



Welcome to the Q3, 2022 issue of the Migraine World Summit (MWS) Quarterly Research Report. This report highlights recent research publications related to migraine and headache. We hope you find it a helpful way to discover some of the latest findings that may be relevant to you.

Each report is intentionally brief in order to provide a quick overview. The goal is to give you an idea of current research and to share some insights that may improve your understanding of migraine.

Consult your headache specialist or primary care physician to discuss how any of the research findings might apply to you.

Some medical publications don't provide free online access. In some cases, your health care professional may be able to print a copy for you.

Please note that our volunteer support team members are patients themselves and are not able to answer questions about the research or comment on these medical studies.

Authors highlighted **in bold** are those who have spoken at the Migraine World Summit.

Quotes are taken directly from the research paper.

We welcome your feedback on this report. Please share via email to [info@migraineworldsummit.com](mailto:info@migraineworldsummit.com)

Disclaimer: The views reflected in this research report do not represent the views of the Migraine World Summit. This report is not designed to replace a consultation with your doctor. Seek medical advice before making any changes to your treatment plan.

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Research Title

Principles and techniques of migraine surgery

Publication Date

2022

Medical Journal

Eur Rev Med Pharmacol  
Sci.

## RESEARCH OVERVIEW

Over a period of a decade, the researchers performed surgical decompression of trigger points on 527 people with migraine disease not responsive to other modalities. The hypothesis is that migraine headache is initiated by compression and irritation by vessels and tissue surrounding peripheral branches of the trigeminal nerve.

They focused on three key sites: frontal, occipital, or temporal. A positive response was achieved for more than 80% of the patients, with complete recovery varying from 32% to 86%. Complications were minor and transient, although 42% of the patients developed (or expressed) secondary trigger points post-surgery.



## QUOTES

“Today, migraine surgery has been widely accepted as an effective surgical solution for chronic headaches refractory to medical treatment, with a success rate close to 90%.”

“The surgical procedure elicited a positive response in:

1. Occipital surgery: remarkable improvement in 95% of patients (86% complete recovery);
2. Frontal surgery: remarkable improvement in 87% of patients (32% complete recovery);
3. Temporal surgery: remarkable improvement in 88% of patients (50% complete recovery).”



## OUR TAKEAWAY

Extracranial trigger point deactivation for migraine was an accidental discovery. Patients who had browlifts began reporting a reduction or elimination of their migraine attacks, which resulted from incidental decompression of a branch of the trigeminal nerve that passes above the eyebrow.

For people who have intractable migraine events that do not respond to medications or preventive treatments, trigger point deactivation may offer an alternative that reduces or eliminates migraine pain and its associated disability.



## RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36111912/>

Full article available free at

<https://www.europeanreview.org/article/29628>

Raposo, G and E. Raposo. Principles and techniques of migraine surgery 2022. *Eur Rev Med Pharmacol Sci.* 26 (17):6110-6113. DOI: 10.26355/eurrev\_202209\_29628.



Research Title

Effectiveness of gastrodin for migraine: A meta-analysis

Publication Date

2022

Medical Journal

Front Neurol.



## RESEARCH OVERVIEW

Gastrodin is the main component of *Gastrodia elata Blume* (GEB), a traditional Chinese medicine used to treat dizziness, limb numbness, and other conditions.

This was a “study of studies,” using information compiled from 16 randomized controlled trials involving 1,332 subjects reported in the medical literature.

The meta-analysis showed that gastrodin was significantly effective in treating migraine, reducing pain, reducing the frequency of migraine attack, shortening the duration of migraine attack, and slowing average arterial cerebral blood flow velocity.



## QUOTES

“Gastrodin is effective and safe in the treatment of migraine.”

“In summary, gastrodin treatment of migraine can reduce serum concentration of biochemical factors which induced migraine (ET, CGRP,  $\beta$ -EP, SP, NO, etc.) and reduce cerebral artery blood pressure, slow cerebral artery blood flow, and improve cerebral artery oxygen supply capacity.”



## OUR TAKEAWAY

Meta-analyses lump together studies that often had differing approaches, differing metrics, and differing degrees of rigor, but they also enable researchers to aggregate and analyze data for a larger number of patients.

