transfusion from HLA antibodies from previous exposure through transfusion or pregnancy, called allogeneization.

Patients number 18 was a man a platelet transfusion which have been in storage over 3 days. This patient was diagnosed with suspected ITP and bleeding gums. These patients did not experience the event may be due to the effects of medication FNHTR pre-transfusion and because there is only a risk factor platelet stored over 3 days.

Patient number 13 was a man with a diagnosis suspect of anemia aplastica and urinary tract infections. Patients never been get platelet transfusion and get sold less than 3 days. The FNHTR did not happen may be due to the effects of medication pre-transfusion.

Another study concluded that the duration of platelet storage less than 3 days associated with the lower incidence of FNHTR. Incidence of FNHTR higher after infusion of platelets stored of about 4 to 5 days. This study has several limitations. First, the number of samples of this study is less than the minimum sample size calculation that will affect the statistical analysis. Second, factors suspected to affect FNHTR not measured quantitatively.

CONCLUSION

Pre-transfusion medications with acetaminophen 650 mg and diphenhydramine 25 mg reduced the incidence of FNHTR compared to placebo in the first platelet recipients in malignancy.

REFERENCES


INTRODUCTION

Today, Non-Alcoholic Fatty Liver Disease (NAFLD) is one of clinical condition often found at hepatology area'. There is an increasing incidence of NAFLD in metabolic syndrome that consists of obesity, hyperinsulinaemia, perifer insulin resistance, diabetes mellitus, hypertigliseridaemia and hypertension’. NAFLD has a very wide clinical spectrum from the lightest to the heaviest, namely simple steatosis or non alcoholic fatty liver (NAFL), fatty liver with espouled inflammation and damage hepatocyte often called as nonalcoholic steato hepatitis (NASH), and hepatic cirrhosis, or hepatocellular carcinoma’. At this time, NAFLD is important in clinical implication as the major cause of transaminase enzyme increment in America. Besides, NAFLD has a potential capability to be liver cirrhosis and hepatocellular carcinoma’. In western population, the NAFLD prevalence ranged from 15%-20%. NAFLD prevalence in adult population at United States, Japanese and Italian revolve 15-20%; and 20-30% presented in severe phase like NASH. Studies in obese population at developed countries found 60% simple steatosis, 20-25% NASH and 2-3% cirrhosis. NAFLD incident in diabetes mellitus type 2 populations was as big as 70% and in patient with hyperlipidaemia 60%. Based on existing studies, the prevalence of NAFLD in Indonesia is 30.6%’.

Leptin is a product of gene ob molecule weighing 16kDA that expressed a lot at white adipose tissue. Leptin also detectable at center nerve system, various organ and perifer such as pancreas, liver, artless muscle, and others’. Leptin works at

ABSTRACT

Background. Non alcoholic fatty liver disease (NAFLD) is a prevalent condition associated with obesity and insulin resistance. Leptin is an adipokine which plays role in decreasing food intake and controlling energy utilization. The role of leptin pathogenesis of NAFLD remains unclear. Former studies associated with the role of leptin in NAFLE were never conducted in diabetic patients.

Aim of study. The aim of the study is to analyze the difference of leptin level in non-diabetic population between subjects with and without non-alcoholic fatty liver disease.

Method. This was a non-matching case control study in general check-up polyclinic Dr. Sardjito Hospital Yogyakarta. The inclusion criteria were aged 30-60 years old, no history of alcohol consumption > 20 gr/day, no diabetes mellitus. The exclusion criteria were viral hepatitis (B and C), rapid weight loss, steroid therapy; and pregnancy. Diagnosis of NAFLD was based on bright liver imaging from ultrasonography.

Result. There were 48 subjects, consisted of 23 subjects with NAFL and 25 subjects without NAFL. Mean of leptin level in NAFL group was higher than non NAFL group and this difference was statistically significant (20.29 ± 15.73ng/ml and 12.27 ± 10.1ng/ml; p=0.040).

Conclusion The conclusion of this study was leptin level significantly higher in non diabetic population with NAFL compared with non NAFL.

Keywords: leptin, non diabetic, non alcoholic fatty liver

RESULT

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INTRODUCTION

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hormones. Dependent variable is non alcoholic fatty liver (NAFL). Independent variable is leptin level. Other variables that evaluated were age, sex, height, body weight, body mass index, waist circumference, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, ALT, AST, and GGT.

