EDUCATION MODULE

PRESCRIBING OPIOIDS FOR PATIENTS WITH RECURRENT HEADACHE*

*This module provides additional details and risk-reduction guidance specific for this risk factor for serious prescription opioid overdose. It **supplements** but does not replace the general best practices for opioid prescribing presented in the **"Considerations for Safe and Responsible Opioid Prescribing"** module.*

Background

1. Migraine headache is common in the U.S., affecting 16% to 20% of women, and 5% to 9% of men.[1]

2. Individuals with migraines have a high prevalence of comorbidities, including mental health disorders (e.g., anxiety, depression, substance use disorders) and other chronic pain conditions such as fibromyalgia, low back pain, and joint pain.[2-4]

    a. Patients with co-occurring chronic pain and mental health disorders have greater intensity and longer duration of pain, poorer clinical outcomes, and increased health care utilization compared with those with either condition alone.[2,5-8]
        i. They are also more likely to be treated with opioid analgesics, to receive higher potency opioids, higher opioid dosages, and/or longer duration (>90 days) of opioid therapy relative to those without mental health disorders.[9-11]

3. Opioids are used to treat 10% to 35% of patients with migraines despite lack of endorsement by headache treatment guidelines.[12-15]

    a. Evidence is limited or insufficient that pain, or function improve with long-term opioid therapy for migraines (with or without aura), tension-type headaches, occipital neuralgia, or myofascial pain.[16-18]
    b. Opioids do not treat the underlying migraine pathophysiology; headaches treated with opioids have a high rate of recurrence after the analgesic effect of the opioid diminishes.[19,20]

4. More than one in four patients with migraine are eligible for prophylactic migraine medications, but only 13% to 49% use such medications.

    a. Poor medication adherence is common due to adverse effects and/or perceived lack of efficacy.[21-26]

Recurrent headache and opioid overdose

1. In individuals with frequent headaches, *underuse* of prophylactic migraine medications may lead to opioid analgesic overuse to manage recurrent migraine attacks.

2. Treating acute episodic migraines with opioid analgesics may increase transformation to chronic headaches.

a. Medication-overuse headache (previously referred to as "analgesic rebound" headache) may be related to triptans, ergots, opioids, combined analgesic products (e.g., butalbital with caffeine and aspirin or acetaminophen), or any combination thereof.
    i. Medication-overuse headache usually, but not invariably, resolves with cessation of medication overuse.[27,30]
    ii. Opioid-related overuse headaches may be a manifestation of opioid-induced hyperalgesia, with paradoxical heightened sensitivity to pain as opioid use increases via central sensitization.[31]

b. Withdrawal-mediated headache is related to the development of *physical* dependence on opioids. The pharmacological phenomena of tolerance and physical dependence often develop in individuals with regular use of certain medications or substances such as opioid analgesics or caffeine. For individuals taking prescription opioids under medical supervision, these 2 criteria do *not* count towards a DSM-5 diagnosis of OUD.[32]

    i. *Tolerance* is defined by the "need for increased amounts of opioids or diminished effect with continued use at the same amount."
    ii. *Withdrawal* is defined by "characteristic opioid withdrawal syndrome or taking opioids to relieve or avoid withdrawal symptoms" due to physical dependence.

3. The subset of patients with co-occurring mental health disorder(s) and chronic pain condition(s) such as recurrent headache has an elevated risk for developing opioid (or other substance) use disorder. The additional use of concomitant opioid analgesics and other CNS-depressant psychotherapeutic drugs place these patients at a particularly high risk for experiencing an opioid-related overdose.[33-36]

Risk mitigation strategies to consider in patients with recurrent headache
(Refer to the full prescribing information in the FDA Label for important product-specific details.)

