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ARTICLE

Nutritional intervention may improve migraine severity: a pilot study

Intervenção nutricional melhora a gravidade da migrânea: estudo piloto

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ABSTRACT

Although some studies have investigated the role of nutritional intervention on migraine, they had focused on triggers or on weight change and, to the best of our knowledge, none studied diet quality. **Objective:** To investigate whether nutritional intervention focused on improving diet quality and healthy weight can promote improvement in clinical parameters of women with migraine. **Methods:** Non-controlled and non-randomized intervention study conducted for 90 days. Women received an individualized diet meal plan and nutritional orientation according to their nutritional diagnosis. Anthropometric, clinical and nutritional data were measured once a month. Diet energy content and macronutrients were evaluated using 24-hour dietary recall. Diet quality was assessed through the Brazilian Healthy Eating Index–Revised (BHEI-R). The Migraine Disability Assessment and Headache Impact Test version 6 were used to assess the severity of migraine, and the Beck Depression Inventory evaluated depressive symptoms. **Results:** Fifty-two women aged 44.0 ± 13.0 years were enrolled. Anthropometric characteristics, energy, macronutrients and fiber intake did not change after intervention. However, the BHEI-R scores improved after 60 and 90 days of intervention. Concurrent to this, the Beck Depression Inventory scores and Headache Impact Test scores decreased after 60 and 90 days, respectively. The change in the BHEI-R score was negatively correlated with the migraine severity as assessed by the Headache Impact Test at the end of the intervention. **Conclusions:** We concluded that the management of diet quality may be a good strategy for improving migraine severity, regardless of the nutritional status and weight change.

Keywords: Migraine disorders; diet; depression.

RESUMO

Estudos investigaram o papel da intervenção nutricional, focada no consumo de alimentos "gatilhos" ou na alteração de peso, na melhora da migrânea. Porém, mudanças na qualidade da dieta ainda não foram abordadas. **Objetivo:** Investigar se intervenção nutricional focada na qualidade da dieta e peso saudável pode melhorar parâmetros clínicos em mulheres com migrânea. **Métodos:** Estudo de intervenção, não controlado e não randomizado. As mulheres receberam plano alimentar individualizado e orientações nutricionais, conforme o diagnóstico nutricional. Dados antropométricos, clínicos e alimentares foram medidos uma vez por mês durante três meses. Recordatório alimentar de 24 horas forneceu informações sobre o consumo alimentar. Qualidade da dieta foi avaliada pelo Índice Brasileiro de Alimentação Saudável (IQD-R). Os questionários *Migraine Disability Test* (MIDAS) e *Headache Impact Test,* versão 6 (HIT-6) avaliaram a incapacidade gerada pela enxaqueca e o Inventário de Depressão de Beck (BDI) investigou sintomas depressivos. **Resultados:** Cinquenta e duas mulheres com 44,0 ± 13,0 anos participaram da amostra. Características antropométricas e consumo de energia, macronutrientes e fibras não se alteraram depois da intervenção. No entanto, os escores do IQD-R melhoraram após 60 e 90 dias de intervenção. Os escores do BDI e do HIT-6 diminuíram após 60 e 90 dias, respectivamente. A mudança no escore do IQD-R correlacionou de maneira negativa com a gravidade da enxaqueca avaliada pelo HIT-6 ao final da intervenção. **Conclusões:** O manejo da qualidade da dieta pode ser estratégia para melhorar a gravidade da migrânea, independente do estado nutricional e da mudança de peso dos pacientes.

Palavras-chave: Transtornos da enxaqueca; dieta; depressão.

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Migraine is a common headache disorder and an important public health problem that affects 11% of adults worldwide[1]. As migraine may cause severe disability, the illness has a significant burden on the patient's life and society[2,3,4].

Migraine attacks may be triggered by exogenous and/or environmental agents[5]. Many of these triggers are related to dietary habits such as fasting, low fluid intake and consumption of specific foods (e.g. coffee, milk, chocolate and citrus fruits)[6,7]. Furthermore, some studies have demonstrated an association between obesity and a worse migraine prognosis[8,9] and clinical improvement after weight loss[10,11], although this has been questioned[12].

