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The ketogenic diet as a potential therapeutic approach for migraine management: a review of current evidence

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Abstract

Introduction

Migraine, a common neurological disorder, significantly reduces quality of life, particularly among women. Despite advancements in treatment, therapeutic options remain limited, and side effects are common. The ketogenic diet (KD), characterized by low carbohydrate and high fat intake, has shown promise in reducing migraine frequency and severity.

Aim of the study

The aim of this study is to review the literature on the effectiveness of of the ketogenic diet on the frequency of migraine attacks and their severity.

Materials

This review analyzed two studies by Di Lorenzo et al. (2018) and Caprio et al. (2023), both demonstrating that KD significantly reduced migraine days compared to non-ketogenic diets. Additional benefits included reduced inflammatory markers and improved body weight.

Results

While findings are promising, limitations such as small sample sizes, focus on overweight individuals, and lack of long-term safety data highlight the need for larger studies.

Conclusions

KD offers potential as an effective alternative for managing migraines, but further research is required to confirm its benefits and safety.

Keywords: migraine, ketogenic diet

Introduction

Migraine, as a chronic and episodic neurological disorder, affects a significant portion of the population, particularly women, with a prevalence of approximately 17% in Europe compared to around 8% in men. [1] It is classified as a primary headache disorder. Apart from moderate to severe headaches, migraine often manifests with symptoms such as nausea, vomiting, hypersensitivity to sound and light, loss of appetite, and general weakness. [2] The pathophysiology of migraine remains incompletely understood. However, it is believed to be associated with abnormalities in energy metabolism within the central nervous system, potentially linked to mitochondrial dysfunction. [3] Factors that predispose individuals to increased migraine frequency include smoking, overuse of analgesics, head injuries, hormonal

imbalances, lower socioeconomic status, sleep disturbances, obesity, diabetes, dyslipidemia, hypertension, autoimmune diseases, and neurological disorders. [4]

Despite the relatively high prevalence of migraine in the European population and the rapid development of new therapeutic methods, the quality of life for migraine patients remains diminished. The underlying mechanisms of the disease are still not fully understood, and available treatment options are limited. [5] Most pharmacological therapies are associated with a high risk of bothersome side effects, highlighting the need for alternative approaches to migraine management.

The ketogenic diet, characterized by low carbohydrate intake, high fat consumption, and moderate protein intake, was developed in the 20th century after it was observed that prolonged fasting with sustained ketosis had anticonvulsant effects. [6] Depending on the daily carbohydrate intake, the diet can be categorized as very low-carbohydrate ketogenic (less than 50 grams per day), low-carbohydrate (50-100 grams), or moderate-carbohydrate (130-225 grams). [7]

Recent studies suggest that maintaining a state of ketosis may be associated with a reduction in migraine frequency, decreased severity of attacks, and a reduced need for strong analgesics. [8-10]

Aim of the study

The aim of this paper is to review current scientific reports and summarize the state of knowledge regarding the effect of the ketogenic diet on the frequency of migraine attacks and their severity.

