THE JOURNAL OF FAMILY PRACTICE

EDITORIAL

John Hickner, MD, MSc
Editor-in-Chief
jfp.eic@gmail.com

doi: 10.12788/jfp.0432

New—and surprising—ways to approach migraine pain

Migraine headaches pose a challenge for many patients and their physicians, so new, effective approaches are always welcome. Sometimes new treatments come as total surprises. For example, who would have guessed that timolol eyedrops could be effective for acute migraine?[1] Granted, the results (discussed in this issue's PURLs on page 222) are from a single randomized trial, but they look very promising.

This is not the only new and innovative treatment for migraine. Everyone knows about the heavily marketed calcium gene-related peptide antagonists, which include monoclonal antibodies and the so-called "gepants." The monoclonal antibodies and atogepant are approved for migraine prevention, and they do a decent job (although at a high price). In randomized trials, these agents reduced migraine days per month by an average of about 1.5 to 2.5 days compared to placebo.[2-5]

Who would have guessed that timolol eyedrops could be effective for acute migraine?

Ubrogepant and rimegepant are approved for acute migraine treatment. In clinical trials, about 20% of patients taking ubrogepant or rimegepant were pain free at 2 hours post dose, compared to 12% to 14% taking placebo.[6,7] Unfortunately, that means 80% of patients still have some pain at 2 hours. By comparison, zolmitriptan performs a bit better, with 34% of patients pain free at 2 hours.[8] However, for those who can't tolerate zolmitriptan, these newer options provide an alternative.

We also now have nonpharmacologic options. The caloric vestibular stimulation device is essentially a headset with ear probes that change temperature, alternating warm and cold. In a randomized controlled trial, it reduced monthly migraine days by 1.1 compared to placebo, from a baseline of 7.7 to 3.9 days.[9] It can also be used to treat acute migraine. There is also a vagus nerve–stimulating device that reduced migraine headache severity by 20% on average in 32.2% of patients in 30 minutes. Sham treatment was as effective for 18.5% of patients, giving a number needed to treat of 6 compared to sham.[10]

And finally, there are complementary and alternative medicine options. Two recent randomized trials demonstrated that ≥ 2000 IU/d of vitamin D reduced monthly migraine days an average of 2 days, which is comparable to the effectiveness of the calcium gene-related peptide antagonists at a fraction of the cost.[11,12] In another randomized trial, intranasal 1.5% peppermint oil was as effective as topical 4% lidocaine in providing substantial pain relief for acute migraine; about 42% of patients achieved significant relief with either treatment.[13]

While we may not have a perfect treatment for our patients with migraine headache, we certainly have many options to choose from. JFP

References

1. Ge Y, Castelli G. Migraine relief in 20 minutes using eyedrops? *J Fam Pract*. 2022;71:222-223, 226.
2. Loder E, Renthal W. Calcitonin gene-related peptide monoclonal antibody treatments for migraine. *JAMA Intern Med*.

CONTINUED ON PAGE 218

CONTINUED FROM PAGE 198

2019;179:421-422. doi: 10.1001/jamainternmed.2018.7536

3. Silberstein S, Diamond M, Hindiyeh NA, et al. Eptinezumab for the prevention of chronic migraine: efficacy and safety through 24 weeks of treatment in the phase 3 PROMISE-2 (Prevention of migraine via intravenous ALD403 safety and efficacy-2) study. *J Headache Pain*. 2020;21:120. doi: 10.1186/s10194-020-01186-3
4. Ament M, Day K, Stauffer VL, et al. Effect of galcanezumab on severity and symptoms of migraine in phase 3 trials in patients with episodic or chronic migraine. *J Headache Pain*. 2021;22:6. doi: 10.1186/s10194-021-01215-9
5. Goadsby PJ, Dodick DW, Ailani J, et al. Safety, tolerability, and efficacy of orally administered atogepant for the prevention of episodic migraine in adults: a double-blind, randomised phase 2b/3 trial. *Lancet Neurol*. 2020;19:727-737. doi: 10.1016/S1474-4422(20)30234-9
6. Lipton RB, Croop R, Stock EG, et al. Rimegepant, an oral calcitonin gene-related peptide receptor antagonist, for migraine. *N Engl J Med*. 2019;381:142-149. doi: 10.1056/NEJMoa1811090
7. Lipton RB, Dodick DW, Ailani J, et al. Effect of ubrogepant vs placebo on pain and the most bothersome associated symptom in the acute treatment of migraine: the ACHIEVE II randomized clinical trial. *JAMA*. 2019;322:1887-1898. doi: 10.1001/jama.2019.16711
8. Bird S, Derry S, Moore R. Zolmitriptan for acute migraine attacks in adults. *Cochrane Database Syst Rev*. 2014;2014:CD008616. doi: 10.1002/14651858.CD008616.pub2
9. Wilkinson D, Ade KK, Rogers LL, et al. Preventing episodic migraine with caloric vestibular stimulation: a randomized controlled trial. *Headache*. 2017;57:1065-1087. doi: 10.1111/head.13120
10. Grazzi L, Tassorelli C, de Tommaso M, et al; PRESTO Study Group. Practical and clinical utility of non-invasive vagus nerve stimulation (nVNS) for the acute treatment of migraine: a post hoc analysis of the randomized, sham-controlled, double-blind PRESTO trial. *J Headache Pain*. 2018;19:98. doi: 10.1186/s10194-018-0928-1
11. Gazerani P, Fuglsang R, Pedersen JG, et al. A randomized, double-blinded, placebo-controlled, parallel trial of vitamin D3 supplementation in adult patients with migraine. *Curr Med Res Opin*. 2019;35:715-723. doi: 10.1080/03007995.2018.1519503
12. Ghorbani Z, Togha M, Rafiee P, et al. Vitamin D3 might improve headache characteristics and protect against inflammation in migraine: a randomized clinical trial. *Neurol Sci*. 2020;41:1183-1192. doi: 10.1007/s10072-019-04220-8
13. Rafieian-Kopaei M, Hasanpour-Dehkordi A, Lorigooini Z, et al. Comparing the effect of intranasal lidocaine 4% with peppermint essential oil drop 1.5% on migraine attacks: a double-blind clinical trial. *Int J Prev Med*. 2019;10:121. doi: 10.4103/ijpvm.IJPVM_530_17