



Welcome to the Q1, 2023 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 individual 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

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

Dietary Zinc Intake and Migraine in Adults: A Cross-Sectional Analysis of the National Health and Nutrition Examination Survey 1999–2004

Publication Date

January 2023

Medical Journal

Headache



RESEARCH OVERVIEW

Neuroinflammatory and oxidative stress are known to be involved in migraine genesis. Zinc is a trace element that has anti-inflammatory and antioxidant properties.

Researchers looked at dietary and supplement data for 11,088 people, 20.2% of whom reported having migraine disease. They found an inverse association between dietary zinc and migraine. When dietary and supplemental zinc (total intake of zinc) were combined, the same relationship (more zinc equals less migraine) was found.



QUOTES

“An expanding body of evidence suggests that migraine disease results from oxidative stress levels exceeding the capacity of antioxidants in the body to reduce the oxidative stress.”

“Our findings suggest zinc is an important nutrient that influences migraine.”

“Participants who consumed more dietary zinc had a lower risk of migraine after adjusting for age, sex, marital status, race/ethnicity, education level, BMI, smoking status, hypertension, diabetes, stroke, coronary heart disease, CRP, and for intake of energy, carbohydrate, protein, and dietary copper.”

“Previous studies have reported lower serum zinc levels in individuals living with migraine disease compared to healthy controls, and that zinc supplementation diminished migraine frequency and severity.”



OUR TAKEAWAY

There is no “magic bullet” for completely preventing migraine, but this study points to a substantial protective role for zinc. The body normally maintains a delicate balance between free radicals (reactive oxygen molecules that play a role in cell signaling) and natural antioxidants. When this balance is upset (oxidative stress), the body recruits pro-inflammatory cytokines. Inflammation, in turn, contributes to migraine. Zinc may help to reduce inflammation by serving as a component of superoxide dismutase (SOD), which is an antioxidant enzyme that research shows is lower in people living with migraine. A lack of zinc could impair the ability to generate SOD.



RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36588459/>

Liu, H., Wang, Q., Dong, Z., & Yu, S. (2023). Dietary zinc intake and migraine in adults: a cross-sectional analysis of the National Health and Nutrition Examination Survey 1999-2004. *Headache*, 63(1), 127-135. <https://doi.org/10.1111/head.14431>



Research Title

Migraine Headache in Childhood

Publication Date

January 2023

Medical Journal

StatPearls



RESEARCH OVERVIEW

Childhood migraine is often overlooked, misdiagnosed, or mistreated. Its impact on children can be harmful physically, psychologically, and socially. This book chapter is an up-to-date, comprehensive review of the etiology, epidemiology, pathophysiology, evaluation, treatment/management, differential diagnosis, complications, and prognosis for children with migraine disease. It includes information about prevention, patient education, and ways of enhancing healthcare team outcomes.



QUOTES

“Up to 18% of patients in the pediatric emergency room are found to be migraine-related.”

“About 1 in 10 children experience recurrent headaches due to migraine, which can significantly impair school performance and quality of life.”

“The most common comorbidity with migraine in childhood is sleep disorders. There is a greater prevalence of parasomnias, obstructive sleep apnea, and sleep-related movement disorders in children [with migraine].”

“Managing migraine in the pediatric population requires an interprofessional team that includes clinicians (MDs, DOs, NPs, and PAs), nurses, and pharmacists.”



OUR TAKEAWAY

Primary care physicians who don't have extensive experience diagnosing or treating childhood migraine may find this paper helpful to them and beneficial for the patient. It provides a helpful overview of everything from differential diagnosis to current treatment options. It can be also be a useful tool for educating providers who may otherwise minimize the reality or significance of migraine-like headache symptoms, which are too frequently attributed to “stress” or other “blame the victim” diagnoses.



