Managing and Preventing Migraine in the Emergency Department: A Review

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Migraine is a leading cause of disability worldwide, and acute migraine attacks are a common reason for patients to seek care in the emergency department (ED). There have been recent advancements in the care of patients with migraine, specifically emerging evidence for nerve blocks and new pharmacological classes of medications like gepants and ditans. This article serves as a comprehensive review of migraine in the ED, including diagnosis and management of acute complications of migraine (eg, status migrainosus, migrainous infarct, persistent aura without infarction, and aura-triggered seizure) and use of evidence-based migraine-specific treatments in the ED. It highlights the role of migraine preventive medications and provides a framework for emergency physicians to prescribe them to eligible patients. Finally, it evaluates the evidence for nerve blocks in the treatment of migraine and introduces the possible role of gepants and ditans in the care of patients with migraine in the ED. [Ann Emerg Med. 2023;82:732-751.]

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INTRODUCTION

Migraine is a leading reason for patients to present to the emergency department.[1] The prevalence of migraine is estimated between 11.7 and 22.7%[2-4,] and it carries substantial morbidity.[1,2,5-9] Worldwide, migraine is the second most common cause of disability, the foremost driver of disability in those under the age of 50, and the third highest driver of lost productivity from absences.[5,10] Additionally, its effect on health care use and costs is monumental: in the USA, annual health care expenditures from ED visits for migraine approximate $700 million.[11]

Most patients in the ED with acute migraine attacks have tried over-the-counter treatment unsuccessfully. Prolonged pain exposure from migraine can lead to central sensitization, contributing to the development of chronic migraine and preventing return to normal functioning.[10,12] Despite how common and disabling migraine is, significant gaps in the care of migraine in the ED persist. Migraine attacks are seldom treated to a pain-free target, and opioid use remains common.[13] Recently, new therapeutic classes have emerged and are playing an increasing role in the outpatient treatment of acute migraine attacks: gepants and ditans.

This review serves as a comprehensive, evidence-based summary of migraine in the ED, aiming to empower emergency physicians to precisely diagnose migraine and provide effective treatment that improves functional outcomes and decreases future ED visits.

MATERIALS AND METHODS

A panel of 5 physicians coauthored this narrative review: 3 Royal College emergency physicians (MACL, MD, and DJ) and 2 neurologists with headache-focused practices (SLO and ACL). One of the emergency physicians subspecialized in pain medicine with a focus on craniofacial pain (DJ), and another has a focus on neurologic emergencies and a secondary practice in a concussion center (MACL). Multiple databases were searched (eg, PubMed, World of Science, Google Scholar, academic textbooks in both emergency medicine and neurology) with no language restrictions, and references were reviewed to further capture relevant studies (Table E1, available at http://www.annemergmed.com). Where available, meta-analyses, systematic reviews, and clinical guidelines were prioritized.

PATHOPHYSIOLOGY

Migraine is a complex chronic neurovascular brain disorder that implicates common brain networks.[14] The trigeminovascular pathway is key in the pain phase of migraine and comprises the trigeminal nerve, its projections to the dura mater and around large intracranial blood vessels, and its afferent projections to the spinal trigeminal nucleus in the brainstem (which also receives afferent projections from the cervical dorsal root ganglia). Second order afferent neurons

project from the spinal trigeminal nucleus to the thalamus with collaterals to several other regions (eg, hypothalamus, periaqueductal gray, and the superior salivatory nucleus that projects to the sphenopalatine ganglion). Third order neurons project from the thalamus to the somatosensory cortex and other cortical regions (eg, visual cortex, insular cortex).[15] Migraine-specific therapies (ie, triptans, ergots, gepants, and ditans) are generally thought to target first order structures in the trigeminovascular pathway. Other reviews focus on migraine pathophysiology in detail.[15-17]

DIAGNOSIS

The first step in diagnosing a primary headache disorder is excluding secondary causes of headache. Features such as thunderclap headache (ie, instant peaking), fever, neurologic deficits, altered mentation, new headache in those more than 50 years, jaw-claudication, and signs of meningeal irritation are some of the characteristics suggestive of a secondary cause (Table 1).[18] Headache relief after analgesia cannot discriminate between primary and secondary headache disorders.[19] Because the diagnostic criteria for migraine include a history of recurrent attacks, caution is advised when assessing a first presentation of suspected migraine.

Next, emergency physicians should elucidate a likely primary headache disorder based on the headache semiology and tailor treatment accordingly (eg, consider high-flow oxygen for cluster headache, occipital nerve block for occipital neuralgia, and carbamazepine for trigeminal neuralgia).[20-23] Many patients in the ED do not meet strict diagnostic criteria for a particular primary headache disorder.[24]

Diagnosing Migraine in the ED

Broadly, migraine can present with or without aura. Migraine without aura—previously "common migraine"—is a syndrome of headache and a specific set of associated symptoms. Migraine with aura—previously "classic migraine"—is characterized by headache that is preceded or accompanied by transient neurologic symptoms (diagnostic criteria in Table 2),[25] The most common migraine aura is visual aura[26]; however, the spectrum is large and can rarely involve complex phenomena: brainstem aura (ie, brainstem dysfunction),[27] hemiplegic migraine (ie, motor weakness),[28,29] and retinal migraine (ie, monocular visual disturbances).[30] Selected migraine-related diagnoses relevant to the ED are depicted in Figure 1.

