies who were admitted in the Department of Neurology of Sri Ramakrishna Hospital, Coimbatore. After taking an informed consent from patients or their relatives the study was initiated.

The study protocol was approved by institutional review board (IRB). Patient information form was given to the subjects; both verbal and written consent was obtained from each subject before initiating the study. Structured proforma was designed which were used to collect various clinical and demographic details of the patient such as age, gender, electrolyte levels, and interactions. Patients' medical and medication history were used as the source for evaluating the risk factors for stroke. Past and present disease conditions of the patient were documented. Patients' social habits like alcohol consumption and smoking were also obtained. To determine the subtype of stroke, clinical examination followed by CT / MRI scan of brain taken was used. A total serum sodium, potassium, chloride and bicarbonate level was determined using serum samples. Study of calcium and magnesium was excluded from the present study as imbalances of these electrolytes are hardly encountered in association with stroke. The patients were followed up for outcome up to 2 weeks during their stay in hospital and before discharge using Glasgow Outcome Scale (GOS).

3. Results

A total of 105 patients were included in the present study. The mean age of the study population was 60.52 ± 12.33 years (Range: 24 – 86 years). There were 78 male patients (74%) and 27 female patients (26%).

Hypertension was present in 50 cases (65.7%) and among those patients, only 25 were taking anti-hypertensive agents (36.7%). Diabetes Mellitus was present in 35 cases (46%) and among those, 10 patients were on anti-diabetic agents (14.7%).

In the present study, social history of 105 patients revealed that 9 patients were alcoholic (8%), 8 patients were smokers (8%), 24 patients were both alcoholic & smokers (23%) and 1 patient was on tobacco use (1%). In this study out of 105 patients, 87 had Ischemic Stroke (ISCHS) and 18 had Haemorrhagic Stroke (HS). The percentage of ISCHS was 83% and HS was 17 % [Table 1].

Table 1: Types of Stroke

Types	No. of Patients (n=105)	%
Ischemic	87	83
Hemorrhagic	18	17

Among all the risk factors of stroke, age group between 51 – 70 years (75.2%), male gender (74.2%), smoking (29.5%), alcohol consumption (32.3%), SHT (47.6%) and DM (33.3%) were present in the study. This data is explained in Table 2.

Table 2: Risk Factors

Risk Factors	No. of Patients (n= 105)	Percentage (%)
Age (51 – 70 years)	79	75.2
Gender (Male)	78	74.2
Smoking	31	29.5
Alcohol	34	32.3
SHT	50	47.6
DM	35	33.3

Hypertension and diabetes were the leading comorbidities documented in this study with 45.7% and 30.4% respectively.

Table 3 shows the electrolyte ranges of the patients in this study. In 105 patients, normal serum sodium was seen in 32 patients (30.5%), hyponatremia was present in 72 patients (68.6%) and hypernatremia in 1 patient (1%). Serum sodium in ISCHS was normal in 27 patients (25.7%) and hyponatremia was seen in 60 patients (57.1%). In HS, serum sodium was normal in 5 patients (4.8%) hyponatremia was seen in 12 patients (11.4%) and hypernatremia was seen in

1 patient (1%). There was association between sodium imbalance and type of stroke (p = 0.046). Mean sodium level was 134.52±5.08.

In 105 patients, 71 patients (67.6%) had normal serum potassium, 31 patients (29.5%) had hypokalaemia and 3 patients (2.9%) had hyperkalaemia. Serum potassium in ISCHS was normal in 63 patients (60%), hypokalaemia was seen in 23 patients (21.9%) and hyperkalaemia was seen in 1 patient (1%). In HS, 8 patients (7.6%) had normal serum potassium, 8 patients (7.6%) had hypokalaemia and 2 patients (1.9%) had hyperkalaemia. There was association between potassium imbalance and type of stroke (p = 0.014). Mean potassium level was 3.82±0.59.

In 105 patients, 78 patients (74.3%) had normal serum chloride, 5 patients (4.8%) had hypochloraemia and 22 patients (21%) had hyperchloremia. Serum chlorides in ISCHS were normal in 63 patients (60%), hypochloraemia was seen in 4 patients (3.8%) and hyperchloremia was seen in 20 patients (19%). In HS, 15 patients (14.3%) had normal serum chloride, 1 patient (1%) had hypochloraemia and 2 patients (1.9%) had hyperchloremia. There was no association between chloride imbalance and type of stroke (p = 0.529). Mean chloride level was 104.16±5.93.

In 105 patients, 76 patients (72.4%) had normal serum bicarbonate, 29 patients (27.6%) had low bicarbonate level. Serum bicarbonate level in ISCHS were normal in 65 patients (61.9%), low bicarbonate level was seen in 22 patients (21%). In HS, 11 patients (10.5%) had normal serum bicarbonate level, 7 patients (6.7%) had low bicarbonate level. There was no association between bicarbonate imbalance and type of stroke (p = 0.186). Mean bicarbonate level was 23.50±2.83.

Graphical representation of the electrolyte levels is shown in Figure 1. The statistical analysis conveyed that serum sodium and potassium levels had an association with stroke.