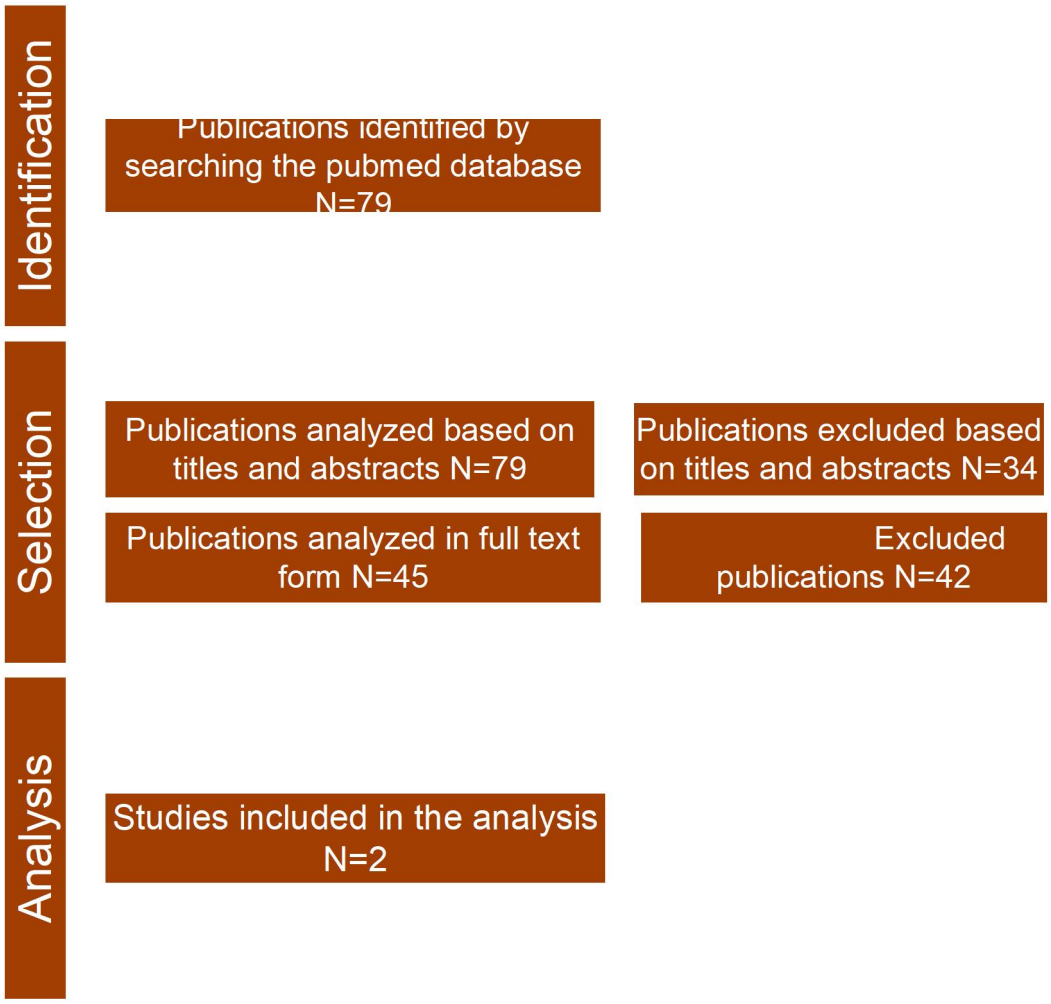
Methods

In November 2024, a review of the available literature was conducted using the PubMed database. Articles were searched using the keywords "migraine" and "ketogenic diet". The search period was not limited. A total of 79 articles were found as a result of the initial search.

Studies were selected based on the following inclusion criteria (1) observational studies, (2) peer-reviewed journals, (3) articles in English, (4) with free access to the full text of the article, (5) concerned the analysis of the effect of the ketogenic diet on the frequency or severity of migraine attacks, (6) included an adult population (>18 years of age). The following exclusion criteria were applied: (1) studies in a group of patients with confounding factors, e.g. other neurological diseases.

A summary of the search process for studies is presented in Figure 1.

Table 1. Characteristics of the analyzed articles



Source: own study

Results

Two papers were subjected to final analysis. The characteristics of the papers discussed in chronological order are presented in Table 1.

First author, month, year of publication	Number of participants, average age	duration of the study	Inclusion criteria	Intervention group	Control group
Cherubino Di Lorenzo, 07.2018 [11]	29, 41	1 month	Overweight/obese adults (Body Mass Index (BMI) > 25) 18 to 65 years, 12 months history of migraines with or without aura, defined according to the criteria of the International Classification of Headache Disorders, a history of between 2 and 14 migraine days per month on average during the 3-months preceding the trial and during the 4-weeks baseline phase.	People on a low-calorie ketogenic diet	People on a low-calorie, non-ketogenic diet
Massimiliano Caprio, 10.2023	57, 42,6	24 weeks	- BMI 27 – 35 - diagnosis of migraine -migraine onset <50 years -preventive migraine treatment discontinuation since at least 3	People who follow a very low-calorie ketogenic diet for 8 weeks, followed by a low-calorie ketogenic diet for 3 weeks, and	People who follow a balanced low-calorie diet for 24 weeks

			moths -negative pregnancy test -use of a valid contraceptive method throughout the study	a balanced low-calorie diet for another 12 weeks	

Ch. Di Lorenzo's team conducted a randomized, double-blind study to analyze the efficacy and therapeutic effect of a low-calorie diet in overweight patients with paroxysmal migraine. The subjects were randomly assigned to a group using a low-calorie ketogenic or non-ketogenic diet. The study was completed by 29 people. The outcome measure was a reduction in the number of migraine days in a monthly follow-up compared to the clinical picture before the intervention. The number of migraine attacks per month, the number of painkillers taken, and the change in body mass index (BMI) were also assessed. As a result of the analysis, it was shown that patients using a ketogenic diet experienced a greater reduction in the number of days per month compared to those using a non-ketogenic diet. / The number of migraine attacks also decreased in this group. However, there were no significant differences in the change in BMI and the number of painkillers taken. The analysis indicates that the ketogenic diet may have a preventive effect in people with migraine attacks. However, the study was conducted on a small group of patients, which indicates the need to conduct a similar analysis in the future with a larger population. [11]

