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# Management of Migraine Using Pain Killers: A Systematic Review

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## Abstract

**Introduction:** Migraine is a disabling disease that can significantly impact work or school productivity and lead to absenteeism. The overuse of analgesics and anti-migraine drugs have been published in recent years. This review aimed to identify the advancement in management of migraine using various types of pain killers.

**Methods:** A systematic search was conducted of English-language articles in PubMed, Cochrane, and EMBASE databases to identify studies on the prevalence and incidence of chronic migraines. The search included terms related to chronic migraines, as well as epidemiological terms such as burden, prevalence, and incidence, and terms related to other types of chronic headache. Studies were included if they were population-based, conducted in adults, and reported prevalence and/or incidence estimates for CM or provided sufficient information to calculate these estimates.

**Results:** A total of 21 studies were included in a review of treatments for migraines. These studies included 11 randomized controlled trials, 5 retrospective reviews, and 4 prospective chart review studies. The studies evaluated a variety of treatments, including intravenous fluids, analgesics, dopamine receptor antagonists, valproic acid, propofol, magnesium, bupivacaine, triptan medications, and dihydroergotamine. The primary outcome in most of the studies was the change in pain on a visual analog scale at 30 minutes. One study found that ibuprofen had nearly three times the odds of efficacy compared to placebo at 2 hours, and was twice as effective as acetaminophen. Another study found that acetaminophen was superior to placebo in reducing headache intensity.

**Conclusions:** The use of recommended first-line therapies varied greatly within the healthcare system and the frequent use of narcotics was concerning due to the limited effectiveness of these drugs in the treatment of migraines and the increased risk of adverse side effects and drug abuse.

**Keywords:** *Migraine, Headache, Analgesics, Narcotics, Therapy.*

## Introduction

Migraine is a neurological disorder characterized by severe, throbbing headaches that are often accompanied by other symptoms such as sensitivity to light and sound, nausea, and vomiting. It is a common condition, affecting about 22.3% of adult women and 10.8% of adult men in the US. Migraine is a disabling disease that can significantly impact work or school productivity and lead to absenteeism [1]. It also has a significant impact on healthcare costs, with an estimated annual direct cost of \$17 billion in the US. The underlying cause of migraine is thought to involve disruptions in the normal neural networks of the head and the role of neurotransmitters such as serotonin. Triptans, a class of medications used to treat migraines, work by activating serotonin receptors. Over-the-counter medications, including acetaminophen, ibuprofen, naproxen, and aspirin, are often the first line of treatment for mild to moderate migraines [2]. In addition to these traditional medications, melatonin and other complementary treatments are being explored as a potential treatment for migraine prevention.

The overuse of analgesics and anti-migraine drugs have been published in recent years, as have randomized clinical trials on the treatment and prevention of this condition [3]. Acetaminophen, ibuprofen, and aspirin are all over-the-counter medications that can be used to treat migraines. Acetaminophen is effective for treating acute migraines, while ibuprofen is often used for the treatment of chronic migraines because of its ability to reduce pain, inflammation, and fever. Aspirin can be used to treat chronic migraines on its own or in combination with other medications. A review conducted by Cochrane found that aspirin is effective for treating acute migraines in adults. Melatonin, a hormone involved in sleep, is also being explored as a potential treatment for preventing migraines. Studies have shown that melatonin may be effective for this purpose, and there is a growing body of literature on the use of melatonin and other complementary treatments for migraine prevention [4]. Over-the-counter medications are generally preferred over the

prescription medications for treating migraines because they are more accessible and cost-effective. Migraine can be treated with a variety of medications, including analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), ergotamine derivatives, and triptans, which work by activating serotonin receptors [5]. However, overuse of these medications can lead to medication-overuse headache, a condition where regular use of headache medications actually increases headache frequency. For people who experience more than two or three migraines per month, preventive treatment may be beneficial, although the optimal frequency for preventive treatment is a matter of debate. Selective cyclooxygenase 2 inhibitors, a type of NSAID, have also been found to be effective in treating migraines, but the most well-studied drug in this class, rofecoxib, is no longer available. Allodynia, a condition where non-painful stimuli are perceived as painful, is common in migraine and affects about two-thirds of people with the condition [6].

