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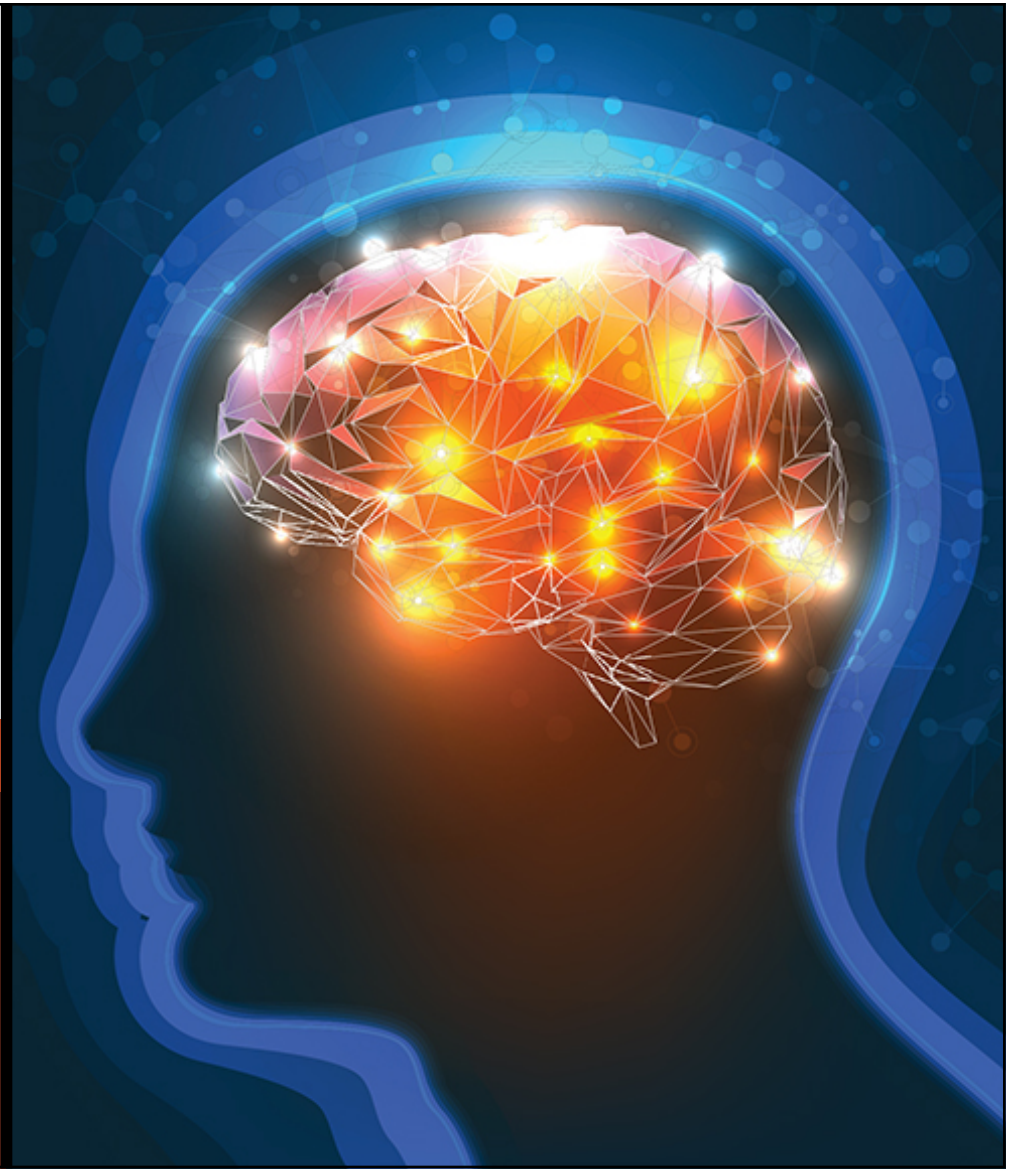
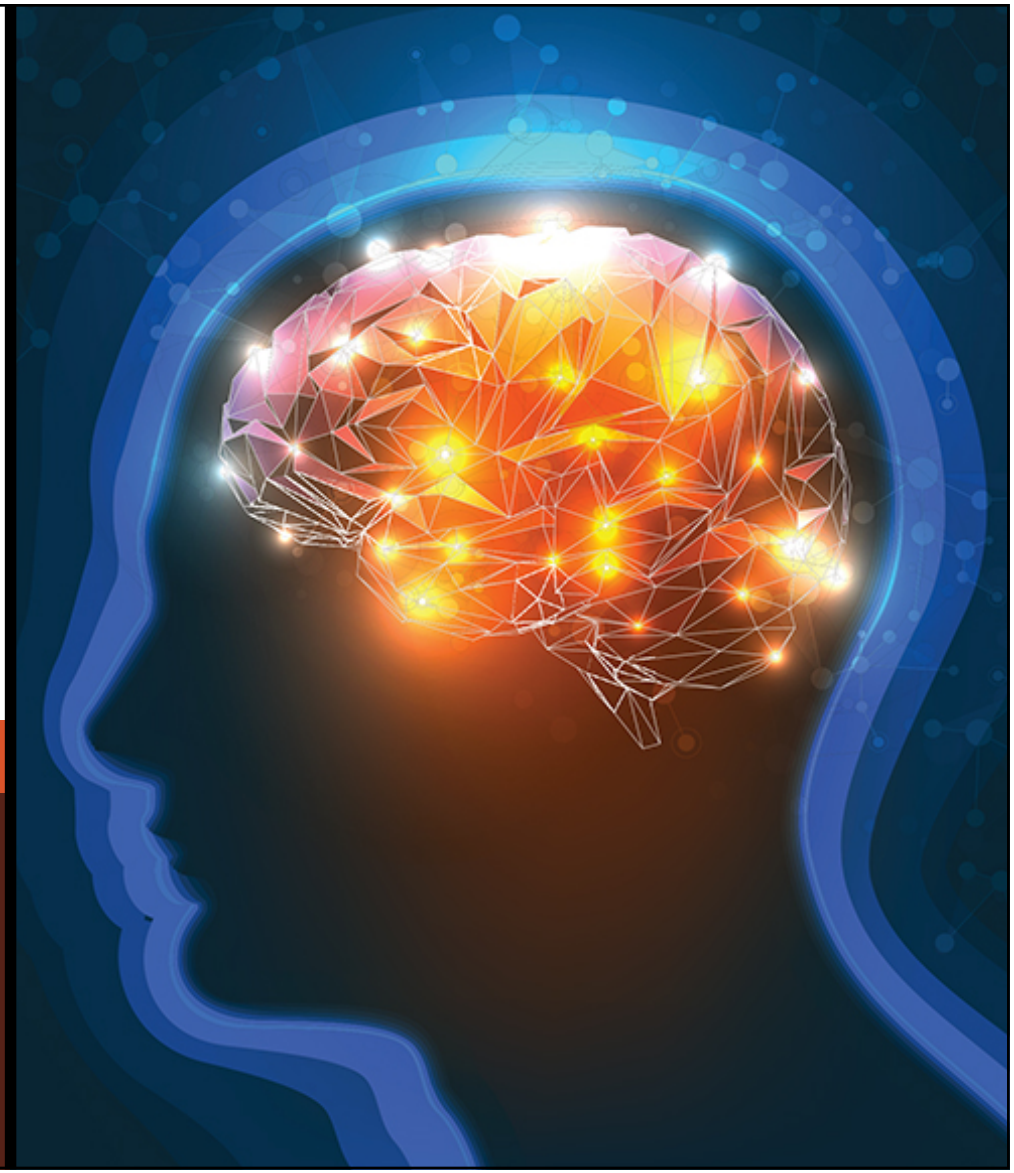