Distinguishing Migraine from Stroke

Occasionally, migraine with aura can mimic stroke. Factors more strongly associated with migraine than stroke include younger age, absence of cerebrovascular risk factors, female sex, previous history of migraine, and milder symptom severity. [31-36] Physicians should not rely on the patient's sex in making this distinction; compared with male patients, female patients with stroke present atypically more frequently[37] and have higher rates of stroke misclassification.[38-40]

Clarifying the temporal profile of the aura can help distinguish migraine aura from stroke or transient ischemic attack (TIA): the onset of stroke or TIA tends to be sudden, whereas migraine with aura classically evolves over minutes and sometimes with a succession of different neurologic symptoms (eg, first visual aura, then sensory). Additionally, whereas stroke or TIA present typically with negative phenomena (eg, weakness, numbness, or visual loss), migraine with aura often presents with positive sensory phenomena (eg, paresthesias, scintillating scotoma) that may then be followed by negative phenomena (Table 3). For symptoms of brainstem dysfunction (eg, diplopia, ataxia), posterior circulation stroke is far more common than migraine with brainstem aura.[27,41] When doubt exists, stroke should be excluded with brain imaging and/or obtaining a neurologist's opinion. In particular, the first presentations of suspected migraine with brainstem aura, hemiplegic migraine, and retinal migraine require the exclusion of secondary causes. Neuroimaging is not recommended for patients with stable headache meeting criteria for migraine.[42]

Vestibular Migraine

Vestibular migraine is among the most common causes of recurrent vertigo and the leading cause of central vertigo.[43,44] The physical examination is necessary to exclude serious causes of central vertigo (eg, unilateral deficits, cerebellar or brainstem dysfunction) or to diagnose a peripheral vestibulopathy;[45] there are no reliable examination findings to diagnose vestibular migraine.[43] Ultimately, the diagnosis is suspected in patients with migraine and recurrent moderate-severe vestibular symptoms (eg, vertigo, head-motion intolerance) not better explained by another vestibular

Table 1. Secondary causes of headache, "SNNOOP10 Mnemonic"*.

Sign or Symptom *(SNNOOP10)*	Secondary Headaches to Consider
Systemic signs and symptoms	Central nervous system infection Intracranial malignancy Metabolic, endocrine, vascular, or inflammatory disorders
Neurological deficits or altered mental status	Stroke Trauma Intracranial mass Meningitis or encephalitis Intracranial hemorrhage Posterior reversible encephalopathy syndrome Cavernous venous sinus thrombosis Carbon monoxide poisoning
Neoplasm history	Cerebral neoplasm or metastasis
Onset—thunderclap	Subarachnoid hemorrhage Cavernous venous sinus thrombosis Reversible cerebral vasoconstriction syndrome Posterior reversible encephalopathy syndrome Pituitary apoplexy Colloid cyst (intracranial hypotension)
Onset—age >50 years	Giant cell arteritis Intracranial mass
Papilledema	Elevated intracranial hypertension
Positional	Intracranial hypotension (worse when standing) Intracranial hypertension (worse when supine)
Precipitated by Valsalva	Elevated intracranial hypertension Chiari malformation
Precipitated by exertion	Dissection Reversible cerebral vasoconstriction syndrome Subarachnoid hemorrhage
Painful eye with autonomic features	Cavernous sinus thrombosis Orbital apex syndrome Acute angle closure glaucoma Intracranial lesions (posterior fossa or pituitary)
Posttraumatic onset	Subdural hematoma Dissection Intracranial hypotension
Pulsatile tinnitus	Idiopathic intracranial hypertension Vascular disorders
Pregnancy or postpartum	Pre-eclampsia/eclampsia Cavernous venous sinus thrombosis Reversible cerebral vasoconstriction syndrome Posterior reversible encephalopathy syndrome Pituitary apoplexy Postdural puncture headache
Pathology of the immune system	Opportunistic infections
Progressive or pattern change	Neoplasms Vascular intracranial disorders Other secondary causes

*Adapted from Do TP, Remmers A, Schytz HW, et al. Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. *Neurology*. 2019;2(3):1349.

disorder.[25] High-quality evidence on optimal vestibular migraine treatment is lacking[46]; until new evidence dictates otherwise, the same pharmacotherapy used for acute migraine attacks can be used for vestibular migraine.

Chronic Migraine

When migraine attacks occur in high frequency, it can be difficult to differentiate individual attacks from a continuous headache. Chronic migraine is diagnosed when a patient experiences headache for at least 15 days/month

Table 2. Diagnostic criteria for migraine types according to the ICHD-3.

