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Hyperlipidemia in migraine: Is it more frequent in migraineurs?

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Migraine, Triglyceride, Cholesterol, Low Density Lipoprotein, High Density Lipoprotein

Abstract

Background: Some coincidental disorders with migraine have been introduced that may have role in its pathogenesis or aggravation. In this study we determined the relative frequency of hyperlipidemia as a coincidental disorder in patients affected by migraine.

Methods: A total of 102 migraine-affected patients according to International Headache Society (HIS) criteria and 103 control subjects adjusted for age participated in this case-control study. Their serum level of triglyceride, total cholesterol, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) were measured.

Results: A total of 84 women and 18 men with mean age of 34.9 ± 11.8 years and 79 women and 24 men with mean age of 32.8 ± 5.7 years constituted case and control groups, respectively. The means of serum triglyceride, total cholesterol, HDL-C and LDL-C levels in case and control groups were 177.0 ± 118.2 versus 108.7 ± 37.2 mg/dl (P = 0.0001), 186.2 ± 44.1 versus 152.9 ± 3.7 mg/dl (P = 0.0001), 49.9 ± 12.5 versus 46.1 ± 10.7 mg/dl (P = 0.023) and 104.8 ± 33.7 versus 84.1 ± 34.0 mg/dl (P = 0.0001), respectively. The prevalence of hypertriglyceridemia and hypercholesterolemia in case and control groups were 41.2% versus 18.4 % (P = 0.0001), and 36.3% versus 9.7% (P = 0.0001). According to multivariate analysis, odds ratios were 3.11 (95% CI: 1.4 -6.6) and 17.4 (95% CI: 2.12-138.3), respectively. Odds ratio for low HDL-C was 0.2 (95% CI: 0.08-0.49).

Conclusion: Hypertriglyceridemia and hypercholesterolemia were more frequent in migraineurs. Conversely, low HDL-C was less frequent among the patients compared with non-migraineurs.

Introduction

Headache is one of the most common chief complaints in referred patients. More than 90% of men and 95% of women experience headache during their life[1] and migraine is one of the most common headaches.[2] In different studies, some complex mechanisms have been introduced for migraine and pointed to some coincidental disorders with migraine such as genetic factors, family history, and environmental factors including psychological stresses, some specific foods, drugs and hunger.[3] On the other hand, sometimes in practice, we approach to some patients with migraine that are intractable to all of medications. However, the control of coincidental factors reduces its therapeutic resistance in these patients. Recognition of coincidental factors with migraine may helps to control it better, although no cause-effect association is found between them. Moreover, it may help to recognize the pathophysiology of migraine more and more. One of these factors that its roles and relationship with migraine is yet in doubt is hyperlipidemia (including hypertriglyceridemia, hypercholesterolemia and abnormal levels of high and low density lipoproteins).

In one study, Tietjen et al. investigated some coincident disorders including hyperlipidemia, diabetes

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mellitus, hypertension and hypothyroidism among migraine affected patients.[4] In some studies, high levels of serum lipids and free fatty acids have been recognized as the cause of migraine headache;[5] but is some other studies, such association was found in specific ranges of age or sex. In one study by Glueck et al.[7] it was concluded that primary or familial lipoprotein abnormalities particularly those involving high levels of low density lipoprotein cholesterol (LDL-C) and or low levels of high density of lipoprotein cholesterol (HDL-C) may be etiologically related to pediatric migraine, in other study similar results were attained;[6,7] but such study has not been conducted in adults. On the other hand, it was seen that the cerebrovascular accidents are more prevalent in migraineurs.[1,8] This increased risk may be due to either migraine nature and the change formation by migraine and their common vascular pathophysiology, or accompaniment of stroke risk factors including hyperlipidemia. Moreover, the cardiovascular accidents are more prevalent in migraineurs[9] that can be explained by the same reasons.

Some limited genetic studies with contradictory results have been done in this regard. Mochi et al. investigated the polymorphism of LDL-C receptor gene (that plays an important role in cholesterol homeostasis) on chromosome 19p13.2 by analyzing two polymorphic markers, a GI42A transition in exon 10 and a tri-allelic (TA)n repeat in exon 18 and concluded that the allelic distributions of (TA)n polymorphism was significantly different between migraine without aura and both controls and migraine with aura.[10] In another study by Curtain et al, the (TA)n polymorphism in exon 18 of the LDL-C receptor gene of the same chromosome was investigated; conversely, the results showed no significant difference between groups for allele frequency distributions of (TA)n polymorphism even after the separation of migraine affected individuals into subgroups of migraine with and without aura.[11] Of course, the author of second study pointed to some sampling error in his study to explain this difference.

