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Case Report

Effectiveness of Oral Magnesium in Chronic and Episodic Migraine: An Evidence-Based Case Review

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A B S T R A C T

Abstrak

Latar Belakang: Migrain kronis (≥15 hari sakit kepala per bulan) dan migrain episodik (<15 hari per bulan) merupakan gangguan neurologis yang melumpuhkan lebih dari satu miliar orang di seluruh dunia. Terapi profilaksis konvensional, seperti beta blocker dan antiepileptik, dapat efektif namun sering dikaitkan dengan masalah tolerabilitas. Magnesium, mineral esensial yang berperan dalam regulasi vaskular dan fungsi neuron, diusulkan sebagai alternatif profilaksis yang aman dan berbiaya rendah.

Tujuan: Mengevaluasi efektivitas suplementasi magnesium oral dalam menurunkan frekuensi dan intensitas migrain melalui evidence-based case review.

Metode: Pencarian literatur sistematis dilakukan pada PubMed, Scopus, Cochrane Central, dan Google Scholar. Uji klinis teracak dan tinjauan sistematis yang membandingkan magnesium oral dengan plasebo atau terapi standar disertakan dan dinilai kritis.

Hasil: Tujuh studi (tiga RCT dan empat tinjauan sistematis) diidentifikasi frekuensi dan keparahan nyeri migrain, meskipun terdapat heterogenitas terkait formulasi, dosis, dan desain penelitian. Secara umum, magnesium oral menurunkan.

Kesimpulan: Magnesium oral aman, murah, dan relatif mudah ditoleransi sebagai terapi tambahan atau alternatif, namun diperlukan uji klinis berkualitas tinggi untuk memastikan dosis optimal dan efektivitas komparatif.

Kata Kunci: migrain, magnesium, profilaksis, sakit kepala, suplementasi

What is already known about this topic?

Magnesium is commonly used as a supplement for migraine prophylaxis; however, the clinical evidence remains inconsistent.

What does this study add?

This evidence-based case review integrates recent randomized trials and meta-analyses and highlights how variation in magnesium formulation and dosage contributes to heterogeneity and influences the certainty of conclusions.

Abstract

Background: *Chronic migraine (≥15 headache days per month) and episodic migraine (<15 headache days per month) are disabling neurological disorders affecting more than one billion people worldwide. Conventional prophylactic therapies, including beta blockers and antiepileptics, may be effective but are often associated with tolerability concerns. Magnesium, an essential mineral involved in vascular regulation and neuronal function, has been proposed as a safe and low-cost alternative for migraine prevention.*

Objective*: To evaluate the effectiveness of oral magnesium supplementation in reducing migraine frequency and intensity through an evidence-based case review.*

Methods*: A systematic literature search was conducted in PubMed, Scopus, Cochrane Central, and Google Scholar. Randomized controlled trials and systematic reviews comparing oral magnesium with placebo or standard prophylactic therapy were included.*

Results*: Seven studies (three randomized controlled trials and four systematic reviews) were identified. Overall, oral magnesium reduced migraine frequency and pain severity, although substantial heterogeneity in formulation, dosage, and study design was observed.*

Conclusion*: Oral magnesium appears safe, inexpensive, and well tolerated, but further high-quality trials are needed to determine optimal dosing and comparative efficacy.*

Keywords: *migraine, magnesium, prophylaxis, headache, pain.*

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Introduction

Chronic migraine is defined by the International Classification of Headache Disorders (ICHD-3) as a debilitating neurological condition with ≥15 headache episode days per month, at least 8 fitting migraine criteria, and lasting longer than 3 months.[1] In contrast, episodic migraine (EM) is characterized by 0 to 14 headache days per month.[2] Each year, migraine affects over a billion people worldwide and is one of the most common neurological impairment, with a high prevalence and morbidity, particularly among young adults and women. Between 1990 and 2021, the worldwide burden of migraine rose significantly: the prevalence increased by 58.15%, from 732.56 million to 1.16 billion; while incidence increased by 42.06%.[3] Additionally, the Disability-Adjusted Living Years (DALYs) increased by 58.27%.[4] The absolute rates of migraine incidence and prevalence were greater in females, while the rate of growth rate in males was four to five times faster than in females.[5] The most noticeable decline in prevalence was seen in Southeast Asia.[5] Despite a substantial investigation, the pathophysiology of migraine has yet to be fully understood.

It is commonly known that migraine is related to a wide range of comorbidities, including stress, sleep difficulties, and (EBCR) will assess whether oral magnesium supplementation (such as magnesium oxide or citrate at therapeutic doses) is effective in reducing frequency and pain intensity in adults with chronic or episodic migraine when compared to placebo or existing standard therapy.

