

Reasons and Management of Headache (Migraine): A Systematic Review

*Hassan Mohammed Hamad Alyami (1) *, Hamad Ali Hamad Al Hotelah (2), Zidane Saleh Muhammad Zabadin (3), Mohammed Abdullah Ali Al Jearah (4), Youssef Muhammad Mansour Al Abbas (5), Rahmah Mabkhoot Alzaqzaq (6), Salmah Ahmad Ameer Alshehri (7), Noora Ali Hussien Al Mukalas (8), Ghaliyah Ali Hussien Almukalas (9), Wafgah Ali Mohd Balhareth (10)*

1. *Social Work (Sociology), King Khalid Hospital, Najran, Saudi Arabia.*
2. *Nursing Technician, King Khalid Hospital, Najran, Saudi Arabia.*
3. *Pharmacist Assistant, Mohammedia Dispensary, Najran, Saudi Arabia.*
4. *Operations Technician, Forensic Medicine Department, Najran, Saudi Arabia.*
5. *Emergency Medical Services, King Khalid Hospital, Najran, Saudi Arabia.*
6. *Nurse, King Khalid Hospital, Najran, Saudi Arabia.*
7. *Nursing Technician, Najran Health Cluster, Najran, Saudi Arabia.*
8. *Nursing Technician, Hai Alfahad Alsh mali Primary Health Care Center, Najran, Saudi Arabia.*
9. *Nursing Technician, Thar General Hospital, Najran, Saudi Arabia.*
10. *Nursing, Administration of Centers, Najran, Saudi Arabia.*

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*Corresponding author

Abstract

Introduction: Migraine represents a significant burden, often impairing individuals' productivity at work or school and increasing the likelihood of absenteeism. Recent literature has highlighted concerns regarding the excessive consumption of analgesics and specific migraine medications. This review seeks to explore recent advancements in the treatment of migraines with an emphasis on pain management strategies.

Methods: A comprehensive literature review was conducted in English on PubMed, Cochrane, and EMBASE databases to gather data on the management of chronic migraines. The search criteria encompassed terms related to chronic migraines, epidemiological measures such as the disease's burden, prevalence, and incidence, and broader chronic headache conditions. Inclusion criteria were set for population-based studies in adult subjects that either reported on the prevalence and incidence of chronic migraines or provided data from which these metrics could be derived.

Results: Out of the pool, 21 studies were deemed relevant for inclusion in this analysis of migraine treatment modalities. This collection comprised 11 randomized controlled trials, 5 retrospective studies, and 4 prospective chart reviews. Investigated treatments spanned a range, including intravenous therapies, various analgesics, dopamine receptor antagonists, valproic acid, propofol, magnesium, bupivacaine, triptan medications, and dihydroergotamine. A common endpoint for these studies was the assessment of pain reduction using a visual analog scale 30 minutes post-treatment. Notably, one investigation revealed that ibuprofen was significantly more effective than both placebo and acetaminophen in alleviating headache symptoms at the 2-hour mark. Another study highlighted acetaminophen's superiority over placebo in diminishing headache severity.

Conclusions: The findings underscore a diverse application of first-line treatments within healthcare settings for migraine management. However, the prevalent prescription of narcotic pain relievers raises concerns due to their questionable efficacy in migraine relief, potential for adverse reactions, and the risk of medication overuse and dependency.

Keywords: *Migraine Management, Chronic Headache, Pain Relief, Medication Overuse, Treatment Strategies*

Introduction

Migraine, a complex neurological condition, manifests as intense, pulsating headaches often accompanied by nausea, vomiting, and heightened sensitivity to light and sound. It prevalently affects approximately 22.3% of adult women and 10.8% of adult men in the United States, significantly impairing their ability to function in work or academic environments [1]. Migraines contribute to substantial healthcare expenditures, with the annual direct costs in the U.S. estimated at around \$17 billion. The pathophysiology of migraines is believed to involve abnormalities in neural networks and neurotransmitter functions, particularly serotonin. Medications such as triptans target serotonin receptors to alleviate migraine symptoms, while common over-the-counter drugs like acetaminophen, ibuprofen, naproxen, and aspirin serve as initial treatments for mild to moderate episodes [2]. Emerging research also suggests the potential of melatonin and other alternative therapies in migraine prevention.

Recent literature has spotlighted the issue of analgesic and anti-migraine medication overuse, alongside studies focusing on their efficacy in treatment and prevention [3]. Acetaminophen is recognized for its effectiveness in acute migraine scenarios, whereas ibuprofen is frequently chosen for chronic conditions due to its analgesic and anti-inflammatory properties. Aspirin has been identified by Cochrane reviews as beneficial for acute migraine relief in adults. The role of melatonin, integral to sleep regulation, is currently being investigated as a preventative measure for migraines, with promising results [4]. Over-the-counter options are generally favored for their accessibility and cost-efficiency. A range of medications, including NSAIDs, ergotamine derivatives, and triptans, are employed in migraine management, though their overuse may lead to medication-overuse headaches, exacerbating the condition. Preventive treatments are recommended for

individuals experiencing frequent migraines, with the debate ongoing regarding the most appropriate regimen. Medications like propranolol, amitriptyline, and topiramate have demonstrated efficacy in clinical trials for reducing migraine frequency. Additionally, new treatments targeting CGRP and nitric oxide pathways are under development, offering hope for more effective migraine management [5-10]. This review aims to survey the latest progress in migraine treatment strategies, focusing on a variety of pain relief methods..

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.