RESEARCH LINK & AUTHORS

Abstract and full document available free at <https://www.ncbi.nlm.nih.gov/pubmed/32491745>

Al Khalili, Y., Asuncion, R. M. D., & Chopra, P. (2023). [Migraine Headache In Childhood](#) StatPearls (internet publication)



Research Title

Presence and Severity of Migraine is Associated with Development of Primary Open Angle Glaucoma: A Population-Based Longitudinal Cohort Study

Publication Date

March 2023

Medical Journal

PLoS One



RESEARCH OVERVIEW

Glaucoma is an eye disease in which there is progressive damage to the optic nerve as a result of excessive eye pressure and other factors. The purpose of this study was to examine the association between the presence and severity of migraine and development of primary open-angle glaucoma (POAG). Subjects were classified into three groups:

1. Healthy control subjects.
2. Subjects with mild migraine.
3. Those with severe migraine.

During the nine-year follow-up period, the incidence rate of POAG per 1,000 person-years was 2.41 and 3.25 in subjects without and with migraine and 3.89 in those with severe migraine, respectively. The researchers concluded that migraine is associated with increased risk of POAG.



QUOTES

“Our study suggests that presence and severity of migraine are both associated with increased risk of subsequent development of [primary open-angle glaucoma].”

“It is noteworthy that glaucoma shares certain characteristics with migraine in that both are possibly associated with vascular dysregulation in terms of pathophysiology of the diseases.”

“The association between migraine and subsequent POAG was consistent in all subgroup analyses.”

“While those with mild migraine showed 1.17 times greater risk, those with severe and chronic migraine showed 1.29 times greater risk of POAG after adjusting for confounding factors.”

“Prevalence of migraine and POAG both increase along with the subjects’ age.”



OUR TAKEAWAY

People with migraine disease benefit from knowing when they are at risk for comorbid conditions. This study, which was a review of data from a large Korean health database, reports an increased risk for open-angle glaucoma, with the risk increasing in parallel with migraine severity. Though the precise mechanisms are unclear, both migraine and glaucoma involve vascular issues and thus to some degree share pathophysiology.



RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0283495>

Ohn, K., Han, K., Moon, J. I., & Jung, Y. (2023). Presence and severity of migraine is associated with development of primary open angle glaucoma: A population-based longitudinal cohort study. *PLoS One*, 18(3), e0283495. <https://doi.org/10.1371/journal.pone.0283495>



Research Title

Safety, Tolerability, and Efficacy of Zavegepant 10mg Nasal Spray for the Acute Treatment of Migraine in the USA: A Phase 3, Double-Blind, Randomised, Placebo-Controlled Multicentre Trial

Publication Date

March 2023

Medical Journal

Lancet Neurol



RESEARCH OVERVIEW

The FDA recently approved zavegepant, the first nasal spray calcitonin gene-related peptide (CGRP) inhibitor for use during a migraine attack. It is expected to be in distribution by July, under the brand name Zavzpret. This study had 1,405 participants, divided evenly between treatment and placebo groups.

Two hours after the treatment dose, more participants in the zavegepant group than in the placebo group were free of pain (24% vs. 15%) and free from their most bothersome symptom (40% vs. 31%). The most common adverse events in either treatment group ($\geq 2\%$) were taste distortion (21% in the zavegepant group vs. 5% in the placebo group), nasal discomfort (4% vs. 1%), and nausea (3% vs. 1%). There was no sign of liver toxicity, which had been an issue for some early medications in this category.



QUOTES

“Zavegepant 10 mg nasal spray was efficacious in the acute treatment of migraine, with favorable tolerability and safety profiles. Additional trials are needed to establish the long-term safety and consistency of effect across attacks.”

“As the only gepant [class of CGRP inhibitors] medication supplied in a non-oral formulation, zavegepant 10 mg nasal spray could be particularly useful in patients with characteristics associated with guideline-based recommendations for non-oral therapies, including headache attacks with severe nausea or vomiting or rapidly escalating headache pain, as well as for patients in whom oral forms are associated with inadequate response, slow onset of action, or poor tolerability.”



OUR TAKEAWAY

This study helped establish both the effectiveness and safety of zavegepant. It delivered pain freedom at the two-hour mark for around a quarter of those tested. It was better than placebo in eliminating other major migraine symptoms, including sensitivity to light and sound. Because it will be available as a nasal spray, zavegepant may prove particularly useful for those who experience gastroparesis, can't keep an oral medication down or whose headaches escalate rapidly, rendering the oral route too slow to be effective.



RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/36804093/>

Lipton, R. B., Croop, R., Stock, D. A., Madonia, J., Forshaw, M., Lovegren, M., Mosher, L., Coric, V., & **Goadsby, P. J.** (2023). Safety, tolerability, and efficacy of zavegepant 10 mg nasal spray for the acute treatment of migraine in the USA: a phase 3, double-blind, randomised, placebo-controlled multicentre trial. *Lancet Neurol*, 22(3), 209-217. [https://doi.org/10.1016/S1474-4422\(22\)00517-8](https://doi.org/10.1016/S1474-4422(22)00517-8)



Research Title

Risk of Migraine after Traumatic Brain Injury and Effects of Injury Management Levels and Treatment Modalities: A Nationwide Population-Based Cohort Study in Taiwan 2022

Publication Date

February 2023

Medical Journal

J Clin Med



RESEARCH OVERVIEW

Traumatic brain injury (TBI) causes several long-term disabilities, including headache. An association between TBI and subsequent migraine has been reported; however, few longitudinal studies have explored the link between migraine and TBI, and the modifying effects of treatment remain unknown. This retrospective cohort study used records from Taiwan's Longitudinal Health Insurance Database 2005 to evaluate the risk of migraine among more than 150,000 patients with TBI and to determine the effects of different treatment modalities. There was a correlation between trauma severity and migraine incidence: major trauma was associated with a higher migraine risk than minor trauma. Migraine risk did not differ significantly after surgery or occupational/physical therapy.



QUOTES

“These results suggest that, in addition to providing acute surgical intervention and chronic rehabilitation, physicians should counsel TBI patients regarding adjuvant strategies to prevent subsequent migraine development.”

“Whether trauma induces migraine or triggers a pre-existing susceptibility to migraine itself remains unclear.”

“Among TBI patients, hospitalization and major trauma were associated with 1.557-fold and 1.670-fold increased risks of migraine, respectively.”



OUR TAKEAWAY

Traumatic brain injury can occur in many ways, from auto and industrial accidents to sports and gunshot wounds. Severity varies considerably, as do lingering symptoms, headache among them. This study, which used a large body of data from a health insurance database, found that those who suffered TBI were more likely to later have migraine disease and that there was a relationship between the severity of TBI and the likelihood of subsequent migraine disease. Subsequent occupational and physical therapy had no significant impact on migraine incidence.



RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9959615/>

Chen, M. H., Sung, Y. F., Chien, W. C., Chung, C. H., & Chen, J. W. (2023). Risk of Migraine after Traumatic Brain Injury and Effects of Injury Management Levels and Treatment Modalities: A Nationwide Population-Based Cohort Study in Taiwan. *J Clin Med*, 12(4). <https://doi.org/10.3390/jcm12041530>



Research Title

Evaluation of Vascular Risk in Patients with Migraine with and without Aura Treated with Erenumab: Post Hoc Analysis of Pooled Long-Term Clinical Trial Data

Publication Date

March 2023

Medical Journal

Headache



RESEARCH OVERVIEW

Cardiovascular risk from hypertension has been posited as a possible risk factor with the calcitonin gene-related peptide (CGRP) inhibitor class of drugs. The intent of this study was to evaluate cardiovascular (CV) risk of erenumab (Aimovig).

Data were pooled from four double-blind, randomized trials and used to assess blood pressure (BP) changes and CV safety in patients. CV safety was assessed as ischemic cardiovascular and cerebrovascular adverse events. Ischemic CV and cerebrovascular adverse events were uncommon, and the incidence rates were similar across the 10-year CV risk categories.

This study provides some reassurance that at least in the case of Aimovig, CV risk is not increased.



QUOTES

“As CGRP causes dilation of blood vessels, hypertension has been considered a theoretical risk associated with the inhibition of the CGRP pathway in migraine management, particularly in a patient population with pre-existing cardiovascular (CV) risk factors.”

“Management of migraine is challenging in people with CV comorbidities. Although erenumab does not show vasoconstrictive effects in human coronary and cerebral arteries, it is necessary to consider potential implications of CGRP pathway inhibition, especially in at-risk patients, as CGRP is a potent vasodilator.”

“This analysis supports the vascular safety profile of erenumab across different CV risk profiles, including patients with high risk.”



OUR TAKEAWAY

Reports of increased hypertension (high blood pressure) in those taking Aimovig prompted this in-depth evaluation of a large data set. Pooling data from other studies provides a means of gaining a larger cohort and thus more statistically valid study. There have been concerns about the unknowns of blocking the CGRP receptors, since CGRP is also involved (as a vasodilator) in blood pressure regulation. This study found that at least for one medication in the category, neither blood pressure nor CV risk were significantly increased for those taking Aimovig.