Magnesium is an essential element involved in a variety of neurological functions, including neurotransmitter modulation and vascular tone. Previous studies have concluded that magnesium probably has an important role in the pathogenesis of migraine.[8,9] The human body contains 25–35 g of magnesium, of which only 1% is found in the blood, 46% is found in muscles and soft tissues, and around 53% is stored in the bones.[10] Magnesium insufficiency has been identified in some people who suffer from migraine,[10,11] sparking interest in magnesium supplementation as a cost-effective, well-tolerated prophylaxis for chronic and episodic migraine. Previous researches have yielded mixed results about the relationship of intravenous or oral magnesium supplementation in migraineurs.[9,12] Some studies indicated the therapeutic benefits of magnesium treatment on acute migraine episodes and migraine prophylaxis.[9] On the other hand, other studies disputed any positive association between magnesium therapy and migraine.[9]

Based on current clinical trial evidence, this evidence-based case review (EBCR) will assess whether oral magnesium supplementation (such as magnesium oxide or citrate at therapeutic doses) is effective in reducing frequency and pain intensity in adults with chronic or episodic migraine when compared to placebo or existing standard therapy.

Case

A 28-year-old female, Ms. A, presents to the neurology outpatient clinic with a history of migraine causing significant impairment in daily functioning. She reports pulsatile right temporal headaches accompanied by photophobia, phonophobia, and occasional nausea. She has no prior history of epilepsy or cardiovascular disease and is not pregnant or breastfeeding.

She previously trialed propranolol and topiramate but discontinued them due to adverse effects (fatigue and cognitive slowing). Under medical supervision, she restarted topiramate at a lower dose (25 mg twice daily). Despite ongoing prophylaxis, she continued to experience migraine attacks on 5 days per month, with an average attack duration of ~60 minutes, mean pain intensity VAS 6/10, and a HIT-6 score of 53, indicating persistent functional impact.

Oral magnesium was then initiated as adjunct prophylaxis (500 mg once daily) alongside topiramate 25 mg twice daily. After 3 months of combination therapy, Ms. A reported improvement in migraine burden, with attacks occurring on 3 days per month, reduced average duration (~45 minutes), lower pain intensity (VAS 4/10), and a modest improvement in disability (HIT-6 score 50). She reported no gastrointestinal adverse effects during treatment.

Methods

Clinical Question

The clinical question was developed using the PICO framework (Population, Intervention, Comparator, Outcome) to ensure a structured and focused evidence-based review (Table 1). Based on this format, a therapeutic-type clinical question for this case can be formulated as follows: " In adults with chronic or episodic migraine, how effective is

oral magnesium supplementation compared to placebo or standard prophylactic therapy in reducing migraine frequency and pain intensity?"

Table 1. PICO Framework

Item	Definition
Population	Adults diagnosed with chronic or episodic migraine
Intervention	Oral magnesium supplementation
Comparator	Placebo or standard prophylactic therapy (e.g., propranolol, topiramate)
Outcome	Reduction in migraine frequency and pain intensity measured by validated scales (VAS, NRS, HIT-6)

Literature Search Strategy

A systematic literature search was conducted on September 2, 2025, in four electronic databases: PubMed, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar.

A structured search strategy was developed for each database using combinations of MeSH terms and free-text keywords related to migraine, oral magnesium supplementation, comparators, and pain outcome measures. The detailed search strategies and results are presented in Table 2.

Table 2. Summary of searching strategy (Sept 2 2025)

Database	Searching Strategy	Hits	Eligible
PubMed	("Migraine Disorders"[Mesh] OR "chronic migraine"[tiab] OR “episodic migraine”[tiab]) AND ("Magnesium"[Mesh] OR "magnesium supplementation"[tiab] OR "oral magnesium"[tiab]) AND ("Placebos"[Mesh] OR "placebo"[tiab] OR "Propranolol"[Mesh] OR "Topiramate"[Mesh] OR "propranolol"[tiab] OR "topiramate"[tiab]) AND ("Pain Measurement"[Mesh] OR "pain intensity"[tiab] OR "migraine severity"[tiab] OR "Visual Analog Scale"[tiab] OR "VAS"[tiab] OR "HIT-6"[tiab] OR "Numeric Rating Scale"[tiab] OR "NRS"[tiab])	2	1
Scopus	TITLE-ABS-KEY("chronic migraine" OR "migraine disorder" OR “episodic migraine”) AND TITLE-ABS-KEY("magnesium supplementation" OR "oral magnesium" OR "magnesium oxide" OR "magnesium citrate") AND TITLE-ABS-KEY("placebo" OR "propranolol" OR "topiramate") AND TITLE-ABS-KEY("pain intensity" OR "pain score" OR "headache severity" OR "visual analog scale" OR "VAS" OR "numeric rating scale" OR "NRS" OR "HIT-6")	6	2
Cochrane	("chronic migraine" OR “episodic migraine” OR "migraine disorder") AND ("magnesium" OR "oral magnesium" OR "magnesium oxide" OR "magnesium citrate") AND ("pain intensity" OR "pain score" OR "headache severity" OR "VAS" OR "NRS" OR "HIT-6") AND ("placebo" OR "propranolol" OR "topiramate")	6	0
Google Scholar	("chronic migraine" OR “episodic migraine”) AND ("magnesium supplementation" OR "oral magnesium" OR "magnesium oxide" OR "magnesium citrate") AND ("pain intensity" OR "pain score" OR "headache severity" OR "VAS" OR "NRS" OR "HIT-6") AND ("placebo" OR "propranolol" OR "topiramate")	362	4

Eligibility Criteria

Study selection was conducted using predefined inclusion and exclusion criteria.