Although some studies have investigated the role of nutritional intervention in migraine, they had focused on triggers[7] or on weight change[10,11] and, to the best of our knowledge, none studied diet quality. Because healthy eating is beneficial for maintaining ideal weight and good health, the aim of this study was to obtain pilot evidence on whether nutritional intervention, focused on improving diet quality and healthy weight, would be able to promote improvement in the clinical parameters of migraine patients.

METHODS

Patients

We conducted a non-controlled and non-randomized intervention study with women treated at the Headache Clinic, University Hospital, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil. All patients had been previously diagnosed with migraine according to the International Headache Society criteria[13]. Pregnant and lactating women were excluded from the study. Pharmacological treatment remained unchanged during the interventional study.

The sample size was estimated at 51 participants considering the mean of medical appointments per month (100 patients) at the Headache Clinic (corresponding to 1,600 patients in the study period), and the expected decrease of migraine severity between 22% to 38% according to previous studies[4,14]. The calculation of sample size was also made considering 5% of alpha error, 80% of statistical power and 50% of possible losses as observed in previous similar studies[15,16]. This study was approved by the Ethics Committee of Universidade Federal de Minas Gerais (Protocol N. 0311.0.203.000-11), and all patients signed a consent form. This study was registered in the Clinical Trials Registry Platform Search (NCT02703129).

Nutritional assessment

Weight, height and waist circumference were measured according to World Health Organization criteria[17]. A digital weight scale, Tanita® (BF-680 model), with a capacity of 150 kg and accuracy of 100 g was used to measure weight, and a stadiometer, Alturexata®, with pinpoint accuracy was used to measured height. Then, the body mass index (BMI) was calculated [BMI = weight (kg)/height^2 (m)] and nutritional diagnosis classified according to the limits proposed by the World Health Organization[17]. The waist circumference was measured using a tape with millimeter precision and was classified according to the increased risk (> 80 cm) and the substantially increased risk (> 88 cm) of metabolic complications associated with obesity[18].

Body composition was measured by bioelectrical impedance analysis using Biodynamics® (model 310E) equipment. Measurements were performed with the patient lying supine with the arms and legs extended about 45° from the body after 12 hours of fasting. This analysis was carried out only in women who did not have a pacemaker or metallic prosthesis (n = 44).

Nutritional intervention

Patients received individualized diet meal plans and nutritional orientations focused on improving diet quality and according to their nutritional diagnosis. For those with a low weight, the aim was to gain weight; for those with an ideal weight, the aim was maintenance; and for overweight or obese patients, the aim was to lose weight. The diet meal plan was prepared by nutritionists based on the estimated energy requirement[19]. The energy requirement was calculated using the ideal weight (equivalent to medium BMI = 21.5 kg/m^2) for women with a BMI below the ideal range, the current weight for women with a BMI in the ideal range, and the current weight plus caloric restriction for women who were overweight or obese. The caloric restriction aimed to decrease 5% of body weight in three months[20]. All nutritional recommendations were based on the Dietary Guidelines for the Brazilian Population[21].

Patients were evaluated three times with an interval of 30 days between visits (Figure 1). Clinical, anthropometric and food evaluations were conducted and nutritional orientations were strengthened. The diet prescription did not change during the interventional period.

Diet assessment

The energy content, macronutrients and quality of the diet were assessed using a single day 24-hour dietary recall applied at each visit by nutritionists. The same day of the week was recalled at each follow up point. The food intake reported was converted to grams and milliliters, and subsequently analyzed using Nutrition Dietwin® software (http://www.dietwin.com.br/). Quantitative analysis considered the energy intake, carbohydrates, proteins, total lipids, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids and fiber.