Common Migraine Types		
Migraine Without Aura	**Migraine With Aura (Typical)**	**Vestibular Migraine**
A. At least 5 episodes fulfilling criteria B-D	**A. At least 2 episodes fulfilling criteria B and C**	**A. At least 5 episodes fulfilling criteria C and D**
B. Headache lasts 4-72 h	**B. At least 1 of the following reversible symptoms:**	**B. History of migraine with or without aura**
C. Headache has at least 2 of the following:	1. Visual	C. Vestibular symptoms of moderate or severe intensity,lasting between 5 min and 72 h
1. Unilateral location	2. Sensory	
2. Pulsating quality	3. Speech and/or language	**D. At least half of episodes are associated with at least 1 of the following:**
3. Moderate or severe intensity	4. Motor	1. Headache with at least 2 of the following:
4. Aggravated by routine physical activity	5. Brainstem	a) Unilateral
D. At least 1 of the following:	6. Retinal	b) Pulsating
1. Nausea and/or vomiting	**C. At least 3 of the following:**	c) Moderate-severe
2. Photophobia and phonophobia	1. Aura spread gradually over at least 5 minutes	d) Aggravated by routine activity
E. Not better accounted for by another ICHD-3 diagnosis	2. At least 2 aura symptoms occur in succession	2. Photophobia and phonophobia
	3. Each individual aura symptom lasts 5-60 min	3. Visual aura
	4. At least 1 aura symptom is unilateral	**E. Not better accounted for by another ICHD-3 diagnosis**
	5. At least 1 aura symptom is a positive phenomenon	
	6. Headache accompanies aura or occurs within 60 min of aura	
	D. Not better accounted for by another ICHD-3 diagnosis	

Rare Migraine Types		
Brainstem Aura	**Hemiplegic Migraine**	**Retinal Migraine**
A. Attacks meeting criteria for migraine with aura	**A. Attacks meeting criteria for migraine with aura**	**A. Attacks meeting criteria for migraine with aura**
B. Aura consisting of both of the following:	**B. Aura consisting of both of the following:**	**B. Aura consisting of both of the following:**
1. At least 2 of the following:	1. Fully reversible motor weakness	1. Fully reversible monocular visual phenomena (positive or negative)
a) dysarthria	2. Fully reversible visual, sensory and/or speech or language symptoms	2. At least 2 of the following:
b) vertigo		a) spreading gradually over at least 5 min
c) tinnitus		b) symptoms last 5-60 min
d) hypoacusis		c) accompanied or followed within 60 min by headache
e) diplopia		
f) ataxia		
g) decreased level of consciousness		
2. No motor or retinal symptoms		

ICHD-3, International Classification of Headache Disorders.

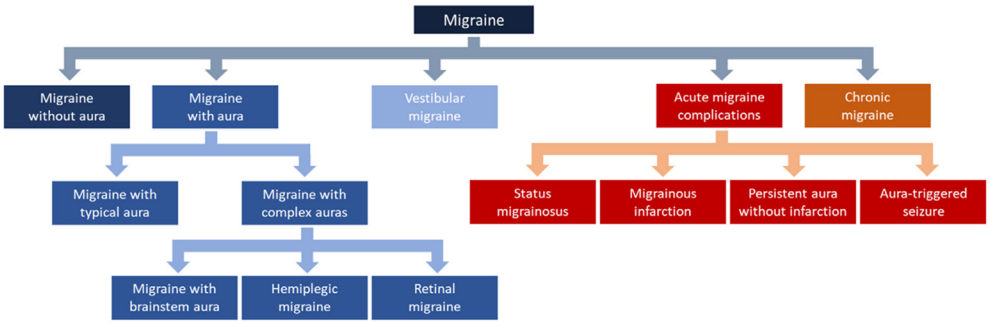

Figure 1. Selected migraine-related diagnoses according to the ICHD-3. *ICHD3*, International Classification of Headache Disorders.

for at least 3 months, and for which at least 8 of these attacks are associated with migraine features.[25]

Other Primary Headache Disorders

At the population level, tension-type headache is more prevalent than migraine;[47] however, owing to the higher severity of migraine, its prevalence in the ED is higher than that of tension-type headache.[9,24] Migraine and tension-type headache can be distinguished on history: migraine attacks are more severe, tend to be unilateral, are generally pulsating or throbbing rather than pressure-like, and are accompanied by photophobia, phonophobia, and nausea (tension-type headache can present with only one of photophobia or phonophobia) (Figure 2).

The trigeminal autonomic cephalalgias are characterized by paroxysmal attacks of unilateral head pain and ipsilateral autonomic findings and include

Table 3. Distinguishing characteristics between migraine aura and stroke or TIA.

Characteristic	Migraine Aura[†]	Stroke or TIA
Onset	Gradual	Sudden
Course	Symptoms typically progress in succession Headache follows aura	Symptoms typically occur simultaneously
Duration	Typically less than 30 min	Variable
Visual Symptoms	**Positive phenomena:** Flashing lights Zigzag lines Scintillating scotoma typically expands gradually or propagates	**Negative phenomena:** Vision loss (quadrantanopia, hemianopia, blindness)
Sensory Symptoms	**Positive phenomena:** Paresthesias (pins-and-needles)	**Negative phenomena:** Sensory loss
Speech and Language Symptoms	**Typically mild:** Word-finding difficulty Paraphasic errors	**Typically more pronounced:** Large spectrum of aphasic disturbances: Receptive and expressive Paraphasic errors Dysarthria
Brainstem Symptoms	Very rare, less than 0.1%[‡]: Present in migraine with brainstem aura	20% of stroke or TIA[§]: Present in posterior circulation stroke or TIA
Motor Weakness	If present, it tends to be milder Isolated weakness as in hemiplegic migraine exceedingly rare (<0.01%) [‖,¶]	Tends to be more severe Common

