Comparison of β-Hydroxylase Enzyme 11 Serum in Obese, Overweight, and Normoweight Young Men

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ABSTRACT

Background: Previous studies showed that cardiovascular risk factor was increased in obese and overweight subjects. Obesity and cardiovascular risk factor are associated with hypothalamic-pituitary-adrenal (HPA) axis hyperactivity that causes hypercortisolism, cortisol level is associated with cardiovascular risk factor on obesity. 11 β-hydroxylase is an enzyme that involved in cortisol synthesis. The aim of this study was to investigate 11 β-Hydroxylase concentration in obesity, overweight, and normal weight young men.
Subjects and Method: This was analytic-observational study using cross-sectional design. The study was conducted at HKBP Nommensen University, Medan. The study subjects included by 76 young men aged 18-28 years old, consisting of 25 obese subjects, 25 overweight, and 25 normoweight. The concentration of 11 β-Hydroxylase was evaluated in blood sample after 10 hours fasting. The data was analyzed bivariately.
Results: Mean of 11 β-Hydroxylase concentration was 52.76 ± 44.27 in obese subjects, 70.16 ± 46.83 in overweight subjects, and 43.42 ± 27.75 in normoweight subjects. The 11 β-Hydroxylase concentration in overweight subjects was statistically higher than normoweight subjects ($p = 0.007$), but the 11 β-Hydroxylase concentration on obese subjects statistically was not different from normoweight subjects ($p = 0.362$).
Conclusion: The 11 β-Hydroxylase concentration on overweight subject is higher than normoweight subject. There is no difference of 11 β-Hydroxylase concentration on obese and normoweight subject. Mitochondrial stress and mitochondrial failure mechanism on overweight and obesity merit further investigation.

Keywords: 11 β-Hydroxylase, cortisol, obesity, overweight

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BACKGROUND

Obesity is a condition with excessive fat accumulation in adipose tissue (McPhee et al., 2011). Obesity is one of the health issues of concern to the World Health Organization (World Health Organization/ WHO) (World Health Organization, 2013). According to WHO data, the prevalence of obesity in the world continues to increase (World Health Organization, 2011; World Health Organization, 2013), including in Indonesia (Riskesdas, 2013).

Increased prevalence of excess weight, whether overweight or obesity, is one of the factors that led to an increase in the death rate from non-communicable diseases (World Health Organization, 2011). Obesity is a risk factor for many diseases such as cardiovascular disease and diabetes mellitus type 2 (Obregon, 2010; Tirosh et al., 2011; Schmidt et al., 2013; Juonala et al., 2011), hypercholesterolemia (Ramzan et al., 2011; Rizk and Yousef, 2012; Thakur and Bisht, 2010), and malignant disease (Obregon, 2010).

Obesity and risk of cardiovascular disease is closely related to hyperactivity axis hypothalamic-pituitary-adrenal which caus-

es Hypercortisolism (Anagnostis et al, 2009). A study in the United States (Russell et al., 2009) and Italy (Prodam et al., 2013) showed that cortisol levels associated with cardiovascular risk factors in obesity.

Glucocorticoid hormone cortisol is dominant in humans. This hormone is produced by the adrenal cortex fasciculate zone with the help of the enzyme 11 β-hydroxylase (Barrett et al., 2010). This enzyme is encoded by the genes cytochrome P450, family 11, subfamily B, polypeptide 1 (P45 0c11) or better known as CYP11B1 gene. This enzyme present in the cell membrane of the mitochondria of the adrenal cortex (Miller and Auchus, 2011).This study aims to compare the levels of 11 β-hydroxylase enzyme in male young adults obese, overweight and normal.

SUBJECTS AND METHOD

Design and Research Samples

This research is an analytic study with cross sectional design. Sampling was carried out research at the University of HKBP Nommensen Medan. Intake and blood tests carried out in the Clinical Laboratory Spectrum International Medan.

The samples used in this study were 75 people, divided into three groups, obese, overweight and normal groups. Obese group were male obese (BMI ≥ 25 kg/ m2 and waist circumference >90 cm), a group of men are overweight (BMI 23 to 24.9 kg/ m2 and waist circumference 80-90 cm), and the group normal is male (BMI 18.5 to 22.9 kg/ m2 and waist circumference <80 cm). Sampling was done by purposive sampling technique. The exclusion criteria were subjects who had a history of hypertension, suffering from Cushing's syndrome (based on history and clinical symptoms).

This study has received permission from the Health Research Ethics Committee Faculty of Medicine, University of North Sumatra and every research subject has given consent after an explanation (informed consent).

Measurement of Body Mass Index and Waist Circumference

The body mass index is calculated by dividing body weight (kg) by height squared (m2) and recorded 1 decimal places. Weight measurement is done using a digital scale brand Kris. Samples are asked only to use thin clothes (shirt and shorts). Height measurement performed by the meter stature breath (inspiration) long. Waist circumference was measured at the time the subject exhaling (expiratory). Measurement is performed three times and the average value of three measurements was reported as waist circumference in centimeters unit.