All 16 of the studies were conducted in China; applicability to other populations is unknown.

This study found gastrodin to be safe and effective in treating migraine, though the authors acknowledge that “the randomized controlled trials included in the meta-analysis have large limitations and large heterogeneity in each study.”



## RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36090869/>

Full article available free at

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9454298/>

Zhou X, Shao J, Xie X, Xu Y, Shao T, Jin Z.

Effectiveness of gastrodin for migraine: A meta-analysis. *Front Neurol.* 2022 Aug 25;13:939401. doi:

10.3389/fneur.2022.939401. PMID: 36090869; PMCID: PMC9454298.



Research Title

Association between sleep quality, migraine and migraine burden

Publication Date

2022

Medical Journal

Front Neurol.



## RESEARCH OVERVIEW

If this report puts you to sleep, that may not be an entirely bad thing because poor sleep quality was significantly and independently associated with total pain burden, severity, headache impact, quality of life, anxiety, and depression in migraine patients.

The researchers observed that “few studies have systematically assessed the association between sleep quality and the risk of developing migraine, and its gender and age differences are unclear.” The study was “aiming to provide new clinical evidence for the prevention and treatment of migraine.”

The study, which consecutively enrolled 134 migraine patients and 70 matched controls, concluded that “Poor sleep quality was significantly independently associated with an increased risk of developing migraine and the migraine-related burdens.”



## QUOTES

“The prevalence of poor sleep quality in migraine patients was significantly higher than that in subjects without migraine.”

“After adjusting for various confounding factors, the risk of migraine with poor sleep quality remained 3.981 times that of those with good sleep quality.”



## OUR TAKEAWAY

Consistently getting a full night of sleep may be one of the best ways to reduce the adverse effects of migraine disease.

Though the study was relatively small (134 people with migraine, 70 matched controls), the statistical analysis was sophisticated and thorough.

What remains uncertain is whether the neurology of people with migraine makes them more vulnerable to poor quality of sleep or whether poor sleep quality is a migraine trigger.



## RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36090858/>

Full article available free at

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9459411/>

Duan S, Ren Z, Xia H, Wang Z, Zheng T, Liu Z. Association between sleep quality, migraine and migraine burden. *Front Neurol.* 2022 Aug 26;13:955298. doi: 10.3389/fneur.2022.955298. PMID: 36090858; PMCID: PMC9459411.



Research Title

Delivery of Dihydroergotamine [DHE] Mesylate to the Upper Nasal Space for the Acute Treatment of Migraine: Technology in Action

Publication Date

2022

Medical Journal

J Aerosol Med Pulm Drug Deliv.



## RESEARCH OVERVIEW

Oral administration of migraine medications during a migraine has limitations that include nausea, inconsistencies in rates of dissolution, and variations in absorption.

The nasal route has advantages that include ease of use, fast, consistent absorption, and avoidance of gastrointestinal (GI) issues; however, traditional nasal sprays only deliver medication to the lower portion of the nasal tract, where absorption is limited.

This report describes Precision Olfactory Delivery (POD<sup>®</sup>), a handheld, manually actuated, propellant-powered administration device that delivers medication to the upper nasal space.



## QUOTES

“Results from clinical studies of INP104 [a formulation of dihydroergotamine, a frequently used migraine medication] demonstrate a favorable pharmacokinetic profile, consistent and predictable dosing, rapid systemic levels known to be effective (similar to other DHE mesylate clinical programs), safety and tolerability on the upper nasal mucosa, and high patient acceptance.”



## OUR TAKEAWAY

Speed is of the utmost importance when dealing with a migraine. Anything that delivers helpful medication more quickly and more effectively deserves careful consideration.

By delivering more DHE to the upper nasal space, the POD device has the potential to overcome the limitations of traditional nasal delivery systems, while utilizing the nasal delivery benefits of GI tract avoidance, rapid onset, patient convenience, and ease of use.

Many new-generation migraine medications are being developed with nasal administration in mind.