TIA, Transient ischemic attack.
[†]Viana M, Sances G, Linde M, et al. Clinical features of migraine aura: results from a prospective diary-aided study. *Cephalalgia*. 2017;37(10):979-989.
[‡]Yamani N, Chalmer M, Olesen J. Migraine with brainstem aura: defining the core syndrome. *Brain*. 2029;142(12):3868-3875.
[§]Gulli G, Marquadt L, Rothwell P, and Markus H. Stroke risk after posterior circulation stroke/transient ischemic attack and its relationship to site of vertebrobasilar stenosis. *Stroke*. 2013;44:598-604.
[‖]Thomsen L, Eriksen M, Roemer S, Andersen I, Olesen J, and Russell M. *Brain*. 2002;125(Pt 6):1379-1391.
[¶]Thomsen L, and Olesen J. Sporadic hemiplegic migraine. *Cephalalgia*. 2004;24:1016-1023.

Features	Migraine	Tension-Type Headache
Duration	4-72 hours	30 min to 7 day
Location	Unilateral	Bilateral
Quality	Pulsating or throbbing	Steady, pressing, or squeezing
Severity	Moderate to severe	Mild to moderate
Aggravation	Routine physical activity	None
Associated Symptoms	Photophobia AND Phonophobia *OR* Nausea OR vomiting	Max one of: Photophobia or Phonophobia
Aura	In migraine with aura	None

Figure 2. Differentiating between migraine and tension-type headache.

cluster headache, paroxysmal hemicrania, hemicrania continua, short-lasting unilateral neuralgiform headache with conjunctival tearing, and short-lasting unilateral neuralgiform headache with cranial autonomic symptoms (SUNA).

Cranial neuralgias involve neuralgic pain along the distribution of a nerve of the head or neck. Among these, trigeminal neuralgia and occipital neuralgia are the most common; glossopharyngeal neuralgia and nervus intermedius syndrome are rarer.[48]

Medication-Overuse Headache

Medication-overuse headache is a chronic condition that develops in patients with a primary headache disorder who frequently use analgesics for at least 3 months.[25] The risk of developing medication-overuse headache increases when simple analgesics (ie, acetaminophen or nonsteroidal anti-inflammatory drugs [NSAIDs]) are used at least 15 days/month in isolation or when acetaminophen and NSAIDs in combination, triptans, ergots, or opioids (which should be avoided) are used at least 10 days/month.[49,50] It is treated by discontinuing the culprit medication, typically while initiating preventive treatment.[51,52]

ACUTE COMPLICATIONS OF MIGRAINE

Migraine can be associated with acute complications that require urgent recognition and management: status migrainosus, migrainous infarction, persistent aura without infarction, and migraine aura-triggered seizure.

Status Migrainosus

Status migrainosus is a debilitating migraine attack unremitting for at least 72 hours. Up to one fifth of patients with migraine experience status migrainosus, and it is associated with poorer prognosis and higher rates of disability.[53,54] The recurrence rate of status migrainosus is high, and it carries an increased risk of progression to chronic migraine.[55] Consequently, it is essential to recognize status migrainosus in order to initiate optimal treatment of acute migraine attacks, consider preventive therapy, and refer to neurology.

Table 4. Treatments and interventions for acute migraine attacks in the ED.

Treatment or Intervention		Strength of Recommendation (Level of Evidence) AHS	Strength of Recommendation (Level of Evidence) CHS	Contraindications and Adverse Effects
		Mild-Moderate Episodes		
First-Line	Acetaminophen 1,000 mg PO	N/A (Level A)*	Strong (High) §	Gastrointestinal, headache, insomnia
	One of the following:			Gastrointestinal, headache, acute kidney injury
	Naproxen 500 mg PO	N/A (Level A)*	Strong (High) §	
	Ibuprofen 200-400 mg PO	N/A (Level A)*	Strong (High) §	
	Diclofenac 50-100 mg PO	N/A (Level A)*	Strong (High) §	
		Moderate-Severe Episodes		
First-Line	Ketorolac 30 mg IV or 60 mg IM	May Offer (Level C) †	Strong (Low) ‖	Gastrointestinal, headache
	One of the following:			Extra-pyramidal syndromes (akathisia)
	Metoclopramide 10-20 mg IV	Should Offer (Level B) †	Strong (Moderate) ‖	
	Prochlorperazine 10 mg IV	Should Offer (Level B) †	Strong (High) ‖	
	One of the following:			
	Sumatriptan 6 mg SC *(may repeat in 2 hours)*	Should Offer (Level B) †	Strong (Moderate) ‖	Chest pain, avoid severe vascular risk factors or ergots within 24 h
	DHE 1 mg IV	No Recommendation (Level U) †	Weak (Low) ‖	Vomiting, avoid if severe vascular risk factors or triptans within 24 h
Second-Line	Valproic acid 800-1,000 mg IV (*if available in ED*)	May Offer (Level C) †	Weak (Low) Against ‖	Transaminitis, cognitive side effects, teratogenic
Third-Line	Magnesium sulfate 1 g IV over 15-20 min	No Recommendation (Level U) †	Weak (Moderate) *Against* ‖	May cause hypotension; avoid in neuromuscular disorder
Experimental	Propofol 0.25-1 mg/Kg IV	No Recommendation (Level U) †	Weak (Low) *Against* ‖	Sedation, hypotension, respiratory suppression
		Nerve Blocks		
First-Line	Sphenopalatine ganglion Greater occipital nerve Lesser occipital nerve	N/A	N/A	Local hypersensitivities
Second-Line	Supraorbital nerve	N/A	N/A	Local hypersensitivities
Experimental	Supratrochlear nerve Auriculotemporal nerve	N/A	N/A	Local hypersensitivities
		Recurrence Prevention		
In the ED	Dexamethasone 10 mg IV in the ED	Should Offer (Level B) †	N/A	Flushing, gastrointestinal, and paresthesias

