STUDY OF ELECTROLYTE IMBALANCE IN ACUTE CORONARY SYNDROME PATIENTS; A HOSPITAL BASED STUDY.

Biochemistry

Dr. Rajiv Ranjan	PG Resident (MD Biochemistry 3rd Year), Department of Biochemistry, SHKM Government Medical College, Nalhar, Nuh, Haryana, India.
Dr. Sangeeta B. Singh	Professor and HOD, Department of Biochemistry, SHKM Government Medical College Nalhar, Nuh, Haryana, India.
Dr. Shikhaa Mahajan*	Associate Professor, Department of Biochemistry, SHKM Government Medical College Nalhar, Nuh, Haryana, India. *Corresponding Author
Dr. Asha Kumari	Assistant Professor, Department of Biochemistry, SHKM Government Medical College, Nalhar, Nuh, Haryana, India.
Dr. Nikita Singh	Ex. Junior Resident, Department of Biochemistry, SHKM Government Medical College Nalhar, Nuh, Haryana, India.
Dr. Harsh Vardhan Chawla	Ex. Junior Resident, Department of Biochemistry, SHKM Government Medical College Nalhar, Nuh, Haryana, India.
Dr. Vivek Sharma	Biochemist, Department of Biochemistry, SHKM Government Medical College Nalhar, Nuh, Haryana, India.

ABSTRACT

Introduction: Electrolytes are very essential for normal functioning of vital organs including heart. Electrical activity of the heart is regulated by Na, K and Ca. Normal homeostasis of these electrolytes are vital for normal functioning of heart. Electrolyte imbalance is often common after episode of acute coronary syndrome (ACS) and electrolyte imbalance may have important role in altering the prognosis of ACS.

Aims & Objectives: To assess the serum electrolytes imbalance (Na, K and Ca) in ACS patients within first 48 hours of onset of symptoms.

Materials and Methods: This hospital based cross sectional study conducted on 50 cases of ACS and 50 healthy controls. Serum Na, K and Ca (total) concentration were estimated in healthy controls and newly diagnosed cases of ACS within 48 hours of onset of symptoms.

Result: Mean value of serum Na, K and Ca (total) in case and control group were 138 ± 4.23 and 140 ± 1.99 mEq/L ($p=0.0018$), 3.87 ± 0.43 and 4.16 ± 0.35 mEq/L ($p=0.0006$), 8.85 ± 0.59 and 9.68 ± 0.44 mg/dL ($p<0.0001$) respectively. Hyponatremia, hypokalaemia and hypocalcemia were found in 14% ($n=7$), 12% ($n=6$) and 18% ($n=9$) of ACS patients respectively.

Conclusion: There were statistically significant lower levels of serum Na, K and Ca (total) found in ACS patients compared to healthy controls.

KEYWORDS

Acute coronary syndrome, Serum Electrolyte, Arrhythmia.

INTRODUCTION:

Acute coronary syndrome (ACS) is a condition due to decrease blood supply in coronary arteries of heart. There are three sub- groups of ACS; 1. ST Segment elevated myocardial infarction (STEMI) 2. Non ST Segment elevated MI (NSTEMI) 3. Unstable Angina (UA), based on ECG finding and cardiac biomarkers. STEMI is characterized by complete occlusion the blood vessel, resulting in transmural infarct to the myocardium and rise in troponins. In NSTEMI, plaque rupture and thrombus formation causes partial occlusion of blood vessel results in subendocardial infarct of myocardium and rise in troponins. In unstable angina, plaque ruptures and thrombus formation occur without infarct, causing partial occlusion of the vessel and normal troponins with angina pain that occurs at rest or progresses rapidly over a short period of time.¹

ACS is one of the manifestations of coronary heart disease (CHD). CHD is worldwide disease with 7.2 million deaths per year and 12.8% of total deaths globally. In India, prevalence of CHD in urban population is 6.4% whereas in rural population prevalence of CHD is 2%.² According to the "global burden of disease study age-standardized estimates (2010)", nearly 24.8% of all deaths in India are due to cardiovascular diseases.³

