The Differences of Electrolyte and Cardiac Markers in STEMI n NSTEMI

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ORIGINAL ARTICLE

The Differences of Electrolyte and Cardiac Markers Levels in NSTEMI and STEMI Patients

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ABSTRACT

Background: Coronary heart disease (CHD) has become the leading cause of mortality in the world. Myocardial infarction is the most common form of CHD, which consists of NSTEMI and STEMI. Differences of sodium, potassium, chloride, troponin I and NT-ProBNP levels on NSTEMI and STEMI were not widely discussed. Previous studies of electrolyte levels and NT-ProBNP gave different results.

Aim: To analyze the differences of serum sodium, potassium, chloride, troponin I and NT-ProBNP levels in NSTEMI and STEMI patients.

Methods: Analytic observational study design with cross sectional approach was conducted in February-May 2019 involving 35 NSTEMI and 35 STEMI patients at the Dr. Kariadi General Hospital ED who were screened according to the inclusion and exclusion criteria. Sodium, potassium and chloride levels were measured using the ISE method of the Advia biochemistry system. Troponin I levels were measured by the ELFA method on Vidas mini and NT-ProBNP levels were using the ELISA method. Differences in sodium, potassium and chloride levels between groups were analyzed using independent t-test, differences in troponin I and NT-ProBNP levels between groups were analyzed using Mann Whitney U Test. p values were considered significant if less than 0.05.

Results: There are significant differences in levels of sodium ($p=0.001$), chloride ($p=0.030$), troponin I ($p<0.001$) and NT-ProBNP ($p=0.001$) between NSTEMI and STEMI patients. The difference of potassium levels is not significant between the two groups ($p=0.721$).

Conclusion: Lower levels of sodium and chloride, higher troponin I and NT-ProBNP levels occur in STEMI rather than NSTEMI.

Keywords: Electrolyte, Troponin I, NT-ProBNP, NSTEMI, STEMI

INTRODUCTION

Coronary heart disease (CHD) has become the leading cause of death in the world. World Health Organization estimates that 13% of deaths worldwide were due to coronary heart disease in 2015.[1] The CHD in Indonesia was the second leading cause of death after stroke in 2014, which is 12.9%.[2]

The most common form of CHD is the myocardial infarction. Myocardial infarction consists of non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI), a condition that occurs due to a prolonged ischemia in the heart muscle, where the availability of blood flow to the heart through the coronary arteries decreases beyond the critical threshold and defeats the repair mechanism of the heart muscle, resulting in irreversible damage and cardiac muscle cell death. Myocardial infarction is characterized by typical chest pain, changes in the electrocardiogram (ECG) and elevated levels of cardiac enzymes such as troponin I.[3]

Electrolyte levels can be affected by myocardial infarction. Electrolyte ions, mainly sodium and potassium, are needed in the myocardial impulses generation and conduction, and undergo continuous exchange between intracellular and extracellular spaces, both through passive and active diffusion. Myocardial infarction causes damage to the heart muscle cell membranes, that it will cause dysfunction of the sodium, potassium channels and the sodium-potassium-ATPase pump. Myocardial infarction also causes a decrease in pressure in the left atrium and in the circulation, which will affect the aldosterone and vasopressin in water reabsorption and electrolyte homeostasis.[4-5]

Previous studies of electrolyte levels in the acute coronary syndrome (ACS) showed different results. Study by Wali et al. showed a decrease in serum sodium and potassium levels in the state of myocardial infarction, but not accompanied by significant differences in chloride levels.[4] Faraj found different results however, an increase in sodium and chloride levels, and decrease of potassium levels in ACS patients.[5] Our previous study have demonstrated that serum sodium levels are lower in STEMI patients than those with NSTEMI, whereas potassium and chloride levels were not significantly different.[6]

Troponin I will increase within 4-6 hours after myocardial infarction, reach the peak in 14-36 hours and can still be detected up to 1 week after infarction. Several previous studies on differences of troponin levels in NSTEMI and STEMI showed different results. Bhatt et al. reported significantly higher troponin I levels in STEMI, however Gonzales et al. found higher troponin I levels in STEMI and type 1 ACS patients than those with NSTEMI and type 2 ACS.[7-8]