The diet quality of the patients was assessed through the Brazilian Healthy Eating Index–Revised (BHEI-R) version. The BHEI-R evaluates 12 components, combining different

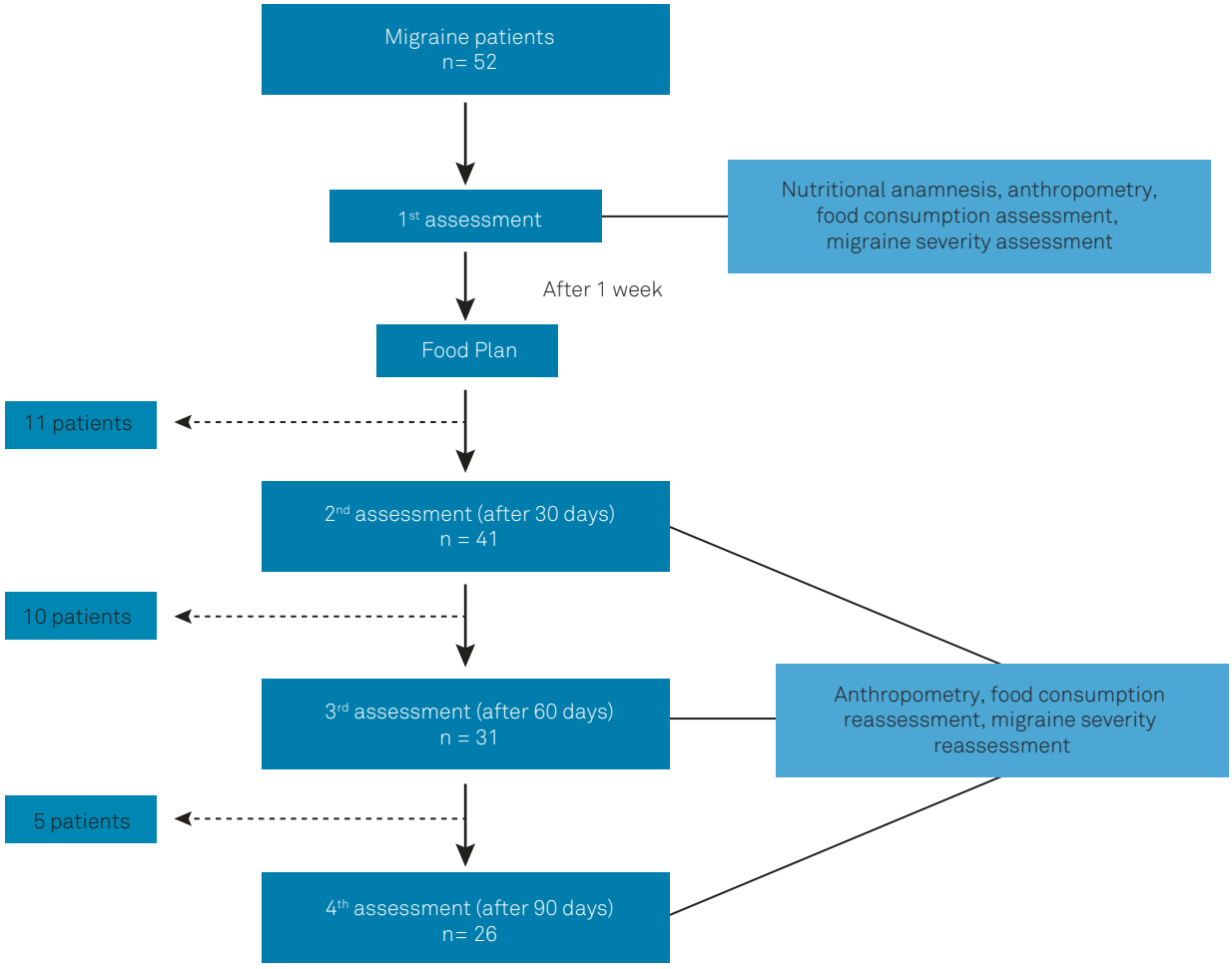

Figure 1. Design of the study. Filled arrows indicate the direction of the patients throughout the study. Dotted arrows represent patients who discontinued the study.

types of foods, nutrients and dietary constituents. These components are analyzed in relation to dietary recommendations and/or health outcomes. The total score of the BHEI-R was obtained by the sum of the values for each component in which the maximum score is 100, with a higher score indicating increased compliance with dietary guidelines[22].

