



HEADACHES & MIGRAINES

Exploring Migraine Management: CGRP Agonist Drugs vs. Acupuncture

Bill Reddy, LAc, Dipl. Ac.

WHAT YOU NEED TO KNOW

- CGRP agonist drugs, developed specifically for migraine treatment, work by targeting and modulating the activity of CGRP receptors.
- CGRP agonist drugs provide a targeted pharmacological intervention, while acupuncture is more patient-centered, taking into account the emotional aspects of stressors in the patients' lives.
- Currently there are no studies directly comparing acupuncture with CGRP meds, and hopefully in the future, there will be more information.

In the ever-evolving landscape of migraine management, where diverse strategies from pharmaceutical interventions to integrative therapies come into play, a recent addition to the repertoire is capturing attention: CGRP (calcitonin gene-related peptide) agonist drugs.

Interestingly, I recently attended an exceptional presentation by Poney Chiang (through Healthy Seminars) on “Using Trigeminal Nerve-Associated Acupoints to Increase Cerebral Blood Flow” in which he talked about CGRP and how to promote (and inhibit) vasodilation using specific acupoints on the head and neck.¹ This article delves into a comparative exploration of these cutting-edge “biologics” with acupuncture, examining their mechanisms, efficacy, and potential side effects to offer a comprehensive understanding of the choices available for individuals seeking relief from migraines.

Understanding CGRP Agonist Drugs

CGRP is a neuropeptide found in our central and peripheral nervous systems, implicated in

migraine pathophysiology, primarily in the trigeminal nerve.²⁻³ CGRP agonist drugs, developed specifically for migraine treatment, work by targeting and modulating the activity of CGRP receptors. Aimed at preventing migraine attacks, these drugs fall into two categories: gepants (non-peptide small molecules) and monoclonal antibodies (injected medications).

Gepants such as ubrogepant (Ubrelvy) and rimegepant act by blocking CGRP receptors, effectively inhibiting the vasodilation and inflammation associated with migraines. Monoclonal antibodies like erenumab (Aimovig), fremanezumab (Ajovy), and galcanezumab (Emgality) are administered monthly through injection, targeting either CGRP itself or its receptor.

Effectiveness / Efficacy of CGRP Agonist Drugs

Clinical trials have demonstrated the efficacy of CGRP agonist drugs in reducing both the frequency and severity of migraine attacks. These medications offer a preventive approach, minimizing the need for acute treatments and enhancing overall quality of life for migraine sufferers. In a scoping review and meta-analysis of anti-CGRP monoclonal antibody medications for migraines, they found a $\geq 50\%$ improvement in responder rates ranging from 40% to 70% in the studies collected.⁴

However, individual responses to CGRP agonist drugs vary, and they can be considered more palliative care than a cure for migraines. Some patients may experience significant relief, while others may not respond as well. Additionally, being a new class of medication, the long-term safety and potential side effects of these drugs are still under investigation, warranting further research. For example, Rimegepant warns against interactions with close to 70 other drugs, including erythromycin, diflucan, dilantin and even St. John's wort.

Mechanism of Acupuncture

While the exact mechanism of action by which acupuncture alleviates migraines remains unclear, it is believed to modulate pain perception, reduce neuroinflammation, and improve blood flow, as well as inhibit the production of nitric oxide (that causes vasodilation). Chen, et al., demonstrated a modulation of CGRP through the stimulation of specific acupoints.⁵

Effectiveness and Efficacy of Acupuncture

Studies on acupuncture's efficacy for migraines have yielded mixed results. Some trials suggest acupuncture may be as effective as prophylactic medications in reducing the frequency and intensity of migraine attacks. However, the variability in study designs, acupuncture techniques, and participant responses complicates the establishment of clear conclusions.

