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DIFFERENCES IN LIPID PROFILES LEVELS BETWEEN MIGRAINE PATIENTS AND TENSION TYPE HEADACHE

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Abstract

Background: Headache is one the most common neurologic disorders. Various mechanism have been proposed as the pathogenesis of headache. Recently evidences have supported that lipid profiles might play a role in headache.

Methods: a cross-sectional study was performed on 62 patients migraine and TTH, aged ≥ 18 years. Diagnosis was made based on The V National Consensus of Indonesian Neurologist Association Headache Study Group. Venous blood samples were obtained from eligible subjects. Laboratory measurements of standard biochemical parameters were performed on computerized laboratory analyzers.

Results: The mean levels of total cholesterol and triglyceride significantly higher in migraine groups when compared to TTH group ($P < 0.001$). LDL was significantly higher in migraine groups than in TTH group ($P = 0.001$). Furthermore, mean HDL was not significantly different in those groups ($P = 0.437$). All of the lipid profile did not show a significant relationship with the intensity of headache ($p > 0.05$).

Conclusion: Total blood cholesterol, triglyceride, and LDL were higher in migraine patients than TTH patients. There is no significant different of HDL in both groups.

Introduction

Headache (cephalgia) is a neurological symptom where pain or discomfort is felt in all areas of the head with a lower border from the chin to the back of the head (occipital area and part of the neck)¹. Migraine and TTH are primary headaches that attack 80% of the population in world and headaches are most common in the productive age (20-55 years)². Despite its high prevalence, the pathophysiology of the logical mechanism underlying this disease is still being debated. Various different theories have been formulated to explain migraine and TTH. The relationship between neurotropic factors and migraine, neurotropic factors and TTH has been investigated as different pathophysiology³. Neurologically the cause of migraine comes from activation of the brain stem or cortical spreading depression (CSD). Pain in migraine as a result of neurogenic inflammation due to release of inflammatory neuropeptides from nerve endings on activation of the trigeminal system resulting in vasodilation, plasma extravasation and mast cell degranulation⁴. The pathogenesis of TTH is still considered to be influenced by myofascial where pericranial tenderness is significantly correlated with the intensity and frequency of chronic TTH attacks⁴.

Adiponectin has anti-inflammatory effects that can inhibit IL-6 and TNF which induce the formation of IL-8, as well as inducing anti-inflammatory cytokines such as IL-10 and IL-1RA (receptor antagonists), so that adiponectin levels are maintained high, having an effect protective against cascade inflammation causing migraines and other types of headaches, so that adiponectin in chronic headache has a pro-inflammatory effect, which was found that HMW adiponectin can educate IL-6 which has implications on the pathway that causes neurogenic inflammation in migraine^{4,5}. In the research of Rist et al (2011) it was said that in some population-based studies from the Netherlands and clinical-based studies in Austria where it was found that an increase in total cholesterol and LDL levels in patients with aura migraine and migraine without aura. Research Hamed et al (2012) reported that significantly total cholesterol, triglyceride and low density lipoprotein (LDL) levels ($P = 0.001$; $P = 0.05$; $P = 0.001$, respectively) were found to be higher in the migraine patient group compared to the migraine group TTH patient⁷. The study also found high density lipoprotein (HDL) values that were not significantly different between the two groups⁷



Method

Study sample

All patients who have been diagnosed with migraine and tension type headache based on history using the IHS Classification questionnaire (Questionnaire adapted from HO KH & Ong BK-C) in accordance with diagnostic criteria in National Consensus V Head of the Indonesian Neurology Specialist Study Group (PERDOSSI) questionnaire All migraine and TTH patients who meet the inclusion criteria will fill out a questionnaire in the form of a Visual Analog Scale (VAS) questionnaire to provide information about the intensity of headache. Taking venous blood as much as 5 cc for laboratory examination of lipid profile levels, examination by the enzymatic method colorimetric test, with Automatic Architech c8000 (Abboth, Laboratories).