Inclusion Criteria:

- Adult patients diagnosed with chronic or episodic migraine

- Intervention involving oral magnesium supplementation, either as monotherapy or adjunct therapy
- Comparator group receiving placebo or standard prophylactic treatment
- Outcomes reporting migraine frequency and/or pain intensity using validated scales (e.g., VAS, NRS, HIT-6)
- Study design: randomized controlled trials (RCTs), controlled clinical trials, or systematic reviews and meta-analyses
- Articles published in English

Exclusion Criteria:

- Preclinical studies, case reports, expert opinions, narrative reviews
- Incomplete or partial studies
- Studies evaluating only intravenous or non-oral magnesium formulations

Article Selection

The study selection process followed PRISMA guidelines.

All retrieved records were screened in three stages:

1. Title screening to exclude clearly irrelevant studies
2. Abstract screening based on eligibility criteria
3. Full-text assessment for final inclusion

Duplicates were removed prior to screening. Full-text articles of potentially relevant studies were independently reviewed for eligibility based on the predefined inclusion and exclusion criteria. The overall selection process is illustrated in Figure 1 (PRISMA flow diagram).

The methodological quality of included studies was critically appraised using appropriate evidence-based appraisal tools:

- Randomized controlled trials were assessed using standard risk-of-bias criteria (randomization, allocation concealment, blinding, completeness of outcome data, and selective reporting).
- Systematic reviews and meta-analyses were evaluated for methodological rigor, comprehensiveness of search strategy, and risk-of-bias assessment.

Each study's level of evidence and risk of bias were considered when interpreting the overall findings.

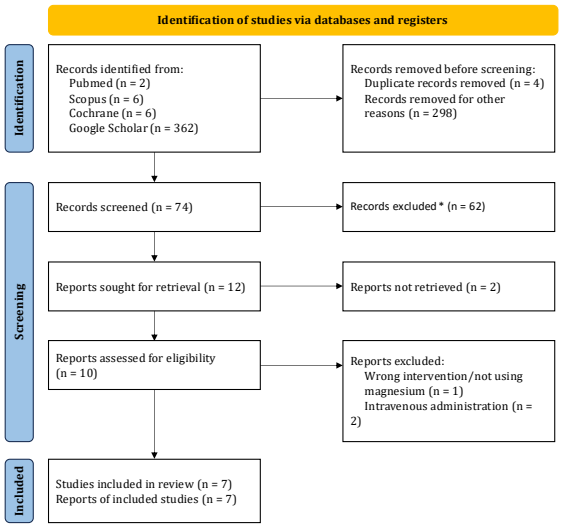

Figure 1. Flow diagram of literature search and study selection.
*Records excluded after title and abstract screening for not meeting inclusion criteria.

Results

Three randomized controlled trials (as summarized in Table 3) and four systematic reviews and meta-analyses (as presented in Tables 3 and 4) examined the efficacy of magnesium in migraine treatment, either alone or in combination with other therapies.

Gaul et al.[14] conducted a three-month multicenter, double-blind, placebo-controlled study of a proprietary supplement comprising magnesium (600 mg), riboflavin (400 mg), and coenzyme Q10 (150 mg) in 130 migraine sufferers. The supplement group had a higher, but not statistically significant, decrease in monthly migraine days (from 6.2 to 4.4 vs. 6.2 to 5.2; $p = 0.23$) than the placebo group. However, there were notable decreases in HIT-6 scores (mean reduction of 4.8 vs. 2.0 in placebo; $p = 0.01$) and migraine severity ($p = 0.03$). Additionally, compared to 0% in the placebo group, 18.2% of patients in the supplement group regarded the effectiveness as "very good" ($p = 0.01$). Only a few gastrointestinal side effects were recorded, indicating excellent tolerability.

Table 3. Characteristics and critical appraisal of included studies according to Oxford Centre of Evidence Based Medicine (CEBM).