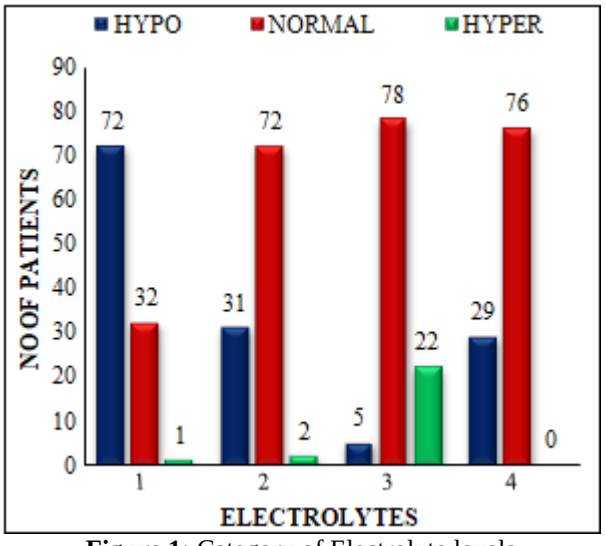

Figure 1: Category of Electrolyte levels

Table 3: Electrolyte Ranges in ischemic and Hemorrhagic Stroke

Electrolytes	Range	IS	HS	Total (n = 105)	%
Na+	Hypo (<137)	60	12	72	68.5
	Normal (137 – 145)	27	32	32	30.4
	Hyper (>145)	0	1	1	0.95
K+	Hypo (<3.5)	23	8	31	29.5
	Normal (3.5 – 5.1)	64	8	72	68.5
	Hyper (>5.1)	0	2	2	1.90
Cl-	Hypo (<98)	4	1	5	4.76
	Normal (98 – 107)	63	15	78	74.2
	Hyper (>107)	20	2	22	20.9
Hco3-	Hypo (<22)	22	7	29	6.66
	Normal (22 – 29)	65	11	76	10.2
	HYPER (>29)	0	0	0	0

Table 4 & 5 represents the treatment given for stroke and electrolyte imbalance.

Table 4: Drugs Prescribed For Stroke

ATC Code	Category	No. of Drugs (n = 13)	No. of Patients (n=105)	%
N06BS	Nootropic Agents	4	83	79
B01AC B01AB	Anti-Platelets & Anti-Coagulants	7	87	82.9
A06A	Glycerol + Mannitol	2	43	40.9

Table 5: Treatment Given For Electrolyte Imbalance

ATC Code	Abnor-Mality	Drugs	No. of Pts. (n=105)	%
B05CB01	Hypo-Natremia	NS	63	60
A12BA01	Hypo-Kalemia	KCl	18	17.1
A12AA 03	Hyper-Kalemia	Calcium Gluco-Nate	1	0.9
B05XA02	Low Bicarbo-Nate	NaHCO3	9	8.5

In 105 prescriptions, a total of 42 interactions were found. Among those, 28 were major (66.6%), 13 were moderate (30.9%) and 1 was minor (2.3%) interaction.

The degree of recovery assessed using Glasgow Outcome Scale (GOS) is depicted in Table 6 & Figure 2. In 105 patients, 8 patients (8%) had a score of 3 which indicates severe disability, 43 patients (41%) had a score of 4 which indicates moderate disability and 54 patients (51%) had a score of 5 which indicates good recovery.

Table 6: Outcome Assessment with GOS

GOS Score	No. of Patients (n=105)	Percentage (%)
1	0	0
2	0	0
3	8	8
4	43	41
5	54	51

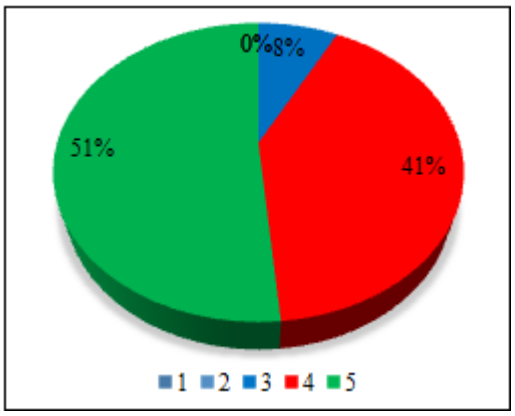

Figure 2: Outcome assessment with GOS

According to this study, as the management for dyselectrolytemia was provided appropriately, the GOS score (p 0.287) had no association with electrolyte disturbance.

4. Discussion

Dyselectrolytemia are quite often associated with acute strokes. In this study we observed that stroke is dominant at the middle age group or above and is commonly found in male than female and most of the patients are above 50 years age group. A similar study was conducted by Mana Swini Panda et al., in which, among 100 stroke patients 30% of them were in the 51-60 years age group and 56.67% of them were in the 61-70 years of age group. Prevalence of stroke is more in men than women as it differs with respect to its risk factors [5]. Women with stroke are older at onset (by an average of about 4 years), and are more likely to have atrial fibrillation and hypertension. There was a study conducted by Meike A.H.N. et al., in which among 85 stroke patients, 61.2% was male.