The inclusion criteria were age 30-60 years old and willingness to join the GCU polyclinic. The study was conducted in General Check up Polyclinic at Dr. Sardjito General Hospital Yogyakarta. All subjects visited GCU in a state of fasting for 12 hours. The patients were examined for leptin, triglyceride, total cholesterol, LDL, HDL, AST, ALT, and GGT. Blood samples were obtained at Proda laboratory Yogyakarta. All subjects were divided into two groups based on USG examination, namely group with NAFL and group without NAFL. The mean of leptin level was compared in group with NAFL and group without NAFL. The sample size calculation was done at Proda Laboratory Yogyakarta. All variables were analyzed using Independent Student t test and Mann Whitney U test.

In table 1, there were differences on the mean of liver enzymes, such as AST, ALT, and GGT between group with NAFL and group without NAFL. The mean of AST in group with NAFL was 32.78±15.73 IU/l, while in group without NAFL was 17.89±12.63 IU/l. Although the mean of AST in group with NAFL was higher compared to group without NAFL, the mean of ALT in group with NAFL was 29.32±18.94 IU/l, while in group without NAFL was 20.29±15.73 IU/l. The mean of GGT in group with NAFL was 34.09±25.70 IU/l, while in group without NAFL was 29.32±18.94 IU/l. The mean of leptin in group with NAFL was 20.29±15.73 ml, while in group without NAFL was 12.27±9.08 ml.

Data displayed in mean ± Standard Deviation, all data were analyzed using Independent Student t test, * analysis X, CI: Confidence Interval, NAFL: non alcoholic fatty liver, BMI: Body Mass Index, LDL: low density lipoprotein, HDL: high density lipoprotein, TG: triglyceride, ALT: alanin aminotransferase, AST: aspartat aminotransferase, GGT: gamma glutamyltransferase.
Table 2 showed that on male subjects, there were significant differences on the mean of TG, ALT, AST, GGT, leptin, BMI, and waist circumference between group with NAFL and without NAFL. The mean of leptin level of male subjects in group with NAFL was 17.64 ± 18.16 ng/ml, while in the group without NAFL was 6.27 ± 9.93 ng/ml.

Table 3. Variation in leptin level on male subjects correlated with BMI, waist circumference, total cholesterol, triglycerides, and AST.

Table 3 showed that on female subjects there were significant differences on the mean of AST, BMI, and waist circumference between group with and without NAFL. The mean of leptin level in female subjects with NAFL was 23.19 ± 12.06 ng/ml, while in the group without NAFL was 15.09 ± 9.023 ng/ml.However, this difference was not statistically significant (p = 0.122).

Results from this study showed that the average concentrations of leptin level were higher in the group with NAFL compared to group without NAFL, and the result was consistent only on male subjects. While the difference in leptin levels between group with NAFL and group without NAFL was not statistically significant in female subjects. Results from this study is differ from previous research conducted by Huang et al. (2008) and Chitturi et al. (2002), which states that both groups of male and female leptin levels were higher in NAFLD and NASG groups compared with control 15,16. Several previous studies have also shown an increase of leptin level in group with NAFLD compared to group without NAFLD, but there is no further study analyzed in the differences of leptin level on each gender 15. Different result showed in the study by Chahalani et al. (2003) and Musso et al. (2005), ie. both studies showed that leptin level did not significantly different in the NASH group and control 15,16.

The increase of leptin levels in NAFLD probably caused by the condition of the hyperleptinemia which is related to pro inflammation. Leptin is estimated to contribute at each stage of the occurrence of NAFLD. Leptin can also strengthen the process of inflammation and fibrosis in the liver. There is an evidence that injections of leptin will lead the increasing of level of procollagen-1, TGF B1, and TNFα, which leading to inflammation and more severe liver fibrosis 15,16. This study conducted by Chitturi et al. (2002), showed the opposite result, whereas, the study showed that leptin level has no correlation with BMI on both subjects, male and female. In the study by Chitturi et al. (2002) found precisely such a significant correlation between leptin level on male with ALT and C-peptide 15,16. Mendez et al. (2005) in his research found that in NAFLD subjects; body weight, body mass index, central obesity and insulin resistance were higher than control group 17. The research on 174 NAFLD subjects with 42 controls showed that bigger waist circumference on NAFLD was indicating central obese 15. Waist circumference portrayed more body fat because it was not consisted of lots of bone structures (spine only), whereas hip circumference portrayed more body fat because it was not consisted of lots of bone structures (spine only).
The normal value of leptin on male is 2.03 to 5.63 ng/ml, whereas on female is 3.63 to 11.09 ng/ml. Based on the normal value, result of this study showed that leptin level is 5.63 ng/ml on male and on female is 10.09 ng/ml leptin levels was concluded as normal, while leptin level on male is 5.63 ng/ml and on female is 11.09 ng/ml as high leptin levels. Table 6 showed the proportion of incidence of NAFL on subjects with high leptin levels than subjects with normal leptin levels.