# Applying Data to Practice: Integrating New Therapies for Migraine in Real-World Patients



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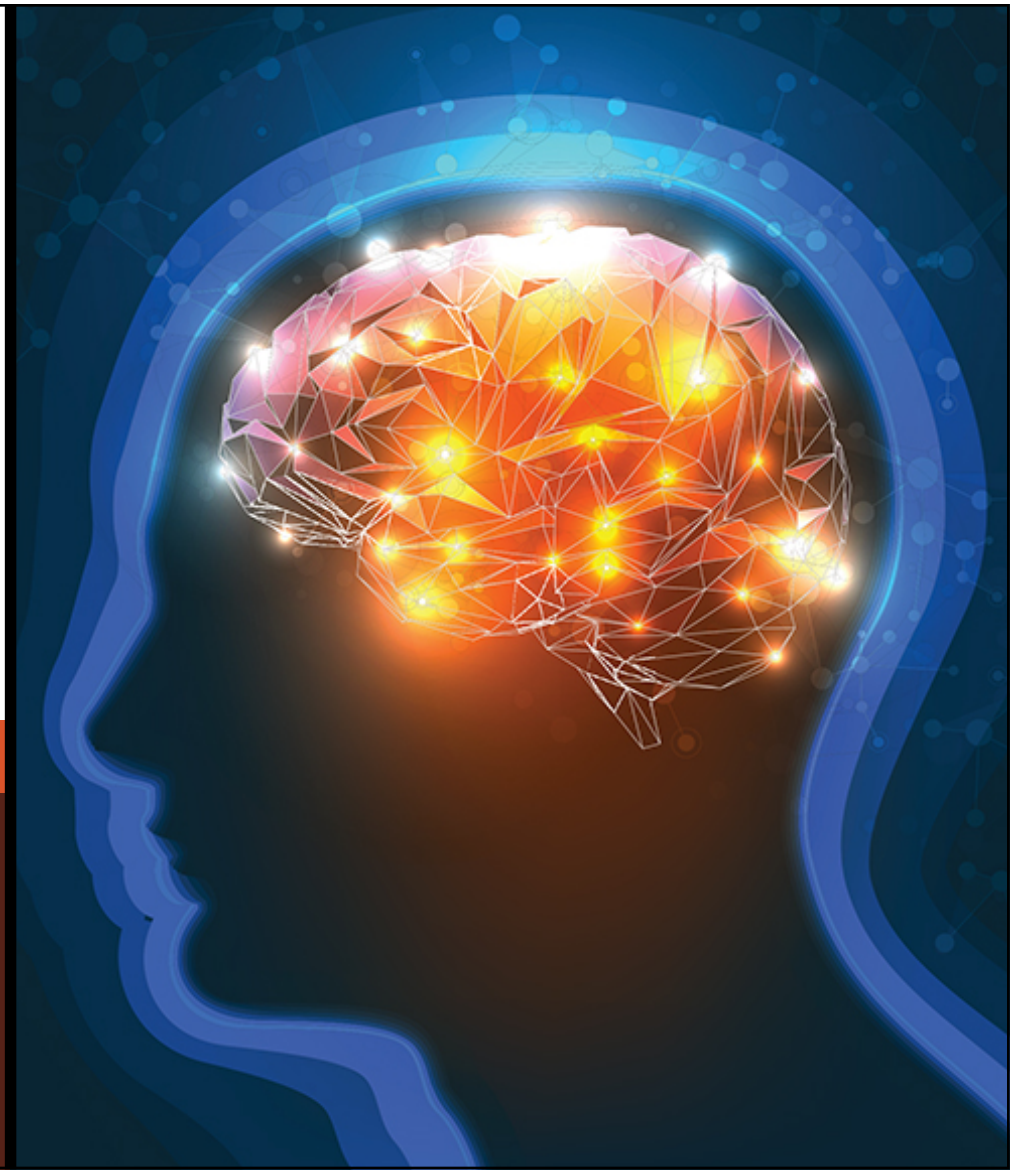
# Learning Objective

Identify patients who are likely to benefit from calcitonin gene-related peptide (CGRP) inhibitors.