NT-ProBNP is a prohormone which, along with BNP, are split from the ProBNP molecule. Ventricular muscle cells secrete NT-ProBNP in response to ventricular volume expansion or increased myocardial stretching. This parameter has been used as cardiac dysfunction detection and evaluation marker in heart failure.[9-10]

Several previous studies found that heart muscle cells that were damaged due to myocardial infarction also secreted NT-ProBNP. Radwan et al. have demonstrated that NT-proBNP levels between STEMI and NSTEMI patients were significantly different, where levels were higher in STEMI patients.[9] Different result were obtained by

Salama et al. who found that higher levels of NT-ProBNP in NSTEMI patients than in STEMI patients.[10]

This study aims to analyze differences of serum sodium, potassium, chloride, troponin I and NT-ProBNP levels between NSTEMI and STEMI patients, in order to comprehend the effect of myocardial infarction degree on the levels of these laboratory parameters.

MATERIAL AND METHODS

This study was an observational analytical study with cross sectional approach. The subjects were patients in the Emergency Department (ED) of Dr. Kariadi General Hospital, who were diagnosed with STEMI and NSTEMI in February – May 2019. All subjects were requested written informed consent. Ethical clearance was obtained from the Dr. Kariadi General Hospital Health Research Ethics Committee.

This study involved 70 patients, 35 of whom were diagnosed with STEMI and 35 diagnosed with NSTEMI that met the inclusion and exclusion criteria. STEMI and NSTEMI are characterized by typical chest pain and elevated cardiac enzymes levels such as troponin I. STEMI is distinguished from NSTEMI by the change in ST segment on the electrocardiogram (ECG). Patients with concomitant diseases such as kidney failure, diarrhea, stroke, COPD, gastrointestinal bleeding, and patients who received electrical cardioversion therapy before sampling, which could interfere with cardiac enzyme and electrolyte levels were excluded from this study. Cardiac ventricular hypertrophy which is known to affect NT-ProBNP levels was excluded via ECG. The specimen used was blood serum.

Electrolyte and troponin I measurements were carried out in Dr. Kariadi General Hospital laboratory and NT-ProBNP levels were measured in the Diponegoro University Faculty of Medicine GAKI (*Gangguan Akibat Kekurangan Iodium*/Iodine Deficiency Disorders) laboratory. Serum sodium, potassium and chloride levels were measured using the ion selective electrode (ISE) method of the Advia biochemistry system. Measurement of troponin I levels were using the ELFA method on a mini Vidas device and NT-ProBNP levels were measured using the ELISA method.

Normality test was carried out by using Saphiro-Wilk test. Normally distributed data of sodium, potassium and chloride levels were presented in the form of mean ± SD (95% CI) and then followed by statistical analysis using t-test. Data on troponin I and NT-ProBNP levels that are not normally distributed were presented in the form of median (lowest value – highest value), data transformation was performed and then analyzed using Mann Whitney U test. Statistical tests were considered significant if p values less than 0.05.

RESULTS

Demographic data of the study subjects can be seen in Table 1 below. Statistically the two groups are homogeneous.

Table 2 shows the basic characteristics of the subjects based on the time span from the onset of chest pain to the time the diagnosis was made. Laboratory parameters results in STEMI and NSTEMI patients are shown in Table 3.

Random blood glucose and creatinine levels are not significantly different between STEMI and NSTEMI patients. Sodium and chloride levels are significantly lower in STEMI patients compared to NSTEMI patients. Potassium levels are also lower in STEMI patients but are not significantly different. Troponin I and NT-ProBNP levels are significantly higher in STEMI patients compared to NSTEMI.

