ABSTRAK

PENGARUH TERAPI DISLIPIDEMIA TERHADAP KADAR AKTIVITAS *CREATININ KINASE* (CK) PADA PENDERITA PENYAKIT JANTUNG DI RS UNIVERSITAS AIRLANGGA

Latar belakang : Penyakit kardiovaskular merupakan masalah kesehatan yang penting di wilayah Asia Pasifik. Beberapa penelitian hingga saat ini menemukan bahwa dislipidemia sebagai penyebab morbiditas, mortalitas, dan memerlukan biaya pengobatan yang tinggi. Dislipidemia merupakan salah satu faktor risiko aterosklerosis. Terapi dislipidemia yang banyak digunakan adalah statin. Statin sering menimbulkan gangguan pada otot berupa mialgia, miopati dan rabdomiolisis yang bisa menyebabkan kematian.

Metode : Rancangan penelitian kohort prospektif dilakukan di RS UNAIR Surabaya pada periode April-November 2019. Sebanyak 26 pasang sampel yang meliputi 13 sampel diterapi atorvastatin dan 13 sampel diterapi simvastatin. Subyek tersebut dilakukan pemeriksaan kadar aktivitas *Creatinine Kinase* (CK). Pemeriksaan CK menggunakan metode enzimatik. Analisis digunakan uji *t–paired* bila distribusi normal, sedangkan bila data terdistribusi tidak normal dihitung dengan *wilcoxon rank test*.

Hasil dan Pembahasan : Rerata kadar CK pada kelompok atorvastatin sebelum diterapi 105,71 IU/L dan setelah terapi 100,03 IU/L, disebabkan karena subyek didiagnosis dengan sindrom koroner akut dan pengambilan darah dilakukan saat kondisi akut. Median kadar CK pada kelompok simvastatin didapatkan 85,5 IU/L sebelum terapi, 118,1 IU/L setelah diterapi, dan terdapat perbedaan bermakna kadar CK sebelum dan setelah terapi. Hal ini dikarenakan simvastatin sangat rentan terhadap interaksi obat tertentu yang dapat meningkatkan konsentrasi statin di serum.

Simpulan: Terdapat perbedaan kadar aktivitas CK sebelum dan setelah terapi simvastatin.

Kata kunci : Dislipidemia, atorvastatin, simvastatin, CK, metode enzimatik

ABSTRACT

EFFECT OF THE DYSLIPIDEMIA THERAPY ON LEVELS OF CREATININ KINASE ACTIVITY IN PATIENTS WITH HEART DISEASE IN THE AIRLANGGA UNIVERSITY HOSPITAL

Background: Cardiovascular disease is an important health problem in the Asia Pacific region. To date, several studies have found that dyslipidemia is a cause for morbidity, mortality, and requires high medical costs. Dyslipidemia is a risk factor for atherosclerosis. The most widely used therapy for dyslipidemia are statins. Statin often cause muscle disorders in the form of myalgia, myopathy, rhabdomyolysis and can cause death.

Method: A prospective cohort study design was carried out at the Airlangga University Hospital Surabaya during April - November 2019. A total of 26 sample pairs containing 13 samples were treated with atorvastatin and 13 samples were treated with simvastatin. The subjects were examined for the activity level of Creatinine Kinase (CK). CK examination used enzymatic methods. The analysis used the T-paired test if the distribution was normal, whereas if the data were not normally distributed Wilcoxon rank test was applied.

Results and Discussion: The mean CK levels in the atorvastatin group before being treated 105.71 IU/L and after being treated 100.03 IU/L,because the subjects were diagnosed with acute coronary syndromes and blood sampling was performed during the acute condition. The median CK levels in the simvastatin group before being treated 85.5 IU/L and after therapy 118.1 IU/L and there were significant differences in CK levels before and after therapy. This was because simvastatin was very suspectible to certain drug interactions that could increase the concentration of statin in the serum.

Conclusions: There were differences in levels of CK activity before and after simvastatin therapy.

Key Words: Dyslipidemia, atorvastatin, simvastatin, CK, enzymatic method

RINGKASAN

Dislipidemia merupakan suatu kelainan metabolik (peningkatan kolesterol dan trigliserida) yang dapat menyebabkan morbiditas, mortalitas dan biaya pengobatan yang tinggi. Dislipidemia merupakan faktor risiko utama untuk aterosklerosis. Manifestasi klinis dari arteriosklerosis ditemukan pada penyakit arteri koroner, stroke iskemik, dan penyakit oklusi vaskular perifer. Perubahan gaya hidup terapeutik merupakan terapi lini pertama untuk mengurangi kadar kolesterol LDL pada orang yang berisiko terjadi aterosklerosis.Selain perubahan gaya hidup diperlukan juga terapi untuk dislipidemia, salah satunya dengan pemberian terapi statin.

Terapi statin merupakan terapi hiperkolesterol yang banyak diresepkan dan berhasil mengurangi risiko yang terkait dengan penyakit kardiovaskuler . Efek samping paling sering dikaitkan dengan terapi statin meliputi kram otot, nyeri otot, kelelahan otot, kelemahan otot, dan kerusakan otot yang dapat menyebabkan suatu kematian. Berdasarkan *National Lipids Association's* (NLA) *Muscle Expert Panel* tahun 2014 menekankan pentingnya standardisasi terapi statin terkait miopati. Pengelolaan yang dilakukan terkait miopati akibat terapi statin adalah menghentikan terapi statin atau *rechallenge* dengan terapi statin yang sama atau golongan statin yang lainnya.