Migraine attacks can be more effectively treated if medication is taken early in the attack, when the pain is still mild, rather than later when the pain is moderate or severe. This has led to a search for nonvasoconstrictor therapies for acute migraines. Preventive therapy, which aims to reduce the frequency and severity of migraines, is important for about a third of people with migraines [7]. Many preventive medications seem to work by inhibiting the process of cortical spreading depression, which is thought to play a role in migraines. Guidelines for when to start pharmacological migraine prophylaxis vary, with some recommending it for people who experience more than two attacks per week and others suggesting it for those with two or more attacks per month. Several medications, including propranolol, amitriptyline, and topiramate, have been shown to be effective in reducing the frequency of migraines in clinical trials. Flunarizine, which is not available in many countries, and verapamil, which has only been tested in small studies, may also be used for this purpose [6,8]. Triptans are a class of medications used to treat migraines, which work by activating serotonin

receptors. They are effective in treating acute migraines and cluster headaches, but may not be suitable for everyone and can have limitations, including the recurrence of symptoms after initial effectiveness [9]. New drugs are being developed as alternatives to triptans for the treatment of migraines, including those that target calcitonin gene-related peptide (CGRP) and nitric oxide, which are thought to be involved in the development of migraines. These new drugs, including olcegepant and telcagepant, have shown promise in clinical studies. Other medications, such as beta blockers, antiepileptics, calcium channel blockers, angiotensin II receptor antagonist inhibitors, and antidepressants, are used for the prevention of migraines. Neuromodulatory methods are also being explored for the treatment and prevention of migraines [10]. This review aimed to identify the advancement in management of migraine using various types of pain killers.

## Methods

A systematic search was conducted of English-language articles in PubMed, Cochrane, and EMBASE databases to identify studies on the prevalence and incidence of chronic migraines (CM). The search included terms related to chronic migraines, as well as epidemiological terms such as burden, prevalence, and incidence, and terms related to other types of chronic headache. Studies were included if they were population-based, conducted in adults, and reported prevalence and/or incidence estimates for CM or provided sufficient information to calculate these estimates.

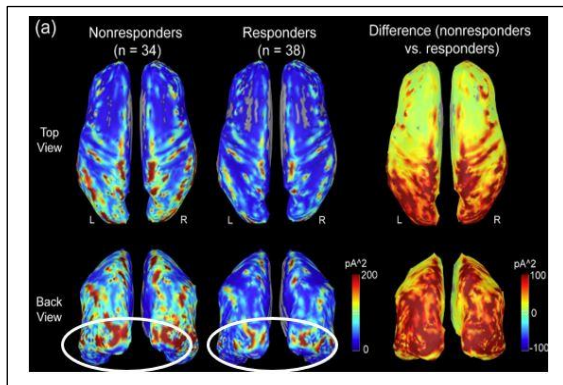
Studies were included in the review if they were population-based, conducted in adults, and reported or provided information on the prevalence and/or incidence of chronic migraines. Studies were excluded if they were case-control studies, did not specifically report on chronic migraines, were not population-based, only included individuals with chronic migraines, or only included adolescents or children. The review included studies that defined chronic migraines as having at least 10 headaches per month, as well as studies that addressed daily headache without a specific cut-off point. The abstracts of all

identified studies were reviewed by two independent researchers, with a sample of 10% of abstracts reviewed by both researchers to assess inter-rater agreement. The remaining abstracts were then divided between the reviewers.

## Results and discussion

A total of 21 studies were included in a review of treatments for migraines. These studies included 11 randomized controlled trials, 5 retrospective reviews, and 4 prospective chart review studies. The studies evaluated a variety of treatments, including intravenous fluids, analgesics, dopamine receptor antagonists, valproic acid, propofol, magnesium, bupivacaine, triptan medications, and dihydroergotamine. The primary outcome in most of the studies was the change in pain on a visual analog scale at 30 minutes. One study found that ibuprofen had nearly three times the odds of efficacy compared to placebo at 2 hours, and was twice as effective as acetaminophen. Another study found that acetaminophen was superior to placebo in reducing headache intensity. There was also an interaction with sex in one study, with boys treated with ibuprofen experiencing relief at a higher rate than girls.

