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The Effect of Kemuning Leaves (*Murraya paniculata* (L.) Jack) Infusion on SGOT and SGPT Enzym Activities in Obese Patients

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ABSTRACT

Obesity or excess body weight may cause fatty liver that can be diagnosed by the increase of SGOT and SGPT enzymes activity. Kemuning leaves, not only act as antiobesity, but also act as hepatoprotecor from its content of flavonoid which act as an antioxidant to liver cells. The aim of this research is to know the effect of kemuning leaves (*Murraya paniculata* (L.) Jack) infusion to SGOT and SGPT enzymes activity in obese patients. This study used 15 obese male aged 25-50 years as participants. The patients was given a 250 mL kemuning leaves infusion treatment twice a day after meal for 15 days. SGOT and SGPT enzymes serum level of participants were measured and compared before and after consumption of kemuning leaves infusion. The average value of SGOT pretest is 35,87 U/l, SGPT 41,20 U/l, and postest SGOT 25,47 U/l, SGPT 31,67 U/l with Paired T test bivariate analysis of SGOT p=0,011 and SGPT p=0,032. Kemuning leaves infusion could decrease SGOT and SGPT enzymes activity in obese patients.

Keywords: Infusion, Kemuning leaves, Murraya paniculata, Obesity, SGOT, SGPT.

INTRODUCTION

There are at least 2,8 million people worldwide die every year because of obesity. Most of the world population lives in the countries which overweight kills more people than underweight. Excess weight leads to bad metabolic effects towards blood pressure, cholesterol, triglyceride and insulin resistance. According to World Health Organization (WHO), the increase of Body Mass Index (BMI) is associated with the increase of coroner heart disease risk, diabetes mellitus, fatty liver, and various kind of cancer such as breast cancer, bowel cancer, prostate cancer and many more. Excess weight that was once considered as a disease that only occured in first world countries is now increasing in second and third world countries, especially suburban[1].

Indonesia, as a developing country that keeps on going to urbanization with sendetary life style, has increasing prevalence of obesity. According to the report of Basic Health Research of Indonesia (Riskesdas) in 2013, the prevalence of obese adult men (>18 years) in 2013 is 19,7%. This number is higher than in 2007 (13,9%) and 2010 (7,8%) and is predicted to keep on increasing in the following years[2].

Excess fat accumulation that occured in obese patients can interfere with the liver function as the main organ that controls fat metabolism of the body. When the input of fatty acid is higher than it's output, a condition called fatty liver may develop. In present times, the prevalence of non-alcoholic fatty liver disease (NAFLD) worldwide is increasing rapidly, reciprocal to the increasing prevalence of obesity[3].

The severe NAFLD spectrum, non-alcoholic steatohepatitis (NASH), is estimatedly occur in 2-3% of world population and increase in the obesity patients up to 80%. Central obesity and diabetes is the main and most occuring risk factors. Survey by Hasan in urban population of Jakarta with liver ultrasonography (USG) showed that the prevalence of NAFLD is estimatedly 30%. In RSUP dr. Kariadi Semarang, with the same method, a survey in 2005-2009 showed an increasing number of NAFLD case from year to year, consecutively 4%, 4.5%, 5%, 6% and 7%[4].

Diagnosis of NAFLD clinically using various types of lab examination, such as: liver radiology such as ultrasonography (USG), computeried tomography (CT SCAN), magnetic resonance imaging (MRI) and fibroscan, lab examination such as serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) enzymes, and liver histopathology. Currently, a liver biopsy remains the only reliable way to precisely diagnose NAFLD and establish the severity of liver injury, presence of fibrosis and architecture remodelling. However, the cost and intrinsic invasive procedure of a liver biopsy rules it out as a gold standard diagnostic test, and the imaging test are not the best choice due to the price, and currently is being refined. A cheap, convenient and non-invasive examinations, such as serum biomarkers including SGOT and SGPT, have been developed to diagnose and also to evaluate treatment response of NAFLD patients, which increase of SGOT, SGPT, or both may be found[5,6,7].

Indonesia is a developing country that is rich in plants variousity that has a huge potential to be developed as medicine. The shifting of people point of view to back to nature habit, leads to increase in herbal medicine growth and development in Indonesia, moreover with the *jamu* scientification program from Health Department that aims to the increasing of *jamu* use in medical site, especially among doctors. This leads to more utilization of herbal medicine to cure diseases. One of the plants that is known to have effects in lowering body weights is kemuning[8].

