



QUARTERLY RESEARCH REPORT

Welcome to the Q2, 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 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
TitleThe Importance of an Early Onset of Migraine
Prevention: An Evidence-Based, Hypothesis-
Driven Scoping Literature Review

Publication Date

May 2022

Medical Journal

*Therapeutic Advances in
Neurological Disorders*

RESEARCH OVERVIEW

MWS Co-producer Paula Dumas joined seven co-authors (including four prior MWS presenters) in reporting that compared to placebo:

- Erenumab [AIMOVIG, three studies] reduced weekly migraine days within 1 week;
- Fremanezumab [AJOVY, six studies] increased reports of no headache of at least moderate severity on Day 1 and significantly reduced migraine frequency within 1 week;
- Galcanezumab [EMGALITY, three studies] significantly reduced the mean number of patients with migraine beginning Day 1 and each day of the first week;
- Eptinezumab [VYEPTI, four studies] significantly reduced migraine attack likelihood on Day 1 by > 50% versus baseline; and
- OnabotulinumtoxinA (BOTOX two studies) reduced headache and migraine days within 1 week.



QUOTES

“Anti-CGRP monoclonal antibodies (erenumab, fremanezumab, galcanezumab, and eptinezumab) and a chemodenervation agent (onabotulinumtoxinA) provide clinically relevant benefits during the first treatment week.”

“The results of this evidence-based scoping literature analysis identified clinically and statistically significant evidence that supports the hypothesis that patients with migraine benefit from an early onset of prevention with currently approved anti-CGRP mAbs and onabotulinumtoxinA.”



OUR TAKEAWAY

It is very important to understand the time frame within which preventive medications can be expected to begin providing protection. This helps establish reasonable expectations for both clinicians and patients, thereby minimizing the premature discontinuation or changing of medications before they have had a chance to work. This study, based on a review of 16 studies, found that CGRP inhibitors and Botox reduce migraine days within one day to one week.



RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/35662957/>

Full article available free at

<https://journals.sagepub.com/doi/full/10.1177/17562864221095902>

Gottschalk C, Buse DC, Marmura MJ, Torphy B, Pavlovic JM, Dumas PK, Lalvani N, Blumenfeld A.

The Importance of An Early Onset of Migraine Prevention: An Evidence-Based, Hypothesis-Driven Scoping Literature Review.

Ther Adv Neurol Disord. 2022 May 31;

15:17562864221095902. doi:

10.1177/17562864221095902. PMID: 35662957;

PMCID: PMC9160905.

Research
Title

The Association Between OnabotulinumtoxinA and Anti-CGRP Monoclonal Antibodies: A Reliable Option for the Optimal Treatment of Chronic Migraine

Publication Date June 2022

Medical Journal *Neurological Science*

RESEARCH OVERVIEW

Some people with migraine get incomplete or diminishing relief using either a CGRP inhibitor or Botox (onabotulinumtoxin-A). This paper summarizes the rationale and existing data on the use of both medications simultaneously.



QUOTES

“The association of two preventive treatments may be a reliable option for these patients. So, onabotulinumtoxinA (BT-A) and anti-CGRP mAbs may be used together, and some pre-clinical and clinical evidence of an additive action of the 2 drugs is emerging.”

“An intriguing possibility may be the association between the BT-A and an anti-CGRP mAb in CM sufferers who experienced an incomplete or null response to one of the abovementioned drug classes.”



OUR TAKEAWAY

CGRP inhibitors work for migraine prevention. Botox (onabotulinumtoxin-A) works for migraine prevention. But sometimes, for some people, neither of them work, or they work for awhile and then become less effective. Exploring the possibility that the two could work better together, the authors consider the physiological pathways that make each medication function, the reasons why they might work synergistically, and the barriers to using them simultaneously.



RESEARCH LINK & AUTHORS

Abstract available free at

<https://link.springer.com/article/10.1007/s10072-022-06195-5>

Guerzoni, S., Baraldi, C., & Pani, L. (2022).

The Association Between OnabotulinumtoxinA and Anti-CGRP Monoclonal Antibodies: A Reliable Option for the Optimal Treatment of Chronic Migraine.