Study (Author, Year)	Study Design	Population	Intervention	Comparator	Outcome Measured	Key Findings
Talandashti et al., 2024	SR/MA	Adults with migraine	Dietary supplements including magnesium, vitamin D, riboflavin, CoQ10, probiotics, omega-3, and alpha-lipoic acid	Placebo	Frequency and duration of migraine attacks, severity (intensity) of migraine pain and Monthly Migraine Days (MMDs)	Mg supplementation reduced migraine attacks, severity, and monthly migraine days vs controls. However, notable heterogeneity was observed among the studies
Veronese et al., 2019	SR/MA	Adults with migraine	Oral Mg in migraine prophylaxis	Placebo or no intervention (control group)	Frequency and intensity of migraine attacks	Magnesium supplementation significantly reduced the frequency and intensity of migraine attacks in adults with migraine.
Luckner and & Rieder, 2018	SR	Adults with migraine	Oral magnesium supplementation (mainly magnesium dicitrate, 600 mg/day)	Placebo	Frequency of migraine days, intensity of migraine attacks, adverse events	Evidence level Grade C (possibly effective). Magnesium supplementation reduced the number of migraine days in some RCTs, but results were inconsistent and heterogeneity was high.
Chiu et al., 2016	MA	Adults with migraine	Oral magnesium supplementation (varied formulations and doses)	Placebo or active control	Frequency and intensity of migraine attacks (measured by VAS, diaries, response rate)	Oral magnesium significantly reduced frequency (OR = 0.20) and intensity (OR = 0.27) of migraine compared with control. Some included studies had methodological limitations.

Table 4. Study Characteristics of Systematic review and Meta-analysis

Author, Year	Population (Sample)	Study Design	Regimen	Validity				Importance		Applicability		LoE
				Randomization	Follow-up	Blinding	Intention	Outcome	NNT	Similarity	Feasibility	
Gaul, 2015	130 adults with ≥3 migraines/month	RCT, multicenter, double-blind	Oral supplement: Mg citrate 600 mg + riboflavin 400 mg + Q10 150 mg vs placebo for 3 mo	Randomized	10 dropped out in the treatment group, 11 dropped out in the control group	Double-blind	ITT not explicitly stated	Decrease in intensity and HIT-6 ($p < 0.005$); decrease in frequency not statistically significant ($p = 0.23$)	No NNT reported	Similar to target population	Feasible	Level 1b
Karimi, 2019	63 adults with episodic migraine	RCT, double-blind, crossover	Oral Mg oxide 500 mg/day vs Na valproate 400 mg/day for 8 weeks each	Randomized	1 dropped out in group 1 during period 1, 6 dropped out during period 2 .	Double-blind	ITT explicitly stated	Both treatments decrease frequency, duration, severity; no significant difference between groups ($p > 0.05$)	No NNT reported	Similar to target population	Feasible	Level 1b
Khani, 2021	222 adults with ≥4 migraines/month, aged 18–65	RCT, 3-arm, double-blind	Oral Mg oxide 500 mg/day, Na valproate 400 mg/day, or both	Randomized	6 dropped out in group A, 16 dropped out in group B, 16 dropped out in group C	Double-blind	ITT not explicitly stated	Decrease in migraine frequency, severity, duration in all groups; combination is superior ($p < 0.001$)	No NNT reported	Similar to target population	Feasible	Level 1b

Table 5. Critical appraisal of included studies according to GRADE tools

Study (Author, Year)	Outcome	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality of Evidence (GRADE)	Comments
Talandashti et al., 2024	Frequency and duration of migraine attacks, severity (intensity) of migraine pain and Monthly Migraine Days (MMDs)	22	12 studies low, 3 studies moderate, 7 studies high	High	Present	High	Possible	High	Results show some inconsistency and imprecision with wide confidence intervals in several outcomes; moderate risk of bias and possible publication bias noted
Veronese et al., 2019	Reduction in frequency and intensity of migraine relapses	36 from RCTs, 19 for observational studies	Moderate	Low	None	Moderate	Possible	High	Results largely consistent with low heterogeneity; some outcomes limited by imprecision and potential publication bias
Luckner and & Rieder, 2018	Effect of oral magnesium for migraine prophylaxis (number of migraine attacks, migraine days)	5 RCTs (2 Class I, 3 Class III)	Mixed: Class I trials low risk, but Class III trials had methodological flaws	High	Low	Present	Possible	Moderate	Evidence classified as Grade C (possibly effective). One high-quality trial (Peikert 1996) showed significant benefit, others mixed. Heterogeneity and methodological flaws lower certainty. Overall, magnesium may be a safe, low-cost option, but evidence insufficient for strong recommendation.
Chiu et al., 2016	Frequency and intensity of migraine attacks (measured by VAS, diaries, response rate)	21 RCTs (11 IV, 10 oral)	Some studies lacked adequate randomization; overall moderate risk	Moderate	Low	Present	Possible	High	Intravenous magnesium showed significant benefit at 15–45 min, 120 min, and 24 h post-infusion; oral magnesium reduced frequency and intensity of migraine. However, methodological limitations, heterogeneity, and possible publication bias reduce certainty.