Daily Preventive Medications	**Nutraceuticals to eligible patients, any or all of the following:**			
	Magnesium citrate, 500-600 mg PO daily	Should Consider (Level B) [‡]	Strong (Low) [¶]	Mild gastrointestinal upset
	Coenzyme Q10, 150 mg PO BID	May Consider (Level C) [‡]	Strong (Low) [¶]	Eructations
	Riboflavin, 400 mg PO daily	Should Consider (Level B) [‡]	Strong (Low) [¶]	Orange colored urine
	Preventive medications to eligible patients, one of the following:			
	Metoprolol, 25-50 mg PO BID (max 200 mg/d)	Should Offer (Level A) [‡]	Strong (High) [¶]	Bradycardia, hypotension, dizziness
	Propranolol, 40-80 mg PO BID (max 160 mg/d)	Should Offer (Level A) [‡]	Strong (High) [¶]	Bradycardia, hypotension, dizziness
	Amitriptyline, 10 mg PO QHS *May be increased by 10 mg/ week to max of 100 mg PO QHS*	Should Consider (Level B) [‡]	Strong (High) [¶]	Drowsiness, weight gain, anticholinergic side effects, long-QT
	Topiramate, 25 mg PO QHS *May be increased by 25 mg/ week to max of 100 mg PO BID*	Should Offer (Level A) [‡]	Strong (High) [¶]	Paresthesia, cognitive side effects, weight loss,renal colic, acute angle closure glaucoma, teratogenic

AHS, American Headache Society; *BID*, twice daily; *CHS*, Canadian Headache Society; *DHE*, dihydroergotamine; *IM*, intramuscular; *IV*, intravenous; *N/A*, not available; *PO*, oral, *SC*, subcutaneous; QHS, nightly.

*Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: The American Headache Society evidence assessment of migraine pharmacotherapies. *Headache.*2015;55:3-20.

[†]Orr SL, Friedman BW, Christie S, et al. Management of adults with acute migraine in the emergency department: the American Headache Society evidence assessment of parenteral pharmacotherapies. *Headache.* 2016;56:911-940.

[‡]Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN Guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. *Headache.* 2012;52:930-945.

[§]Worthington I, Pringsheim T, Gawel MJ, et al. Canadian Headache Society guideline: acute drug therapy for migraine headache. *Can J Neurol Sci.* 2013;40(S3):S1-S80.

[‖]Orr SL, Aubé M, Becker WJ, et al. Canadian Headache Society systematic review and recommendations on the treatment of migraine pain in emergency settings. *Cephalalgia*. 2014;0:1-14.

[¶]Pringsheim T, Davenport J, Mackie G, et al. Canadian Headache Society Guideline for Migraine Prophylaxis: Supplement 2. *Can J Neurolog Sci*. 2012;39(S2):i-63.