Men are more prone to stroke due to reasons like:

- High blood pressure
- Smoking damages blood vessels
- Being overweight or obese
- Diabetes can cause disease of blood vessels in the brain.
- Alcohol [9]

The majority of the stroke cases were ischemic (83%). Other studies have also reported ischaemic stroke as the most common type. In the present study, 78% of stroke patients had some electrolyte imbalance. Other studies have reported electrolyte imbalance in 60% to 70% of stroke patients. Most common electrolyte imbalance in ischaemic stroke was hyponatremia. The reason for hyponatremia may be due to Syndrome of Inappropriate Anti Diuretic Hormone (SIADH) or Cerebral Salt Wasting Syndrome (CSWS).In a study conducted by Siddiqui et al., in haemorrhagic stroke & ischaemic stroke patients, hyponatraemia (17% & 13%), hypernatraemia (1% & 3%), hypokalaemia (19% & 11%), hyperkalaemia (0% & 1%), hypochloraemia (9% & 6%) were observed respectively.

SIADH consists of hyponatraemia, inappropriately elevated urine osmolality, excessive urine sodium and decreased serum osmolality in a euvolemic patient without oedema. In SIADH, ADH is produced continuously despite body fluid hypotonicity. This leads to expanded effective circulatory volume so that the negative feedback mechanism that normally controls ADH fails and ADH continues to be released. Hyponatraemia in SIADH is due to excess water (dilutional hyponatraemia) and is not primarily due to serum sodium deficiency. It is a combination of water retention together with secondary solute loss, which results in reduction in serum sodium.

CSWS is defined by the development of excessive natriuresis and subsequent hyponatraemia, dehydration in patients with intracranial disease. Though many hypotheses have been given, but the exact mechanism of CSWS is not known. CSWS is a centrally mediated process characterized by renal loss of sodium resulting in polyuria, natriuresis, hyponatraemia, and hypovolaemia. The postulated mechanisms include decreased sympathetic input to the kidney or the presence of circulating natriuretic factors such as Atrial Natriuretic Peptide (ANP) or BNP or both. Decreased sympathetic tone leads to a decreased Glomerular Filtration Rate (GFR), a decreased renin release and decreased renal tubular sodium reabsorption [10].

Sometimes electrolyte disturbances may cause complications like coma, seizure and even death. Anyone can develop an electrolyte disorder. Certain people are at an increased risk because of their medical history. Conditions that increase the risk for an electrolyte disorder includes cirrhosis, CHF, kidney disease and eating disorders, such as anorexia and bulimia.

Diagnostically, the initial step is to differentiate hypotonic from non-hypotonic hyponatremia. Hypotonic hyponatremia is further differentiated on the basis of urine osmolality, urine sodium level, and volume status. Recently identified parameters, including fractional uric acid excretion and plasma copeptin concentration, may further improve the diagnostic approach.

The treatment for hyponatremia is chosen on the basis of duration and symptoms. Although fluid restriction remains the first-line treatment for most forms of chronic hyponatremiatherapy to increase renal free water excretion is often necessary. Vasopressinreceptor antagonists, urea, and loop diuretics serve this purpose [11].

Vasopressin receptor antagonists (Vaptans) includes Tolvaptan, Lixivaptan, Satavaptan can be given at a dose of 15mg – 30mg/day, less than 7.5mg, 50mg/day respectively. Loop diuretic furosemide at a dose of 40mg.

For the treatment of hypokalemia, potassium supplements (potassium chloride as injection and syrup) are given at a dose of 1.5gm/5ml, 1.5gm/15ml respectively. Intravenous calcium gluconate at a dose of 1.5-3gm IV infused over 2-5 mins is administered to patients with hyperkalemic electrocardiographic changes [12].

There are number of scales available for the assessment of outcome in stroke patients. It includes Barthel Index, Functional Independence Measurement (FIM), Glasgow

Outcome Scale (GOS) & Community Integration Questionnaire.

In this study, we assessed the outcome of patients using Glasgow Outcome Scale (GOS). This scale allows a prediction of the long-term course of rehabilitation to return to work and everyday life. This scale includes five scores: (i) 1 – Death, (ii) 2 – Persistent vegetative state, (iii) 3 – Severe disability, (iv) 4 - Moderate disability, (v) 5 – Good recovery.

According to the study, 54 patients had good recovery, 43 patients had moderate disability and 8 patients had severe disability. None of the patients had severe disability or death. Since appropriate medical management was provided for dyselectrolytemia, most of the patients had good recovery. Thus, dyselectrolytemia must be addressed in every stroke patient for better recovery.

Further multi-centred studies with a greater number of patients are needed to assess the impact of electrolyte disturbances in stroke and the quality outcomes of the patient.

5. Conclusion

The results of the present study demonstrated that electrolyte disturbances especially hyponatremia and hypokalaemia were highly prevalent in CVA patients. The cause of hyponatremia may be SIADH or CSWS. Thus, early assessment of electrolyte disturbance is essential to prevent morbidity and mortality and for better prognosis. This should be further carried out in large population.

6. Declarations

Conflict of Interest
The Author(s) declare(s) that they have no conflicts of interest to disclose.

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