Migraine parameters

Migraine Disability Assessment (MIDAS) questionnaires[23] and Headache Impact Test, version 6 (HIT-6)[24] were used to assess the severity of migraine. The MIDAS measures the disability caused by migraine over a period of 90 days, and the total score is categorized according to severity as follows: I – little or no disability; II – mild disability; III – moderate disability; IV – severe disability[23]. The HIT-6 also measures the disability caused by migraine over a period of 30 days. It provides a migraine score that can be classified as little or no impact; some impact; substantial impact; and very severe impact[24].

Patients were educated about the use prophylactic medication. Depressive symptoms were evaluated by the Beck Depression Inventory (BDI)[25].

Statistical analyses

Categorical variables were described as absolute and relative frequencies. The Kolmogorov-Smirnov test was used to test normality of quantitative variables. All quantitative data were presented as means and standard deviations (SD). Clinical and nutritional parameter evolution was assessed by the paired Student t-test for parametric, Wilcoxon for nonparametric, and McNemar for proportions comparison. Additional analysis included Pearson's correlation between the difference observed in the intervention period [Δ = {(end point value) – (baseline value) / (baseline value)} x 100] for quality diet, HIT-6, MIDAS and BDI. A p-value $\leq$ 0.05 was considered statistically significant. Statistical analyses were performed using SPSS, version 19.0 software (IBM Corp., Armonk, NY, USA).

RESULTS

Fifty-two women were evaluated at the baseline. The mean age ± SD was 44.0 ± 13.0 years. Before nutritional intervention, 45 patients (87%) were diagnosed with episodic

migraine and 33 (64%) had migraine without aura. In additional, 23 (44%) had a positive family history for migraine. The mean ± SD BDI score was 15.3 ± 10.7. Thirty-two patients (64%) had some degree of headache-related disability according to the MIDAS, and the majority (67%) was classified as very severe impact according to the HIT-6. In relation to the nutritional data, most of the patients (62%) were overweight and had increased visceral fat according to their waist circumference (Table 1).

Patients returned for another three visits that occurred 30, 60 and 90 days after the first evaluation. During the period of nutritional intervention, 26 women (50%) discontinued the study (Figure 1). At the baseline, patients who completed the protocol had had more depressive symptoms (BDI: 18.9 ± 11.8 vs. 11.8 ± 8.3; p = 0.015) and lower diet quality [BHEI-R: 56.7 (42.6 - 80.5) vs. 65.0 (28.8 - 85.6); p = 0.028] than those who discontinued. There was no significant difference for the other variables (p > 0.05).

After nutritional intervention, weight, BMI and waist circumference did not change significantly. The BDI (p = 0.010 at 60 days and p = 0.001 at 90 days) and HIT-6 (p = 0.012) scores decreased, respectively, after 60 and 90 days (Table 2). Analysis of the improvement in migraine parameters according to weight loss showed that both women who maintained/gained weight (n = 12) or lost weight (n = 14) had better HIT-6 and BDI scores after intervention. However, the improvement of HIT-6 scores was statistically significant only among those who maintained or gained weight after 90 days (p = 0.029). For BDI scores the improvement was statistically significant for both groups: for women who maintained or gained weight (p = 0.002) and for those who lost weight (p = 0.034).

Figure 2 shows the distribution of patients in HIT-6 categories throughout the study. There was a migration of patients from the "very severe impact" category to the "substantial impact" category, which is consistent with the improvement in the means of the HIT-6 score. Reduction in the HIT-6 scores 90 days after the beginning of the nutritional intervention was observed for most patients (64%). Women who improved migraine severity with nutritional intervention had higher HIT-6 scores at baseline in comparison with those who did not improve (65.7 ± 7.4 vs. 58.8 ± 8.7; p = 0.045). There was no association between reduction of HIT-6 score and nutritional status at baseline.