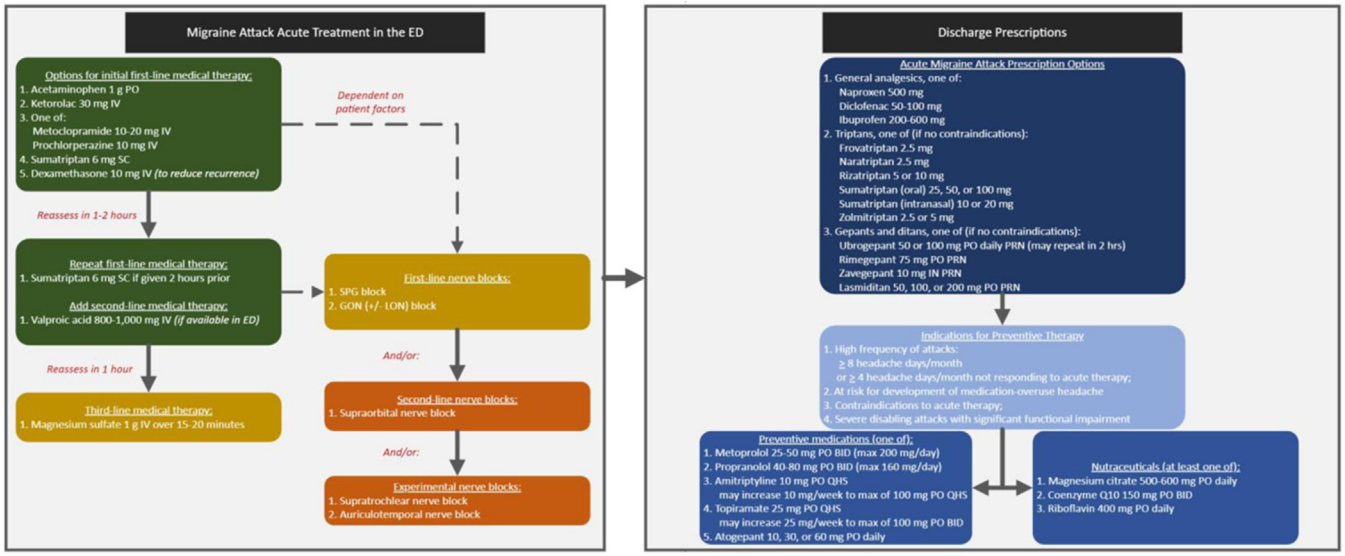

Figure 3. Treatment algorithm for acute migraine attacks in the emergency department. *BID*, twice daily; *GON*, greater occipital nerve; *IM*, intramuscular; *IV*, intravenous; *LON*, lesser occipital nerve; *PO*, oral; *PRN*, as needed; *QHS*, nightly; *SC*, subcutaneous; *SPG*, sphenopalatine ganglion.

Migrainous Infarction and Persistent Aura Without Infarction

Migraine with aura has been associated with an increased risk of ischemic stroke.[56-59] It is unclear whether stroke is a complication of migraine or if stroke triggers migraine attacks; however, it is postulated that migrainous infarction may result from hypoperfusion associated with aura.[60] Relatedly, in persistent aura without infarction, patients experience migraine aura for at least one week without evidence of infarction.[25] In such cases, physicians should exclude stroke with cerebral imaging. Both of these complications are exceedingly rare: the incidence of migrainous infarction in adults with migraine ranges from 1.44 to 3.36 per 100,000 annually,[61] and accounts for fewer than 0.5% of strokes.[62-64]

Migraine Aura-Triggered Seizure

Seizures triggered by migraine with aura—or *migralepsy*—are considered rare events characterized by epileptic activity occurring during or within 60 minutes of migraine with aura.[25] Given that migraine with aura and seizure can both result in positive phenomena, distinguishing the 2 can be challenging. Occipital seizures, for example, can mimic or coexist with migraine with aura,[65] Referral to a neurologist is warranted for suspected aura-triggered seizure.

ACUTE MIGRAINE MANAGEMENT

The management of acute migraine has evolved over the last decade. Since the last publication of the Canadian Headache Society and the American Headache Society guidelines in 2014[66] and 2015,[67] respectively, new pertinent trials were published, and new categories of medications became available for acute migraine attacks: gepants and ditans. Still, despite numerous guidelines recommending avoidance of opioids and barbiturates in acute migraine care, they continue to be commonly prescribed, increasing the risk of medication-overuse headache and dependence.[68]

The goals of treating migraine in the ED are to relieve pain, relieve migraine-associated symptoms, and enable patients to return to normal functioning.[69,70] The 3 medication classes with the strongest level of evidence and highest level of recommendation in treating acute migraine attacks are acetaminophen, NSAIDs, and triptans.[66] A treatment summary and an approach for treating patients with acute migraine in the ED are summarized in Table 4 and Figure 3, respectively.

Mild to Moderate Attacks

Acetaminophen and NSAIDs are first-line therapy for mild-moderate migraine attacks.[67,69] An initial dose of 1,000 mg oral acetaminophen along with any 50 or 100 mg oral diclofenac, 400 mg oral ibuprofen, or 500 mg oral naproxen is a safe and effective combination.[68] Patients requiring acute medications more than 15 days/month as monotherapy or more than 10 days/month in combination are at increased risk of developing medication-overuse headache.

Moderate to Severe Attacks

Most patients visiting the ED for migraine have tried acetaminophen and NSAIDs without success. Parenteral NSAIDs, triptans, and dopamine antagonists should be