Electrolytes are very essential for normal functioning of cells and vital organs including heart. Sodium (Na), Potassium (K) and calcium (Ca) are among the most important electrolytes for vital function in the body. Chloride, bicarbonate ion, magnesium (Mg) and phosphate ions are other important electrolytes. Electrical activity of the heart is regulated by normal level of Na, K and Ca. Normal homeostasis of these electrolytes are vital for normal functioning of heart. Electrolyte imbalance is often common after episode of ACS and electrolyte imbalance may have important role in altering the prognosis of ACS.⁴

Potassium is the major intracellular cation. It is required for depolarization of cardiac muscle and transmission of nerve impulses. Normal serum level of K is 3.5 to 5.5 mEq/L. Cardiac arrhythmias particularly malignant ventricular arrhythmia is often common in post ACS events and it is due to hypokalemia.⁵ Sodium is the most abundant extracellular cation and play vital role in extracellular fluid balance and facilitates neuromuscular functioning. Normal serum Na level is 135 to 145 mEq/L. Hyponatremia occurs when serum Na level below 135 mEq/L and its often seen in post ACS events.⁶

Calcium is involved in depolarization of myocytes and myocardial contractility. Normal range of serum Ca (total) is 8.5 to 10.5 mg/dL. Hypocalcemia may lead to coronary spasm, thrombus formation and disruption of atherosclerotic plaque.⁷

Electrolyte imbalance has prognostic importance in very early hours after ACS events. So, present study was conducted with aim to assess the electrolytes imbalance (Na, K and Ca) in ACS patients.

MATERIALS AND METHODS:

This hospital based cross sectional study was conducted in the Department of Biochemistry in collaboration with Department of General Medicine, SHKM Govt. Medical College Nuh, Haryana from November 2018 to February 2020. A total of 100 study subjects were enrolled for this study which comprise of 50 diagnosed cases of ACS and 50 age and sex matched healthy volunteers according to inclusion and exclusion criteria. Patient informed consent and institutional ethical clearance was taken from SHKM Govt. Medical College Nuh, Haryana for conducting this study.

Inclusion Criteria: 1. Newly diagnosed cases of ACS (Age $\leq$ 60 years) attending/ admitted in SHKM Hospital, Nuh, Haryana within 48 hours of onset of symptoms. 2. Both male and female 3. Those willing

to participate

Exclusion Criteria: 1. Patients suffering from chronic diseases like diabetes mellitus, hypertension, thyroid disorders and diseases affecting serum electrolyte concentration like patients suffering from acute diarrhoea, dehydration and malabsorption syndromes.

2. Patients on I.V fluid lines before sampling. 3. Patients on drugs like proton pump inhibitors, Cisplatin, Cyclosporine, Aminoglycoside, Amphotericin B, Cetuximab and diuretics. 4. Renal insufficiency like acute renal failure (ARF) and chronic renal failure (CRF). 5. Those not willing to participate.

Three ml of venous blood sample was taken from the antecubital vein under all aseptic conditions in plain vacutainer after informed consent of study subjects. Samples were transported to lab immediately. Serum Na and K were estimated by electrolyte analyser (Erba Transasia). Serum Ca (total) was estimated by fully autoanalyser (Roche P800).

Statistical Analysis: All data were tabulated and compiled using Microsoft Excel 2010. The data were analysed by using SPSS Version 22 (Chicago, Inc. USA). All values were expressed as mean $\pm$ SD. Difference of mean of two variables (case and control group) were compared and analysed by unpaired student t-test. For all analysis, p value <0.05 was considered as statistically significant.

RESULTS:

In this study, case group was comprised of 32 male and 18 female ACS patients. Control group comprised of equal number of age and sex matched healthy controls. Average age of study subjects in case group was 52.1 ± 7.32 years and in control group, it was 50.14 ± 7.03 years. Demographic profile of study subjects were mentioned in table 01.