Study design

This descriptive analytic study with cross sectional data collection method was carried out on 62 patients aged \geq 18 years in 2 groups; 31 migraine patients and 31 TTH patients. With primary data sources obtained from all migraine sufferers and tension type headaches in the Neurology Department of the H Adam Malik General Hospital Medan and the Network Hospital. The diagnosis is based on history taking in accordance with the diagnostic criteria of the National Consensus V Group of the Head Pain Study Group of the Indonesian Neurologist Specialist (PERDOSSI) 2018.

Statistical analysis

Research data will be analyzed statistically with the help of a computer program using SPSS (Statistical Product and Science Service). Descriptive analysis was used to see the demographic characteristics of the group of tension type headache sufferers. To see the difference in total cholesterol levels between migraine patients and tension type headache, the unpaired T test is used when the data is normally distributed and the Mann Withney test if the data is not normally distributed.

Result

This research was conducted at the General Hospital. Haji Adam Malik Medan and Network Hospital in Medan. The study subjects obtained a total of 62 people who suffer from primary headaches, namely 31 people experienced migraines and 31 people experienced tension type headache (TTH). Demographic characteristics data indicate that in both groups, both migraine and tension type headache groups, the dominant research subjects were female (56.6%); with a mean age of 42 years and 47 years; body mass index is overweight; risk factors most subjects do not have risk factors; and the intensity of headache is moderate. the mean total cholesterol level in migraine patients (256.42 ± 62.278 mg / dl) was higher than in patients with TTH (201.32 ± 38.336 mg / dl), triglyceride levels in migraine patients were 160 (90-372) mg / dl higher than TTH patients 102 (70-239) mg / dl, LDL levels in migraine patients 122 (72-371) mg / dl higher than those in TTH patients 89 (50-192) mg / dl, HDL levels in migraine patients (36 mg / dl) is not much different from HDL levels in TTH patients (38 mg / dl). For complete data about the characteristics of the subject of this study are presented in table 1 below.

Table 1. Demographic Characteristics of Research Subjects

Demographic Characteristics	Migraine (n=31)	TTH (n=31)	Total (n=62)
Sex, n (%)			
Male	16 (51,6%)	11 (35,5%)	27 (43,5%)
Female	15 (48,8%)	20 (64,5%)	35 (56,5%)
Age (years), Mean\pmS.D	47,65 \pm 6,85	42,48 \pm 6,287	45,08 \pm 7,024
BMI, n(%)			
Normoweight	4 (12,9%)	11 (35,5%)	15 (24,2%)



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Overweight	13 (41,9%)	17 (54,8%)	30 (48,4%)
Obesitas	14 (45,2%)	3 (9,7%)	17 (27,4%)
Risk Factor, n(%)			
No	15 (48,4%)	14 (45,2%)	29 (46,8%)
Hypertension	0 (0,0%)	8 (25,8%)	8 (12,9%)
Hypercholesterolemia	3 (9,7%)	5 (16,1%)	8 (12,9%)
Hypertension dan Hypercholesterolemia	13 (41,9%)	4 (12,9%)	17 (27,4%)
Intensity Pain ,n(%)			
Moderate	31 (100,0%)	27 (87,1%)	58 (93,5%)
Severe	0 (0,00%)	4 (12,9%)	4 (6,5%)
Lipid Profiles Level(mg/dl)			
Total Cholesterol ,(Mean±S.D)	256,42±62,2	201,32±38,3	228,87±58,3
Triglycerides,Median (Min-Maks)	160(90-372)	102 (70-239)	122 (70-372)
LDL,Median (Min-Maks)	122 (72-371)	89 (50-192)	110 (50-371)
HDL Median (Min-Maks)	36 (28-71)	38 (14-55)	38 (14-71)