# Indications for Calcitonin Gene-Related Peptide (CGRP) Inhibitors

Patients with migraine may benefit from preventive treatment if:

- ≥ 4 migraine attacks per month
- Disabling symptoms associated with attacks (e.g., status migrainosus, hemiplegic attacks, severe vertigo, profound emesis, prolonged aura)
- Impaired function and reduced disability: MIDAS (grade III-IV)
- Ineffective acute treatment, medication overuse, and contraindications or unwanted side effects to abortive medications
- Patient preference (e.g., reduce psychological distress, enhance personal control)
- Contraindications to standard oral migraine preventive treatments due or medication use or comorbid conditions
- History of lack of response (when used for at least 2 months on an optimal dose) or poor tolerability to prior preventive treatment for migraine
- History of non-adherence to oral medications (e.g., patients who might be cognitively impaired)

American Headache Society. *Headache*. 2019;59(1):1-18.

# Case 1

**Background:** This 24-year-old Brazilian woman has had a history of headaches since age 8. More problematic headaches developed at age 15. For a period of time in high school, she had headaches approximately 3 days per week that lasted 1-2 days in duration. For the past 5 years, she has had high frequency of headaches correlating with the time her mother has been sick with cancer.

**Current Presentation:** The headaches occur 10-14 days per month. She has worse headaches 9 days per month. The attacks last 3 days. The pain is described as 8-10, on a numeric rating scale of 0-10, and may be throbbing and sharp. Her headaches are associated with sensitivity to light, sound, and movement. She also has nausea and vomiting a few days per month; the nausea has been associated with a few episodes of syncope/lightheadedness. During her headaches, she occasionally also experiences flashing lights for 15-30 minutes. Cranial autonomic symptoms are not present. Attacks may accompany vertigo, lightheadedness, fatigue, blurry vision, neck pain, and difficulty concentrating. She sometimes has concentration impairment and fatigue a few hours before and after acute attacks.

# Case 1 (Continued)

**Triggers and Lifestyle/Risk Factors:** Triggers include menses, lack of sleep, and stress. She sometimes has a migraine prior to the onset of her menstrual period. She has not been able to identify any types of foods that may trigger attacks. Alcohol is not associated with the headaches. She played soccer as a child and often endured blunt impacts to the head. At age 20, she had a loss of consciousness when hitting her head and had more headaches for about 1 year.

**Current Medications:** Sertraline, clonazepam, alprazolam

**Acute Treatment:** Excedrin 10 days per month; works for short time but pain returns in hours

**Preventive Treatment:** None

**Past Preventive Medication Trials:** Melatonin was used in college for 1 month but did not affect headaches.

**Past Acute Medication Trials:** No triptan but has tried acetaminophen, ibuprofen 100-200 mg sometimes aggravates her stomach.

**Other Intervention Trials:** Acupuncture did not help.

**Allergies:** None

# Case 1 (Continued)

**Past Medical History:** Insomnia. Irregular menstrual period at age 12 and thyroid problems at age 19

**Past Psychiatry History:** Anxiety, depression

**Past Surgical History:** None

**Family History:** Migraine in her mother and brother

**Social History:** Single and lives with her boyfriend but is in the middle of a break up. She works as a medical student and does not smoke, use illicit drugs, or drink alcohol. She drinks coffee 2-3 times per day. Exercise includes yoga 1-2 times per week for about 45 minutes

**Review of Systems:** A complete 11 point review of systems was performed. Poor memory, difficulty with speech, difficulty reading and writing, forgetting appointments, change in sleep habits, excessive daytime drowsiness, loss of consciousness, blurred vision, diminished hearing, spinning sensation, muscle twitching, muscle pain, tremor, numbness, lightheadedness, fainting, intolerance to heat, chills, palpitations, joint pain, nausea, vomiting, constipation, and diarrhea.