Table 01: Demographic profile of study subjects.

Variables	Case (n=50) mean $\pm$ SD	Control (n=50) mean $\pm$ SD	P value
Age in years	52.1 ± 7.32	50.14 ± 7.03	0.34
Male (n %)	32 (64%)	32 (64%)	-
Female (n %)	18 (36%)	18 (36%)	-
BMI (kg/m ³)	23.31 ± 2.92	21.71 ± 3.10	0.009
Pulse	90 ± 18	74 ± 2	<0.001
DBP (mm of Hg)	71 ± 8	82 ± 5	<0.001
SBP (mm of Hg)	114 ± 20	132 ± 5	<0.001

There was statistically significant difference between mean values of serum electrolytes (Na, K and Ca) in case and control group. Serum electrolytes levels were significantly lower in cases compared to control group. Mean value of serum Na, K and Ca in case and control group were 138 ± 4.23 and 140 ± 1.99 mEq/L ($p=0.0018$), 3.87 ± 0.43 and 4.16 ± 0.35 mEq/L ($p=0.0006$), 8.85 ± 0.59 and 9.68 ± 0.44 mg/dL ($p<0.0001$) respectively as shown in table 02.

Table 02: Comparison of Serum Na, K and Ca (total) in case and control groups using unpaired student t-test.

Serum Electrolytes.	Case (n=50) Mean $\pm$ SD	Control (n=50) Mean $\pm$ SD	p value
Serum Na (mEq/L)	138 ± 4.23	140 ± 1.99	0.001
Serum K (mEq/L)	3.87 ± 0.43	4.16 ± 0.35	<0.001
Serum Ca; Total (mg/dL)	8.85 ± 0.59	9.68 ± 0.44	<0.001

p value <0.05 was considered as statistically significant.

Hyponatremia found in 14% (n=7) of ACS patients, hypokalemia found 12% (n=6) of ACS patients, whereas hypocalcemia found in 18% (n=9) of ACS patients. Minimum level of serum Na, K and Ca found in ACS patients were 123 mEq/L, 2.6 mEq/L and 7.1 mg/dL respectively. Study subjects in control group were healthy and their serum electrolytes levels were in normal reference range as shown in table 03.

Table 03: Distribution of serum electrolytes in ACS patients and in healthy controls

S. Electrolyte (with normal range)	ACS cases having lower S. Electrolytes (n, %)	Controls having lower S. Electrolytes (n, %)	Range in case group	Range in control group
Na (135 to 145 mEq/L)	7 (21.9%)	0 (0%)	123-145 mEq/L	136-144 mEq/L
K (3.5 to 5.5 mEq/L)	6 (18.8%)	0 (0%)	2.6-4.8 mEq/L	3.6-5.0 mEq/L
Ca (8.5 to 10.5 mg/dL)	9 (28.1%)	0 (0%)	7.1-10 mg/dL	8.8-10.5 mg/dL

Na (135 to 145 mEq/L)	Hyponatremia; n = 7, 14%	Hyponatremia; n=0	123-145 mEq/L	136-144 mEq/L
K (3.5 to 5.5 mEq/L)	Hypokalaemia; n= 6, 12%	Hypokalaemia; n= 0	2.6-4.8 mEq/L	3.6-5.0 mEq/L
Ca (8.5 to 10.5 mg/dL)	Hypocalcaemia ; n= 9, 18%	Hypocalcaemia ; n=0	7.1-10 mg/dL	8.8-10.5 mg/dL

DISCUSSION:

There were statistically significant lower levels of serum Na, K and Ca found in ACS patients compare to healthy controls. Fourteen percent of ACS patients had hyponatremia, 12% of ACS patients had hypokalaemia and 18% of ACS patients had hypocalcaemia as shown in table 03. Patil et al also found the significant lower level of serum Na, K and Ca in AMI patients. They observed in their study that 27% of all AMI patients were hyponatraemic, 24% were hypokalaemic and 49% of cases were hypocalcaemic and mean sodium level was 135.93 ± 3.96 mEq/L with lowest value being 125 mEq/L, mean potassium was 3.81 ± 0.48 mEq/L with lowest value was 2.6 mEq/L and mean Calcium was 8.51 ± 0.66 mg/dl with lowest value being 7.2mg/dl.⁸

Normal electrolyte balance depends on working of different types of ion channels. Na⁺/K⁺-ATPase (also known as the Na⁺/K⁺ pump) is an trans-membrane ATPase found in the cell membrane. For every ATP molecule that pump uses, three Na ions are exported and two K ions are imported across the cell membrane and hence there is a net export of a single positive charge per pump cycle.⁹

Ca²⁺ ATPase is an active Ca pump. There are two types of calcium ATPase; 1. Plasma membrane Ca²⁺ ATPase (PMCA) and 2. sarcoplasmic reticulum Ca²⁺ ATPase (SERCA). PMCA serves to remove Ca from cytoplasm of cells. It is vital for regulating the amount of Ca²⁺ within cells so that intracellular Ca ion concentration should be maintained. The PMCA and Na⁺/Ca²⁺ exchanger are together the main regulators of intracellular Ca²⁺ concentrations. In myocytes, Ca²⁺ is normally sequestered into sarcoplasmic reticulum (SR). SERCA transfers Ca²⁺ from the cytosol of the cell to the lumen of the SR at the expense of one ATP during muscle relaxation.¹⁰

Na⁺/Ca²⁺ exchanger is an antiporter membrane protein that removes Ca from cells. It uses the energy that is stored in the electrochemical gradient of Na⁺ by allowing Na⁺ to flow down its gradient across the plasma membrane in exchange for the counter transport of Ca²⁺. A single Ca²⁺ is exported for the import of 3 Na⁺. It can transport the ions rapidly (has a high capacity and low affinity), transporting up to five thousand Ca²⁺ ions per second.

In cardiac myocytes, the L-type (long-lasting type) calcium channel passes inward Ca²⁺ current and triggers calcium release from the SR by activating ryanodine receptor 2 (RyR2). Phosphorylation of these channels increases their permeability to calcium and increases the contractility of cardiac myocytes.¹² T-type calcium channels are low voltage activated calcium channels allow entry of calcium into cardiac myocyte, initiates contraction directly by allowing the cytosolic concentration of Ca²⁺ to increase. T-type calcium channels control the pace-making activity of the SA Node.¹³

Nordrehaug et al have suggested that ion channels may be unable to function properly to maintain normal electrolytes homeostasis due to ischemia during ACS episode. They concluded that possible mechanism for the low concentrations of Na and K in post AMI was impairment of the Na⁺/K⁺-ATPase pump and the Na-Ca exchanger in their study on malignant cardiac arrhythmia following AMI.¹⁴

Besides impairments of ion channels, Flear et al had suggested that the hypoxia and cardiac ischemia increased the cell membrane permeability to sodium ions, activation of sympathetic nervous system and rennin-angiotensin system. This might lead to decrease serum Na in ACS patients.¹⁶ Madias et al suggested in their study that hypokalaemia in post AMI was most likely due to the stress induced catecholamine secretion from the adrenal medulla that increased K uptake into cells leading to decreased level of serum K.¹⁶ (summarised in figure 01)

Figure 01: summary of possible mechanism behind electrolyte imbalance in ACS patients.

CONCLUSION:

There were statistically significant lower levels of serum electrolytes (serum Na, K and Ca) found in ACS patients compared to healthy controls during first 48 hours of ACS events. Early estimation and intervention to correct these electrolytes imbalance in ACS patients may have positive impact on better prognosis of ACS and it may minimise fatal outcomes including cardiac arrhythmias.

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