<table>
<thead>
<tr>
<th>Leptin</th>
<th>NAFL</th>
<th>Without NAFL</th>
<th>p</th>
<th>OR</th>
<th>CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (%)</td>
<td>18 (37.5)</td>
<td>11 (22.9)</td>
<td>0.015</td>
<td>4.582</td>
<td>1.291 – 16.267</td>
</tr>
<tr>
<td>Normal (%)</td>
<td>5 (10.4)</td>
<td>4 (29.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6. Proportion of NAFL on subject with high and normal leptin level

Analysis were using U2 test. High leptin when 2.563 ng/ml on male and 11.09 ng/ml on female. Normal leptin when < 5.63 on male and < 11.09 on female. OR: odds ratio

Table 6 showed that from the total of patients with NAFL, there were 37.5% which have high leptin level. Statistically, there were significant relation between high leptin level and NAFL (p=0.015). This study showed that subjects with high leptin levels had a higher chance 4.582 times to be NAFL compared to subjects with normal leptin levels.

Table 7. Multivariate analysis on the influence of variables to NAFL

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>S.E.</th>
<th>p</th>
<th>Exp (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.282</td>
<td>0.463</td>
<td>0.542</td>
<td>1.326</td>
</tr>
<tr>
<td>Waist Circumference</td>
<td>0.279</td>
<td>0.217</td>
<td>0.198</td>
<td>1.322</td>
</tr>
<tr>
<td>TG</td>
<td>0.038</td>
<td>0.026</td>
<td>0.146</td>
<td>1.038</td>
</tr>
<tr>
<td>HDL</td>
<td>0.051</td>
<td>0.089</td>
<td>0.091</td>
<td>1.163</td>
</tr>
<tr>
<td>ALT</td>
<td>0.006</td>
<td>0.085</td>
<td>0.727</td>
<td>1.030</td>
</tr>
<tr>
<td>AST</td>
<td>0.203</td>
<td>0.127</td>
<td>0.109</td>
<td>1.225</td>
</tr>
<tr>
<td>Leptin</td>
<td>-0.104</td>
<td>0.111</td>
<td>0.348</td>
<td>0.901</td>
</tr>
</tbody>
</table>


Table 7 showed that the logistic regression analysis on variables which influence the presence of NAFL. Table 7 showed that none of the variables tested can be used as a predictor of the occurrence of NAFL. Concentration of leptin tends to increased on group with NAFL compared to group without NAFL, but from the logistic analysis regression was meaningless.

Logistic analysis regression showed that none of the BMI, waist circumference, HDL, triglycerides, ALT, AST, and leptin can be used as a predictor for the incidence of NAFL, whereas leptin, although the levels are elevated in conditions of NAFL, was not a factor predictor of incident NAFL. This is consistent with research conducted by Chitturi et al. (2002), which states that leptin is not an independent predictor of the occurrence of inflammation of the liver or severity of liver fibrosis. Possible mechanisms underlying this was that leptin level can be influenced by many factors, such as age, sex, obesity, and the presence of diabetes mellitus. Meanwhile, the study was done by excluding patients with diabetes mellitus as the research subjects. However, the study did not control the influence of obesity, thus the research showed that most groups of NAFL were obese (BMI=25-30 kg/m²).

Insulin resistance has known to have a role in the etiology of insulin resistance and NAFLD. Diabetes mellitus is a condition which mostly associated with insulin resistance. To reduce the influence of insulin resistance in diabetes mellitus on hyperleptinemia conditions, this study was conducted in populations without diabetes mellitus. Whereas, previous studies showed that the effect of leptin on NAFLD conducted in a heterogeneous population, which also included diabetic population.

There were several weaknesses in the study. First is the study design, which did not have matched control to group with and without NAFL. Second, the subjects of the study were not randomized, so that they cannot represent the population of the study. Third, there were several factors which affect leptin level that cannot be controlled in this study, such as physical activity, diet and obesity.

Conclusion and Suggestion

From the study, we can conclude that there were differences in the mean leptin level in group with NAFL and NAFLD in non-diabetic population. The mean of leptin level concentration in group with NAFL was higher than the control group. Need to conduct further research by using a better study design, such as design with matched control cases on age, gender, BMI, or a prospective design, which will show a better known under the stronger role of leptin as a risk factor for NAFL. Besides, research must be done by using liver biopsy as a definitive diagnosis of NAFL.

REFERENCES


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