Research Article

Comparative study of lipid profile between episodic migraineurs and healthy volunteers

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Abstract

Background: The lipid profile of migraineurs showed atherogenic condition. Cardiovascular and cerebrovascular events were found to be frequent and appeared one decade earlier in migraine patients compared with the general population. No comprehensive study is available regarding these aspects in migraineurs in India.

Objectives: To compare lipid profile parameters between episodic migraineurs and healthy volunteers.

Materials and Methods: This was a case–control study performed in a sample of migraine cases selected from the Outpatient Department, G.B. Pant Hospital, New Delhi, India, and normal healthy individuals as control group were chosen from the students of medicine, Maulana Azad Medical College, New Delhi, India. Migraineurs were selected based on the clinical diagnosis by neurologists, each fulfilling the International Headache Society criteria 2004. Subjects aged between 20 and 40 years were enrolled for study irrespective of the aura status. Lipid profile parameters studied were total cholesterol, high-density lipoprotein (HDL), very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and triglycerides.

Results: The lipid profile of migraineurs showed abnormal condition. When LDL levels were compared, 24 of 54 cases and 5 of 30 controls showed abnormal levels ($P = 0.020$), whereas the remaining lipids showed no statistical significance between the two groups.

Conclusion: Atherogenic lipid profile of migraineurs in our study coincided with the results of earlier studies. LDL levels were higher in cases when compared with those of controls. The values of total cholesterol, triglycerides, HDL, and VLDL levels did not differ significantly between the controls and the cases.

KEY WORDS: Episodic migraine, lipid profile, healthy volunteers

Introduction

Migraine is a common, primary, chronic/intermittent neurovascular headache disorder characterized by episodic severe headache accompanied with autonomic nervous system dysfunction and, in some patients, transient neurologic symptoms known as migraine aura.[1,2]

An association between migraine and chest pain has been described earlier.[3,4] The increased frequency of ischemic stroke among women with migraine[5] has led to the speculation that migraine may be a risk factor for ischemic stroke.[6–8] Indeed, initial retrospective case–control studies found increased risk of ischemic stroke, in particular among cases of migraine with aura. A retrospective assessment of lifetime history of migraine with aura and prevalent TIA symptoms might reveal a strong association as both have similar clinical features that even experienced neurologists cannot distinguish.[9]

Indeed, several studies have found association between migraine with aura and increased risk of ischemic stroke. Some studies have suggested that migraine, particularly migraine with aura, is associated with unfavorable cardiovascular risk profile and prothrombotic or vasoactive factors[10–14] and that the vascular dysfunction of migraine may also extend to coronary arteries.[15,16] It is plausible that migraine, especially migraine with aura, may be associated with other vascular disorders and not just stroke.

These findings warrant a proper evaluation of lipid profile in migraine patients to see if the increase in stroke and cardiovascular events is perhaps because of altered lipid profile.

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Materials and Methods

This case–control study was conducted in the Department of Physiology, Maulana Azad Medical College, in association with the Department of Neurology, G.B. Pant Hospital, and the Department of Biochemistry, Maulana Azad Medical College, New Delhi, India.

Inclusion Criteria

All adult patients of either sex, aged 20–40 years, presenting with history of headache satisfying the International Headache Society 2004 criteria for primary episodic migraine were enrolled for the study.

All secondary causes of headache were excluded by appropriate clinical and radiological examinations.

Exclusion Criteria

Migraine patients with diabetes mellitus, those with hypercholesterolemia disorders, those on oral contraceptives, and those with obesity were excluded from the study.

Selection of Controls

Normal healthy adults of either sex, aged 20–40 years, without any history of migraine attacks were taken as controls.

The study was conducted on 84 subjects, of which 54 were migraine patients (cases) selected from the Neurology Outpatient Department, G.B. Pant Hospital, New Delhi. The remaining 30 subjects formed the control group comprising healthy students of medicine (MBBS), senior residents, and junior residents from the Department of Physiology, Maulana Azad Medical College, New Delhi. Thus, the two study groups were as follows: group A (controls) composed of 30 healthy adults aged 20–40 years with no clinical signs and symptoms of migraine and group B composed of 54 migraine patients aged 20–40 years.

Lipid Profile

All subjects were tested under similar laboratory conditions. The blood samples for lipid profile were taken early morning after 12-h fasting and the samples centrifuged in an ultracentrifuge; the serum was stored in cryogenic conditions (–80°C) in the Department of Biochemistry. Lipid profile was performed in the Central Biochemistry Laboratory, Maulana Azad Medical College, New Delhi, using Accurex and Erba kits in DxC800 analyzer (Beckman Coulter).

Cholesterol

Quantitative determination of cholesterol was done using cholesterol oxidase–peroxidase enzymatic colorimetric method.[17] The intensity of the color formed is proportional to the cholesterol concentration in the sample. Normal value is <200 mg/dL.

HDL-Cholesterol

High-density lipoprotein (HDL)-cholesterol precipitating reagent in conjunction with cholesterol reagent was used for enzymatic determination of the HDL-cholesterol level in serum.[18] Normal value: men, 27–67 mg/dL; women, 29–89 mg/dL.

Triglycerides

The enzymatic method using lipoprotein lipase, glycerol kinase, glycerol phosphate oxidase, and peroxidase in discrete semiautomated analyzer was used for the serum triglyceride (TG) estimation.[19] Normal value is <150 mg/dL.