Karimi et al.[15] compared oral magnesium oxide (500 mg twice daily) with sodium valproate (400 mg twice daily) in 63 adult patients with episodic migraine in a randomized, double-blind, crossover study. There was a 4-week washout in between each 8-week treatment phase. When compared to baseline, both therapies significantly decreased the incidence of migraines, the duration of headaches, and the number of days with moderate to severe pain ($p < 0.001$). The magnesium group experienced 1.72 ± 1.18 migraine attacks on average per month, while the valproate group experienced 1.27 ± 1.27 migraine attacks. The two regimens had no statistically significant difference, despite sodium valproate exhibiting somewhat larger numerical decreases ($p > 0.05$). There were few reported adverse effects, and both were well tolerated.

Khani et al.[16] evaluated the three-month preventative effects of sodium valproate (400 mg/day), magnesium oxide (500 mg/day), and their combination in 222 individuals. The frequency, intensity, and duration of migraines were all considerably decreased by all therapies ($p < 0.001$). Combining treatment outperformed monotherapies in terms of lowering severity, duration, and the need for analgesics. Interestingly, magnesium increased the effectiveness of sodium valproate without increasing its dosage. The combo group also had the most improvement in MIDAS and HIT-6 scores.

In addition, Chiu et al.[9] performed a meta-analysis of 21 randomized controlled trials, 11 evaluating intravenous magnesium for acute migraine attacks (n = 948) and 10 assessing oral magnesium for prophylaxis (n = 789). Intravenous magnesium significantly relieved acute migraine within 15–45 minutes, 120 minutes, and 24 hours after infusion (ORs 0.23, 0.20, and 0.25, respectively), while oral magnesium significantly reduced migraine frequency and intensity (ORs 0.20 and 0.27). Although promising, the analysis highlighted limitations such as inadequate randomization in several studies and moderate heterogeneity.

Similarly, Luckner and Rieder[8] conducted a systematic review of five double-blind, placebo-controlled trials assessing oral magnesium for migraine prophylaxis. One of the two Class I trials and two of the three Class III trials demonstrated significant reductions in migraine attacks compared with placebo, particularly with high-dose magnesium dicitrate (600 mg/day). However, results were inconsistent across studies, with some failing to show benefit. The authors concluded that magnesium may be "possibly effective" (Grade C) as a preventive strategy, noting its favorable safety profile and cost-effectiveness.

Veronese et al.[17], an umbrella review of 16 meta-analyses comprising 55 outcomes from both RCTs and observational studies. Among RCTs, magnesium supplementation demonstrated strong evidence for reducing the frequency and intensity of migraine relapses, alongside decreasing the need for maternal hospitalization during pregnancy. In observational studies, higher dietary magnesium intake was associated with a significantly lower risk of type 2 diabetes (28% reduction; class II evidence) and stroke (class III evidence). The review highlighted that, while evidence for migraine prevention was strong and consistent, results for cardiometabolic outcomes were heterogeneous and mostly limited to suggestive associations.

Most recently, Talandashti et al.[18] conducted a systematic review and dose–response meta-analysis including 22 trials assessing dietary supplements for migraine prophylaxis. Magnesium supplementation significantly reduced migraine attack frequency (MD = –2.51), severity (MD = –0.88), and monthly migraine days (MD = –1.66) compared with control. Other supplements, including coenzyme Q10, riboflavin, alpha-lipoic acid, probiotics, and vitamin D, also demonstrated reductions in various migraine parameters, while omega-3 fatty acids did not show significant benefit

Discussion

This review investigates the role of oral magnesium for migraine prophylaxis based on two randomized controlled trials.

Up until now, studies are still being conducted to better understand the complex pathophysiology of migraine. More recent research highlights the role of ion channel dysfunction, glutamatergic neurotransmission, and abnormalities in energy metabolism—often influenced by genetic and mitochondrial factors—as major contributors to cortical spreading depression (CSD), vascular dysregulation, and neurogenic inflammation.[19–21] The neuroprotective function of magnesium is particularly interesting, moreover its control over NMDA receptors, where magnesium has an

important role as a natural calcium channel blocker.[8,10,11,22] Hypomagnesaemia may cause migraine episodes by lowering the threshold for CSD onset, increasing excitatory glutamate release, and promoting oxidative stress.[23,24] This process provides reasoning to the therapeutic justification for magnesium supplementation in regulating neuronal activity and delaying the onset of migraine.

Newer research has provided more evidence that magnesium insufficiency may be a cause for migraine episodes, especially in migraine with aura.[11] Magnesium plays an important role in various physiological activities, including ATP generation, neuronal excitability modulation, vascular tone, and neurotransmitter release.[25,26] As a natural NMDA receptor blocker, magnesium aids in two points in migraine pathogenesis: calcium excess and central sensitization after nociceptive stimuli.[27] Magnesium imbalances have been linked to CSD, oxidative stress, and brainstem activation, all of which are linked to migraine. Additionally, magnesium affects platelet aggregation, inflammatory cascades, and CGRP release, further proving that magnesium has an important role in the development and recurrence of migraine.[11,19,21,22] These pathways contribute to the rationale of magnesium administration for migraine.

