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Chronic migraine prevention from the perspective of a family doctor: a literature review

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Abstract

Chronic migraine is a disease that significantly reduces the quality of life of patients. It affects millions of people around the world, and is common particularly among young women. Family physicians often encounter the problem of migraine headaches in their daily practice. The diagnostic problem results from absence of tests or imaging studies that can clearly indicate the cause of the headache. In order to establish a diagnosis and exclude secondary sources of pain, doctors focus on a detailed medical history and analysis of symptoms presented over time. Preventive treatment of migraine requires appropriate drug selection after weighing the benefits and risks for each patient. This review paper presents and briefly discusses selected pharmacological and non-pharmacological methods used in migraine prevention. They were selected by searching the PubMed Internet database. The presented non-pharmacological methods include the use of nutraceutics, acupuncture and behavioral therapy. The discussed pharmacological methods include treatment with beta-blockers, topimarate, flunarizine or one of the latest methods - the use of monoclonal antibodies against CGRP. In addition, the use of botulinum toxin type A in the treatment of chronic migraine has also been demonstrated. It should be remembered that the type of therapy chosen should be individualized: according to the patient's preferences, treatment effectiveness, possible side effects or accompanying diseases. Proper management of chronic migraine prophylaxis can significantly improve the quality of life of patients and reduce the frequency of headache attacks.

Keywords: migraine; headache; preventive therapy

Aim of the study:The aim of the study is to represent recommendations, based on EBM, for preventive treatment of chronic migraine for family physicians. Into consideration were taken non-pharmacological and pharmacological methods.

Materials and methods:

Current information about treatment of migraine headaches is important for family physicians. In this study available literature about migraine headaches is introduced. Significant studies

were identified by searching literature in internet database PubMed. Selection of articles was done focusing on the following key points: modification of lifestyle, non-pharmacological treatment of migraine, prophylactic pharmacological treatment of migraine, new methods of migraine treatment. In addition, from available studies on pharmacological treatment, mainly those from years 2018-2022 were chosen.

Introduction

Migraine is a disease that affects millions of people around the world, impairing functioning not only during attacks, but also affecting daily activities and reducing the quality of life of patients. [1]*Chronic migraine*We define it as a headache that lasts at least 15 days a month, at least 8 of which meet the criteria for migraine headaches, is sensitive to treatment with triptans or ergotamine, and lasts longer than 3 months. [2]

It also constitutes a diagnostic and therapeutic challenge for practicing physicians. According to the latest Global Burden of Disease research, migraine ranks as the second leading disability in the world and is the leading cause among young women. [3] The diagnosis is based on a detailed interview and physical examination of the patient. There is currently no imaging, blood or cerebrospinal fluid test available to confirm the diagnosis of migraine. [4] Typically, additional tests are needed only in the case of differential diagnosis and exclusion of secondary origin of headaches. [5]

Treatment is based on both pharmacological and non-pharmacological methods. Pharmacological treatment can be divided into prevention and treatment of acute pain. [6,7,8] Thanks to the progress of science, patients can now be offered many different methods of prevention tailored to the individual needs of each of them.

Non-pharmacological methods.

In 2019, primary care physicians attempted to provide recommendations on lifestyle modifications to help prevent migraine and identify pain triggers hidden under the acronym*SEEDS*(*Sleep, Exercise, Eat, Diary, and Stress*) - sleep, exercise, diet, dairy and stress. [9] It is generally accepted that migraines are related to diet and that certain dietary components can trigger migraine attacks. Potential list*triggers*is long. The following items were recorded in the literature: chocolate, dairy products, onion, citrus fruits, nuts, ice cream, tomatoes, alcoholic beverages, coffee, caffeine, gluten, monosodium glutamate (MSG), histamine, tyramine, phenylethylamine, nitrites, aspartame, sucralose. [10,11,12] Identification of the elements that trigger attacks allows the use of an exclusion diet. Despite the known impact of triggers on migraine attacks, the exact mechanism is not yet

known and requires further research. [13] It should also be remembered that completely eliminating certain products from the diet may lead to malnutrition. [14]

They can support your diet*nutraceuticals*, i.e. food products or supplements that have medicinal or health effects. Nutraceuticals are increasing in popularity among migraine patients and are likely to be widely underestimated. [15] The most commonly used in migraine prevention are riboflavin (vitamin B12), magnesium, coenzyme Q10, and butterbur root extract (*Petasites hybridus*) and pyrethrum maruna (*Tanacetum parthenium*). [16] Riboflavin is a precursor of flavin mononucleotide and flavin adenine dinucleotide and a water-soluble B vitamin [17]. The properties of this nutraceutical were first investigated in a randomized study in 1998 in Belgium conducted by Schoenen and a team of researchers. The effect of a 400 mg daily dose was studied in 55 adult patients with episodic migraine, with and without aura - riboflavin showed a significant effect on reducing the number of headache days and attack frequency, with only minor and rare side effects compared to placebo. [18] However, a randomized controlled trial in 48 children with episodic migraine found no difference between a 50% lower dose (200 mg) of riboflavin and placebo in reducing the number of headache days, their duration, or the severity of migraine attacks and associated symptoms . [19]*Behavioral methods*consist of various strategies such as relaxation, thermal and electromyographic biofeedback, and cognitive behavioral therapy. They are used in the treatment of migraine mainly to teach patients to cope with symptoms more effectively and recognize potential headache triggers. Relaxation techniques include progressive muscle relaxation, autogenic training, and meditation.[20] Use*acupuncture*in the prevention of migraine headaches has been the subject of research for years. Several randomized controlled trials have been conducted comparing the effects of acupuncture (both real (*verum)*, What sham*(sham)*and standard therapy, show a slight effect on headaches. However, blinding in these studies proves difficult and the strength of the evidence is low. [20]

One of the largest clinical trials (960 patients) was conducted in Germany. Three types of therapy were then compared: true acupuncture*(verum)*, sham*(sham)*and standard preventive therapy, showing that all types were effective in reducing the number of migraine days from baseline, but there was no significant difference between the three groups. This allows us to assume that the therapeutic effect of acupuncture does not depend on the positioning of the needles themselves. [22] The effectiveness of needle therapy requires expanded research.