Creatine Kinase (CK) adalah enzim dengan berat molekul sekitar 82 KDa yang terkait dengan regenerasi Adenosine Trifosfat (ATP) pada sistem kontraksi otot atau trasportasi. CK pertama kali diidentifikasi pada tahun 1934 oleh K. Lohman di jaringan otot. Pertengahan tahun 1990-an kadar CK diteliti sebagai marker dalam mendiagnosis suatu infark miokard pada penderita yang mengalami nyeri dada yang dirawat di ruang gawat darurat. Adanya peningkatan kadar CK terkait erat dengan kerusakan sel otot atau penyakit. Gangguan selular ini akan menyebabkan CK keluar dari sel dan masuk ke dalam serum darah. CK diekspresikan sangat tinggi dalam jaringan yang mudah tereksitasi sehingga membutuhkan aliran energi yang besar. Tujuan dari penelitian ini adalah menganalisis perngaruh efek samping terapi dislipidemia terhadap kadar aktivitas CK pada penderita jantung di RS Universitas Airlangga Surabaya.

Penelitian ini merupakan penelitian analitik observasional dengan desain kohort prospektif. Pengambilan sampel dilakukan di RS Universitas Airlangga selama periode Agustus–November 2019. Penelitian ini mendapatkan 26 pasang sampel yang meliputi 13 sampel diterapi atorvastatin dan 13 sampel diterapi simvastatin.

Uji normalitas dengan uji Saphiro-Wilk menunjukkan data kadar aktivitas CK pada pasien yang diterapi atorvastatin menunjukkan data terdistribusi normal, sedangkan yang diterapi simvastatin tidak terdistribusi normal. Hasil penelitian didapatkan rerata kadar CK pada kelompok atorvastatin sebelum diterapi 105,71 IU/L dan setelah terapi 100,03 IU/L. Rerata perbedaan CK sebelum dan setelah terapi pada kelompok atorvastatin menggunakan uji *t-paired* menunjukkan tidak

terdapat perbedaan bermakna dengan p = 0,738. Median kadar CK pada kelompok simvastatin didapatkan 85,5 IU/L sebelum terapi, 118,1 IU/L setelah diterapi, dan terdapat perbedaan bermakna kadar CK sebelum dan setelah terapi. Uji *Wilcoxon* digunakan untuk menilai perbedaan CK sebelum dan setelah terapi pada kelompok simvastatin menunjukkan terdapat perbedaan bermakna. Uji *Mann-Whitney* untuk analisis perubahan kadar CK pada atorvastatin dan simvastatin menunjukkan tidak terdapat perbedaan bermakna.

Penelitian ini menyimpulkan bahwa terdapat perbedaan bermakna kadar aktivitas CK sebelum dan setelah terapi simvastatin. sehingga perlu dilakukan penelitian lebih lanjut untuk mencari faktor lainnya yang mempengaruhi peningkatan kadar aktivitas CK dan menentukan nilai *cut off* CK pada penderita jantung yang diterapi statin.

SUMMARY

Dyslipidemia is a metabolic disorder (an increase in cholesterol and triglycerides) that can cause morbidity, mortality and high medical costs. Dyslipidemia is a major risk factor for atherosclerosis. Clinical manifestations of arteriosclerosis are found in coronary artery disease, ischemic stroke, and peripheral vascular occlusion. Therapeutic lifestyle changes are the first-line therapy to reduce LDL cholesterol levels in people who are at risk of atherosclerosis. Besides lifestyle changes, therapy for dyslipidemia is also needed, one of which is by giving statin therapy.

Statin therapy is an anti hypercholesterolemia therapy that is widely prescribed and successfully reduces the risk associated with cardiovascular disease. Side effects most often associated with statin therapy include muscle cramps, muscle aches, muscle fatigue, muscle weakness, and muscle damage that can cause death. Based on the National Lipids Association's (NLA) Muscle Expert Panel in 2014 stressed the importance of standardization of statin therapy related to myopathy. Management carried out related to myopathy due to statin therapy is to stop statin or rechallenge therapy with the same statin therapy or other statin classes.

Creatine Kinase (CK) is an enzyme with a molecular weight of about 82 KDa that is associated with the regeneration of Adenosine Triphosphate (ATP) in the muscular contraction or transportation system. CK was first identified in 1934 by Lohman in muscle tissue. In the mid 1990s CK levels were studied as markers in diagnosing a myocardial infarction in patients with chest pain who were treated in the emergency room. An increase in CK levels is closely related to cell damage to muscle cells or disease. This cellular disorder will cause CK to exit the cell and enter the blood serum. CK is expressed very high in an easily excited tissue that requires a large flow of energy. The purpose of this study was to analyze the effect of side effects of dyslipidemia therapy on the level of CK activity in cardiac patients at the Airlangga University Hospital, Surabaya.

This was an observational analytical study with a prospective cohort design. Sampling was carried out at the Airlangga University Hospital during August-November 2019. This study obtained 26 pairs of samples which included 13 samples treated with atorvastatin and 13 samples treated with simvastatin.

The normality test with the Saphiro-Wilk test showed data on the level of CK activity in patients treated with atorvastatin having normally distributed data, while those treated with simvastatin were not normally distributed. The results showed mean CK levels in the atorvastatin group before being treated 105.71 IU / L and after therapy 100.03 IU/L. The mean CK difference before and after therapy in the atorvastatin group using the t-paired test showed no significant difference with p = 0.738. Median CK levels in the simvastatin group were 85.5 IU / L before therapy, 118.1 IU / L after treatment, and there were significant differences in CK levels

before and after therapy. The Wilcoxon test was used to assess differences in CK before and after therapy in the simvastatin group showed significant differences. Mann-Whitney test for analysis of changes in CK levels in atorvastatin and simvastatin showed no significant difference.

This study concluded that there were significant differences in levels of CK activity before and after simvastatin therapy. So further research is needed to look for other factors that influence the increase in the level of CK activity and determine the CK cut-off value in cardiac patients treated with statins.