Kemuning (*Murraya paniculata* (L.) Jack) grows wild and blooms every year in tropical countries and commonly found in Indonesia. Kemuning has been known and used since ancient era by Indonesian people as family herbal medicine. An in-vivo study of the effectivity of kemuning leaves extract in lowering body weight in obese rats showed a significant result. The flavonoid in kemuning leaves also proven to be antioxidant that may be hepatoprotector. Therefore, we are attracted to do a research on the effects of kemuning leaves simplicia to SGOT and SGPT enzymes activity in obese patients[9].

MATERIALS AND METHODS

Patients eligibility

Fifteen adult men employees of Unila (University of Lampung) aged 25-50 years with obesity (BMI >25 kg/m^2) were treated with 250 mL kemuning leaves infusion twice a day after meal for 15 days around December 2016. All patients were screened to make sure that they are not: (a) in a diet program; (b) taking any prescriptions; (c) having medical history of congenital or acquired liver disease; (d) suffering from metabolic syndromes or degenerative diseases (such as diabetes mellitus, hypertension, cancer, etc.) that made them excluded. Prior to the treatment, participants were informed about the entire procedure, effects and possible side effects of the treatment that might occur and written informed consent was obtained afterwards. The procedure of the reasearch was approved by the Ethical Commitee of Medical Faculty of Unila.

Treatment

The participants underwent 15 days treatment of kemuning leaves infusion made from boiling 15 g of dry kemuning leaves simplicia in 500 cc boiled water (70^{o}C) for about 15 minutes or until the volume reduced by half (250 cc). Than the solution was being strained from the leftover sludge

to make an infusion for one drink. Two cups of one dose (250 cc) of infusion was given to the patients every day at their workstation for them to drink twice a day, subsequent to breakfast and dinner. During the treatment, patients were not given any restrictions to their daily diet.

Measurements

Medical history, body weight (kg) and height (m) to measure BMI (kg/m^2) were measured and recorded prior to the tretment. Serum level of SGOT and SGPT enzymes (U/l) were measured twice, before and afrer the treatment. Participants were continously monitored and observed for adverse reactions and any specific symptoms that appeared during the study were recorded for safety. The participants were explained about the possible side effects of kemuning leaves infusion consumption such as light headedness, mild dizziness, nausea, vomit, constipation, or polyuria, and were ordered to subjectively record if any of those symptoms occured during the treatment[10].

The presentation of the data were in mean ± standard deviation. Normality tests of Shapiro-Wilk were conducted and showed the result of $p > 0.05$ which signified that the distribution of the data variables were normal. The mean difference between before and after treatment of the participants were evaluated using paired t-tests method and showed a statistical significant level of $p < 0.05$[11].

RESULTS

Participants characteristics

Of the 15 participants, the average of age were 41.87 ± 8.193 years and the average of BMI were 30 ± 4.595. When classified according to WHO guidelines for Asia-Pacific Region, 11 patients were obese and 4 patients were severely obese[1].

SGOT and SGPT

The SGOT level decreased from 35.87 ± 12.35 to 25.47 ± 4.60 U/l with statistical significance (p = 0,011) and the SGPT level decreased from 41.20 ± 9.56 to 31.67 ± 9.57 U/l with statistical significance (p = 0,032). The result of SGOT and SGPT changes is shown in Table 1.

DISCUSSION

Obesity patients has 60-80% of developing NAFLD that is marked by mild to moderate increase of liver enzymes serum level. The pathogenesis of NAFLD is still not completely explained; however, current evidence suggest that lipid peroxidation and insulin resistance play a significant role in the development of NAFLD[12]. Excess fat accumulation for a long period of time in obese patients leads to oxidative stress of liver cells which is responsible for fat metabolism. Oxidative stress in cells activate the inflamation cytokines to start inflammatory response to destroy the excess fats. But, the cytokines end up destroying the normal cells as well and caused changes in cell morphology, cell injury and death, and formation of fibrotic tissue in liver[10]. So, the treatment for obesity also requires a protection for the liver cells. Based on Indonesia Department of Health Constitution No. 6/2016 about Indonesian Herbal Drugs Formularium (FOHAI) kemuning leaves is a recommended herbs to used as antiobesity with no reported side effects[10].