The Canadian Headache Society (CHS) 2024 update and the American College of Physicians (ACP) 2025 guidelines offer the most up-to-date recommendations for migraine prophylaxis that are under current clinical practice standards.[28,29] A systematic review and meta-analysis were incorporated into the CHS's revised guideline to offer evidence-based suggestions for the prevention of both episodic and chronic migraines.[28] It provides significant support for more recent medications, such as gepants (e.g., atogepant) and calcitonin gene-related peptide (CGRP) monoclonal antibodies, especially for individuals who have high-frequency migraines or do not respond to conventional medicines.[28] Onabotulinumtoxin A is also suggested by the guidelines for those with persistent migraines.[28] These suggestions are meant to help doctors optimise migraine prophylactic tactics and are based on the most recent clinical trial results.[28] Both recommendations stress the value of customised treatment programs that take patient preferences, cost, safety, and efficacy into account.[28] The ACP recommendation is centered on the use of medications to prevent episodic migraines in individuals who are not pregnant in outpatient settings.[29] It suggests starting therapy with well-known agents such as beta-blockers (e.g., example, propranolol), tricyclic antidepressants (e.g., amitriptyline), and antiseizure meds (e.g., topiramate), pointing out that they are more readily available and equally effective as more recent ones.[5] When choosing a therapy, the recommendation highlights the significance of patient preferences, financial concerns, and possible adverse effects.[29] Additionally, if no sufficient response is shown within two to three months or if side effects arise, it suggests reevaluating the selected therapy.[29]

Among individual randomized controlled trials, findings remain mixed. A double-blind crossover study comparing magnesium oxide 500 mg/day with sodium valproate demonstrated significant reductions in migraine frequency, duration, and intensity from baseline, with no statistically significant difference between groups.[15] Nevertheless, this trial was not designed as a formal non-inferiority study, confidence intervals were not reported, and no placebo arm was included, limiting interpretation of therapeutic equivalence. In contrast, a multicenter placebo-controlled parallel trial evaluating a combination supplement containing magnesium (600 mg), riboflavin, and coenzyme Q10 showed improvements in pain intensity and HIT-6 scores but failed to demonstrate a statistically significant reduction in migraine days compared with placebo ($p = 0.23$).[14] The use of a multi-ingredient formulation prevents isolation of magnesium's independent effect and contributes to treatment heterogeneity. Another three-arm randomized trial found that magnesium oxide monotherapy was inferior to valproate in reducing migraine frequency at three months ($P < 0.001$), while combination therapy did not significantly outperform valproate in frequency reduction ($P = 0.525$), suggesting that magnesium may function more effectively as an adjunctive rather than standalone therapy in certain populations.[16]

Systematic reviews further illustrate this variability. A focused review applying American Academy of Neurology classification identified five eligible placebo-controlled trials totaling approximately 253 patients and concluded that magnesium provides Grade C (possibly effective)

evidence for migraine prevention.[8] Only one of two Class I trials demonstrated significant benefit, whereas two of three Class III trials were positive,[8] underscoring limitations in both study size and consistency. A meta-analysis including 10 oral magnesium trials reported significant reductions in migraine frequency (OR 0.20, 95% CI 0.05–0.89) and intensity (OR 0.27, 95% CI 0.12–0.61), but heterogeneity was substantial (I^2 92.87% and 80.57%, respectively).[9] Sensitivity analyses demonstrated instability of pooled effects after removal of outlier studies,[9] suggesting that methodological differences meaningfully influence overall estimates. A more recent dose–response meta-analysis including 22 randomized trials confirmed statistically significant reductions in migraine frequency, severity, and monthly migraine days; however, heterogeneity remained extremely high (I^2 > 96%), and several outcomes were downgraded due to inconsistency and imprecision.[18] Interestingly, an umbrella review evaluating the credibility of evidence across health outcomes classified magnesium supplementation for migraine relapse reduction as strong evidence according to GRADE criteria, although the number of contributing randomized trials was relatively small.[17] These differences in evidence grading reflect variability in methodological approach and emphasize that statistical significance does not necessarily equate to high certainty regarding magnitude of clinical benefit.

Multiple factors likely contribute to heterogeneity across studies. Magnesium was administered in various salt forms, including magnesium oxide, trimagnesium dicitrate, magnesium aspartate, and compound formulations. Notably, trials demonstrating significant reductions in migraine attacks frequently used 600 mg of trimagnesium dicitrate, whereas lower doses (360–480 mg) or alternative salts were more often associated with nonsignificant findings.[8] Differences in bioavailability between formulations may therefore influence treatment response. Study design variability—including crossover versus parallel trials, placebo-controlled versus active comparator studies, and monotherapy versus combination interventions —further complicates direct comparison. In addition, several earlier trials exhibited limitations in allocation concealment, blinding, and sample size,[9] which may partially explain inconsistent results. Heterogeneous interindividual response has also been proposed, potentially reflecting benefit predominantly in migraineurs with intracellular magnesium deficiency,[8] although most trials did not stratify participants by baseline magnesium status.