Table 1. Demographic data

Variable	NSTEMI	STEMI	*p*
Sex (n(%))			
Males	25 (71,4%)	27 (77.1%)	0.584*
Females	10 (28,6%)	8 (22.9%)	
Age (years)	61.63 ± 9.37	58.60 ± 9.49	0.183*

Annotation: **Independent t-test; *Pearson chi square. Normally distributed data are displayed as mean ± standard deviations

Table 2. Time span from the onset of chest pain until the diagnosis was made

Group	n	Time span from the onset of chest pain until the diagnosis was made (hours) Median (min – max)
NSTEMI	35	9 (1 – 48)
STEMI	35	7 (1 – 38)

Annotation: min: minimum; max: maximum

Table 3. Laboratory parameters results in STEMI and NSTEMI

Parameter	NSTEMI	STEMI	*P*
Random blood glucose (mg/dL)	122,77 ± 28,83	126,37 ± 34,95	0,638+
Creatinine (mg/dL)	0,9 (0,7 – 1,3)	1,01 (0,51 – 1,3)	0,292‡
Sodium (mmol/L)	139.11 ± 3.65	135.69 ± 4.34	0.001+*
Potassium (mmol/L)	4.15 ± 0.61	4.09 ± 0.84	0.721+
Chloride (mmol/L)	103.89 ± 4.67	101.34 ± 4.91	0.03+*
Troponin I (µg/L)	0.09 (0.05 – 1.4)	25.82 (0.13 – 40)	<0.001‡*
NT-ProBNP (ng/ml)	0.45 (0.03 – 1.07)	1.08 (0.07 – 2.88)	0.001‡*

Annotation: *Significant (p<0.05); +Independent t-test; ‡Mann whitney test. Normal reference values for serum sodium levels are 135-145 mmol/L, serum potassium levels are 3.5-5.5 mmol/L, and chloride levels are 95-108 mmol/L. The reference value for cardiac troponin I in adults is <0.01 µg/L with a cut-off value for myocardial infarction is >0.3 µg/L or a serial change with an increase of >20% troponin value and a baseline increase above the 99th percentile.[3] NT-ProBNP reference value in myocardial infarction have yet to be determined.

DISCUSSION

The results of this study indicate a greater percentage of male patients compared to women in both the NSTEMI and STEMI groups (Table 1). The cause of the difference which shows that men are more prone to suffer from ACS compared to women is still being debated by experts, but it is suspected that there are several contributing factors such as the estrogen in women, lifestyle differences that cause men tend to have a higher cholesterol levels, blood pressure and body mass index. Differences in physical activity and stress response between the sexes are also thought to play a role.[11] The results of this study are in accordance with the statistical reports of heart disease from AHA in 2016.[12]

This study find a time span from the onset of chest pain to the time the diagnosis was established in the NSTEMI group is 9 hours and in the STEMI group is 7 hours (Table 2). Study by Widyarani in Yogyakarta Indonesia found the average time span of NSTEMI patients to arrive in the ED was 7.89 ± 6.44 hours.[13]

Gruden's (2012) study found NT-ProBNP levels were affected by blood glucose, therefore in this study high blood glucose levels were excluded and random blood glucose levels of the two groups did not differ significantly.[14] Creatinine levels which used to exclude kidney failure were within normal range and were not significantly different in the two groups.

The serum sodium and chloride levels in this study are lower in STEMI patients. This because the greater degree of infarction in STEMI will further reduce the contractility ability of heart muscle cells so that the pressure in the left atrium of the heart will decrease further, which then will lead to higher non-osmotic stimulation of vasopressin hormone secretion by the posterior pituitary. The vasopressin hormone will increase water reabsorption in the kidney tubules by increasing the water permeability in the distal tubule and collecting duct cells. Increased water reabsorption will cause a decrease in the levels of sodium. Chloride which is in a state of equilibrium with sodium, will also decrease due to dilution by increased plasma fluid.[15]

Further decrease in sodium levels can also be caused by a more severe anoxic state in STEMI causing dysfunction in greater numbers of voltage-gated sodium channels of heart muscle cells so that permeability of sodium ions increases and sodium ions diffuse into heart muscle cells, go down the concentration gradient. This state of anoxia can also cause a decrease in intracellular ATP concentrations which will caused sodium-potassium-ATPase pump dysfunction.[16]

The disrupted function of the sodium channel and the sodium-potassium-ATPase pump will increase the positivity within the cell, so that the membrane potential will increase with a higher electrical baseline. This can be seen as ST segment elevation on the ECG of STEMI.[17]