## RESEARCH LINK & AUTHORS

Abstract available free at

<https://www.liebertpub.com/doi/full/10.1089/jamp.2022.0005>

Cooper, W., Ray, S., Aurora, S. K., Shrewsbury, S. B., Fuller, C., Davies, G., & Hoekman, J. (2022). Delivery of Dihydroergotamine Mesylate to the Upper Nasal Space for the Acute Treatment of Migraine: Technology in Action. *J Aerosol Med Pulm Drug Deliv.* <https://doi.org/10.1089/jamp.2022.0005>



Research Title

Time course of efficacy of atogepant for the preventive treatment of migraine: Results from the randomized, double-blind ADVANCE trial

Publication Date

2022

Medical Journal

Cephalalgia



## RESEARCH OVERVIEW

Atogepant (Qulipta) is an oral, small-molecule, calcitonin gene-related peptide receptor antagonist for the preventive treatment of migraine. Other gepants medications are Ubrelvy and Nurtec.

In this study, 873 participants with 4-14 migraine days/month were randomized to atogepant 10 mg, 30 mg, 60 mg, or placebo once daily for 12 weeks.

The day after the first dose, 25.2% of those in the placebo group reported a migraine, while 10.8-14.1% of the atogepant groups on varying doses reported migraine.

The advantage remained with the treatment group for each 4-week interval of the 12-week trial.



## QUOTES

“Considering the significant impact of migraine on an individual’s life both during and between attacks, there is a need for treatments that reliably address preventive treatment goals and provide a rapid onset of action.”

“Atogepant demonstrated treatment benefits as early as the first full day after treatment initiation, and sustained efficacy across each 4-week interval during the 12-week treatment period.”



## OUR TAKEAWAY

The gepants class of medications work by preferentially binding to the receptor site for calcitonin gene-related peptide, a substance known to be involved in the migraine biochemical cascade. Unlike triptans and other medications, the gepants medications do not cause constriction of blood vessels and are thus safe for those with cardiovascular risk factors.

This study found that atogepant has a rapid onset of efficacy and that its impact compared to a placebo was sustained throughout the study period.



## RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://journals.sagepub.com/doi/10.1177/03331024211042385>

Schwedt, T. J., Lipton, R. B., Ailani, J., Silberstein, S. D., Tassorelli, C., Guo, H., Lu, K., Dabruzzo, B., Miceli, R., Severt, L., Finnegan, M., & Trugman, J. M. (2022). Time course of efficacy of atogepant for the preventive treatment of migraine: Results from the randomized, double-blind ADVANCE trial. *Cephalalgia*, 42(1), 3-11. <https://doi.org/10.1177/03331024211042385>



Research Title

Association of increased pain intensity, daytime sleepiness, poor sleep quality, and quality of life with mobile phone overuse in patients with migraine: A multicenter, cross-sectional comparative study

Publication Date

2022

Medical Journal

Brain Behav



## RESEARCH OVERVIEW

Researchers in this study recruited 400 people with migraine. They were divided into two groups, high and low users, based on their cell phone usage. For each group the researchers measured patients' level of disability, pain intensity, sleep quality, daytime sleepiness, and quality of life. The respondents' average age was 27.6 years.

Greater pain intensity, poor sleep quality, and reduced medication effectivity were found in the high cellphone use group.



## QUOTES

“Smartphone overuse could worsen pain, sleep, and reduce treatment efficacy in individuals with migraine.”

“Controlled smartphone use is recommended to avoid worsening symptoms.”



## OUR TAKEAWAY

High cell phone use may be a contributing factor to the discomfort and disability of migraine disease.

This study found that higher rates of cell phone use were correlated with migraine attacks of greater pain intensity and reduced effectiveness of medication.

The study did not attempt to describe what the mechanism might be by which cell phones cause these adverse effects.

It is interesting to note that the *lower-use group* reported increased duration of migraine and medication intake.



## RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36128652/>

Full article available free at

<https://onlinelibrary.wiley.com/doi/10.1002/brb3.2760>

Butt, M., Chavarria, Y., Ninmol, J., Arif, A., Tebha, S. S., Daniyal, M., Siddiqui, U. M., Shams, S. S., Sarfaraz, Q., Haider, S. F., & Essar, M. Y. (2022). Association of increased pain intensity, daytime sleepiness, poor sleep quality, and quality of life with mobile phone overuse in patients with migraine: A multicenter, cross-sectional comparative study. *Brain Behav*, e2760.

