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Correlation between Ubiquinone Levels, Lactate Dehydrogenase, and Lactate on Acute Myocardial Infarction

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ABSTRACT

Ubiquinone is an antioxidant that plays a role in preventing endothelial damage, thereby reducing the risk of myocardial infarction. In myocardial infarction, there is a decrease in ubiquinone levels and energy production in the form of ATP. Both stimulate anaerobic metabolism, which increases lactate dehydrogenase and lactate levels. This study aimed to analyze the correlation between ubiquinone levels, lactate dehydrogenase levels, and lactate levels in patients with acute myocardial infarction. This study was an analytical observational study with a cross-sectional approach. The normality of data was analyzed using the Kolmogorov-Smirnov test, and the correlation among variables was analyzed using the Spearman Rank test. The number of research subjects was 52, consisting of 25 research subjects with STEMI and 27 with NSTEMI. The median of ubiquinone, LDH, and lactate levels was 12.52 ng/mL (5.6–412.2); 310 U/L (3-1212); and 4 mmol/L (0.8 – 22), respectively. The correlation test results between ubiquinone levels with LDH levels obtained p=0.4 with r=-0.35; correlation test results between LDH levels and lactate levels obtained p=0.09, with r = -0.14. There was no correlation between acute myocardial infarct patients' ubiquinone levels, LDH levels, and lactate levels in AMI patients.

Keywords: Acute myocardial infarct, ubiquinone, lactate

INTRODUCTION

Atherosclerosis is a chronic condition, which occurs slowly due to an imbalance between free radicals and antioxidants facilitated by lipid levels in the blood. Complications of atherosclerosis are very dependent on the site of the affected blood vessels, including during a heart attack or known as Acute Myocardial Infarction (AMI). [1,2]

Ubiquinone or also called coenzyme Q-10 (CoQ10) is an antioxidant that neutralizes free radicals, thus playing a role in preventing endothelial dysfunction. There are many ubiquinone functions, including antioxidants, transport electrons, and produce energy. The higher levels of free radicals circulating in the human body result in lower ubiquinone levels due to excessive use.[3]

At myocardial infarction, lack of oxygen will cause heart muscle cells to not contract. This is caused by a lack of energy supply in adenosine triphosphate (ATP). Ubiquinone plays an essential role in providing ATP through the electron transport mechanism. Cardiac metabolism will continue anaerobically, which requires the enzyme lactate dehydrogenase (LDH) and produces lactic acid. LDH is in the cell in high concentration; it escapes from damaged cells after the MI or anoxia. LDH levels in serum are related to the size, site, and severity of the myocardial infarction.[3,4]

Anaerobic metabolism is needed for the heart to contract properly. However, this metabolic compensation will increase lactate levels in heart muscle cells. LDH is also a marker of cardiac infarction in addition to troponin and Creatine Kinase Myocardial Band (CKMB). Elevated LDH and lactate in myocardial infarction are strongly associated with patient mortality.[4,5]

Based on the background, this study aimed to analyze the correlation between ubiquinone levels with LDH and lactate levels in acute myocardial infarction patients.

METHOD

This research design was an analytic observational study with a cross-sectional approach.

This research was conducted at the Dr. Kariadi Central Hospital and Diponegoro National Hospital, Semarang. This research was conducted from February to September 2020. It has received approval from ethical clearance from the Ethics Commission of Dr. Kariadi Central General Hospital with number 576/EC/KEPK-RSDK/2020 and permission from both hospitals.

Electrocardiography, Troponin I, and CKMB parameters were tested at each hospital to confirm the diagnosis of myocardial infarction, according to America Heart Association.[3] Ubiquinone test was carried out at the "Gangguan Akibat Kekurangan Yodium" Laboratory, Faculty of Medicine Diponegoro University, Semarang. LDH and lactate levels were measured in the central clinical pathology laboratory, Faculty of Medicine Diponegoro University. The CKMB levels were measured using an Indiko chemical analyzer using reagents from thermo-scientific. Troponin I levels were measured using the I-Chroma analyzer with reagents from Boditech. Ubiquinone levels were measured using the biosensor ELISA method.