Neurol Sci. <https://doi.org/10.1007/s10072-022-06195-5>

Research
TitleReal-World Experience of Interictal Burden
and Treatment in Migraine: A Qualitative
Interview Study

Publication Date

June 2022

Medical Journal

Journal of Headache Pain

RESEARCH OVERVIEW

The objective of this study was to understand the interictal burden of migraine, from the patient perspective, and to explore patient experience with migraine treatments.



QUOTES

“In contrast to the substantial body of evidence regarding the specific impact of migraine attacks, relatively little is known about the interictal burden, or burden of disease between migraine episodes.”

“Emotional impacts were reported by all participants, including anger, depression, anxiety and hopelessness. Many participants who took preventive treatments reported improvements in HRQL and functioning but still experienced breakthrough attacks.”



OUR TAKEAWAY

Often lost in the analysis of migraine impact is what happens to people with migraine between attacks. The impact of migraine does not stop when the postdrome ends. This “interictal” period has received relatively little attention, yet as this research shows, it has a major impact on the quality of life for people with migraine disease.



RESEARCH LINK & AUTHORS

Full article available free at

<https://thejournalofheadacheandpain.biomedcentral.com/articles/10.1186/s10194-022-01429-5>

Lo, S. H., Gallop, K., **Smith, T.**, Powell, L., Johnston, K., Hubig, L. T., Williams, E., Coric, V., Harris, L., L'Italien, G., & Lloyd, A. J. (2022).

Real-World Experience of Interictal Burden and Treatment in Migraine: A Qualitative Interview Study. *J Headache Pain*, 23(1), 65.

<https://doi.org/10.1186/s10194-022-01429-5>



Research Title

Triggers of Migraine: Where Do We Stand?

Publication Date

June 2022

Medical Journal

Current Opinion in Neurology



RESEARCH OVERVIEW

This review article examines the literature relating to migraine “triggers” and finds that triggers, at least partially actually correspond with premonitory symptoms because:

1. migraine attacks are not reliably induced by daily life triggers;
2. experimental evidence suggesting that sensory stimuli and food substances are reliable triggers is poor; and
3. there is a close correspondence between the trigger factors and premonitory symptoms (odor/osmophobia, light/photophobia, noise/phonophobia).



QUOTES

“Commonly reported trigger factors lack a strong causative relationship with migraine, especially when considered alone.”

“The studies aimed at evaluating the causal relationship between trigger factors and a migraine attack suggest that reported trigger factors are, in most cases, just symptoms of the premonitory phase of migraine experience.”

“Trigger avoidance may prove ineffective or even deleterious when the cause-effect relationship between the supposed trigger and the migraine attack is not proven. A healthy lifestyle and, when necessary, a cognitive behavioural therapy approach may have a positive effect on migraine severity.”



OUR TAKEAWAY

What if migraine “triggers” aren’t triggers? Citing triggers for migraine onset is common for many people with migraine disease. It may have costs such as self-blame and guilt. This research suggests that what many cite as triggers may instead be prodromal symptoms signaling the start of a complex process in the brain whose result is the migraine headache. The next time you experience a trigger that leads to an attack, ask yourself - could this be the start of the prodrome?



RESEARCH LINK & AUTHORS

Abstract available free at

<https://pubmed.ncbi.nlm.nih.gov/35674080/>

Martinelli, D., Pocora, M. M., De Icco, R., Putorti, A., & Tassorelli, C. (2022).

Triggers of Migraine: Where Do We Stand? *Curr Opin Neurol*, 35(3), 360-366.

<https://doi.org/10.1097/WCO.0000000000001065>

Research
TitleType and Severity of Migraine Determines
Risk of Atrial Fibrillation in Women

Publication Date May 2022

Medical Journal

*Frontiers in
Cardiovascular Medicine*

RESEARCH OVERVIEW

This study, which included a 10-year follow up period, sought to identify gender differences in the frequency with which men and woman with migraine had developed atrial fibrillation (AF) and whether the severity of their migraine attacks were linked to the incidence of AF. Severe migraine with aura significantly increased the risk of incident AF in women, but not in men.



QUOTES

“To the best of our knowledge, this is the first study to provide sex-stratified results regarding the effect of the type and the severity of migraine on AF development.”

“Women who had severe migraine with aura were at the highest risk for AF in the future, while the effect of migraine with aura on the development of AF was not significant in men.”