<https://doi.org/10.1002/brb3.2760>



Research Title

Prevalence and Predictors of Fatigue in Patients with Episodic Migraine

Publication Date

2022

Medical Journal

Wiad Lek.



## RESEARCH OVERVIEW

This study examined the frequency of fatigue in people with episodic migraine (EM). Fatigue, as a general and persistent symptom, interferes with activities of daily living and the quality of life.

In the 85 people studied who met the definition of having episodic migraine, 41.2% reported experiencing fatigue as a general symptom; in a matched control group, 11.4% of the people reported reported experiencing general fatigue.

The presence of fatigue in the study participants was associated with a higher number of headache days per month, with more severe headache episodes, as well as with more frequent occurrence of migraine prodromal phenomena.



## QUOTES

“In recent years, evidence has emerged that fatigue in migraine patients is different from fatigue in healthy people.”

“Thus, in patients with EM, fatigue is a common phenomenon that has migraine-related predictors.”

“It’s very likely that proper migraine treatment may also indirectly affect fatigue characteristics and improve patients’ well-being.”



## OUR TAKEAWAY

Migraine disease has a large footprint with an impact on quality of life beyond the acute headache phase.

The results of this study suggest that there are underlying biological reasons why episodic migraine results in persistent fatigue.

## RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36129080/>

Full article available free at

<https://wiadlek.pl/wp-content/uploads/archive/2022/08/WLek202208205.pdf>

Delva, M., Delva, I., Pinchuk, V., Kryvchun, A., & Purdenko, T. (2022). Prevalence and Predictors of Fatigue in Patients with Episodic Migraine. *Wiad Lek.* 75(8 pt 2), 1970-1974.

<https://doi.org/10.36740/WLek202208205>





Research Title

Management of Chronic Migraine in Children and Adolescents: Where are we in 2022?

Publication Date

2022

Medical Journal

Pediatric Health Med Ther.



## RESEARCH OVERVIEW

This is a “state of the state” review article providing an overview of acute and preventive treatments for the management of chronic migraine (>15 headache days per month) in youth.

The paper describes diagnostic criteria for chronic migraine and highlights the state of evidence for acute and preventive treatment in children and adolescents.

The authors then discuss emerging treatments currently receiving rigorous clinical research effort, special considerations for the treatment of chronic migraine in children and adolescents, and avenues for improving existing treatments and expanding access to evidence-based care.



## QUOTES

“Chronic migraine is a disabling migraine subtype that affects a substantial proportion of children and adolescents and tends to persist into adulthood.”

“Once a chronic migraine diagnosis has been established, a biopsychosocial approach to care that incorporates both medical treatment and non-medicine intervention strategies is recommended.”

“Inadequate hydration, skipping meals, poor sleep, and insufficient exercise are factors associated with increased headache risk.”

“The best available evidence, as described in current guidelines from the AAN [American Academy of Neurology] and American Headache Society, supports use of a combined pharmacotherapy (i.e., amitriptyline) and behavioral approach (i.e., cognitive-behavioral therapy) for migraine prevention in children and adolescents.”



## OUR TAKEAWAY

Chronic migraine in children and adolescents receives relatively little attention, yet it is disruptive and debilitating socially, academically, and in all the ways adults are affected. Diagnosis and treatment of this population is different and challenging, and even neurologists are less familiar with it than they are with adult chronic migraine.

This paper is an excellent summary of current best practices in diagnosis and treatment for this population. The authors emphasize the applicability of non-pharmacological modalities in combination with medication.



## RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://www.dovepress.com/management-of-chronic-migraine-in-children-and-adolescents-where-are-w-peer-reviewed-fulltext-article-PHMT>

Gibler RC, Knestruck KE, Reidy BL, Lax DN, Powers SW. Management of Chronic Migraine in Children and Adolescents: Where are We in 2022? *Pediatric Health Med Ther.* 2022;13:309-323 <https://doi.org/10.2147/PHMT.S334744>