The population reached in this study were patients who suffered from angina and chest pain. The target population was patients with angina who came to Dr. Kariadi Central Hospital and National Diponegoro Hospital and were diagnosed with acute myocardial infarction by the doctor in charge. Diagnosis of AMI was supported by laboratory test results of cardiac enzyme marker troponin I > 0.03 ng/ml or creatinine kinase myocardial band (CKMB) > 25ng/mL.[6] The research subjects were obtained by consecutive sampling.

The inclusion criteria for the research subject were age 35 years and above, was not febrile (temperature < 37.5^{0}C), and was not suffering from severe anemia (Hb>7g/dL). Meanwhile, the exclusion criteria were patients who had been diagnosed with malignancy and consumed ubiquinone.

Data were collected from anamnesis interviews, physical examinations, and laboratory test results of research samples. The collected data were then processed using computer software. Univariate analysis was performed on each subject characteristic. Bivariate analysis was conducted to analyze the correlation between ubiquinone levels, LDH levels, and blood lactate levels.

RESULTS AND DISCUSSIONS

The research was conducted at Dr. Kariadi Central Hospital and National Diponegoro Hospital Semarang from April to September 2020. The number of samples was 52 patients with AMI who received treatment at both hospitals within less than 1 day of the chest pain. The characteristics of the research data can be seen in Table 1.

The Spearman's rank test used to analyze the correlation between ubiquinone levels and LDH levels showed p=0.40; r = -0.35. These results indicated that there was no significant correlation between ubiquinone levels and LDH levels (Figure 1).

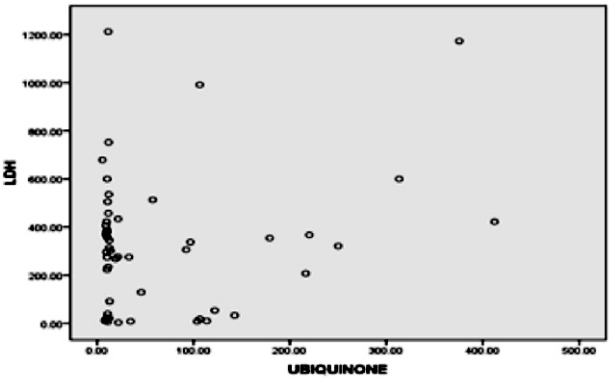

Figure 1. No significant correlation between ubiquinone and LDH levels in myocardial infarction

Table 1. Characteristics of research subjects

Variable	Mean±SD	Median (minimum-maximum)	p*
Age (years)	57.96±9.83	57 (35–87)	0.07
Gender			
Male n= 34 (65.4%)			
Female n= 18 (34.6%)			
Ubiquinone (ng/mL)	65.71±97.70	12.52 (5.60–412.20)	<0.001
LDH (U/L)	322.21±281.51	310 (3–1212)	<0.001
Lactate (mmol/L)	5.20±4.22	4 (0.80–22.00)	<0.001
Troponin I (ng/mL)	17.10±20.72	3.06 (0.1–50.00)	<0.001
CKMB (U/L)	259.02±379.90	60 (12–2090)	<0.001

(*) Normality test using Kolmogorov-Smirnov, p> 0.05 indicated normality

The Spearman's rank test used to analyze the correlation between LDH levels and lactate levels showed p=0.09; r= -0.18. These results indicated that there was no significant relationship between LDH levels and lactate levels (Figure 2).

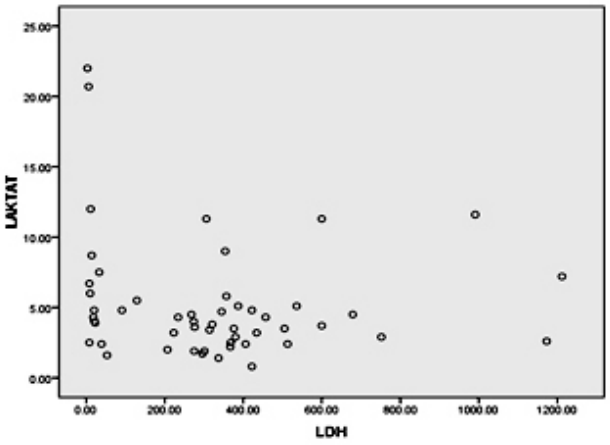

Figure 2. No significant correlation between LDH levels and lactate in myocardial infarction