Table 3 shows data for changes in eating habits. There was no significant difference in energy, macronutrients and fiber intake after nutritional intervention (p > 0.05). However, in qualitative analyses, there were increases in the total vegetable score, and the dark green and orange vegetable scores after 30 days of nutritional intervention. We also observed an increase in the total fruit score and decrease of calories from saturated fat-alcohol-sugar added to the meal, after 60 days of intervention. Additionally, there was an increase in the whole grains score after 90 days of nutritional intervention.

Table 1. Clinical and nutrition characteristics in patients with migraine.

Characteristics	% or Mean ± SD
Migraine	
Chronic	13
Episodic	87
Aura	
With aura	36
Without aura	64
Family history of migraine	
Yes	44
No	56
Prophylactic medication	
Beta-blocker	35
Tricyclic antidepressants	31
Valproic acid	18
Migraine Disability Assessment questionnaire (MIDAS)[23]	20.6 ± 29.5
Little or no disability	36
Mild disability	18
Moderate disability	16
Severe disability	30
Headache Impact Test (HIT-6)[24]	62.6 ± 8.9
Little or no impact	10
Some impact	13
Substantial impact	10
Severe impact	67
Beck Depression Inventory (BDI)[25]	15.3 ± 10.7
Weight (kg)	67.2 ± 12.1
Body mass index (kg/m^2)[20]	27.9 ± 4.7
Malnutrition	2
Normal range	36
Overweight	33
Obese	29
Waist circumference (cm)[21]	82.3 ± 10.6
No risk of metabolic complications	38
Increased risk of metabolic complications	33
Substantially increased risk of metabolic complications	29
Body composition	
Lean mass percentage	64.6 ± 8.3
Fat mass percentage	34.5 ± 8.0

SD: Standard Deviation.

The BHEI-R total score improved after 60 days (p < 0.001) and 90 days (p < 0.014) of nutritional intervention. Both normal weight or overweight woman showed improvement in the total BHEI-R score after 60 days of nutritional intervention (p = 0.007 and p = 0.010, respectively).

Table 2. Evolution of anthropometric parameters, severity of migraine and manifestation of depressive symptoms in patients before and after dietary intervention.

Characteristics*	Time			
	Baseline	30 days	60 days	90 days
Weight (kg)	66.3 ± 9.7	65.6 ± 9.4	65.3 ± 9.7	65.5 ± 10.2
Body mass index (kg/ m^{-2})	26.4 ± 4.5	26.1 ± 4.5	26.0 ± 4.5	26.1 ± 4.8
Waist circumference (cm)	81.7 ± 10.1	81.1 ± 9.6	80.2 ± 9.7	80.8 ± 9.6
% Fat mass	33.9 ± 6.3	33.7 ± 8.4	32.8 ± 6.3	32.8 ± 5.7
% Lean mass	66.1 ± 6.4	66.3 ± 8.4	67.2 ± 6.3	67.2 ± 5.6
Headache Impact Test, version 6 (HIT-6)	63.5 ± 8.4	60.0 ± 10.2	59.4 ± 9.5	57.9 ± 9.8[a]
Migraine Disability Assessment (MIDAS)	20.8 ± 24.9	-	-	16.1 ± 21.6
Beck Depression Inventory (BDI)	18.2 ± 11.8	15.9 ± 8.2	11.5 ± 5.7[a]	10.5 ± 6.0[a]

*Presented as mean ± standard deviation; [a]p ≤ 0.05. Student t-test or Wilcoxon paired.