RESEARCH LINK & AUTHORS

Abstract available free at <https://pubmed.ncbi.nlm.nih.gov/36942409/>

Kudrow, D., Dafer, R., **Dodick, D. W., Starling, A., Ailani, J., Dougherty, C.**, Kalidas, K., Zhang, F., Jeswani, R., Patel, N., & Khodavirdi, A. C. (2023). Evaluation of vascular risk in patients with migraine with and without aura treated with erenumab: Post hoc analysis of pooled long-term clinical trial data. *Headache*, 63(3), 418-428. <https://doi.org/10.1111/head.14485>



Research Title

Sex Differences in Migraine Attack Characteristics: A Longitudinal E-Diary Study

Publication Date

March 2023

Medical Journal

Headache



RESEARCH OVERVIEW

Women are reported as having episodic or chronic migraine disease more frequently than men, but the studies on which this is based have been mostly cross-sectional – one group of people at one point in time. This study assessed differences in migraine attack characteristics between men and women who were prospectively followed for three-and-a-half years using a previously validated electronic headache diary. The primary outcome measured was "attack" duration. Differences between perimenstrual (days -2 to +3 of the menstrual cycle) and non-perimenstrual attacks in women versus attacks in men were corrected for age, chronic migraine, and medication overuse headache. Researchers concluded that compared to attacks in men, both perimenstrual and non-perimenstrual migraine attacks are of longer duration and are more often accompanied by associated symptoms.



QUOTES

“Both perimenstrual and non-perimenstrual migraine attacks in women differ from migraine attacks in men.”

“A sex-specific approach to migraine treatment and research is needed.”

“Treating physicians should be aware of a longer attack duration in women, despite the use of long-acting triptans, and particularly the increased risk of relapse during the perimenstrual window.”

“To what extent differences between men and women have a biological basis or result from psychosocial and cultural factors requires further research, but it seems too simplistic to assume that women are merely more likely to report more frequent and more severe symptoms than men. Our results highlight the need for a sex- and gender-informed approach in migraine treatment and research.”



OUR TAKEAWAY

The way in which migraine affects women is distinct from how it affects men. That is the bottom line of this study, which points to a compelling need for sex-specific research and sex-specific treatment. Perimenstrual migraine attacks, which may result from changes in sex hormone levels prior to menstruation, have a longer duration and increased relapse risk compared to non-perimenstrual migraine attacks. The present study confirmed that similar differences exist between perimenstrual migraine attacks and migraine attacks in men. These differences may be most pronounced in a subgroup of women with menstrual migraine, as has been found in previous studies. In addition, the researchers identified smaller differences in attack duration between non-perimenstrual migraine attacks and attacks in men.



RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://headachejournal.onlinelibrary.wiley.com/doi/full/10.1111/head.14488>

Verhagen, I. E., van der Arend, B. W. H., van Casteren, D. S., le Cessie, S., **MaassenVanDenBrink, A., & Terwindt, G. M.** (2023). Sex differences in migraine attack characteristics: A longitudinal E-diary study. *Headache*, 63(3), 333-341. <https://doi.org/10.1111/head.14488>



Research Title

Diagnosis, Knowledge, Perception, and Productivity
Impact of Headache Education and Clinical
Evaluation Program in the Workplace at an
Information Technology Company of More than
70,000 Employees

Publication Date

March 2023

Medical Journal

Cephalalgia



RESEARCH OVERVIEW

Education is highly valuable not only for people with migraine disease but also their co-workers. The Japanese company Fujitsu collaborated with the International Headache Society-Global Patient Advocacy Coalition to create the Fujitsu Headache Project. Activities for participating employees included an e-learning program, video seminars and online headache consultation with a staff physician and industrial health nurses. Of the 81,159 Fujitsu employees in Japan, 90.5% participated. Of those, 16.7% provided a self-diagnosis of migraine. The proportion of participants who found headaches to be part of a disease with a significant impact on someone's life increased from 46.8% to 70.6%. More than three-quarters of total participants (76.9%) said that their attitudes towards their colleagues' headache disorders changed as a result of the e-learning, and 82.9% said that their attitudes changed toward their colleagues as a result of the e-learning.