OUR TAKEAWAY

Atrial fibrillation is a heart arrhythmia in which the heart loses its normal pacing and beats either very slowly or (more often) very quickly. This creates an elevated risk of blood clots forming in the heart and migrating to the brain or lungs. Studies have previously reported that people with migraine with aura are at greater risk of atrial fibrillation. This study reports that the risk is specifically increased for women who have migraine with aura.



RESEARCH LINK & AUTHORS

Abstract available free at
<https://pubmed.ncbi.nlm.nih.gov/35711356/>

Full paper available free at
<https://www.frontiersin.org/articles/10.3389/fcvm.2022.910225/full>

Rhee, T. M., Choi, E. K., Han, K. D., Ahn, H. J., Lee, S. R., Oh, S., & Lip, G. Y. H. (2022).

Type and Severity of Migraine Determines Risk of Atrial Fibrillation in Women. *Front Cardiovasc Med*, 9, 910225.

<https://doi.org/10.3389/fcvm.2022.910225>

Research
TitleOnabotulinumtoxinA [Botox] in Chronic
Migraine: Is the Response Dose Dependent?

Publication Date June 2022

Medical Journal *BMC Neurology*

RESEARCH OVERVIEW

This is the first paired comparison study to evaluate responses to different doses of Botox. The study was conducted on chronic migraine patients at the Mayo Clinic (Rochester). Data were gathered from electronic medical records of people who received at least 3 rounds of 150 units of onabotulinumtoxinA followed by at least 3 rounds of 200 units of onabotulinumtoxinA.

The higher dose was associated with fewer headache and severe headache days and a decreased wearing-off period.



QUOTES

“The highly disabling nature of chronic migraine dictates the need for more effective treatments. Overall, the prophylactic migraine treatments are underutilized, although their use results in lower healthcare costs.”

“Our results dispute the “follow-the-pain” strategy. We suggest clinicians do not necessarily need to use the “follow-the-pain strategy” in order to improve the headache control. This is especially important when injecting extra units of onabotulinumtoxinA to a certain location like forehead, can increase the risk of adverse events.”



OUR TAKEAWAY

Although the role of onabotulinumtoxinA (Botox) in treatment of chronic migraine is well studied, it has not been clear if its beneficial effects are dose dependent. This research found increased benefits at a higher dose.



RESEARCH LINK & AUTHORS

Abstract available free at
<https://pubmed.ncbi.nlm.nih.gov/35698027/>

Article available free at
<https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-022-02742-x>

Zandieh, A., & Cutrer, F. M. (2022)

OnabotulinumtoxinA in Chronic Migraine: Is the Response Dose Dependent? *BMC Neurol*, 22(1), 218. <https://doi.org/10.1186/s12883-022-02742-x>

Research
TitleDiagnosis, Consultation, Treatment, and
Impact of Migraine in the US: Results of the
OVERCOME (US) Study

Publication Date

April 2022

Medical Journal

*Headache: The Journal of
Head and Face Pain*

RESEARCH OVERVIEW

The Observational survey of the Epidemiology, Treatment and Care of Migraine (OVERCOME) study is a longitudinal, multicohort, web-based annual study of a demographically representative sample of the US population. In the most recent data, lifetime use of migraine preventive medication was 26.1%.

76.8% reported having used a prescription medication in their lifetime, but only 40.0% currently used prescription medication.

In total, 47.7% reported lifetime use of an opioid for migraine and 19.1% reported currently using an opioid for migraine. Lifetime use of triptans was reported by 35.0% whereas 22.7% reported current use.



QUOTES

“This current study demonstrates that, at the time of the survey in 2018, progress is being made related to diagnosis and the preventive treatment of migraine. This is encouraging as it shows that slow but steady progress has continued over time and suggests that efforts to inform persons living with migraine and healthcare professionals caring for/about migraine regarding the value in recognizing and treating migraine are worth continuing.”



OUR TAKEAWAY

OVERCOME provides useful insights into the ways in which migraine disease is being recognized and treated across the U.S. over time. There is slow improvement, but use of preventive medication remains low, reflecting the fact that many people do not have access to a headache/migraine specialist, and primary care physicians are less likely to prescribe preventives.