Pharmacological methods.

Pharmacological migraine prophylaxis is used to reduce the frequency, length and severity of attacks, which facilitates the treatment of acute episodes.

Preventive medications should be used in the following cases: [23,24]

1. Frequent headaches (≥4 attacks per month or ≥8 headache days per month)
2. Presence of contraindications to use, occurrence of side effects or overuse of drugs to treat acute episodes
3. Individual patient preferences
4. Presence of prolonged auras
5. Direct impact on the patient's quality of life and interference with everyday life, despite proper treatment of acute attacks and lifestyle modifications.
6. Menstrual migraine.

The most frequently used drugs are: propranolol, metoprolol, flunarizine, valproic acid, topiramate, amitriptyline, naproxen, acetylsalicylic acid, bisoprolol, gabapentin.

Table 1. *Drugs recommended for the preventive treatment of migraine*

	Bow	Daily dose
First choice	Metoprolol	50-200
	Propranolol	40-240
	Flunarizine	5-10
	Valproic acid	500-1500
	Topiramate	25-200
Second choice	Amitriptyline	50-150
	Naproxen	2 x 250-500
	Bisoprolol	5-10
Other medicines	Gabapentin	1200-1600 mg
	Acetylsalicylic acid	300 mg
	Magnesium	24 mmol
	Riboflavin	400 mg
	Coenzyme Q	300 mg

The choice of treatment should be individualized for the patient based on his/her comorbidities, lifestyle, age and gender. The choice of drugs should be determined by both the doctor and the patient, taking into account side effects and drug effectiveness. [25]

*Beta-blockers*are one of the classes of first-line drugs most frequently chosen by family physicians. Lipophilic beta-blockers, more specifically metoprolol and propranolol, have the ability to cross the blood-brain barrier and have class A recommendations for the preventive treatment of migraine. [26] Side effects that can be expected during treatment with beta-blockers include dizziness and fatigue. Clinical trials have not shown significant differences between the use of beta-blockers and placebo and the occurrence of side effects such as depression, gastric problems, paresthesia and weight gain. [27]

Efficiency*topiramate*and*flunarizine*is comparable - the average reduction in migraine intensity is 59% for topiramate is 59%, and for flunarizine 58.5%. There were also no significant side effects reported in both study groups. [26]

Monoclonal antibodies, directed against calcitonin gene-related peptide (CGRP), is a relatively new form of prevention available to patients with migraine headaches.CGRP is a neuropeptide that modulates the nociceptive signaling pathway and a vasodilator. It has been found that CGRP release is observed during the headache phase. At the same time, intravenous administration of CGRP causes a migraine-like headache. Due to the above facts, it was assumed that CGRP plays a significant role in the pathophysiology of migraine and clinical trials were initiated.[28] Currently, the following drugs are registered by the European Medicines Agency (EMA) for the treatment of migraine: erenumab, fremazezumab, galcanezumab, eptinezumab and rimegepant. It is reported that up to half of patients receiving the antibodies experienced a 50% reduction in the severity of headaches, and given that they work for more than a month after administration, they can be used as a preventive drug, administered in monthly or even quarterly doses. [29]

*Botulinum toxin type A*has been used in the preventive treatment of chronic migraine for over a decade. This option is relatively well tolerated by patients and has a favorable safety profile. The use of botulinum toxin type A reduces the number of pain days by an average of 2 per month (recommendation level A for reduction of the number of days).

[30] It is used in the form of multiple injections, depending on the location - subcutaneous, intradermal or into the superficial layer of the muscle, based on specially developed protocols and should rather be reserved for
neurologists specializing in the treatment of migraine headaches using botulinum toxin type A [31]

Summary

Primary care physicians, as first-contact specialists, have various methods of preventing chronic migraine. Non-pharmacological forms (neuraceptives, acupuncture, behavioral therapy) may prove effective in special cases, such as patients suffering from multiple diseases, or be a good support for pharmacological treatment.
Preventive medications such as beta-blockers, topiramate, flunarizine, and monoclonal antibodies are used to reduce the frequency and severity of migraine attacks. The choice of drugs should be tailored to the patient's individual preferences and comorbidities and take into account effectiveness as well as possible side effects. Monoclonal antibodies such as erenumab, fremazezumab, galcanezumab, eptinezumab and rimegepant are used as a new form of migraine prophylaxis. Clinical studies have shown their effectiveness in reducing the severity of headaches in migraine patients.
The use of botulinum toxin type A also shows good effectiveness in reducing the number of headache days, but its use requires special qualifications and is usually performed by neurology specialists.

CONFLICT OF INTEREST
Author Contributions

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