Taken together, the current body of evidence suggests that oral magnesium provides a statistically significant but clinically modest prophylactic benefit. While pooled analyses consistently demonstrate reductions in migraine frequency and intensity, high heterogeneity, formulation variability, and methodological differences reduce certainty regarding optimal dosing strategy and comparative efficacy relative to established pharmacologic agents. Magnesium appears most appropriately positioned as a safe, low-cost adjunctive option or alternative therapy in selected patients, particularly those with contraindications or intolerance to standard preventive medications. However, claims of equivalence to agents such as valproate or beta-blockers should be interpreted cautiously given limited non-inferiority data and inconsistent primary endpoint findings. Future adequately powered, multicenter, placebo-controlled trials using standardized high-bioavailability formulations and uniform outcome measures are necessary to clarify optimal therapeutic parameters and strengthen the evidence base.

Conclusion

Oral magnesium, either as monotherapy or as an adjuvant to standard therapy, can reduce migraine intensity, improve function, and decrease the frequency of acute migraine episodes. Its clinical relevance is supported by its excellent safety profile, low cost, and wide accessibility, making it a reasonable option for individuals who cannot tolerate standard therapy or have contraindications. Larger, multicenter trials with magnesium preparations of higher bioavailability, standardized dosing, and diverse populations are needed. Future studies should also compare magnesium directly with standard therapies and evaluate relevant biomarkers such as magnesium or CGRP levels. In conclusion, oral magnesium is a viable, evidence-supported option for migraine prevention, particularly in decreasing the intensity and frequency of episodes, and shows greater effectiveness when combined with existing standard therapies.

Conflict of Interest

Authors declare no conflict of interest related to this article.

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References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38(1):1-211. doi:10.1177/0333102417738202.
2. Katsarava Z, Buse DC, Manack AN, Lipton RB. Defining the differences between episodic migraine and chronic migraine. Curr Pain Headache Rep. 2012;16(1):86-92. doi:10.1007/s11916-011-0233-z.
3. Murray CJL, GBD 2021 Collaborators. Findings from the Global Burden of Disease Study 2021. Lancet. 2024;403(10440):2259-62. doi:10.1016/S0140-6736(24)00769-4.
4. Fan L, Wu Y, Wei J, Xia F, Cai Y, Zhang S, et al. Global, regional, and national time trends in incidence for migraine from 1990 to 2019: an age-period-cohort analysis for the GBD 2019. J Headache Pain. 2023;24(1):79. doi:10.1186/s10194-023-01619-9.
5. Dong L, Dong W, Jin Y, Jiang Y, Li Z, Yu D. The global burden of migraine: a 30-year trend review and future projections by age, sex, country, and region. Pain Ther. 2025;14(1):297-315. doi:10.1007/s40122-024-00690-7.
6. Amiri P, Kazeminasab S, Nejadghaderi SA, Mohammadinasab R, Pourfathi H, Araj-Khodaei M, et al. Migraine: a review on its history, global epidemiology, risk factors, and comorbidities. Front Neurol. 2022;12:800605. doi:10.3389/fneur.2021.800605.
7. Abo-Elghiet F, Elosaily H, Hussein DK, El-Shiekh RA, A'aqoulah A, Yousef EM, et al. Bridging gaps in migraine management: a comprehensive review of conventional treatments, natural supplements, complementary therapies, and lifestyle modifications. Pharmaceuticals (Basel). 2025;18(2):139. doi:10.3390/ph18020139.
8. von Luckner A, Riederer F. Magnesium in migraine prophylaxis-is there an evidence-based rationale? A systematic review. Headache. 2018;58(2):199-209. doi:10.1111/head.13217.
9. Chiu HY, Yeh TH, Huang YC, Chen PY. Effects of intravenous and oral magnesium on reducing migraine: a meta-analysis of randomized controlled trials. Pain Physician. 2016;19(1):E97-E112.
10. Domitrz I, Cegielska J. Magnesium as an important factor in the pathogenesis and treatment of migraine-from theory to practice. Nutrients. 2022;14(5):1089. doi:10.3390/nu14051089.
11. Dolati S, Rikhtegar R, Mehdizadeh A, Yousefi M. The role of magnesium in pathophysiology and migraine treatment. Biol Trace Elem Res. 2020;196(2):375-83. doi:10.1007/s12011-019-01931-z.
12. Fernández-De-Las-Peñas C, Florencio LL, Plaza-Manzano G, Arias-Buría JL. Clinical reasoning behind non-pharmacological interventions for the management of headaches: a narrative literature review. Int J Environ Res Public Health. 2020;17(11):4126. doi:10.3390/ijerph17114126.
13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71.
14. Gaul C, Diener HC, Danesch U. Improvement of migraine symptoms with a proprietary supplement containing riboflavin, magnesium and Q10: a randomized, placebo-controlled, double-blind, multicenter trial. J Headache Pain. 2015;16:32. doi:10.1186/s10194-015-0516-6.
15. Karimi N, Razian A, Heidari M. The efficacy of magnesium oxide and sodium valproate in prevention of migraine headache: a randomized, controlled, double-blind, crossover study. Acta Neurol Belg. 2021;121(1):167-73. doi:10.1007/s13760-019-01101-x.
16. Khani S, Hejazi SA, Yaghoubi M, Sharifipour E. Comparative study of magnesium, sodium valproate, and concurrent magnesium-sodium valproate therapy in the prevention of migraine headaches: a randomized controlled double-blind trial. J Headache Pain. 2021;22(1):21. doi:10.1186/s10194-021-01234-6.
17. Veronese N, Demurtas J, Pesolillo G, Celotto S, Barnini T, Calusi G, et al. Magnesium and health outcomes: an umbrella review of systematic reviews and meta-analyses of observational and intervention studies. Eur J Nutr. 2020;59(1):263-72. doi:10.1007/s00394-019-01905-w.
18. Talandashti MK, Shahinfar H, Delgarm P, Jazayeri S. Effects of selected dietary supplements on migraine prophylaxis: a systematic review and dose-response meta-analysis of randomized controlled trials. Neurol Sci. 2025;46(2):651-70. doi:10.1007/s10072-024-07794-0.
19. Gawde P, Shah H, Patel H, Bharathi KS, Patel N, Sethi Y, et al. Revisiting migraine: the evolving pathophysiology and the expanding management armamentarium. Cureus. 2023;15(2):e34553. doi:10.7759/cureus.34553.
20. Puledda F, Silva EM, Suwanlaong K, Goadsby PJ. Migraine: from pathophysiology to treatment. J Neurol. 2023;270(7):3654-66. doi:10.1007/s00415-023-11706-1.
21. Mungoven TJ, Henderson LA, Meylakh N. Chronic migraine pathophysiology and treatment: a review of current perspectives. Front Pain Res (Lausanne). 2021;2:705276. doi:10.3389/fpain.2021.705276.
22. Hajhashemy Z, Golpour-Hamedani S, Eshaghian N, Sadeghi O, Khorvash F, Askari G. Practical supplements for prevention and management of migraine attacks: a narrative review. Front Nutr. 2024;11:1433390. doi:10.3389/fnut.2024.1433390.
23. Assarzadegan F, Asgarzadeh S, Hatamabadi HR, Shahrami A, Tabatabaey A, Asgarzadeh M. Serum concentration of magnesium as an independent risk factor in migraine attacks: a matched case-control study and review of the literature. Int Clin Psychopharmacol. 2016;31(5):287-92. doi:10.1097/YIC.0000000000000130.
24. Karim MR, Bhattacharjee M, Islam MS, Banerjee S, Hossain S, Hossain MI, et al. Relation between serum magnesium level and migraine. Mymensingh Med J. 2021;30(2):301-6.