Antioxidants represent potential therapeutic target for NAFLD patients. Vitamin E, vitamin C, and betaine have all been studied in NAFLD populations, with evidence supporting some modest benefit from vitamin E, although this is tempered by concerns about effects on cardiovascular health, all-cause mortality, and prostate cancer.[13,14] Medications classified as cytoprotective agents, including

Tabel 1: Changes of serum liver markers after treatment of kemuning leaves infusion

Item	Before Treatment	After Treatment	Z score
SGOT (U/l)	35.87 ± 12.35	25.47 ± 4.60	- 0.147*
SGPT (U/l)	41.20 ± 9.56	31.67 ± 9.57	- 0.310*

ursodeoxycholic acid and pentoxifylline, have also been investigated with mixed results.[15,16] Similarly, medications designed to improve serum cholesterol panels have been evaluated in NAFLD populations. The evidence to date has suggested that 3-hydroxy-3-methylglutaryl-coenzyme A reductase or statins can be used safely in NAFLD populations for hyperlipidemia, but cannot be recommended for histologic benefit in NASH[17]. Weight loss medications such as orlistat have shown modest efficacy, but only when accompanied by weight loss of at least 9% body weight[18,19].

Kemuning leaves infusion promotes the healing and protecting effects to the liver cells by 3 methods: (1) lowering body weight by decreasing appetite and increasing excretion that leads to reduction of fat accumulation; (2) bonds competitively with lipase enzym so fat absorption is reduced; (3) flavonoid content acts as antioxidant and immunomodulator. Kemuning leaves effect as a hepatoprotector is measured by the repair of liver cells marked by reduction of liver enzymes serum level[20,21].

Aminotransferase enzymes are sensitive to abnormalities in liver, making it the most widely used and commonly measured liver enzymes in diagnosis of clinical liver pathology. The two aminotransferases that are checked are SGOT and SGPT. These enzymes are a major element of the liver cells. But also found in lesser concentration in the muscle cells. A damaged or injured liver cell will secrete these enzymes into the blood stream, raising their blood levels. Hence raised blood levels of SGOT and SGPT signifies liver disease or injury[22]. The most common etiology of elevated SGPT levels is NAFLD[23,24]. NAFLD is a probable explanation for abnormal liver enzyme levels and a cause of asymptomatic elevation of SGPT levels[25]. NAFLD is considered to be associated with metabolic disorders, including obesity[23,26].

The aminotransferases, also referred as transaminases, catalyze the chemical reactions of amino acids by transferring amino group from the donor to the recipient of amino acid molecule[22,27]. In normal condition, SGOT is present in heart, muscle, liver, kidney and brain. When any of these tissue gets damaged, SGOT is released into the blood stream. For instance, blood SGOT level is increased in muscle injury and heart attacks. Hence, SGOT is not a specific indicator for liver tissue damage as it is elevated in other conditions than liver cells damage[22,28]. On the other hand, SGPT is normally present in large concentrations in the liver. Hence, on the condition of liver damage its level in the blood rises, thereby, serving as a specific indicator for liver injury[29]. SGPT is considered to be the most specific indicator of hepatic diseases and most closely related to liver fat accumulation[30].

To regard SGOT and SGPT as liver function tests is a commonly prevalent misnomer in medical community as they do not reflect the function of the liver. They only detect liver injury or damage caused by any type of infection and inflammatory changes. The liver may still functioning normally even in conditions when both of these enzymes are highly elevated. The normal ranges of SGOT and SGPT might differ depending on the protocols to measure them by different laboratories. In this study, the laboratory used the range of <31 U/l for normal SGOT and <41 U/l for normal SGOT serum level[22,31].

The level of SGOT and SGPT measured in this study was significantly decreased after 15 days treatment. In particular, patients with abnormal ranges of SGOT and SGPT levels before the study has recovered to the normal range. This result showed that kemuning leaves infusion promote regeneration of liver cells in obese patients due to its hepatoprotector effects[9,12].

CONCLUSSION

This study investigated the effect of kemuning leaves infusion on SGOT and SGPT enzymes activity in obese patients and the result showed that there was a statistically significant decreased of SGOT and SGPT after 15 day treatment. Additional studies with greater sample size and different dose will be necessary.

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