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How do neurologists choose an acute treatment for migraine?

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STOWE, VT. – A large and growing number of medications is available for the acute treatment of migraine. Effective acute treatment enables patients to re-engage in their work and other daily activities, as well as reducing the likelihood that their disease will progress from episodic to chronic migraine. Considering appropriate routes of delivery, assessing efficacy and tolerability, and communicating well with the patient are essential components in the acute treatment of migraine, according to Barbara L. Nye, MD <https://www.dartmouth-hitchcock.org/findaprovider/provider/1556/Barbara-L-Nye> , assistant professor of neurology at the Geisel School of Medicine at Dartmouth, Hanover, N.H.. Dr. Nye discussed the acute treatment of migraine at the annual meeting of the Headache Cooperative of New England.

Choosing an initial treatment

Nonspecific medications are perhaps the first treatments to consider for a patient with acute migraine. This class includes NSAIDs such as naproxen sodium, piroxicam, diclofenac, celecoxib, and indomethacin. Emerging data indicate that some NSAIDs are associated with an increased risk of stroke, which is an important consideration as the population ages, said Dr. Nye. Other nonspecific options are neuroleptics such as prochlorperazine, metoclopramide, promethazine, and chlorpromazine. Many neuroleptics have sedative effects, however, so they do not necessarily help a patient return to function. Nevertheless, these drugs can be good rescue medications, said Dr. Nye.

Triptans are effective in the acute treatment of migraine, and seven drugs in this class are available. Most, such as rizatriptan, almotriptan, eletriptan, naratriptan, and frovatriptan, are available only as tablets. Other routes of delivery are available, however. Sumatriptan, for example, is available in injectable and intranasal formulations, and zolmitriptan is available as an orally dissolving tablet.

Another option to consider is dihydroergotamine (DHE), which has long been used for migraine. The injectable formulation of DHE can be cumbersome because it requires the patients with a headache to open a vial, draw the medication into a filter needle, and inject themselves, said Dr.

Nye. “The nasal sprays that are available right now aren’t as effective as we’d like them to be,” she added. But overall, DHE is effective. Associated adverse events include flushing, nausea, and diarrhea.

Lasmiditan received approval from the Food and Drug Administration for the acute treatment of migraine in October 2019. Compared with placebo, the drug increases the likelihood of pain freedom and freedom from the most bothersome symptom at 2 hours. Driving tests indicated that patients were impaired for about 8 hours after treatment, and lasmiditan is a Schedule V drug. It is available in doses of 50 mg/day, 100 mg/day, and 200 mg/day.

The class of drugs known as the “gepants” provides further options. The most recently approved therapy in this class, which targets calcitonin gene–related peptide, is ubrogepant. Because the drug is metabolized through the CYP3A4 system, they are not appropriate for patients who use strong CYP3A4 inhibitors. The most common side effects are nausea, hypersensitivity reaction, and somnolence.

Neuromodulation can provide effective treatment without provoking side effects, said Dr. Nye. Options include transcutaneous supraorbital stimulation, single-pulse transcutaneous magnetic stimulation, noninvasive vagal nerve stimulation, and remote nonpainful stimulation.

If a patient presents during an acute attack, neurologists could consider using a nerve block. The latter may administer occipital nerve blocks, trigger point injections, auriculotemporal nerve blocks, and supraorbital and supratrochlear nerve blocks. This treatment can bring immediate relief, which is gratifying for patients and neurologists. But no consensus about which medications to use or how to administer them has been established. Neurologists most often use a combination of bupivacaine and lidocaine. Another possibility is a sphenopalatine ganglion nerve block, which requires treatment to be inserted through the nose. This treatment can be delivered in the office using the Sphenocath device or the Allevio device. Another device, the Tx360, is intended to enable patient self-administration.

Addressing treatment failure

If a patient returns and reports that the current treatment is ineffective, the neurologist must reevaluate the therapy. A helpful way to conduct this reassessment is to administer the Migraine Treatment Optimization Questionnaire <https://www.ncbi.nlm.nih.gov/pubmed/19239676> (MTOQ), which was developed by Lipton et al., to the patient. Neurologists ask whether the patient can function normally 2 hours after treatment or whether the medication is, for example, causing a side effect that makes this outcome less likely. Other questions for the patient are whether the

headache pain disappears within 2 hours and whether the medication provides consistent relief. Finally, the neurologist can ask whether the patient is comfortable taking the medication. A score lower than 2 on the MTOQ indicates that the acute treatment should be changed, said Dr. Nye.

Gastroparesis is common during migraine attacks. It is inadvisable to give an oral medication to a patient who vomits within 20 minutes of attack onset, said Dr. Nye. "It's a little less intuitive for those people who are nauseous immediately to think that that oral tablet is probably going to sit in their stomach and not get absorbed in the intestines as intended." Nasal sprays, injectable medicines, and oral dissolving tablets are appropriate options for patients with gastroparesis.

Treating migraine during pregnancy

Special consideration must be given to treatment when the patient is pregnant. Decreased headache frequency is common in pregnancy, but not universal. Occipital nerve blocks are a good option for prevention and acute management in pregnant patients. They may be administered every 2 weeks. Sphenopalatine ganglion nerve block is another option, and it can be administered several times per week. Data "suggest that stacking the injections 2 or 3 days per week for up to 6 weeks can eliminate headaches for up to 6 months," said Dr. Nye.

Tylenol is appropriate for acute headache in pregnant patients, "but we do warn about medication overuse headache and limiting its use." Ondansetron and promethazine are acceptable treatments for nausea. Although ondansetron has less central activity than promethazine, and thus does not reduce the headache, it lessens nausea, said Dr. Nye.

Triptan exposure during the first trimester is not significantly associated with major congenital malformations, which is reassuring, given that many patients take triptans before they realize that they are pregnant. During the second and third trimesters, triptan exposure is significantly associated with atonic uterus and increased blood loss during labor. In a 16-year registry, sumatriptan, naratriptan, and treximet were not associated with teratogenicity.

Nonpharmacological treatments, too, may help pregnant patients. Lifestyle management, including a regular sleep schedule, exercise routine, and diet, can be beneficial. Massage therapy may reduce stress, and cognitive-behavioral therapy and biofeedback are additional options. Behavioral therapy, however, should be initiated before the patient plans the pregnancy, said Dr. Nye. These therapies require training that a patient having an exacerbation of migraine is less likely to have the motivation to begin.

Many medications are transferred to infants through breast milk. The American Pediatric Association considers a relative infant dosing of less than 10% to be safe. A clinician or patient can look up a medication on websites such as LactMed <https://www.ncbi.nlm.nih.gov/books/NBK501922/> to understand the relative infant dose and possible effects. Another helpful reference is Medications and Mothers' Milk <https://www.halesmeds.com/> , said Dr. Nye. Acetaminophen, steroids, ibuprofen, riboflavin, indomethacin, ketorolac, and naproxen are generally safe during lactation. "Eletriptan is the triptan that's least likely to be in the breast milk," said Dr. Nye. Aspirin, atenolol, ergotamine, and lithium, however, should be given with caution. The safety of amitriptyline, nortriptyline, and SSRIs during lactation is unknown.

Dr. Nye is on advisory boards for Alder, Allergan, Biohaven, electroCore, Pernix, and Xoc.

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