In a study of prochlorperazine as a treatment for migraines, 75% of patients reported a 50% reduction in headache severity at 1 hour, with 95% experiencing this level of reduction at 3 hours. By 24 hours, 90% of patients were pain-free [11]. In another study, 94% of patients with a confirmed diagnosis of migraines observed a 50% reduction in intensity following treatment with prochlorperazine at the first evaluation. However, 50% of these patients experienced headache recurrence within the first week after treatment. Some patients experienced symptoms of akathisia, a condition characterized by restlessness and an inability to sit still, but this was successfully treated with an additional dose of diphenhydramine in half of the patients. In a comparison study, prochlorperazine was found to be more effective than ketorolac in treating migraines, with 85% of patients receiving prochlorperazine experiencing success compared to 55% of patients receiving ketorolac [12]. However, there was a higher rate of recurrent headache within 48 hours in the group that received prochlorperazine.



These headaches can be disabling and can significantly impact productivity and quality of life. There are various medications that can be used to treat acute migraine attacks, including over-the-counter medications like acetaminophen, ibuprofen, and aspirin, as well as prescription medications like triptans and other drugs. These medications can be effective at reducing the duration and severity of migraines, but they may also have limitations and side effects. There is also a need for new treatments for acute migraines, as current options may not be effective or well-tolerated for all patients. Research has been conducted on a variety of potential new treatments for acute migraines, including CGRP receptor antagonists, nitric oxide inhibitors, and various medications [13,14]. However, more research is needed to fully understand the effectiveness and safety of these treatments. In addition to treatment for acute migraines, preventive therapies may be necessary for patients with frequent migraines. These therapies can include medications like beta blockers, antiepileptics, and antidepressants, as well as neuromodulatory methods. The choice of preventive therapy will depend on the individual patient and the specific characteristics of their migraines [15].

It is a highly burdensome and disabling condition that affects a significant percentage of the population and has a significant impact on healthcare costs. The underlying cause of migraine is thought to be related to disruptions in the normal neural networks in the head, and certain neurotransmitters, such as serotonin, play a role in its pathophysiology [16]. There are various medications and treatments available for managing migraines, including over-the-counter pain

relievers, triptans, and other prescription medications. In addition to these pharmacological approaches, relaxation techniques such as progressive muscle relaxation, autogenic training, and meditation, and physical treatments like massage, postural correction, and chiropractic therapy may also be effective in managing migraines. Topiramate, a medication used for the prevention of migraines, has been found to be effective in reducing the frequency of migraines across a range of frequencies and may also prevent the escalation of migraines from episodic to chronic [17]. It may also be useful in reverting chronic migraines to episodic ones. The use of over-the-counter or prescription medications for acute headaches, known as medication overuse, is a common factor in the escalation of episodic migraines to chronic migraines and can increase the frequency and severity of migraines in people with chronic migraines. However, there is a lack of large-scale, controlled studies evaluating the effectiveness of medication withdrawal and preventive medications in patients with chronic migraines and medication overuse [18].

A number of clinical trials have been conducted to assess the efficacy of different treatments for relieving the headache associated with acute migraine [12, 17-19]. When the data from these trials is analyzed together, it can provide more accurate information about the safety and effectiveness of these treatments. Some treatments, such as Excedrin, have been found to be effective in reducing the severity of migraines in certain patient groups, but the results of these trials may not be directly comparable to those of other interventions due to differences in the design of the trials [20, 21]. The lack of high-quality clinical trials for many treatments currently recommended for the treatment of acute migraines is also noted [22]. There are several relaxation techniques that may be helpful in managing migraines, including progressive muscle relaxation, autogenic training, and meditation. These techniques involve tensing and relaxing specific muscle groups, using self-instructions to promote relaxation, and silently repeating a word or sound to achieve mental calm. Physical manipulation or treatments, such as massage, postural correction, neck exercises, chiropractic therapy, and osteopathic manipulation, are also commonly recommended and sought out by patients [23,24].

## Conclusions

A study found that the majority of patients with acute migraines in emergency departments (EDs) received narcotic analgesics as their first line of treatment, even though professional organizations recommend using non-narcotic medications as the first line of treatment. The use of recommended first-line therapies varied significantly within a linked healthcare system. The frequent use of narcotics correlated with the results of two other studies in the US, and is concerning due to the limited effectiveness of first-line narcotics in ED treatment of migraines, as well as the increased risk of adverse side effects and drug abuse. Patients with shorter duration of headaches, those deemed less urgent by triage nurses, and those reporting medication allergies were more likely to receive narcotics as first-line treatment. However, patients treated with first-line narcotics were more likely to return to the same ED for headache treatment, suggesting ineffectiveness or a desire for narcotics. The study recommends using other more effective agents as the first choice for emergency treatment of migraines.

## Conflict of interests

The authors declared no conflict of interests.

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