۳۰ درصد تخفیف نوروزی ویژه کارگاه‌ها و فیلم‌های آموزشی

اصول تنظیم قراردادها
پروپوزال نویسی
آموزش مهارت‌های کاربردی در ندوین و چاپ مقاله
Hyperlipidemia in migraine: Is it more frequent in migraineurs?

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Keywords
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 (IHS) 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 life¹ and migraine is one of the most common headaches. 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.⁵ 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
mellitus, hypertension and hypothyroidism among migraine
affected patients. In some studies, high levels of serum lipids
and free fatty acids have been recognized as the cause of
migraine headache; but is some other studies, such
association was found in specific ranges of age or sex. In one
study by Glueck et al. 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 cholesterol (HDL-C) may be etiologically related to pediatric migraine, in
other study similar results were attained, 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. 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
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
dominance of LDL-C receptor gene (that plays an important role in cholesterol homeostasis) on chromosome
19p13.2 by analyzing two polymorphic markers, a G42A 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. 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. 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 case-control 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 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 χ² test,
Fisher’s exact test and logistic regression using SPSS
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 ± 73.2 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 ± 3.0 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

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

| Gender | Groups | N  | Mean  | Std. Deviation | p-value | 95% CI     |
|--------|--------|----|-------|----------------|---------|------------|
|        | TG     |     |       |                |         |            |
| Female | Case   | 84 | 176.5 | 107.9          | 0.000   | 43.8 94.4  |
|        | Control| 79 | 107.3 | 37.4           |         |            |
|        | chol   |     |       |                |         |            |
| Female | Case   | 84 | 188.8 | 43.4           | 0.000   | 21.8 47.7  |
|        | Control| 79 | 154.0 | 40.1           |         |            |
|        | HDL    |     |       |                |         |            |
| Female | Case   | 84 | 49.2  | 9.6            | 0.098   | -0.5 5.8   |
|        | Control| 79 | 46.6  | 10.8           |         |            |
|        | LDL    |     |       |                |         |            |
| Female | Case   | 84 | 104.6 | 34.9           | 0.000   | 9.3 31.2   |
|        | Control| 79 | 84.4  | 35.7           |         |            |
|        | TG     |     |       |                |         |            |
| Male   | Case   | 18 | 179.8 | 161.7          | 0.104   | -2.2 135.2 |
|        | Control| 24 | 113.2 | 36.9           |         |            |
|        | chol   |     |       |                |         |            |
| Male   | Case   | 18 | 174.5 | 46.8           | 0.042   | 0.9 49.5   |
|        | Control| 24 | 149.2 | 31.1           |         |            |
|        | HDL    |     |       |                |         |            |
| Male   | Case   | 18 | 52.7  | 21.7           | 0.118   | -2.1 18.3  |
|        | Control| 24 | 44.6  | 10.5           |         |            |
|        | LDL    |     |       |                |         |            |
| Male   | 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     |
|--------|---------|-----|------------|
|        |         |     |            |
| Hypertriglyceridemia |         |     |            |
| Case   | N       | 36  | 0.000      | 3.8     | 1.8 7.9 |
| Control| N       | 13  | 0.000      | 1.6     |         |
| Hypercholesterolemia |         |     |            |
| Control| N       | 9   | 0.000      | 5.0     | 2.2 11.4|
| Total  | N       | 42  | 0.003      | 0.3     | 0.1 0.7 |
| Low HDL-C |         |     |            |
| Control| N       | 23  | 0.066      | 2.1     | 0.9 4.9 |
| Total  | N       | 32  | 0.003      | 0.3     | 0.1 0.7 |
| High LDL-C |         |     |            |
| Control| N       | 10  | 0.066      | 2.1     | 0.9 4.9 |
| Total  | N       | 30  | 0.003      | 0.3     | 0.1 0.7 |

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. Suggested mechanisms in migraine are the change of cortical irritability, neural system inflammation and vascular endothelial dysfunction. The effect of hyperlipidemia may be inducing platelet aggregation and triggering neurogenic inflammation. 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 PGs (such as PGE\textsubscript{2}) and potent leukotrienes are produced. These changes lead to vasodilatation and migraine headache. 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.

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 |   |        |         |           |           |
|----------------------|------|---|--------|---------|-----------|-----------|
|                      | Case | N | %     | Control | N         | %         |
| hypertriglyceridemia | Case | 6 | 33.3% | Control | 6         | 25.0%     |
|                      | N    | 4 | %     | 1       |           |           |
|                      | Hypercholesterolemia | P value | OR 95% CI | F Fisher’s exact test |
| low HDL-C            | Case | N 2 | 11.1% | Control | N 8       | % 33.3%   |
| high LDL-C           | Case | N 2 | 11.1% | 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 |
|----------|------|--------------|---------|
| HTG      | 0.387| 3.11         | 1.4     |
| HCHOL    | 1.065| 17.1         | 2.1     |
| LHDL     | 0.457| 0.2          | 0.08    |
| HLDL     | 1.103| 0.1          | 0.02    |
| Constant | 0.196| 0.7          | 0.01    |

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 cardiovascular 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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