# Case 1 (Continued)

**Physical Exam Findings:**

| | |
|---|---|
| Blood Pressure: | 107/57 |
| Pulse: | 78 |
| Respirations: | 18 |
| Temperature: | 99°F (37.2°C) |
| SpO2: | 100% |
| Weight: | 120 lb (54.4 kg) |
| Height: | 5' 2" (1.575 m) |
| Body Mass Index: | 21.95 kg/m$^2$ |

**General:** Cervical paraspinal tenderness and spasm, allodynia, some emotional distress

**Mental Status:** Alert, oriented with intact recent and remote memory, full attention span, concentration, fund of knowledge. Speech is fluent.

**Cranial Nerves:** Clear discs. Pupils are equal, round, and reactive to light. Visual fields are full. There is no ptosis. Extraocular movements are intact without nystagmus. Facial strength and sensation is symmetric. Normal tongue position and palate elevation. Speech is clear with no dysarthria. Shoulder shrugs are full. Hearing is normal and symmetric to finger rub.

# Case 1 (Continued)

**Motor:** Normal tone and bulk, no tremors, 5/5 strength throughout

**Sensation:** Intact to light touch, absent Romberg sign

**Reflexes:** Biceps, triceps, patellars, ankle jerks symmetric bilaterally; plantar responses are flexor

**Coordination:** No axial instability; accurate finger to nose and heel-knee-shin bilaterally

**Gait:** Normal, narrow-based gait; tandems well

**Diagnostic Test/Screening:**

CT negative

**Psychiatric Interview Findings:** GAD 7 = 10 (moderate anxiety), PHQ-9 = 17 (moderate depression)

**Questionnaire Results:** MIDAS 32 (grade IV disability), HIT-6 60 (class IV)

# Measuring Treatment Response

- Headache history
- Migraine diary (internet based programs and apps available (i.e., migraine buddy apps)

**Tools:**

- Monitor for reduction in MIDAS (5 points if between 11-20, or 30% if > 20)
- HIT-6 measures (by 5 points)
- Migraine-Specific Quality of Life Questionnaire version (MSQ)
- McGill Pain Questionnaire

## HIT-6 Questionnaire (Evaluation of Headache Disability)

1. When you have headaches, how often is the pain severe?
2. How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?
3. When you have a headache, how often do you wish you could lie down?
4. In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?
5. In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?
6. In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Never 6, Rarely 9, Sometimes 10, Very often 11, Always 13

Class I: 36-49; Class II: 50-55; Class III: 56-59; Class IV: 60 and more; it is suggested to talk to your physician for class II and more

## Migraine Disability Assessment (MIDAS) Test

1. On how many days in the last three months did you miss work or school because your headaches?
2. How many days in the last three months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.)
3. On how many days in the last three months did you not do household work because of your headaches?
4. How many days in the last three months was your productivity related to household work reduced by half of more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.)
5. On how many days in the last three months did you miss family, social, or leisure activities because of your headaches?

0-5: MIDAS grade I, little or no disability; 6-10: MIDAS grade II, mild disability; 11-20: MIDAS grade III, moderate disability; 21 or higher: MIDAS grade IV, severe disability

Kosinski M, et al. *Qual Life Res*. 2003;12(8):963-974. Stewart WL, et al. *Neurology*. 2001;56(6 Suppl 1):S20-S28.

# Case 1 (Continued)

**Impression/Plan:** Migraine with and without aura. Comorbid risk factors include multiple concussions, hypothyroidism, depression, anxiety, and insomnia. Attack frequency correlates with a traumatic life event/chronic stress state.