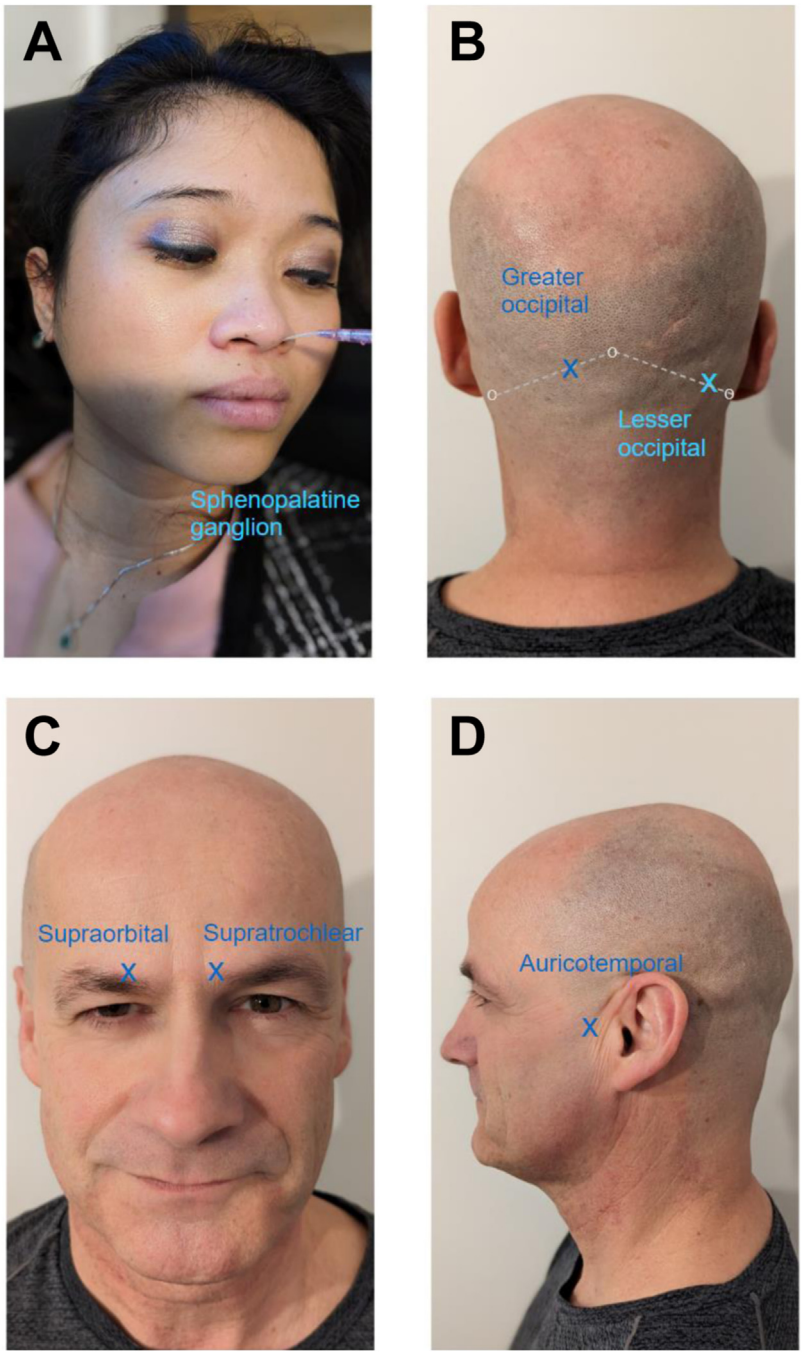

Figure 4. Injection sites for nerve blocks for acute migraine attacks. Each nerve block can be performed with a 27- or 30-gauge needle and injecting 2 mL of either 2% lidocaine or 0.5% bupivacaine. The injection site should first be cleaned with either alcohol or chlorhexidine. *A*, sphenopalatine ganglion block. The left sphenopalatine ganglion is blocked by having the head rotated toward the left and using a soft-tipped angiocatheter to inject either lidocaine or bupivacaine. *B*, the greater occipital nerve site of injection is 1 third along the line between the occipital protuberance and the mastoid process, and the lesser occipital nerve 2 thirds along the same line. *C*, the supraorbital notch is between the pupil and the medial edge of the iris under the eyebrow, and the supratrochlear nerve is located 5-10 mm medial to the orbital notch. *D*, the auriculotemporal nerve is located just anterior to the tragus; for safety, the temporal artery can be palpated, and the injection can be performed cranial to the zygoma.

offered for more severe attacks [66,70]. Parenteral routes are preferred over oral, given their rapid onset and tolerability when patients are nauseated.

Intravenous fluids. Intravenous fluid administration is commonly used in the ED treatment of migraine attacks. No randomized controlled trials evaluating the influence of