Total cholesterol level has a normal distribution of data and then analyzed by independent T test, obtained the average total cholesterol level in patients with migraine (256.42 ± 62.278 mg / dl) is higher than in patients with TTH (201.32 ± 38.336 mg / dl) with a p value <0.001 , which means that there are significant differences in total cholesterol levels between patients with migraine and TTH. Triglyceride, LDL, and HDL levels have abnormal distribution of data, so they are tested by Mann-Whitney non-parametric analysis. Triglyceride levels in migraine patients are 160 (90-372) mg / dl higher than TTH patients 102 (70-239) mg / dl, with a p value <0.001 , which means that there are significant differences in triglyceride levels between patients with migraine and TTH. LDL levels in migraine patients 122 (72-371) mg / dl are higher than TTH patients 89 (50-192) mg / dl, with a p value <0.001 , which means that there are significant differences in LDL levels between patients with migraine and TTH. HDL levels in migraine patients (36 mg / dl) are not much different from HDL levels in TTH patients (38 mg / dl), with a p value = 0.437 which means there is no significant difference in HDL levels between patients with migraine and TTH. VAS score in patients with migraine and patients with TTH is not much different, namely VAS 5, with a P value = 0.376 which means that there is no significant significant difference between VAS scores in migraine patients with TTH patients. This can be seen in table 2 below.

Table 2. Differences in lipid profile levels between migraine patients and TTH

Lipid profiles level	Migraine (n=31)	TTH (n=31)	P
Total Cholesterol (mg/dl)	256,42±62,278	201,32±38,336	$<0,001^a$
Triglycerides (mg/dl)	160 (90-372)	102 (70-239)	$<0,001^b$
LDL (mg/dl)	122 (72-371)	89 (50-192)	0,001 ^b
HDL (mg/dl)	36 (28-71)	38 (14-55)	0,437 ^b
VAS	5 (4-6)	5 (4-8)	0,376 ^b

^a Uji T- Independent ^b Uji Mann Whitney

Total cholesterol level has a normal distribution of data and then analyzed by independent T test, obtained the average total cholesterol level in the group with moderate pain was 228.83 ± 59.937 mg / dl and in the severe pain group was 229.50 ± 30.128 mg / dl, with a value of p = 0.982, which means that there is no significant



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significant difference between the average total cholesterol level of moderate pain intensity and the average total cholesterol level of severe pain intensity. Triglyceride, LDL, and HDL levels have abnormal distribution of data, so they are tested by Mann Whitney's non-parametric analysis. Based on triglyceride levels, it was found that there was no significant significant difference between triglyceride levels in moderate pain intensity (124mg / dl) and triglyceride levels in severe pain intensity (115mg / dl) with $p = 0.901$. LDL levels obtained also showed that there was no significant significant difference between LDL levels in moderate pain intensity (112.5 mg / dl) and LDL levels in severe pain intensity (93 mg / dl) with p values = 0.233. Likewise, HDL levels also showed that there was no significant significant difference between HDL levels in moderate pain intensity (38 mg / dl) and HDL levels in severe pain intensity (38 mg / dl) with $p = 0.923$. This can be seen in table 3 below.

Table 3. Differences in lipid profile levels on headache intensity

Lipid Profiles level	Pain Intensity		p
	Moderate	Severe	
Total Cholesterol	228,83±59,937	229,50±30,128	0,982 ^a
Triglycerides	124 (70-372)	115 (102-160)	0,901 ^b
LDL	112,5(50-371)	93 (78-98)	0,233 ^b
HDL	38 (14-71)	38 (35-39)	0,923 ^b

^a Uji T- Independent ^b Uji Mann Whitney

Discussion

In this study, subjects in the two majority groups were 35 women (56.5%). This study is in line with the study of Winsvold et al (2011) in the HUNT study reporting that a higher percentage of women was 62.2% in the group non migraine and 73.5% - 75.6% in the migraine group. In this study, the mean age in the migraine group was 47.65 ± 6.85 years and in the TTH group 42.48 ± 6.287 years. This study is in line with the research of Winsvold et al (2011) in the HUNT study showing the mean age in the non migraine group at 45.2 years and in the migraine group at 39.6 years and 40.6 years (migraine without aura and migraine with aura)⁸.

