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Low-lipid diet reduces frequency and severity of acute migraine attacks

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Abstract *Background and aim:* There is uncertainty regarding the prevention of migraine crises by changing the lifestyle of patients. The aim of this randomized, crossover intervention trial was to evaluate the effects of a low lipid intake on the incidence and severity of migraine crises, in comparison to a diet with moderate lipid intake.
Methods and results: After a 2-month run-in when patients received preventive medication but were left on their habitual diet, a low-lipid or a normal-lipid diet was randomly prescribed for 3 months and thereafter diets were crossed over for the following 3 months. Headache was diagnosed based on the International Classification of Headache Disorders (IHCD) III criteria. The number and severity of attacks were assessed using a self-reported calendar. Adherence to the diet was assessed by a food frequency questionnaire. An analysis was performed on the 83 episodic or chronic migraineurs (63 female and 20 male), in the age range of 18–57 years, who completed both intervention periods. Obese subjects had a significantly higher number of attacks than those overweight or with normal body weight (24.7 ± 8, 16.3 ± 12, and 15.6 ± 11, respectively, $p < 0.03$) with a significant relationship between the body mass index (BMI) and the number of monthly attacks ($r = 0.238$, $p < 0.03$). The number (2.9 ± 3.7 vs. 6.8 ± 7.5, $p < 0.001$) and severity ($1.2 + 0.9$ vs. 1.7 ± 0.9, $p < 0.01$) of attacks significantly decreased during both intervention periods, with a significant difference in favour of the low-lipid diet.
Conclusions: In this group of patients, the low-lipid diet significantly affected the number and severity of migraine attacks in comparison to a normal-lipid diet.
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Introduction

Headache is a common disease in the general population that affects adult women more frequently than men [1]. Among different factors that might be involved in the pathophysiology of the disease, eating particular foods such as aged cheese or drinking red wine may trigger acute migraine attacks [2,3].

Moreover, a close relationship has been detected between overweight/obesity and migraine severity [4–7] although other authors have shown that obesity at baseline does not seem to be related to follow-up refractoriness to preventive treatment [8–10].

For this reason, some studies have been designed in order to investigate the effects of dietary intervention on the number and severity of headache attacks. First, in a small trial including only seven patients with no control

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group, a carbohydrate-rich diet, low in protein-tryptophan, was shown to favourably affect headache, and the efficacy of the dietary intervention was related to a reduced intake of migraine-precipitating foods with a concomitant increase in the brain serotonin levels [11]. Thereafter, the lipid components of the diet were investigated: it has been suggested that a lipid-rich diet might be responsible for headache because the plasma serotonin levels are reduced in relation to the increased platelet aggregation [12], whilst a very low-lipid diet (about 20 g daily) might help in preventing headache [13]. More recently, the use of a ketogenic diet has been proven to reduce the frequency of migraine attacks [14,15].

The aim of the present study was to investigate the possibility of affecting the frequency and severity of headache attacks by reducing only moderately the intake of lipids to amounts usually prescribed in a low-lipid diet in the Mediterranean area (never reducing total fat <45 g daily with a marked prevalence of the monounsaturated olive oil), without inducing a drastic reduction in the energy intake coming from carbohydrates.

Patients and methods

Over a period of 1 year, 128 patients consecutively presenting to the Headache Outpatient clinic of the Department of Clinical Medicine were invited to enter the study group.

The inclusion criteria were as follows:

- Age range of 18–60 years
- One or more monthly attacks of episodic or chronic migraine without aura
- Arterial blood pressure <180/110 mmHg
- No renal, hepatic or inflammatory chronic bowel diseases
- No use of nitrates or dihydropyridines
- No neurological disease

Before participating in the study, the protocol was fully explained to the patients and their informed consent was obtained.

At the first visit, the patients underwent a complete clinical examination including measurement of body weight (BW), height (Ht), blood pressure (systolic blood pressure (SBP)/diastolic blood pressure (DBP)), and heart rate (HR). The body mass index (BMI) was calculated as BW/Ht^2 and expressed in kilogram per square metre. Headache was classified in the Headache Outpatient Clinic according to the III beta International Headache Classification criteria (IHCD [16]).

Obesity was defined as BMI ≥30, whilst patients were classified as overweight if their BMI was ≥25 and <30 [17].

After the baseline visit, patients who accepted to enter the study were prescribed the calcium entry blocker *flunarizine* 5 mg daily as preventive medication of headache, and they were left on their habitual diet for a run-in period of 2 months.

At the end of this run-in period, all patients were randomly attributed to one of the following two dietary regimens: a low-lipid diet with a lipid content <20% of the total daily energy intake and a normal-lipid diet with a lipid intake between 25% and 30% of the total daily energy intake. The diets were similar in terms of total energy (1977 vs. 2048 in the low- and normal-lipid diets, respectively), proteins (77 vs. 75 g) and fibres (32 g for both). Carbohydrates were slightly higher in the low-lipid diet (330 g, 63% of the total energy vs. 307 g, 56%). In both diets, the lipid intake was mostly represented by monounsaturated fatty acids (14% in the low-lipid diet and 19% in the normal-lipid diet) with a low intake of saturated fats (<8% of the total calories, which is the percentage usually recommended in our diets). Patients were followed up for 3 months at the end of which they were switched to the alternative dietary regimen.

After baseline control, the patients were followed up at the Headache Outpatient Clinic of our department at 1-month intervals during the observation period. At each visit, they were given a form to be filled in at home, summarizing the number of monthly headache attacks, the severity of each one graded from mild to severe pain (1 indicated mild, 2 moderate and 3 very severe headache) and which drug and how many times they had assumed for the therapy of the attacks during the last month. Headache attacks with severe pain were considered those receiving the score of ≥2.5. Moreover, at each visit, patients filled in a food questionnaire, validated in comparison to the 7-day food record [18], with the help of a well-trained dietician. The data were expressed as daily percentage caloric intake from each macronutrient and as the weekly number of a medium-sized serving. Finally, they were invited to fill in a questionnaire regarding physical activity both at work and during leisure time: according to the response, patients were classified as sedentary, moderately active and active [19].

In addition to the medication for headache prevention, patients could use drugs of their choice for pain relief (the selective serotonin receptor agonists triptans, which are abortive migraine medications, or non-steroidal anti-inflammatory agents).

Statistical analysis

Results were analyzed using the SPSS Statistical Package. Data are expressed as mean ± standard deviation. The differences between means were analyzed by paired and unpaired *t*-tests and one-way analysis of variance. Non-parametric variables were analyzed using the χ^2 test. The strength of correlation between variables was evaluated by the Pearson correlation analysis. The differences were considered significant when $p < 0.05$. The sample size was determined in order to detect a difference of four headache attacks monthly between the two dietary periods, with a first-type error (α) of 0.05 and a second-type error (β) of 0.1. The allocation sequence was generated by one of the authors (LAF), who also assigned participants to the groups. Patients were enrolled by doctors of the