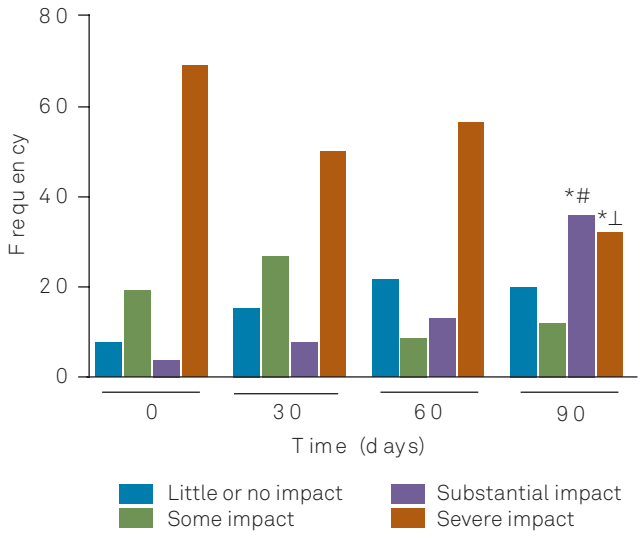

Figure 2. Evolution of the HIT-6 classification in women with migraine before and after nutritional intervention (n = 26). *Represents the difference with respect to the frequency of time zero; # Represents difference with respect to the frequency at 30 days; ⊥ represents differences regarding the frequency at 60 days. McNemar test.

The change in the diet quality score as assessed by the BHEI-R was negatively correlated with the migraine severity measured by HIT-6 (r = -0.45; p = 0.026) at the end of the interventional period.

DISCUSSION

Nutrition seems to play an important role in migraine as specific foods can be triggers for headache attacks, and inadequate diets can lead to weight gain with a consequent increase of illness severity[26]. The current study had two main findings: 1) nutritional intervention was able to improve the quality of diet of patients with migraine; 2) improvement in dietary habits was followed by improvement in migraine severity and reduced expression of depressive symptoms.

Evans et al.[27] found that women with migraine had a worse diet than women without this disease. To our knowledge, our study was the first to measure the quality of diet of migraine patients after nutritional intervention. The evaluation of diet quality considers the synergistic effects of food intake in which the interaction between nutrients and bioactive compounds are important, not only the effect of isolated components on health outcomes. This specific analysis contributes to an overall analysis of food consumption[18,28,29].

Cross-sectional studies have associated low diet quality with obesity[30], cardiovascular risk factors[31] and systemic inflammation[32]. A meta-analysis of cohort studies concluded that diets with high quality scores were associated with a significant reduction in the risk of all-cause mortality, cardiovascular disease, cancer and type 2 diabetes mellitus[28]. These findings are consistent with our results and reduction of inflammation may have been the mechanism by which the improvement in diet quality reduced the severity of migraine. In the present study, the sample consisted only of women who had a high degree of disability related to migraine. Most of them were overweight and had elevated adiposity. Previous studies have investigated the relationship between adiposity and migraine[8,9]. For instance, Bigal and Lipton[9] found that the increase in BMI was followed by an increase in chronic migraine frequency. Overweight patients had more frequent and severe headache attacks than normal weight patients[8,9], which may explain the high degree of disability related to migraine observed in our sample.

Depression also contributes to migraine severity. Ashina et al.[26] found that depressed migraineurs were more prone to developing chronic migraine than migraineurs with no depression (odds ratio = 1.65, 95 %CI 1.12–2.45). Teixeira et al.[33] reported a prevalence of around 30% of major depression

Table 3. Dietary calories, macronutrients, fiber and quality among women with migraine before and after nutritional intervention.