References

1. Colman, I., Rothney, A., Wright, S. C., Zilkalns, B., & Rowe, B. H. (2004). Use of narcotic analgesics in the emergency department treatment of migraine headache. *Neurology*, 62(10), 1695-1700.
2. Bigal, Marcelo. and Lipton, Richard. Excessive acutemigraine medication use and migraine progression. (2008) *Neurology*. 71(22); 1821-1828.
3. Bigal, M. E., & Lipton, R. B. (2009). Overuse of acute migraine medications and migraine chronification. *Current pain and headache reports*, 13(4), 301-307.
4. Diener, H-C., Diener, Hans-Christoph., Diener, Hans-Christoph., Charles, Andrew., Goadsby, Peter., Holle, Dagny., Roche, La., Medica, ., Fabre, Pierre. and Foundation, Jude. The Efficacy of Propofol vs. Subcutaneous Sumatriptan for Treatment of Acute Migraine Headaches in the Emergency Department: A Double-Blinded Clinical Trial. (2015) *Pain Pract*. 15(8); 701-705.
5. Bendtsen, L., Mattsson, P., Zwart, J. A., & Lipton, R. B. (2003). Placebo response in clinical randomized trials of analgesics in migraine. *Cephalalgia*, 23(7), 487-490.
6. Le ´onie Damen, ., Bruijn, Jacques., Verhagen, Arianne., Berger, Y., Passchier, Jan. and

Koes, Bart. Symptomatic Treatment of Migraine in Children: A Systematic Review of Medication Trials. (2005) 116(2); e295-e302.

7. Diener, H-C., Dodick, D., Goadsby, P., Bussone, G., Silberstein, S., Mathew, N., Ascher, S., Morein, J., Hulihan, J., Biondi, D., Greenberg, S. and Diener, Hans-Christoph. Utility of Topiramate for the Treatment of Patients with Chronic Migraine in the Presence or Absence of Acute Medication Overuse. (2009) *Cephalalgia*. 29(10); 1021-1027.

8. Goadsby, Peter., Sprenger, Till. and Group, Headache. Combined occipital and supraorbital neurostimulation for the treatment of chronic migraine headaches: Initial experience. (2010) *Cephalalgia*. 30(3); 260-271.

9. and Linde, Mattias. Migraine: a review and future directions for treatment. (2006) *Acta Neurol Scand*. 114(2); 71-83.

10. Ra, Moore., Derry, Sheena., Rabbie, Roy. and Moore, R. Diclofenac with or without an antiemetic for acute migraine headaches in adults. (2013) 2019(5);

11. Pfaffenrath, V., & Scherzer, S. (1995). Analgesics and NSAIDs in the treatment of the acute migraine attack. *Cephalalgia*, 15(S15), 14-20.

12. Diener, H. C., Holle, D., Dresler, T., & Gaul, C. (2018). Chronic headache due to overuse of analgesics and anti-migraine agents. *Deutsches Ärzteblatt International*, 115(22), 365.

13. Golikhatir, Iraj., Cheraghmakani, Hamed., Bozorgi, Farzad., Jahanian, Fatemeh., Sazgar, Mohammad., Montazer, Hosein. and Montazer, S. The Efficacy and Safety of Prochlorperazine in Patients With Acute Migraine: A Systematic Review and Meta-Analysis. (2019) *Headache: The Journal of Head and Face Pain*. 59(5); 682-700.

14. Mathew, N. T. (1997). Transformed migraine, analgesic rebound, and other chronic daily headaches. *Neurologic clinics*, 15(1), 167-186.

15. Natoli, Jaime., Manack, A., Dean, B., Butler, Q., Stovner, L. and Lipton, R. Global prevalence of chronic migraine: A systematic review. (2010) *Cephalalgia*. 30(5); 599-609.

16. Oldman, A. D., Smith, L. A., McQuay, H. J., & Moore, R. A. (2002). Pharmacological treatments for acute migraine: quantitative systematic review. *Pain*, 97(3), 247-257.

17. Patniyot, Irene. and Gelfand, Amy. Acute Treatment Therapies for Pediatric Migraine: A Qualitative Systematic Review. (2016) *Headache: The Journal of Head and Face Pain*. 56(1); 49-70.

18. Thorlund, Kristian., Sun-Edelstein, Christina., Druyts, Eric., Kanters, Steve., Ebrahim, Shanil., Bhambri, Rahul., Ramos, Elodie., Mills, Edward., Lanteri-Minet, Michel. and Tepper, Stewart. Risk of medication overuse headache across classes of treatments for acute migraine. (2016) *J Headache Pain*. 17(1);

19. Peck, Jacquelin., Urits, Ivan., Zeien, Justin., Hoebee, Shelby., Mousa, Mohammad., Alattar, Hamed., Kaye, Alan. and Viswanath, Omar. A Comprehensive Review of Over-the-counter Treatment for Chronic Migraine Headaches. (2020) *Curr Pain Headache Rep*. 24(5);

20. Silberstein, Stephen. and Kori, Shashidhar. Dihydroergotamine: A Review of Formulation Approaches For the Acute Treatment of Migraine. (2013) *CNS Drugs*. 27(5); 385-394.

21. Goadsby, P. J. (2003). Migraine: diagnosis and management. *Internal Medicine Journal*, 33(9-10), 436-442.

22. Silberstein, S. D., Goadsby, P. J., & Lipton, R. B. (2000). Management of migraine: an algorithmic approach. *Neurology*, 55(9 Suppl 2), S46-52.

23. Becker, W. J. (2015). Acute migraine treatment in adults. *Headache: The Journal of Head and Face Pain*, 55(6), 778-793.

24. Cady, R., & Dodick, D. W. (2002, March). Diagnosis and treatment of migraine. In *Mayo Clinic Proceedings* (Vol. 77, No. 3, pp. 255-261). Elsevier.