In this preliminary study, we determined the serum levels of triglyceride (TG), total cholesterol (total Chol), HDL-C and LDL-C and the relative frequency of hyperlipidemia as a coincidental disorder, in migraine affected patients and compared them with non-migraineurs.

Materials and Methods

In this case0control study, according to a pilot study with 40 cases and 40 control subjects, sample size was determined as 102 persons in each group. All migraine affected patients according to International Headache Society (IHS) criteria, who were referred to a neurology clinic of a University Centre in Guilan, Iran, after complete examination and excluding other reasons of headaches were enrolled. All the cases and controls signed the informed consent. These 2 groups were matched according to age and sex and the prevalence of hypertension, diabetes mellitus. The patients, who were pregnant or had history of cardio-cerebrovascular or peripheral vascular disorders, seizure, inflammatory disorders and who had used oral contraceptive pills in 3 months before, were excluded from the study.

From each subject, 3 cc of whole blood was taken and centrifuged, and then the serum TG, Chol, HDL-C and LDL-C levels were measured by using spectrophotometry technique. The normal ranges of these parameters based on TIETZ reference[12] were: TG < 150 mg/dl, total Chol < 200 mg/dl, LDL-C < 130 mg/dl, and HDL-C > 40 mg/dl. The tests of all patients were performed in Poursina Hospital laboratory.

At the end of study, the serum levels of TG, total Chol, HDL-C and LDL-C and the prevalence of hypertriglyceridemia, hypercholesterolemia, low HDL-C and high LDL-C were determined and compared between case and control groups. The data were analyzed by χ^2 test, Fisher's exact test and logistic regression using SPSS software version 16.

Results

A total of 102 patients (84 women and 18 men) with mean age of 34.9 ± 11.8 years in cases group and 103 persons (79 women and 24 men) with mean age of 32.8 ± 5.7 years in controls group participated in this study.

According to univariate analysis, the means of serum TG level were 177.0 ± 118.2 in case group versus 108.7 ± 37.2 mg/dl in control group (P = 0.0001). Serum total Chol was 186.2 ± 44.1 versus 152.9 ± 3.7 mg/dl (P = 0.0001), HDL-C level was 49.9 ± 12.5 versus 64.1 ± 10.7 mg/dl (P = 0.023) and LDL-C level was 104.8 ± 33.7 versus 84.1 ± 34.0 mg/dl in case and control groups, respectively (P= 0.0001).

The prevalence of hypertriglyceridemia was 41.2% in case group versus 18.4% in control group (P = 0.0001) with a corresponding odds ratio (OR) of 3.09 (95% CI: 1.6- 5.8). Hypercholesterolemia was 36.3% in cases versus 9.7% in controls (P = 0.0001) and OR was 5.29 (95% CI: 2.4-11.4). Low HDL-C was 10.8% versus 30.1% (P = 0.0001) in case and control groups with OR of 0.28 (95% CI: 0.13- 0.6) and high LDL-C was 22.5% versus 10.7% (P = 0.022) and OR was 2.43 (95% CI: 1.1-5.3).

Analysis of data was performed in men and women separately. Except serum level of LDL-C that had statistically significant difference in both populations and serum level of HDL-C that did not have any significant difference in each population, the differences of other factors were significant only in women but not in men (Tables 1-3).

To control of confounding effects, all of factors with P-value lower than 0.1 were entered in logistic regression equation. Final model shows the chances of coincidence of these factors with migraine by multivariate analysis (Table 4).

Discussion

Our findings indicated that hypertriglyceridemia and hypercholesterolemia were coincident with migraine. This conclusion may be only a simple achievement or even a

Table 1. The mean amount of lipids in males and females

Gender		Groups	N	Mean	Std. Deviation	p-value	95% CI	
							Lower	Upper
Female	TG	Case	84	176.5	107.9	0.000	43.8	94.4
		Control	79	107.3	37.4			
	chol	Case	84	188.8	43.4	0.000	21.8	47.7
		Control	79	154.0	40.1			
	HDL	case	84	49.2	9.6	0.098	-0.5	5.8
		Control	79	46.6	10.8			
	LDL	Case	84	104.6	34.9	0.000	9.3	31.2
		Control	79	84.4	35.7			
Male	TG	Case	18	179.8	161.7	0.104	-2.2	135.2
		Control	24	113.2	36.9			
	chol	Case	18	174.5	46.8	0.042	0.9	49.5
		Control	24	149.2	31.1			
	HDL	Case	18	52.7	21.7	0.118	-2.1	18.3
		Control	24	44.6	10.5			
	LDL	Case	18	105.5	28.3	0.016	4.4	40.1
		Control	24	83.2	28.4			

Table 2. The prevalence of hypertriglyceridemia, hypercholesterolemia, low HDL-C and high LDL-C among females