QUOTES

“One of the major objectives of the Fujitsu Headache Project was to raise awareness of headache disorders company-wide, and not just among those with headache. One of the most important outcomes is that the e-learning led to a substantial decrease in stigma; 83% of participants without headache changed their attitude towards colleagues with headache disorders as a result of the e-learning.”

“The Fujitsu Headache Project therefore responded to two of the biggest needs of people with headache disorders in the workplace: feeling understood and supported. Lack of understanding by colleagues and/or supervisors and stigma are associated with feelings of guilt, impaired work interpersonal relationships, and decreased productivity.”



OUR TAKEAWAY

This is an important example of the substantial impact education can have for people with migraine disease, especially in the workplace. More than three-quarters of the participants in the Fujitsu Headache Project said their attitude toward colleagues' headaches disorders *changed* as a result of what they learned, and a remarkable 82.9% changed their attitudes toward the colleagues themselves, helping to greatly reduce the stigma of migraine and other headache disorders. This study was unique in its size, scope, and impact, and it provides a model for how to change attitudes in the workplace.



RESEARCH LINK & AUTHORS

Abstract and full article available free at
<https://journals.sagepub.com/doi/10.1177/03331024231165682>

Sakai, F., Igarashi, H., Yokoyama, M., Begasse de Dhaem, O., Kato, H., Azuma, Y., Koh, R., Phillips, H., Singh, N., **Craven, A., Dodick, D. W.**, & Miyake, H. (2023). Diagnosis, knowledge, perception, and productivity impact of headache education and clinical evaluation program in the workplace at an information technology company of more than 70,000 employees. *Cephalalgia*, 43(4), 3331024231165682.
<https://doi.org/10.1177/03331024231165682>.



Research Title

Anti-Calcitonin Gene-Related Peptide Monoclonal Antibodies for the Treatment of Vestibular Migraine: A Prospective Observational Cohort Study

Publication Date

April 2023

Medical Journal

Cephalalgia



RESEARCH OVERVIEW

Vestibular migraine is thought to be the most frequent cause of vertigo, yet it is often not immediately diagnosed as migraine. Only about 10% of those with migraine disease have vestibular migraine. This study examined the effectiveness of calcitonin gene-related peptide (CGRP) inhibitors for treatment of vestibular migraine.

Fifty patients at an Italian clinic were treated with Aimovig, Ajovy, or Emgality. Response to treatment was excellent: 90% had at least a 50% reduction in vertigo frequency, 86% had at least a 50% reduction in headache frequency, and 80% had a reduction of at least 50% on a standardized migraine evaluation test. Overall, 78% had a reduction of all three parameters.



QUOTES

“Response to treatment was excellent as 45 (90%) patients had at least a 50% reduction in vertigo frequency, 43 (86%) had at least a 50% reduction in headache frequency, and 40 (80%) had a Migraine Disability Assessment (MIDAS) score reduction of at least 50%. Overall, 39 (78%) patients had a concomitant reduction of all three parameters.”

“[Vestibular migraine (VM)] is an unmet clinical need as specific treatments are missing, and the disease burden is incredibly high. This is supported by the mean baseline value of the MIDAS score of 52.8 in our patient population, indicating severe disability.”

“Our data suggests that treatment of VM with anti-CGRP [monoclonal antibodies] is effective and should be started early in the disease course.”



OUR TAKEAWAY

These findings offer hope for those with vestibular migraine, which causes vertigo and is highly disabling. While the CGRP inhibitors have been widely tested and deployed against other forms of migraine disease, this is the first prospective study to definitively find that this class of drug is effective in those with vestibular migraine. There are CGRP receptors in the vestibular area of the inner ear, which would explain both the origin of vertigo and the reason CGRP inhibitors are effective in treating vestibular migraine.



RESEARCH LINK & AUTHORS

Abstract and full article available free at <https://journals.sagepub.com/doi/epub/10.1177/03331024231161809>

Russo, C. V., Sacca, F., Braca, S., Sansone, M., Miele, A., Stornaiuolo, A., & De Simone, R. (2023). Anti-calcitonin gene-related peptide monoclonal antibodies for the treatment of vestibular migraine: A prospective observational cohort study. *Cephalalgia*, 43(4), 3331024231161809.

<https://doi.org/10.1177/03331024231161809>