



Potential interrelation analysis between lipid levels and migraine pain in patients with aura symptoms

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Abstract

Background: Prevalence of migraine aura (MA) is more among patients with vascular diseases. Research on many population studies have concluded the involvement of lipid levels in migraine patients but did not portray the exact mechanism behind it. **Objective:** This study aims in determining the possible link between lipid levels and pain in migraine aura patients. **Methods:** About 50 MA patients and 50 control volunteers were recruited after proper ethical clearance and informed consent and 5ml of 12hr fasting blood was isolated to check the lipid profile. **Results:** Statistically significant observations were made that confirms the altered lipid levels of TC, HDL, VLDL, LDL, TG, TG/HDL in MA patient when compared with control. **Conclusion:** Further investigations on the molecular mechanism and gene analysis are to be made to conclude the potential involvement of altered lipid levels and MA pain.

Keywords: migraine with aura, lipid profile, headache

Introduction

The International Classification of Headache Disorder (ICHD) developed by the International Headache Society (IHS) defines migraine as a common disabling primary headache disorder showing high prevalence with more personal and socio-economic impact ('Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition' 2018). They

have classified migraine into two types based on the symptoms experienced as migraine with aura (MA) and migraine without aura (MO). Migraine is listed as the third most disabling disorder as per the Global burden of disease study 2010 (GBD2010). Migraine prevalence across every population is reported to be between 2.6% and 21.7% (Burch et al., 2018). Years of life lived with disability (YLDs) is found to be around 6.5% for migraine and tension type headache with 5.1% among men and 7.7% among women.

The burden of headache is high in people between the ages 15-49 having 9.5% YLDs in 7.5% men and 11.2% women; the effects is found to be negligible among patients aged between 5-14 years (5.1%), 50-69 years (4.9%) and above 70 years (1.6%) (Stovner et al., 2018). Research on migraine is very limited due to its complex nature. But in recent years, advancements in technology for studying the human physiology and neuroscience with improved imaging studies rekindled the hope to further investigate the disorder in detail (Lance and Goadsby, 2000).

Migraine is reported as one of the symptoms in many neurological disorders like epilepsy, Parkinson's disease, stroke, dementia etc. Much research evidence is available to prove the involvement of migraine with ischemic stroke which is a vascular disorder (MacClellan et al., 2007). Improper functioning of the vascular system is the major reason behind many vascular diseases and deposition of lipids is one major concern. Involvement of lipid deposition in migraine pain progression is being investigated in many population and various observations were made (Gruber et al., 2010; Bigal, 2010). MA type as per ICHD is defined as "recurrent attacks, lasting minutes, of unilateral fully reversible visual, sensory or other central nervous system symptoms that usually develop gradually and are usually followed by headache" ('Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition' 2018). Since the symptoms are more related to vascular functioning, deposition of lipids in vessels might be a possible cause for the aura of migraine. This cross-sectional study aims in determining the levels of lipids in migraine patients with aura symptoms.

Methodology

Subject recruitment: 50 MA patients (fulfilling the ICHD-3 criteria) and 50 control (without any personal and family history of migraine) volunteers were recruited for the study after obtaining the ethical approval by the Institutional Human Ethics Committee (IHEC) of PSG Institute of Medical Sciences and Research

(Proposal No: 16/070). The Declaration of Helsinki guidelines framed by the World Medical Association (WMA) was strictly followed. The nature of the study was explained to the patient as well as the control group and written informed consent was obtained from them.

Clinical data and Sample collection: A standard questionnaire was used to collect the information regarding the current health status of the patient and control group. Migraine Disability Assessment (MIDAS) questionnaire and Headache Impact Test (HIT-6) were also used to determine the disability and impact score. About 5ml of venous blood has been collected from the subject and control group after an overnight fast of 12-hrs for lipid extraction

Lipid profile study: The total Cholesterol (T-Chol) and triglycerides were analysed using PAP enzymatic triglyceride & cholesterol kit. The standard Vertical Auto Profile (VAP) test is used to measure the subfractions of cholesterol like Very Low-Density Lipoprotein Cholesterol (VLDL-C), Low Density Lipoprotein Cholesterol (LDL-C) and High-Density Lipoprotein Cholesterol (HDL-C). The ratios of T-Chol/HDL-C and TG/HDL-C were also calculated.

Statistical Analysis: The baseline characters of MA and control were compared. The continuous and categorical values were calculated by Kruskal-Wallis and chi-square test. The IBM SPSS version 26.0 was used to statistically analyze the results obtained. The significance level was set at $p < 0.05$.

Results

Clinical data analysis

The clinical data of MA patients compared with the control group is tabulated (Table 1). The median age of the control group is 27.75 and MA group is 38.75. High blood pressure is found in patient group when compared with the control group. Severe disability is observed in women MA patients in comparison to the men MA patients. BMI and obesity are dependent variables and women MA patients are highly prone to the obesity and heavy BMI.