This study showed significant differences in total cholesterol levels ($p < 0.001$), triglycerides ($p < 0.001$) and LDL ($p = 0.001$) between the migraine and TTH groups, where the values of the three parameters were higher in the migraine group, while HDL showed differences which is not significant ($p = 0.437$) this is in line with research conducted by Hamed et al (2012) which reported that the levels of total cholesterol, triglycerides, and LDL were significantly ($p = 0.001$; $p = 0.05$; $p = 0.001$, as sequentially) was higher in the migraine group than in the TTH group. The study also found insignificant HDL values between the two groups. Increased levels of total cholesterol, triglycerides, and LDL were found to be more increased in the migraine patient group, this was related to body mass index, where in the migraine patient group in this study about 27 (87.1%) samples had excess body weight or above normal. In obesity, the formation of excess adipocyte tissue and secreting a number of factors that contribute to systemic and vascular inflammation. Proinflammatory cytokines, such as TNF- and IL-6, are produced and released from adipocytes (Konukoglu et al, 2016). Excess adipocyte tissue increases macrophage recruitment. Adipocytes are infiltrated by macrophages that locally produce pro-inflammatory cytokines, and then cause chronic inflammatory conditions^{7,8}.

In this situation, pro-inflammatory conditions also occur, which increase inflammatory mediators, vascular hyperreactivity, plasma calcitonin gene-related peptide (CGRP) concentrations, and decreased adiponectin concentrations. These changes can increase the frequency, severity, and duration of migraine attacks, which then cause central sensitization. Repeated central sensation is induced by permanent neuronal damage in the area around the periaqueductal area with poor modulation of pain and continues with chronic migraine. This theory can be attributed to the results of several studies of obese individuals, who are known to have lipid profiles that tend to be unfavorable. In a study conducted by Horev et al (2005) on obese women, 48.15% of the sample suffered from migraine and 14.81% had TTH. Peres et al. (2005) reported headache in 75% of the sample of obese women in their study, of which 66% had migraines^{7,8,9}.



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In this study, the only lipid profile that was not significantly different between the two groups was HDL. The results of this study showed no significant difference between HDL levels in migraine samples and TTH samples. This result might be attributed to HDL which has a protective role for both. As previously reported, HDL biochemically has anti-oxide, anti-inflammatory and anti-thrombotic effects on endothelial function, where endothelial dysfunction is reported to play an important role in the pathogenesis of migraine and TTH¹⁰. This study showed that the four lipid profiles did not show a significant difference between moderate and severe headache intensity ($p > 0.05$). These results are in line with the research of Gozke et al (2013) which showed no significant correlation between triglyceride and HDL levels with VAS TTH values ($p = 0.556$; $p = 0.053$, respectively) and migraine ($p = 0.883$; $p = 0.543$, respectively)¹¹. Likewise, the results of the study of Demiryurek et al (2016) reported no significant relationship between VAS and total cholesterol, LDL, HDL, and triglycerides ($p = 0.39$; $p = 0.42$; $p = 0.47$; $p = 0.24$, sequentially) on headache samples. This is because based on the theory it has been said that the intensity of headaches in migraine and TTH is the same ie moderate to severe. The pathogenesis of migraine headaches and TTH is also known together through the mechanism of peripheral sensitization and central sensitization in the trigeminovascular system, central sensitization that occurs will change normal peripheral stimulus into nociceptive stimulus^{11,12}.

Conclusion

There are significant differences in total cholesterol, triglyceride, and LDL levels between migraine and TTH patients, where total cholesterol, triglyceride, and LDL levels are higher in migraine patients. There were no significant differences in HDL levels between migraine and TTH patients. There was no significant difference in lipid profile levels on headache intensity between migraine and TTH.

Suggestion

Future studies should also involve other parameters in examining the relationship of lipid profile with migraine headaches and tension type headache so as to improve the pathophysiological understanding of headache.

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