The most common acupoints used in these studies include GB 20, DU 20, *Taiyang* (EX-HN 5) on the head, and LI 4, LIV 3, SP 6 and ST 36 on the limbs. Some studies use auricular acupuncture (or press needles for longer retention), e-stim (usually around 100 hz), and I found a few that used Botulinum toxin A (Botox) injection into acupoints. Treatment frequency ranged from 1-5 times per week and duration of treatment ranged from 4-12 weeks in the majority of studies.⁵⁻⁶

Currently, acupuncture is often considered a complementary therapy rather than a standalone treatment for migraines. Keep in mind that many individuals suffering from migraines are low in magnesium, so recommending a good-quality transdermal magnesium chloride spray and having patients apply it to the nape of their necks twice a day is advisable.

Comparative Analysis

Mechanism of Action: CGRP agonist drugs target the neuropeptide CGRP and its receptors, modulating vasodilation and inflammation associated with migraines.⁴ Acupuncture works on a holistic level, influencing pain perception, neuroinflammation, and blood flow through the stimulation of acupoints, whether manually or with electrical stimulation.⁶

Efficacy: CGRP agonist drugs have demonstrated efficacy in reducing the frequency and severity of migraine attacks, offering a preventive approach.⁴ Acupuncture's efficacy varies among individuals, with some studies suggesting it can be as effective as prophylactic medications.⁵

Safety: CGRP agonist drugs may have potential long-term side effects that require further investigation.⁴ Acupuncture is generally considered safe when performed by trained practitioners, with minimal side effects reported.

Cost: (Self-injected) monthly CGRP injections cost roughly \$6,900 per year.⁷ Acupuncture treatment at twice a week for four weeks, followed by once a week for 12 weeks, and then once per month for the remaining year at \$85 per treatment (roughly the national average), would cost \$2,295; however, treatment would realistically end before an entire year of treatment.

Individual Response: Response to CGRP agonist drugs can vary among patients, with some experiencing significant relief and others showing limited improvement.⁴ Acupuncture's effectiveness may depend on individual responsiveness, making it more suitable for some patients than others.

Clinical Pearls

Both CGRP agonist drugs and acupuncture offer unique approaches to migraine management. CGRP agonist drugs provide a targeted pharmacological intervention, while acupuncture is more patient-centered, taking into account the emotional aspects of stressors in the patients' lives. The choice between these approaches may depend on individual preferences, response to treatment, and the severity of migraines. Acupuncture, however, has a much longer effect than the drug, "influencing" the tonus of cerebral vasculature to be less prone to vasodilation.

If your patient isn't responding to acupuncture, however, it may be worthwhile to recommend they speak to their physician about trying a CGRP agonist medication. Currently there are no studies directly comparing acupuncture with CGRP meds, and hopefully in the future, there will be more information to provide our patients with more of an informed decision on which route to take.

References

1. Meltz L, Ortiz D, Chiang P. The anatomical relationship between acupoints of the face and the trigeminal nerve. *Med Acupunct*, 2020 Aug 1;32(4):181-193.
2. Iyengar S, Johnson KW, Ossipov MH, Aurora SK. CGRP and the trigeminal system in migraine. *Headache*, 2019 May;59(5):659-681.
3. Karsan N, Gosalia H, Goadsby PJ. Molecular mechanisms of migraine: nitric oxide synthase and neuropeptides. *Int J Mol Sci*, 2023 Jul 26;24(15):11993.
4. Hong JB, Lange KS, Overeem LH, et al. A scoping review and meta-analysis of anti-CGRP monoclonal antibodies: predicting response. *Pharmaceuticals*, 2023;16(7):934.
5. Chen Y, Liu Y, Song Y, et al. Therapeutic applications and potential mechanisms of acupuncture in migraine: a literature review and perspectives. *Front Neurosci*, 2022 Oct

20;16:1022455.

6. Zijlstra FJ, van den Berg-de Lange I, Huygen FJ, Klein J. Anti-inflammatory actions of acupuncture. *Mediators Inflamm*, 2003 Apr;12(2):59-69.
7. DiGrande S. The current landscape of CGRP inhibitor coverage. *Am J Man Care*, March 2019.

FEBRUARY 2024