Examination of Blood Samples

Blood samples were taken in the morning (08:00 to 09:00) after a sample of fasting for 10-12 hours. 3 ml of blood is taken in the cubital vein, and then inserted into the tube without ethylene diaminetetraacetic acid (EDTA). Blood serum is separated and stored in a refrigerator at a temperature of -20 ° C. This serum is stable up to 4 months. The level of serum 11-β hydroxylase performed by quantitative sandwich enzyme immunoassay technique. Levels of 11-β hydroxylase samples was determined using a standard curve created by using a program Curve Expert 1.3.

Data analysis

Data analysis was done using computer software. The results are reported in the average (mean)±SD. The test results revealed statistically significant when the $p < 0.05$. Any data distribution is determined first by the Kolmogorov-Smirnov normality test. The data were not normally distributed, the transformation first. do not paired T test with 95% confidence level ($\alpha = 0.05$) is

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used to see a comparison of the average levels of the enzyme 11 β-hydroxylase in obese and overweight groups against the normal group.

RESULTS

General Characteristics of Samples

Samples were aged 18-28 years, with an average of 21 years. Samples majority (66. 7%) is Batak Toba, 14.7% are ethnic Nias, 12% Batak Karo, and Simalungun 6.7%. Picture of body mass index and waist circumference subjects of research can be seen in Table 1.

Table 1. Overview of body mass index and waist circumference research subjects

Variables	n	Min.	Max.	Mean	SD
BMI (kg/m²)	75	18.6	38.2	25.20	5.11
- Obesitas	25	26.4	38.2	31.24	3.60
- *Overweight*	25	23.0	24.9	24.29	0.67
- Normal	25	18.6	22	20.07	1.05
Waist Size (cm)	75	65	117	87.97	13.73
- Obesitas	25	94	117	104.24	7.52
- *Overweight*	25	80	90	85.54	4.09
- Normal	25	65	80	73.74	3.62

Comparative Levels of 11 β-hydroxylase in the Third Group of Samples. The average levels of 11 β-hydroxylase in the group of obese and overweight was higher than normal. The average levels of 11 β-hydroxylase is highest in the overweight group. 11 β-hydroxylase levels in the overweight group was significantly higher than normal (p= 0.013) (Table 2).

Table 2. Levels of 11 β-hydroxylase on obesity, overweight and normal

Subject	n	Mean ± SD	p
Obese	25	52.76 ± 44.27	0.007
Overweight	25	70.16 ± 46.83	0.362
Normal	25	43.42 ± 27.75	

DISCUSSION

The average value of body mass index in the obese group (31.24 kg / m2) belongs to the category of obesity grade 2 with a risk of severe morbidity (Inoue et al., 2000). The average value of waist circumference obese group (104.24 cm) was also well above normal values (Zimmet and Alberti (2006) in WHO (2008)). This shows the tendency of the high risk of morbidity in the obese group sample of this research given the age of the sample is still young (18-30 years). Previous research suggests that body mass index was positively correlated with age. The higher the age, people tend to be more easily fat (Humayun et al., 2009). The study in India showed a tendency to increased morbidity with increasing age (Andrabi et al., 2013).

The average levels of 11 β-hydroxylase in the group of obese and overweight was higher than normal group. 11 β-hydroxylase enzyme is an enzyme that catalyzes the 11-deoxycortisol into cortisol in the adrenal cortex. Increased activity of 11 β-hydroxylase showed an increase in the rate of synthesis of cortisol. This is consistent with the results of research that says that an increase in body mass index was associated with increased rate of synthesis of cortisol (Purnell et al., 2004).

Levels of 11 β-hydroxylase in overweight obtained significantly higher than

the normal group. The average levels of 11 β-hydroxylase is highest in the overweight group. Bureik et al. in Kaminski & Rogawski (2011) states that 11 β-hydroxylase is a mitochondrial enzyme that is located in the zone of the adrenal cortex fasikulata. Prasad et al. (2014) mention oxidative stress in mitochondria can occur as a result of the production of Reactive Oxygen Species (ROS) produced during the process of steroidogenesis. This will lead to oxidative stress and mitochondrial disorders in turn will affect steroidogenesis. This may explain why the average level of 11 β-hydroxylase is highest in the group of overweight and obese group the average level of 11 β-hydroxylase obtained close to the normal group. Previous research also showed that cortisol levels in basal conditions were not elevated in the obese group (Pasqualli et al in Kargi and Iacobellis, 2014).

In conclusion, the levels of 11 β-hydroxylase in the overweight group was statistically higher than the normal group, but the levels of 11 β-hydroxylase obese group did not differ significantly with the normal group. The average levels of 11 β-hydroxylase enzyme present in overweight group. The mechanism of mitochondrial stress and mitochondrial failure that occurs in overweight and obese need to be investigated further to explain why the 11 β-hydroxylase levels were higher in the obese group than the overweight group.

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