Acute myocardial infarction is heart muscle cell damage caused by coronary atherosclerosis. Atherosclerosis is caused by endothelial dysfunction in the tunica intima of blood vessels. Endothelial dysfunction is caused by the accumulation of free radicals that exceed the ability of antioxidants to neutralize and cause oxidative stress. Oxidative stress plays an essential role in developing this disease, thus leading to a theory suggesting that antioxidants can reduce the risk of AMI.[6]

Ubiquinone is the oxidized form of coenzyme Q10 produced by the inner mitochondrial membrane. Ubiquinone is found in all organ systems, with the highest concentrations observed in the heart, kidneys, liver, and muscles. An essential role of ubiquinone is as an intercellular antioxidant that protects the plasma membrane against peroxidation reactions.[7]

This study results showed that all the 52 research subjects had ubiquinone levels below the reference value (<2100 ng/mL).[8] This is due to the accumulation of free radicals in the atherosclerosis process, which will reduce ubiquinone levels. Ubiquinone plays a role in supporting proper cell function. Many degenerative diseases and conditions are associated with ubiquinone deficiency, such as diabetes mellitus, disease, muscular dystrophy, Alzheimer's, Parkinson's, etc.[9]

Atherosclerosis will cause a reduced supply of oxygen to the heart muscle cells. Oxygen is needed by the heart muscle to produce ATP as an energy source for contraction. Lian revealed that the higher amount of ATP will result in a greater cardioprotective effect.[7,10] Ubiquinone also plays a role in forming ATP through the electron transport process. Ubiquinone is vital when there is a reduction in ATP in AMI.[11-13]

The process of glycolysis is the most important metabolic pathway in cardiac contractility because ATP as its product is needed as an energy component in cardiac muscle cells to distribute blood and oxygen to other organs. When an infarct is found in the heart muscle, the oxygen supply decreases, reducing ATP production. However, even in infarction conditions, the required amount of ATP remains the same as in normal conditions.[14,15]

There was no correlation between ubiquinone levels and LDH in this study. This is because LDH is a late infarct myocardial marker or cardiac enzyme parameter that increases last compared to other parameters. One of the reasons why LDH is no longer used in the diagnosis of myocardial infarction is because LDH increases approximately 24 hours after myocardial infarction and lasts up to 4 days after AMI occurs. This is the main reason for LDH use in the diagnosis of AMI, which is delayed in getting treatment at the hospital. LDH is the most recent marker of myocardial infarction to rise compared to other infarct parameters. AMI emergencies that require rapid treatment have caused the use of LDH for diagnosis less popular than troponin and CKMB.[16,17] Hermanindes revealed that LDH levels may be elevated at the onset of myocardial infarction but have a poor mortality prognosis.[18]

The end product of lactate metabolism is lactic acid.[19] Hyperlactatemia in patients with myocardial infarction can be caused by type A and type B lactic acidosis. Myocardial infarction decreases tissue oxygenation, renal perfusion, and cardiac output. This tissue hypoperfusion causes type A lactic acidosis. The local inflammation caused by myocardial infarction can increase glycolysis and cause type B lactic acidosis.[20]

This study obtained different results from the existing theory because LDH levels and lactate levels did not correlate to AMI. This is because the production of lactate with glucose is closely related. Jorge found that the stress response triggers hyperlactatemia and hyperglycemia. Adrenergic stimulation triggers the glycolysis process, which enables lactate production in a coma; therefore, lactate levels are influenced by high and low glucose levels in the body.[21]

The requirement to consider the time of infarction remained the limitation of this study. The

role of time dramatically affects LDH and lactate levels as markers of myocardial infarction.

CONCLUSIONS AND SUGGESTIONS

There was no correlation between ubiquinone levels, LDH levels, and lactate levels in AMI patients. Ubiquinone cannot be used in cases of acute myocardial infarction.

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