LDL-Cholesterol

It was calculated using Friedewald equation:

$$\text{Low} - \text{density lipoprotein (LDL)} - \text{cholesterol} = (\text{Total cholesterol} - \text{HDL} - \text{cholesterol} - \frac{\text{TG}}{5}$$

Normal value is <100 mg/dL.

VLDL

The very-low-density lipoprotein (VLDL) was calculated using the following equation:

$$\text{VLDL} = \frac{\text{TG}}{5}$$

Values between 5 and 40 mg/dL are considered normal. This is based on the average ratio of TG to cholesterol in VLDL.

All values are in milligrams per deciliter.

Ethics

The study was conducted after obtaining clearance from the institute ethics committee for human studies and carries less than minimal risks.

Statistical Analysis

Data for all parameters were collected as per the study protocol and computerized in Microsoft Excel database. Because the distribution of frequency showed a skewed pattern for the parameters of lipid profile, nonparametric test (Fisher's exact test) was used for statistical analysis. Statistical analyses were done at 5% level of significance, and $P < 0.05$ was considered as statistically significant.

Results

Table 1 shows that of 54 cases, 7 cases had abnormal total cholesterol levels, and of 30 controls, 4 had abnormal levels. By applying nonparametric test, we could not establish any statistical significance between the two study groups ($P = 0.604$, Fisher's exact test).

When comparing TGs and HDL profile, 1 of 54 cases and 1 of 30 controls had abnormal levels for both the parameters, whereas the remaining subjects in both the study groups showed normal levels for the same. Results revealed no statistical significance on comparison ($P = 0.589$, Fisher's exact test).

Table 1: Lipid profile parameters between episodic migraine patients (cases) and healthy volunteers (controls)

Lipids	Cases (*N* = 54)		Controls (*N* = 30)		*P*-value
	n	%	*n*	%	
Cholesterol					
Normal	47	87.03	26	86.67	0.604
Abnormal	7	12.97	4	13.33	
Triglycerides					
Normal	53	98.15	29	96.66	0.589
Abnormal	1	1.85	1	3.34	
HDL					
Normal	53	98.15	29	96.66	0.589
Abnormal	1	1.85	1	3.34	
LDL					
Normal	30	55.55	25	83.33	0.020
Abnormal	24	44.45	5	16.67	(<0.05)
VLDL					
Normal	54	100	30	100	–
Abnormal	0	0	0	0	

HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.

Abnormal levels of LDL were observed in 24 of 54 cases and 5 of 30 controls, a statistically statistical difference toward the cases, which suggests a poorer lipid profile compared with that of controls ($P = 0.020$, χ^2- test). None of the cases or the controls had abnormal levels of VLDL. Hence, of all the lipid profile parameters, only LDL showed a statistical significance, with abnormally elevated levels in migraineurs compared with controls.

As LDL-cholesterol was higher in the cases, the lipid profile was atherogenic in nature; the rest of the lipid parameters showed no statistical significance.

Discussion

Literature reveals that the incidence of cardiovascular and cerebrovascular events appeared to be more in cases of migraine. Several studies[20,21] evaluated the association between migraine and stroke and found increased risk for migraine with aura. Hence, in this study, we studied whether the lipid profile of migraineurs is different in the Indian population, as it was in the Western population.

In this study, the total cholesterol, TGs, LDL-cholesterol, HDL-cholesterol, and VLDL were the biochemical parameters measured to assess the cardiovascular and cerebrovascular risks.

Several studies had shown abnormal high levels of total cholesterol in migraineurs.[22–26] However, in this study, the total cholesterol level between the control and the case groups did not show a statistically significant difference. This could be because the Indian population generally has lower lipid levels than the Western population. In a study performed in Chennai, India, 75% people with myocardial infarction had plasma cholesterol levels less than 200 mg/dL.[27] In another study from India, even lower level of plasma cholesterol (<150 mg/dL) in patients with coronary artery disease has been reported.[28] Comparison of values with those reported in different populations in prosperous communities indicated that serum cholesterol levels in India are low in all the age groups.[29] The lipid kit used for our study had the cutoff value of 200 mg/dL, above which the values are considered abnormal. Hence, we could not establish the clinical significance between the cases and controls.

In our study, the LDL-cholesterol estimation showed an increased level, which was in agreement with several previous studies.[22,24,30,31] The case group had a higher level of LDL-cholesterol than the control group, and the difference was found to be statistically significant.

The HDL-cholesterol levels showed no statistical significance between the cases and controls on comparison, similar to the results of the study by Gruber et al.[22] A study of plasma lipids in migraine by Monastero et al.[24] also found no statistical significance for HDL.

Comparison of TGs showed no significance, similar to the study by Monastero et al.,[24] and VLDL level comparison between the cases and controls was also statistically insignificant. These parameters need further elaborate evaluation to find out their association with migraine.

There is a nonspecific sympathetic hyperactivity in migraine patients in headache-free intervals.[32] The LDL levels might have increased because of an increased release of catecholamines during this sympathetic hyperactivity. Epinephrine decreases LDL uptake (binding + internalization) and degradation in a dose-dependent manner. These results are in agreement with the general view that epinephrine increases cyclic AMP intracellular level, as it was previously shown that dibutyryl cyclic AMP or isoproterenol treatment of cultured fibroblasts had similar effect on these pathways. The decrease in LDL processing induced by epinephrine could be involved in the worsening effect of epinephrine on the lipid profile.[33]

Conclusion

The lipid profile status in migraine has been found to be proatherogenic, and this may lead to increased incidences of cardiovascular and cerebrovascular events in migraineurs, which necessitates that their lipid profile should be constantly monitored to prevent any future vascular events.

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