RESEARCH LINK & AUTHORS

Paper available free at

<https://headachejournal.onlinelibrary.wiley.com/doi/10.1111/head.14259>

Lipton, R. B., Nicholson, R. A., Reed, M. L., Araujo, A. B., Jaffe, D. H., Faries, D. E., ... & Pearlman, E. M. (2022).

Diagnosis, Consultation, Treatment, and Impact of Migraine in the US: Results of the OVERCOME (US) Study. *Headache: The Journal of Head and Face Pain*, 62(2), 122-140.

Research
TitleTemporomandibular Disorder and Headache
Prevalence: a Systematic Review and Meta-
analysis

Publication Date

May 2022

Medical Journal

Cephalalgia

RESEARCH OVERVIEW

Temporomandibular disorders (TMD) and headaches are prevalent among the global population. Patients often suffer from both conditions, and they are likely to be associated in a bidirectional way. However, the nature of the association remains unclear.

31 studies were included in the review. Meta analyses revealed moderate-to-large heterogeneities across the studies but overall migraine was more commonly observed in TMD patients (40%) versus tension-type headache (19%). In painful-TMD the prevalence of headache was high at 83%.



QUOTES

“Our review showed that the prevalence of headache in the TMD population was 61.58%”

“Migraine is the most common headache subtype in all TMD patients with a prevalence of 40.25%, which is much higher than the prevalence of headaches in the general population and twice as high as the prevalence of tension-type headache (18.89%).”

“The prevalence of comorbid headache in TMD and concurrent TMD in headache from this review are quite similar (61.58% and 59.42%). Despite the large variance across included studies, the review therefore suggests a high co-occurrence of the two disorders in the general and clinical populations.”



OUR TAKEAWAY

The study suggests that an association between TMD and migraine may exist. The findings also highlight the importance of discussing grinding, clenching or TMD in relation to a migraine diagnosis. When these two conditions coexist, the management of both may lead to a better outcome.

RESEARCH LINK & AUTHORS

Paper available free at

<https://journals.sagepub.com/doi/full/10.1177/25158163221097352>

P. Yakkaphan, J.G. Smith, P. Chana, T. Renton, G. Lambru.

Temporomandibular Disorder and Headache Prevalence: A Systematic Review and Meta-Analysis
Cephalalgia, 5 (2022): 25158163221097352.

Research
TitleDetoxification Vs Non-detoxification Before
Starting an Anti-CGRP Monoclonal Antibody in
Medication Overuse Headache

Publication Date

February 2022

Medical Journal

Cephalalgia

RESEARCH OVERVIEW

Medication overuse headache is a substantial challenge for people with migraine. It can easily lead to a continuous cycle of headache-medication-headache-medication.

The intent of this study was to test whether the newer anti-CGRP medications were effective in patients with medication overuse whether or not they discontinued other medications.

After three months of treatment with either Aimovig or Emgality, 59% of the patients reverted from medication overuse headache and 51% achieved $\geq 50\%$ reduction in monthly headache days



QUOTES

“However, the additional benefit of in-hospital abrupt overused drug(s) discontinuation preceding the start of anti-CGRP [monoclonal antibodies] was never investigated; hence, our study is the first to specifically address this issue.”

“Notably, in our cohort, hospital admission for abrupt acute medication withdrawal did not influence the effectiveness of anti-CGRP [monoclonal antibodies].”

“The results of our study also confirm the effectiveness of these anti-CGRP mAbs even in a severely impaired population.”



OUR TAKEAWAY

This study starts to answer the question of whether it is necessary for patients with medication overuse headaches (aka “rebound” headaches) need to “detox” by going cold turkey before starting on one of the new anti-CGRP monoclonal antibodies.

The findings were that it did *not* matter if people discontinued other medications before starting on Aimvig or Emgality. Both groups responded equally well, with more than half achieving a reduction of 50% or more in monthly headache days.



RESEARCH LINK & AUTHORS

Paper available free at

<https://journals.sagepub.com/doi/full/10.1177/03331024211067791>

Pensato, U., Baraldi, C., Favoni, V., Mascarella, D., Matteo, E., Andriani, G., ... & Cevoli, S. (2022).

Detoxification vs non-detoxification before starting an anti-CGRP monoclonal antibody in medication overuse headache.
Cephalalgia, 42(7), 645-653.