25. Dunn J, Grider MH. Physiology, adenosine triphosphate. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK553175/
26. Daniel O, Mauskop A. Nutraceuticals in acute and prophylactic treatment of migraine. Curr Treat Options Neurol. 2016;18(4):14. doi:10.1007/s11940-016-0398-1.
27. Fila M, Chojnacki C, Chojnacki J, Błasiak J. Nutrients to improve mitochondrial function to reduce brain energy deficit and oxidative stress in migraine. Nutrients. 2021;13(12):4433. doi:10.3390/nu13124433.
28. Medrea I, Cooper P, Lagman-Bartolome AM, Sandoe CH, Amoozegar F, Hussain WM, et al. Updated Canadian Headache Society migraine prevention guideline with systematic review and meta-analysis. Can J Neurol Sci. 2025;52(3):450-72. doi:10.1017/cjn.2024.285.
29. Qaseem A, Cooney TG, Etxeandia-Ikobaltzeta I, Wilt TJ, Harrod CS, Tice JA, et al. Prevention of episodic migraine headache using pharmacologic treatments in outpatient settings: a clinical guideline from the American College of Physicians. Ann Intern Med. 2025;178(3):426-33. doi:10.7326/ANNALS-24-01052.
30. Burch R. Epidemiology and treatment of menstrual migraine and migraine during pregnancy and lactation: a narrative review. Headache. 2020;60(1):200-16. doi:10.1111/head.13665.
31. Bhurat R, Premkumar S, Manokaran RK. Serum magnesium levels in children with and without migraine: a cross-sectional study. Indian Pediatr. 2022;59(8):623-5. doi:10.1007/s13312-022-2576-4.
32. Al-Futaisi A. Pediatric migraines: a comprehensive review and perspectives on diagnosis and treatment. Oman Med J. 2023;38(3):e499. doi:10.5001/omj.2023.45.
33. Morel V, Pickering ME, Goubayon J, Djobo M, Macian N, Pickering G. Magnesium for pain treatment in 2021? State of the art. Nutrients. 2021;13(5):1397. doi:10.3390/nu13051397.