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Conventional and unconventional treatments for migraine

Katarzyna Mielniczek¹, Diana Dołomisiewicz², Weronika Dalmata¹, Ilona Gąbka¹,
Jan Dąbrowski¹

¹ Students' Scientific Circle at the Department of Epidemiology and Clinical Research Methodology, Medical University of Lublin

² Student Research Group at the Department of Neurology “NEKON”, Medical University of Warsaw

Abstract

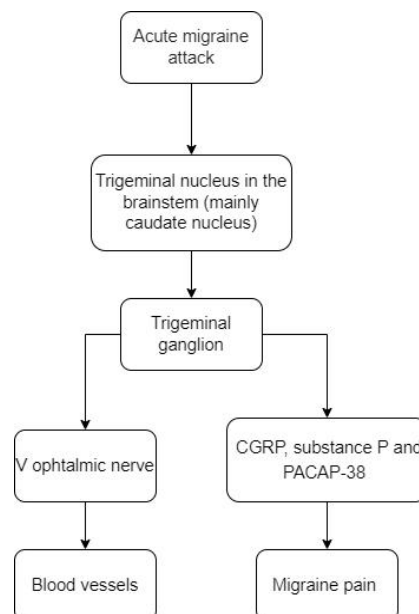
Migraine is one of the leading causes of disability in humans. It causes significant deterioration in patients' lives and prevents daily functioning. Its main symptoms include photophobia, an enormous stabbing headache, nausea and vomiting. In addition, it can be accompanied by tinnitus, visual disturbances or dizziness. Before diagnosing migraine, serious intracranial pathology or other neurological conditions should be ruled out. Treatment of acute migraine is difficult due to significant rates of nonresponse to medications and the difficulty in predicting individual response to a particular agent or dose. A new class of drugs, calcitonin gene-related peptide (CGRP) antagonists, has been approved for the prevention of migraine in adults. In contrast, effective first-line therapies for mild to moderate migraine are over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs) and combination analgesics containing paracetamol, aspirin and caffeine.

Keywords: acute migraine attack, migraine treatment, migraine headache, headache

1. Introduction:

Migraine is one of the more common current conditions. Its prevalence is estimated to be higher than diabetes and asthma. The World Health Organisation has listed migraine among the 10 most common disabling conditions. It has been shown to affect women more often than men. Migraine was ranked as the sixth cause of years lost due to disability worldwide in 2013 [1]. Headache is accounted for 3% of emergency department visits per year and was the fourth or fifth most common reason for patients visits to the emergency room. The prevalence of migraine decreases with age. It causes a significant deterioration in quality of life and its diagnosis and treatment require the involvement of physicians from several specialties [2]. Migraine can often be confused with tension headaches. Migraine sufferers may even go undiagnosed for a long time and thus receive inadequate treatment [1].

The process of migraine is complex, affecting both the central and peripheral nervous systems. However, each attack is heralded by characteristic symptoms i.e. aura, headache or photophobia. The process is illustrated in the diagram below [2]:



Ryc. 1. Process of migraine step by step [2]

Migraines are classified as with and without aura. Migraines with aura have fully reversible sensory, visual or other central nervous system related symptoms. The aura usually begins before the onset of the migraine, but may occur with the onset of the headache or after the headache has subsided. Visual auras are most common, followed by sensory disturbances, while speech disturbances are the least common.

2. Purpose of the work:

The aim of this study is to present both convective and non-convective treatments for migraine.

3. Material and methods:

A review of the scientific literature on PubMed and Google Scholar was conducted. Current knowledge was reviewed using the following keywords: “migraine”, “headache”, “migraine treatment”, “acute migraine attack”.

4. Discussion:

Migraine treatment usually consists of ad hoc or ineffective medications, while preventive medications are used by a minority of people with migraine. Triptans, which are selective serotonin 5-HT_{1B/1D} receptor agonists, have been approved for the treatment of acute migraine, unlike all other migraine agents that are also used for other conditions [1,3].

A new class of drugs, calcitonin gene-related peptide (CGRP) antagonists, has been approved for the prevention of migraine in adults. The newly approved CGRP antagonists are erenumab,

fremanezumab and galcanezumab. Lasmiditan, urogepant and rimegepant are currently emerging therapies for acute migraine that may be added to the arsenal of current migraine treatment [1]. It has been shown that administration of CGRP can trigger migraine in some individuals, while blocking CGRP can alleviate it. As a result of the release of the neurotransmitter from the trigeminal ganglion during an attack, there is an elevated level of the neurotransmitter in the blood, which is picked up by appropriate receptors located in the cortex, thalamus, brainstem, solitary nucleus and the trigeminal and dorsal root ganglia, among others. CGRP itself is a potent vasodilator [3].

4.1. Treatment via CGRP receptor antagonists

Amongst the CGRP receptor antagonists, olcegepant (administered intravenously to treat an acute seizure, which has been shown to work as effectively as triptans) and then telcagepant (oral preparation) were prominent - hence 'gepants' were born. However, they show greater tolerance by not causing vasoconstriction. Among the gepants, ubrogepant and rimegepant have been distinguished as drugs used to treat an acute migraine attack. So far, gepants have not been shown to constrict blood vessels [2].