Another study included in the review assessed the effectiveness of a low-calorie ketogenic diet compared with a low-calorie balanced diet in reducing migraine attacks in overweight or obese people. Fifty-seven people were randomly assigned to either a low-carbohydrate intervention group or a balanced diet control group. The measure of effectiveness of the intervention was the change in migraine days per month from baseline, visual analogue scale (VAS) scores, lymphocyte counts and inflammatory markers in the blood, and aldosterone and renin levels. The analysis showed that the reduction in the number of migraine days per month was greater for people in the intervention group. This group also showed greater effectiveness in reducing body weight. Inflammatory markers also decreased. It was shown that the ketogenic diet can be an effective alternative method of reducing the number of migraine attacks. [12]

Discussion

The ketogenic diet, characterized by very low carbohydrate intake, moderate protein consumption, and high fat intake, is gaining increasing attention as a potential method to support migraine therapy. The results of available studies, such as those conducted by Di Lorenzo and Caprio's teams, provide promising data on the effectiveness of this intervention. Di Lorenzo's study showed that following a ketogenic diet was associated with a significant reduction in the number of migraine days and attacks compared to a low-calorie but non-ketogenic diet. Similarly, the EMIKETO study results confirm that the ketogenic diet was not

only more effective in reducing the number of migraine days but also in improving other health parameters, such as body weight and levels of inflammatory markers.

The proposed mechanisms of action for the ketogenic diet include its potential anti-inflammatory properties, which may be relevant in the context of migraine pathogenesis related to inflammatory processes. Research also indicates the possibility of modulating brain metabolism through ketones, such as beta-hydroxybutyrate, which serve as an alternative energy source for the brain, stabilizing its function under metabolic stress conditions. Additionally, ketosis may influence the balance of neurotransmitters like GABA and glutamate, promoting a reduction in neuronal hyperexcitability characteristic of migraines.

Despite the promising results, these studies have certain limitations. Both Di Lorenzo's analysis and the EMIKETO study involved small sample sizes, making it difficult to generalize the findings to a broader population. Moreover, the research focused on individuals with overweight or obesity, introducing additional variables such as the impact of weight loss itself on migraine frequency. Furthermore, there is a lack of long-term data on the sustainability of the ketogenic diet's effects and its safety over extended periods.

The current literature still lacks large-scale studies on the impact of the ketogenic diet on migraines, particularly in the context of large, randomized, and multicenter analyses. Nevertheless, preliminary findings suggest that the ketogenic diet could represent a promising therapeutic alternative for patients suffering from chronic episodic migraines. Furthermore, the anti-inflammatory action of the ketogenic diet may provide additional benefits in preventing migraine attacks. However, further large-scale studies are necessary to confirm these conclusions and better understand the potential mechanisms and limitations of this intervention.

Conclusions

The conclusions from available studies indicate that the ketogenic diet may be an effective method for reducing migraine attacks in individuals with overweight or obesity. Results suggest that this diet is more effective than low-calorie, balanced, or non-ketogenic diets in terms of decreasing the number of migraine days and reducing the severity of attacks. Its anti-inflammatory effects and the potential modulation of brain metabolism by ketones are proposed mechanisms underlying the observed benefits.

Despite the promising outcomes, the studies were conducted with a small number of participants, limiting the ability to generalize the results to a broader population. Additionally, the focus was primarily on patients with overweight or obesity, a confounding factor since weight loss alone can influence the reduction in migraine attacks. Long-term analyses of the ketogenic diet's safety and efficacy in this patient group are also lacking.

For these reasons, more extensive and comprehensive studies involving larger and more diverse patient groups are needed. Long-term, multicenter analyses would provide a better understanding of the ketogenic diet's therapeutic potential, its enduring effects, and possible limitations. Nonetheless, the available data suggest that the ketogenic diet could be a promising alternative for the prevention and treatment of episodic migraine.

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Author does not report any disclosures.

Author contribution

The author is responsible for the conception, literature review, data analysis, and writing of the manuscript. All aspects of the study were conducted independently by the author.

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Conflicts of Interest

The author declares no conflict of interest

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