Characteristics*	Time			
	Baseline	30 days	60 days	90 days
Energy intake kj (kcal)	5,296.3 (1,265.0 ± 584.8)	4,483.2 (1,070.8 ± 460.8)	4,993.2 (1,192.6 ± 465.6)	4,955.9 (1,183.7 ± 557.9)
Carbohydrates (%)***	54.3 ± 7.4	54.8 ± 8.5	53.5 ± 17.7	56.0 ± 7.9
Protein (%)***	16.6 ± 5.1	17.0 ± 5.5	17.6 ± 7.9	15.3 ± 4.0
Lipids (%)***	29.1 ± 6.4	28.4 ± 6.9	27.4 ± 9.4	28.7 ± 6.0
Saturated fatty acids (%)***	9.4 ± 3.2	9.3 ± 4.0	9.3 ± 4.0	8.2 ± 3.5
Polyunsaturated fatty acids (%)***	5.4 ± 3,7	6.1 ± 4.1	5.7 ± 3.2	5.5 ± 2.5
Monounsaturated fatty acids (%)***	6.1 ± 1.7	6.3 ± 2.0	6.3 ± 3.7	6.5 ± 2.8
Fiber (g)	11.6 ± 8.4	18.4 ± 19.7	15.8 ± 12.7	13.4 ± 6.1
BHEI-R total score	57.9 ± 10.5	64.4 ± 13.8	71.5 (13.5)[a]	68.1 ± 17.5[a]
Fruits score	1.5 ± 2.1	2.6 ± 2.5	3.4 ± 2.0[a]	2.6 ± 2.1
Whole fruits score	1.9 ± 2.4	2.9 ± 2.4	3.8 ± 2.0[a]	3.1 ± 2.4
Vegetables score	2.5 ± 2.3	3.9 ± 1.9[a]	3.6 ± 1.9	4.1 ± 1.7[a]
Dark green-orange vegetables score	2.0 ± 2.4	3.2 ± 2.4[a]	3.4 ± 2.2[a]	4.0 ± 2.0[a]
Grains score	4.5 ± 1.2	4.5 ± 1.2	4.7 ± 1.0	4.9 ± 0.2
Whole grains score	0.5 ± 1.2	0.5 ± 1.4	1.1 ± 1.9	1.7 ± 2.1[a]
Dairy score	5.9 ± 3.3	4.5 ± 3.9	4.9 ± 3.8	4.5 ± 3.5
Meat score	7.2 ± 3.3	7.1 ± 4.0	8.6 ± 2.1	7.8 ± 2.9
Oil score	8.8 ± 2.8	9.8 ± 1.0	9.6 ± 2.0	9.9 ± 0.3
Saturated fat score	7.9 ± 3.0	7.9 ± 2.9	8.5 ± 2.4	8.0 ± 2.4
Fat-sugar-alcohol score**	8.5 ± 7.0	11.2 ± 6.2	12.8 ± 6.2[a]	10.7 ± 9.1

BHEI-R: Brazilian Healthy Eating Index Revised. *Presented as mean ± standard deviation; **Sum of calories as saturated fat and trans, added sugar and alcohol; ***Percentage of the total calorie intake; [a]p ≤ 0.05. Paired Student t-test and Wilcoxon.

among chronic migraineurs. Conversely, migraine patients have twice the chance of developing depressive and anxiety disorders, suggesting that there is a bidirectional association between migraine and depression[34,35]. In addition, depression may be associated with being overweight in migraine patients. Tietjen et al.[36] found that the prevalence of depression was higher among obese migraineurs than normal weight migraineurs. Accordingly, the improvement of migraine severity observed in the current study may be related, at least in part, to the improvement of depressive symptoms.

Although other studies have already demonstrated an association among being overweight, depression and severity of migraine[9,10,37], very few studies have evaluated the impact of nutritional interventions and weight loss on migraine severity. Gunay et al.[10] reported that, after bariatric surgery, patients showed a decrease in migraine severity after mean reduction of 56% their weight. Verrotti et al.[11] evaluated obese adolescents before and after a program involving diet, physical activity and behavioral therapy. They observed a decrease of weight, BMI, waist circumference, frequency and intensity of migraine attacks, use of acute medication and the MIDAS score. In the current study, as there were no significant modifications in weight or body composition, changing the diet quality may have played the main role in migraine improvement. The lack of a control group prevents a definite conclusion in this regard, as it was not possible to control for nonspecific effects related to the clinician-patient interaction.

The present study has some limitations, including sample size, lack of a control group, and the large number of dropouts. Since adherents and dropouts were similar in sociodemographic and clinical parameters, we believe that this does not impair the meaning of our results. Our study dealt with patients with severe forms of migraine, thus findings must be interpreted with caution to milder forms of migraine.

The current study highlights the potential of nutritional intervention as a strategy to reduce migraine severity. Further examination of the relationship between the quality of diet and severity of migraine is warranted.

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