Wali et al. found decreased sodium and chloride levels in acute coronary syndrome patients compared with healthy control patients.[4] Choi et al. and our previous study also have demonstrated lower sodium levels in STEMI patients compared to NSTEMI.[6,18] Hyponatremia is known to affect the prognostic of ACS patients.[18]

Potassium levels in STEMI patients are lower than NSTEMI but do not have a significant difference and this result is in accordance with our previous study.[6] This insignificant difference could be due to blood sampling in this study conducted early at the time of admission, with NSTEMI patients coming to the emergency room at the time span of 9 hours and STEMI patients at 7 hours from the onset of chest pain until diagnosis was established (Table 2), so that the myocardial infarction state has not had an effect on potassium levels, which is due to the opposite mechanism between the dilution effect by vasopressin with effects caused by myocardial infarction in the sodium-potassium-ATPase pump. Anoxia in the heart muscle cell membrane can cause a decrease in intracellular ATP concentration so that it will disrupt the work of the sodium-potassium-ATPase pump causing the potassium ions cannot be pumped into the cell resulting in an increase of plasma potassium levels. This would be contrary to the effects of potassium dilution by the vasopressin.

Study by Shlomai et al. in the Acute Coronary Syndrome Israeli Survey patients database with a total of 1413 ACS patients, found 1277 patients with normokalemia, 76 patients with hypokalemia and 60 patients with hyperkalemia.[19] Kaya et al. study in STEMI patients in Turkey found the changes in potassium levels from normokalemia to hypokalemia or hyperkalemia occurred in 18 – 24 hours after admission.[20]

Troponin I levels in STEMI patients in this study are significantly higher compared to NSTEMI patients. Troponin is a marker of myofibril damage and increases proportionally to the size of the infarction. The greater degree and extent of infarction in STEMI (transmural infarction) will cause more heart muscle cells to undergo necrotic lesions, leading to greater troponin I secretion. Total and persistent occlusion of the coronary arteries that occur in STEMI patients, will cause ischemia to occur in a larger area, conversely in patients with NSTEMI, the level of coronary artery obstruction varies, but without total blockage of blood vessels. The wider area of infarction will also cause greater troponin leakage from heart muscle cells undergoing myocardial necrosis.[8,10] The results of this study are in accordance with previous studies by Bhatt et al., Gonzales et al. and Salama et al. who found significantly higher cardiac troponin levels in STEMI patients compared with NSTEMI.[7-8,10]

NT-ProBNP has been known to increase in heart failure caused by the effect of distension on heart muscle cells, but the specificity of NT-ProBNP for heart failure is still quite low (44 – 57% for non-acute heart failure and 66 – 67% for acute heart failure), indicating that there is a mechanism other than ventricular stretching that can stimulate the release of NT-ProBNP.[21]

This study find that NT-ProBNP levels in STEMI patients are significantly higher compared to NSTEMI patients. Study by Gegenava et al. found that plasma NT-ProBNP levels increased significantly in patients with cardiac ischemia without concomitant left ventricular dysfunction.[22] Durak-Nalbantić et al. have demonstrated that released NT-ProBNP levels in myocardial infarction was positively related to the extent and degree of infarction affected by the number of blood vessels involved and the

percentage of stenosis.[23] Higher NT-ProBNP secretion in STEMI is thought to be a direct response of heart muscle cells in infarct and peri-infarct areas to the STEMI's greater ischemic insult and longer ischemic duration.[21-23] Higher NT-ProBNP levels in STEMI can also occur because distension effect on heart muscle cells due to greater ventricular dysfunction in STEMI.[24]

CONCLUSION

Lower sodium and chloride levels, higher troponin I and NT-ProBNP levels tend to occur in STEMI patients compared with NSTEMI. Although still in the normal range, sodium levels were found to be significantly lower in STEMI conditions compared to NSTEMI, so STEMI patients are more susceptible to hyponatremia. This must be considered in STEMI patients so that management of electrolyte disturbances can be early carried out. Although there were different results in various previous studies on NT-ProBNP levels in myocardial infarction, this study found significantly higher NT-ProBNP levels in STEMI compared to NSTEMI patients.

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