**Non-pharmacological approach:** Consider cognitive behavioral therapy (CBT) for insomnia; patient will first try a relaxation app, exercise daily > 5 times per week, avoid skipping meals, maintain hydration, and keep caffeine to < 200 mg/day

**Preventive treatment:** Consider monoclonal drugs to CGRP or receptor if topiramate is not tolerated.

**Acute treatment:** Trial of rizatriptan 10 mg as orally disintegrating tablet, discontinue Excedrin and start Naproxen 500 mg twice per day as needed (i.e., menstrual migraine), maximum of 10 days per month

Follow up with psychiatrist for anxiety and depression; consider biofeedback with psychology

# Case 2

**Background:** This 33-year-old woman has had a history of headaches since age 14. She has a longstanding history of recurrent abdominal pain and frequent bouts of vomiting as a child. At age 28, she developed more problematic headaches. Previously, she had attacks that occurred twice per month. In 2015 while in law school, the patient had sudden head pain upon awakening that seemed different. She went to the emergency room and had an MRI of the brain, which was normal. She has had persistent headache and was on disability for 3 months. The patient did well on candesartan for a few years and was back to low-frequency migraines; however, her headaches have recently increased over the past 8 months.

She has headaches on a daily basis and has migraine attacks 10-15 days per month. The attacks are described as 6-9, on a numeric rating scale of 0-10, and may last 8 hours with treatment. Her worse attacks are approximately 3 days. She has pain that is generalized at the front of the head, back, side, around the eyes, and the jaw. The pain is described as throbbing and stabbing. Associated features include sensitivity to light, sound, smell, movement, nausea, and vomiting, blurry vision, neck stiffness, and difficulty concentrating. The patient may experience tunnel vision for 1-2 hours. She also has blurry vision and word-finding difficulties with some substitutions. Attacks are not associated with numbness, tingling, weakness, vertigo, diplopia, slurred speech, or imbalance. Cranial autonomic symptoms include rhinorrhea. She has frequent yawning prior to a severe attack.

# Case 2 (Continued)

**Triggers and Lifestyle/Risk Factors:** Triggers include dehydration, alcohol, and lack of sleep. She works as a lawyer, up to 65 hours per week, and perceives her job as stressful. She also has vomiting that is often triggered by certain odors.

**CURRENT PRESENTATION**

**Chief Complaint:** Severe migraine attacks, increasing in frequency

**Current Medications:** Cetirizine, drospirenone and ethinyl estradiol, clonazepam, candesartan

**Acute Treatment:** Flexeril 10 mg as needed, prochlorperazine 10 mg as needed

**Preventive Treatment:** Candesartan 16 mg, seems to no longer be working as well

# Case 2 (Continued)

**Past Preventive Medication Trials:**

- Topiramate 25 mg for 2 months, cognitive side effects/weight loss/tingling, not effective
- Valproate (previously for mood) caused weight gain
- Gabapentin for one month, not effective
- Amitriptyline 25 mg for 6 weeks, not effective
- Botox injections x 3, not effective (appears to be with the PREEMPT protocol)
- Magnesium, not effective
- Riboflavin, not effective

**Past Acute Medication Trials:** Sumatriptan tablets, injectables, which caused side effects, rizatriptan, sumatriptan, nortriptyline, and triptan. All these were ineffective, and sumatriptan injections caused worsening headache and only made her feel slightly improved. Ibuprofen was discontinued due to a gastric ulcer. She also was started on oxycodone multiple times per day, which was complicated by “rebound headaches” when used for 4-5 months. She used up to 10-30 mg per day.

**Other Intervention Trials:** Botox injections (X2), not effective

# Case 2 (Continued)

**Past Medical History:** Pancreatitis/gastric ulcer, IBS, kidney stones, irregular menses, low blood pressure, arrhythmia, and insomnia.

**Past Psychiatric History:** Anxiety, prior history of anorexia

**Past Surgical History:** None

**Family History:** No history of migraine

**Social History:** Married, no children, former smoker, no alcohol or illicit drugs. She works as a lawyer in a commercial law firm, as a senior partner, and works 24-hour shifts on call. She does not exercise.