4.2. Acute migraine attack

The treatment of an acute migraine attack includes ergot, triptans and non-steroidal anti-inflammatory drugs. The triptans are the most effective for short-term treatment. These include sumatriptan, naratriptan, rizatriptan, zolmitriptan, eletriptan, almotriptan, frovatriptan and the sumatriptan/naproxen combination. These drugs can be administered by various routes (oral, intravenous, intranasal), showing effects on serotonin metabolism. Naratriptan and frovatriptan show the longest and most effective effect. Triptans also inhibit the release of CGRP [2]. An acute migraine attack can be treated via either a stratified or stepped strategy.

Stratified treatment is preferable to stepped treatment [1,11,12]. The stratified treatment method is optimised when patients are able to recognise the headache and select the most effective medication for themselves. However, step therapy has the advantage of drug synergy. An example would be a patient who initially takes an NSAID before the migraine peaks and then takes a triptan or dihydroergotamine (DHE) as soon as possible. Despite everything, step therapy may result in a delay in headache relief [1,10,11]. For mild attacks, acetaminophen, aspirin and NSAIDs are recommended [1,12]. For the treatment of moderate to severe migraine, triptans or DHE are suggested [1,11].

4.3. Migraine attacks

Migraine is an intractable condition that prevents you from functioning on a daily basis, so it makes sense to prevent attacks. Many medications can be used to prevent migraine, including beta-blockers, calcium channel blockers, tricyclic antidepressants and anticonvulsants (especially topiramate and valproate) [2,4,5]. In addition, the efficacy of Onabotulinum toxin A has been confirmed [5]. It acts by releasing a number of different neurotransmitters: CGRP, substance P, serotonin, glutamate, gamma-aminobutyric acid (GABA), norepinephrine, dopamine, enkephalin and glycine. It can also affect pain receptors such as TRPV1, TRP1a, GABAA and even opioid receptors [6].

4.4. Mechanical treatments for migraine.

Name of mechanism	Indications	Mechanism of action	Side effects/contraindications
Neuromodulation	acute chronic migraine, cluster headache	non-invasive vagus nerve stimulation (gammaCore), transcranial magnetic stimulation (SpringTMS), supraorbital stimulation (Cefaly) and remote electrical neuromodulation (Nerivio Migra)	Paresthesia; vasovagal syncope Contraindicated with other implanted devices (e.g. pacemaker, cochlear implant)
Transcranial magnetic stimulation	migraine, depression	disruption of cortical spreading depression, which is thought to underlie migraine aura; affects neurotransmission and thus cortical excitability	Due to their low side effect profile, the devices are attractive for the treatment of migraine in pregnancy, as well as in other sensitive groups; contraindicated in people with other implanted devices (e.g. pacemakers and cochlear implants).
Remote electrical neuromodulation	acute migraine attack	controlled by mobile phone with stimulation for 45 minutes and is said to work by inhibiting pain pathways	Low side effects: sensations in the extremity.

Tab. 1. Mechanical treatments for migraine [2]

4.5 Migraine prevention

Preventive treatment of migraine is used daily to reduce the frequency, severity and duration of migraine attacks [1,7]. This treatment is considered for patients complaining of > 6 pain attacks per month [1,8]. FDA-approved migraine preventatives include propranolol, thymolol, divalproex sodium and topiramate. Other agents have established efficacy but are not FDA-approved [1,9]. Prophylactic therapy is selected on the basis of the patient's side-effect profile and comorbidities (e.g. comorbid hypertension can be treated with propranolol or thymolol; comorbid depression or insomnia can be treated with tricyclic antidepressants; comorbid seizure disorder or bipolar affective disorder can be treated with anticonvulsants) [1,8,10]. It takes up to 6 months to achieve full therapeutic effects [1].

4.6 Other effective therapies

Antiemetics have been shown to be effective in the treatment of nausea and vomiting during an acute migraine attack [13]. It has also been stated that intravenously administered metoclopramide should be considered as a primary drug in hospital emergency departments [13,14].

Intravenous dexamethasone is used as an adjunctive therapy for migraine in emergency departments due to its analgesic effect [13,15].

The drug combination acetaminophen/isometepten/dichloralfenazone (Midrin) includes a sympathicomimetic (isometepten) and a muscle relaxant (dichloralfenazone).

Intranasal lidocaine (xylocaine) has a rapid onset of action and may be useful as a deferral agent until a longer-acting therapy is working. A 4% lidocaine solution administered intranasally rapidly reduces unpleasant migraine symptoms [15].

5. Summary and conclusions

In addition to the already proven medications with legitimate effects, there are a number of modern therapies used to treat migraine that can make life easier for patients. Due to the huge number of the population suffering from this condition, keeping up with this rapidly developing field is important in reducing the disability caused by a common condition such as migraine [1,2,14].

Wkład autorski

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Konflikt interesów

Autorzy deklarują brak konfliktu interesów.

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