1. Treat acute migraines with nonsteroidal anti-inflammatory drugs, triptans, or other non-opioid medications such as dihydroergotamine, prochlorperazine, or promethazine.[17,30]

    a. Limit use of acute headache medications to a maximum of 2 to 3 times per week to avoid medication overuse.[17,30]

2. Reserve opioid therapy for headache as a last resort for moderate to severe pain when other treatments have failed, are not tolerated, or are contraindicated.[13,17,29.30]

3. Consider daily prophylactic therapy for patients with more than 3 or 4 migraine attacks per month who have significant disability related to the severity and duration of attacks, and for patients in whom acute migraine medications do not effectively control the attacks, are contraindicated, or are overused.[24,30]

    a. Preventive migraine therapies include selected beta-adrenergic antagonists, anticonvulsants, triptans, and antidepressants.[17,38]

b. Educate the patient regarding expected benefits, side effects, and the importance of adhering to the regimen.[30,39]

c. Maximal response to prophylactic therapy may take 2 to 6 months.

4. Monitor opioid-treated patients with episodic headache disorders for opioid use disorder (misuse, abuse, dependence, addiction), particularly if headaches become more frequent or chronic.[13,28,29] (See 'Follow Up' section in the **"Considerations for Safe and Responsible Opioid Prescribing "** module)

    a. Conduct periodic urine drug testing during ongoing opioid treatment to monitor therapeutic adherence by the presence of prescribed controlled medications and to detect undisclosed use of nonprescribed controlled medications or illicit drugs.[40-42]
    b. Weigh the analgesic and functional benefits against the increased risks of overdose and active OUD.

5. Closely monitor the patient for respiratory depression or over-sedation during opioid initiation and after dosage escalation. The risk for overdose is greatest at this time because tolerance to an opioid's respiratory depressant effects is slower to develop and less complete than tolerance to its analgesic or euphoric effects.[40,41,43,44]

    a. Adults are considered opioid-tolerant if they have been receiving a total daily opioid dosage equivalent to at least 60 mg of oral morphine (60 MME/day) for one week or longer. See 'Treatment' section 5a in the "**Considerations for Safe and Responsible Opioid Prescribing"** module. This dosage is comparable to:
        - 25 mcg transdermal fentanyl per hour
        - 30 mg oral oxycodone per day
        - 60 mg oral hydrocodone per day
        - 8 mg oral hydromorphone per day
        - 25 mg oral oxymorphone per day

6. Avoid concurrent use of other medications or substances that are central nervous system depressants, such as benzodiazepines, sedatives/hypnotics, and alcohol in opioid-treated patients with recurrent headaches. The combination can result in profound sedation, respiratory depression, coma, and death and should be restricted to the minimum required dosage and duration in patients for whom alternative treatment options are inadequate.[40,41,45] (see also: FDA Label)

7. Consider prescribing take-home naloxone to patients treated with opioids to reverse life-threatening respiratory depression if an overdose occurs. Educate the patient, family/household members, and caregivers about signs and symptoms of opioid overdose and train them to properly use naloxone if an opioid-related overdose is suspected.[40,41] Educate the patient, family members, and caregivers about signs and symptoms of opioid overdose and train them to properly use naloxone if an opioid-related overdose is suspected.[40,42] (see the 'Follow Up' section, #5 in the "**Considerations for Safe and Responsible Opioid Prescribing"** module)

Additional Resources

**The information presented in this module highlights some fundamental concepts of opioid prescribing for adult outpatients. It excludes certain populations (pediatrics, pregnancy, patients with active cancer or receiving palliative or end-of-life care) and settings (perioperative, emergency, in-patient). The information provided is intended to support safe and effective opioid therapy and minimize serious adverse outcomes, particularly overdose. It is not intended to be exhaustive nor substitute for consulting a medication's full prescribing information for complete details and warnings. Links and references to selected, more comprehensive clinical and prescribing resources are provided to facilitate safe and effective opioid prescribing.*

1. **FDA-approved drug label information:** FDA Online Label Repository or Daily Med (NIH/National Library of Medicine)
1. In the Clinic: Migraine (American College of Physicians, 2017)
2. American headache society Resources
3. American Academy of Neurology Guidelines
4. Acute treatment of migraine. UpToDate, Jan 2018.

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