**Allergies:** Ceclor [cefaclor] and sulfa drugs

**Review of Systems:** Change in sleep habits, blurred vision, lightheadedness, heartburn, nausea, and vomiting

# Case 2 (Continued)

## Physical Exam Findings:

| | |
|---|---|
| Blood Pressure: | 99/67 |
| Pulse: | 80 |
| Respirations: | 16 |
| Temperature: | 99°F (37.2°C) |
| Weight: | 119 lb (54 kg) |
| Height: | 5’ 6" (1.676 m) |
| Body Mass Index: | 19.21 kg/$m^2$ |

**General:** Paracervical muscle spasm

**Mental Status:** Alert, oriented with intact recent and remote memory, full attention span, concentration, fund of knowledge. Speech is fluent.

# Case 2 (Continued)

**Cranial Nerves:** Clear discs. Pupils are equal, round, and reactive to light. Visual fields are full. There is no ptosis. Extraocular movements are intact without nystagmus. Facial strength and sensation is symmetric. Normal tongue position and palate elevation. Speech is clear with no dysarthria. Shoulder shrugs are full. Hearing is normal and symmetric to finger rub.

**Motor:** Normal tone and bulk, no tremors, 5/5 strength throughout

**Sensation:** Intact to light touch, absent Romberg sign, allodynia present

**Reflexes:** Biceps, triceps, patellars, ankle jerks symmetric bilaterally; plantar responses are flexor

**Coordination:** No axial instability; accurate finger to nose and heel-knee-shin bilaterally

**Gait:** Normal, narrow-based gait; tandems well

**Psychiatric Interview Findings:** PHQ-9 = 6; GAD-7 = 17

# Case 2 (Continued)

**Headache Assessment Scales:**

**MIDAS (Migraine Disability Assessment) score: 45; grade: IV = severe**

| | |
|---|---|
| 1-Miss work/school (days) | 3 |
| 2-Productivity reduced >50% (days) | 6 |
| 3-Housework not done (days) | 17 |
| 4-Housework reduced >50% (days) | 15 |
| 5-Miss activities family/social/leisure (days) | 4 |
| MIDAS Total (days) | 45 |
| MIDAS Grade | IV = severe |

**HIT-6 (Headache Impact Test) score: 65**

| | |
|---|---|
| 1-Severe Pain | 11 |
| 2-Limit daily activities | 11 |
| 3-Wish to lie down | 11 |
| 4-Too tired for activities | 10 |
| 5-Fed up or irritated | 11 |
| 6-Limit concentration | 11 |
| HIT-6 Total | 65 |

# Case 2 (Continued)

**Diagnostic Tests:** MRI of the brain (in 2015), which was negative with the exception of multiple subcortical punctate hyperintensities seen on T2 FLAIR. MR angiogram of the head was also negative.

**Impression/plan:** Chronic migraine refractory to multiple preventive options and with a history of migraine disability and remote medication overuse. Anxiety, insomnia, and occupational stress are risk factors.

- **For prevention:** Trial of monoclonal antibody to CGRP or its receptor
- **For acute treatments:** Ketorolac 30 IM, dihydroergotamine nasal spray, prochlorperazine/ondansetron PRN, cyclobenzaprine for now, limit nonsteroidal anti-inflammatory drugs due to history of ulcer
- **Non-pharmacological approaches:** Consider CBT, relaxation techniques
- **Follow up:** 3 months

# Criteria for Treatment Continuation

- 50% reduction in the frequency of days with headache or migraine (and sometimes less)
- Significant decrease in attack duration as defined by patient
- Significant decrease in attack severity as defined by patient
- Improved response to acute treatment
- Reduction in migraine-related disability and improvements in functioning in important areas of life (work, school, social activities)
- Improvements in health-related quality of life and reduction in psychological distress, anxiety, depression, and insomnia due to migraine
- Consider trial for at least 3 months and possibly more

American Headache Society. *Headache*. 2019;59(1):1-18.

# SMART Goals

## Specific, Measurable, Attainable, Relevant, Timely

- Assess migraine-related disability and psychiatric comorbidities such as anxiety and depression
- Create individualized treatment plans that incorporate newer treatments to achieve optimal patient outcomes.