Female				P value	OR	95% CI	
						Lower	Upper
Hypertriglyceridemia	Case	N	36	0.000	3.8	1.8	7.9
		%	42.9%				
	Control	N	13				
		%	16.5%				
Hypercholesterolemia	Case	N	33	0.000	5.0	2.2	11.4
		%	39.3%				
	Control	N	9				
		%	11.4%				
	Total	N	42				
		%	25.8%				
Low HDL-C	Case	N	9	0.003	0.3	0.1	0.7
		%	10.7%				
	Control	N	23				
		%	29.1%				
	Total	N	32				
		%	19.6%				
High LDL-C	Case	N	20	0.066	2.1	0.9	4.9
		%	23.8%				
	Control	N	10				
		%	12.7%				
	Total	N	30				
		%	18.4%				

cause-effete association. According to the results shown in table 4, hypertriglyceridemic patients had 3.11 folds and hypercholesterolemic patients 17.14 folds more chance for migraine coincidence.

In one study, it was seen that low fat regimen reduces the frequency, severity, and duration of headache and medication use.[13] Suggested mechanisms in migraine are the change of cortical irritability, neural system inflammation and vascular endothelial dysfunction.[14] The effect of hyperlipidemia may be inducing platelet aggregation and triggering neurogenic inflammation.[15] After platelet aggregation, changes in serum serotonin and platelet serotonin level occurred and after this events the cascades of prostaglandins (PG) and leukotrienes (LT) initiate and potent PG_S (such as PGE_2) and potent leukotrienes are produced. These changes lead to vasodilatation and migraine headache.[1,5,6] Regarding the effect of hyperlipidemia on vasodilation, the study by Gokce et al. concluded that acute hypertriglyceridemia is associated with peripheral vessels vasodilatation and increased blood flow.[16]

In our study, when the analysis was performed separately in men and women, none of factors except serum level of LDL-C had significant relation with migraine in men.

Table 3. The prevalence of hypertriglyceridemia, hypercholesterolemia, low HDL-C and high LDL-C among males

male				P value	OR	95% CI	
						Lower	Upper
hypertriglyceridemia	Case	N	6	0.55	1.5	0.4	5.8
		%	33.3%				
	Control	N	6				
		%	25.0%				
hypercholesterolemia	Case	N	4	.146	6.6	0.7	64.9
		%	22.2%	fisher's exact test			
	Control	N	1				
		%	4.2%				
low HDL-C	Case	N	2	.147	0.2	0.04	1.4
		%	11.1%	fisher's exact test			
	Control	N	8				
		%	33.3%				
high LDL-C	Case	N	2	.147	0.2	0.05	1.4
		%	11.1%	fisher's exact test			
	Control	N	8				
		%	33.3%				

Table 4. Odds ratio and predictive value of serum lipids abnormalities according to logistic regression model and multivariate analysis

	S.E.	OR	95.0% C.I		P value
			Lower	Upper	
HTG	0.387	3.11	1.4	6.6	0.003
HCHOL	1.065	17.1	2.1	138.3	0.008
LHDL	0.457	0.2	0.08	0.5	0.000
HLDL	1.103	0.1	0.02	1.2	0.074
Constant	0.196	0.7			0.158

S.E.: standard error, OR: odds ratio

These different findings could be due to small sample size of men (18 men in case group and 24 men in control group). Although the serum level of LDL-C had significant relation with migraine in both populations, but the high LDL-C did not have any relationship with migraine and according to logistic regression equation, high LDL-C did not have independent effect and predictive role in migraine.

On the contrary, serum level of HDL-C did not have any relation with migraine in both men and women. These results may be due to the small sample size in subgroup analysis. Indubitably, the significance of this relation in total population was not as powerful as two other factors including TG and total Chol and just as it was said, low HDL-C had significant relationship with migraine in women but not in men. Of importance is that low HDL-C had negative predictive value in migraine, so that the patients with low HDL-C had 5 fold lower chances for migraine. In other words, low HDL-C had a protective role in migraine in contrary to its negative role in cardio vascular and cerebrovascular disorders.

Accordingly, we may be able to use lipid controlling medication in prophylaxis of migraine. In this regard, some studies about the effect of niacin (vitamin B3) on migraine control can be noticeable. It was seen to be effective in increasing the serum level of HDL-C and reduction of triglyceride and LDL-C.[17] In one case-report, niacin was used for treatment of migraine; this effect may have been due to its role in lipid homeostasis.[18]

Conclusion

Hypertriglyceridemia and hypercholesterolemia were more frequent and low HDL was less frequent among migraine affected patients comparing with non-migraineurs.

Conflict of interest

The authors have no conflict of interest.

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