Table 1: Baseline characteristics of the control and MA patient groups

Parameters	Control (n=50)		Migraine with Aura (n=50)	
	Men (n=18)	Women (n=32)	Men (n=18)	Women (n=32)
Median age, years (IQR)	27 (3.25)	28.5 (4.75)	39 (5.5)	38.5 (4)
BMI, kg/m ² (IQR)	23.1 (1.65)	20.35 (1.25)	27.4 (6.43)	26.3 (5.43)
Obesity (%)	2%	5%	21%	32%
High blood pressure (%)	Nil	Nil	88%	53%
MIDAS (Severe disability %)	Nil	Nil	38%	42%
HIT-6 (Mean ± SD)	Nil	Nil	34.211 (±1.97)	56.68 (2.07)

Lipid profile analysis

The lipid profile analysis for MA and control group were stratified according to sex and tabulate in Table 2. The results show that the high levels of lipid parameters like total cholesterol, LDL cholesterol, VLDL cholesterol,

HDL cholesterol, Triglycerides and TG/HDL-cholesterol ratio show possible involvement in migraine pain of aura patients having significance at p<.05 when compared with the control group. Non-HDL cholesterol and TC/HDL-C ratio did not show possible involvement with migraine pain with no significant p values.

Table 2: Lipid profile analysis of control and MA patient groups

Lipid parameters	Control (n=50)		Migraine with Aura (MA) Median (IQR)		2	p value
	Men (n=18) Median (IQR)	Women (n=32) Median (IQR)	Men (n=18) Median (IQR)	Women (n=32) Median (IQR)		
Total cholesterol, mg/dl	171.5 (32.62)	172 (33.25)	226.15 (21.6)	218.2 (29.87)	5.0051	0.025273*
LDL- cholesterol, mg/dl	92.05 (26.75)	94 (32.75)	162 (15.5)	161.5 (20)	47.8681	<.00001*
VLDL-cholesterol, mg/dl	24.15 (7.67)	23.15 (8.87)	30.45 (1.95)	27.4 (17.52)	32.9715	<.00001*
HDL-cholesterol, mg/dl	57.55 (5.75)	57.9 (4.6)	34.35 (8.2)	34.5 (4.55)	84.64	<.00001*
Triglycerides, mg/dl	120.75 (38.37)	115.75 (44.37)	152.25 (9.75)	137 (87.62)	39.3174	<.00001*
Non-HDL cholesterol, mg/dl	115.1 (24.5)	114.75 (33.87)	190.9 (25.77)	1887.1 (26.35)	1.0417	.307434
T-Chol/HDL-C ratio	2.98 (0.53)	3.00 (0.62)	6.47 (1.97)	6.29 (1.01)	3.8402	.050036
TG/HDL-C ratio	2.00 (0.71)	2.01 (0.85)	4.45 (1.71)	3.27 (2.72)	27.4286	<.00001*

Discussion

This is a preliminary cross-sectional study involving limited participants in the patient as well as the control group to understand the possible involvement of lipid parameters in migraine aura patient. Since migraine is described as a vascular disorder with proven involvement, disruption in the vascular functioning due to accumulation of lipids in them might be one of the many possible reasons behind pain progression in the migraine aura patients (Pamela et al., 2011). The clinical evaluation revealed the presence of high blood pressure, high BMI and obesity among the migraine aura patients when compared with the control group. These are few factors that denotes the presence of high lipid levels in the body. Lipid accumulation in body can be due to many factors like consuming lipid rich food, hereditary factors, improper breakdown of lipids by the body etc. (Gordon et al., 1981; Fahy et al., 2011)

The levels of some lipid parameters like total cholesterol, LDL cholesterol, VLDL cholesterol, HDL cholesterol, Triglycerides and TG/HDL ratio were statistically found to be significant in MA patients. The exact mechanism by which the lipid levels cause migraine pain in MA patients is still a mystery, but certain theories like neuroinflammation, vascular dysfunction etc. can be related to this condition (Gruber et al., 2010). Deposition of lipids in blood vessels and other cells due to improper metabolism fails in supplying the oxygen to all the parts of the body and in particular the brain. Brain needs continuous and rich supply of oxygen for its proper functioning. Deposition of triglycerides in the arterial walls due to excess lipid intake blocks the blood supply to the brain and is found to be the major cause for aura symptoms in patients (Goulart et al., 2016). VLDL and LDL along with the HDL are known for their role in transporting the lipids to then liver for metabolism and when its levels fall, the lipids get stored up in cells causing disruption in the normal functioning (Chapman et al., 2011; Bruce et al., 2017).

This study brought out the possible involvement of lipid levels in causing the pain of MA patients. There is strong evidence for high lipid levels in MA patients but the exact cause and reason for it is to be studied. With the limitations of the study, further investigations on the pathway study and other gene analysis are to be made in relation to lipid levels and migraine patients with the aura symptoms.

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Conflict of Interest Statement

The authors declare that there is no conflict of interest in publishing this manuscript.

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