Treating an Acute Migraine Attack	
1. General pain medications	Maximum 15 days per month (if taking only ONE), or 10 days per month (if taking TWO). ❑ **Acetaminophen** 1,000 mg ❑ **Naproxen** 500 mg or **Ibuprofen** 200, 400 or 600 mg or **Diclofenac** 50, 75, or 100 mg
2a. Migraine-specific medications: triptans	Take at the onset of symptoms and repeat the dose in 2 hours if your symptoms persist. Maximum 10 days per month. ❑ **Frovatriptan** 2.5 mg ❑ **Naratriptan** 2.5 mg ❑ **Rizatriptan** 5 or 10 mg ❑ **Sumatriptan** (oral) 25, 50, or 100 mg ❑ **Sumatriptan** (intranasal) 10 or 20 mg ❑ **Zolmitriptan** 2.5 or 5 mg
2b. Other migraine-specific medications: gepants and ditans	❑ **Ubrogepant** 50 or 100 mg once, may repeat in 2 hours *(max 8 days per month)* ❑ **Rimegepant** 75 mg once daily as needed *(max 18 days per month)* ❑ **Zavegepant** 10 mg intranasal once daily as needed *(max 8 days per month)* ❑ **Lasmiditan** 50, 100, or 200 mg once daily as needed *(max 4 days per month)*
Lifestyle Modifications to Prevent a Migraine Attack	
1. Limit or avoid	- Caffeine, max 2 days per week - Alcohol - Dehydration: consume 1-2 litres of water per day - Hunger: consume protein with breakfast within 1 hour of waking and keep snacks
2. Sleep Hygiene	- Keep a regular sleep schedule, aiming for a full night rest - Avoid naps - Avoid using screens late at night
3. Physical activity	- Routine physical activity: 150 minutes per week in at least 10 minute intervals
4. Ergonomics	- Adjust home and office settings to minimize eye strain - Rule of 20s: every 20 minutes look 20 feet away for 20 seconds
Medications to Prevent a Migraine Attack	
1. Nutraceuticals	Take at least one of: ❑ **Magnesium citrate** 500 to 600 mg daily ❑ **Coenzyme Q10** 150 mg twice daily ❑ **Riboflavin** (vitamin B2) 400 mg daily
2. Preventive Medications	These daily medications reduce the frequency and severity of migraine attacks. ❑ **Metoprolol** 25 to 100 mg twice daily (side effects: dizziness, low energy, low blood pressure) ❑ **Propranolol** 40 to 80 mg twice daily (side effects: dizziness, low energy, low blood pressure) ❑ **Amitriptyline** 10 mg at night; may increase by 10 mg/week, max of 100 mg/night (side effects: sleepiness, fatigue, weight gain, mood disturbance) ❑ **Topiramate** 25 mg at night; may increase by 25 mg/week, max of 100 mg/night (avoid in pregnancy; side effects: tingling, drowsiness, feeling "in a fog", weight-loss, kidney stones, glaucoma) ❑ **Atogepant** 10, 30, or 60 mg once daily (side effects: nausea, tiredness, and constipation)

Figure 5. Discharge instructions handout after treating acute migraine attacks in the emergency department.

intravenous fluid on migraine outcomes have been published. One post hoc analysis of randomized controlled trials evaluating metoclopramide in treating migraine found no significant difference in pain scores in patients who received intravenous fluid compared with those who did not.[71] There were several limitations: uncertainty of volume administration, lack of randomization and blinding, and no measures beyond pain recorded. Given that migraine often presents with vomiting and that dehydration is a risk factor for migraine.[72,73] It is reasonable to administer intravenous fluid alongside other therapy, though it remains unclear whether this improves outcomes.

Parenteral NSAIDs. Ketorolac 30 mg intravenously (60 mg intramuscularly) is similarly effective to other strong comparators in treating migraine attacks.[74] No randomized

controlled trial has examined whether lower doses of ketorolac are equally effective. Specific safety data regarding the use of parenteral NSAIDs in those who had used NSAIDs at home within 8 hours are lacking. The most common side effects of ketorolac are gastrointestinal disturbances and dizziness.

Triptans. Multiple triptan formulations exist, including tablets, wafers, nasal sprays, or subcutaneous injections. Only sumatriptan is currently available subcutaneously and carries the highest level of evidence, among the triptans, for ED use.[66] Whereas the efficacy of oral triptans diminishes when administered beyond 2 hours from symptom onset,[75] subcutaneous sumatriptan appears to retain its benefit.[76] Patients should be offered subcutaneous sumatriptan 6 mg as first-line therapy in the ED; it can be repeated in 2 hours if needed.[66-68] Contraindications to triptans include uncontrolled hypertension, cardiovascular/cerebrovascular or peripheral artery disease, or ergot use within 24 hours. Concerns have been raised about using triptans in migraine with brainstem aura or hemiplegic migraine because of their vasoconstrictive properties and fear they may precipitate stroke; although the risk is likely low, they are best avoided in these cases. The risk of serotonin syndrome when triptans are used in combination with selective reuptake inhibitors (SSRI) or serotonin reuptake inhibitors (SNRI) is exceedingly low for most patients, with an estimated incidence of less than 0.1%.[69,77-79]

Dopamine antagonists. The Canadian Headache Society and American Headache Society guidelines strongly recommend offering either prochlorperazine 10 mg intravenously or metoclopramide 10 to 20 mg intravenously to patients with acute migraine attacks in the ED.[66,70] Side effects include dystonic reactions, in particular akathisia. The risk of akathisia from prochlorperazine is higher than from metoclopramide (36 to 44% compared with 2 to 32%),[80-85] and a slower infusion of metoclopramide (over 15 to 30 minutes) has been shown to lower this risk.[86] Although haloperidol may provide a comparable reduction in symptoms to metoclopramide,[87] it is associated with more adverse events.[88] Diphenhydramine can be administered to treat extrapyramidal side effects.[84,89-91]

Ergots. Dihydroergotamine is a synthetic ergot that can be administered intranasally or intravenously. It is a 5-$HT_{1B/1D/1F}$ agonist and antagonist of 5-HT_{1A}, 5-HT_{2A}, adrenergic, cholinergic, and dopaminergic receptors.[68] Dihydroergotamine may be useful for migraine-associated allodynia or prolonged migraine attacks. Dihydroergotamine is dosed 1 mg intravenously over 2 minutes and can be repeated in 8 hours if needed. Vomiting—the most common side-effect—can be mitigated by preadministering an antiemetic. Ergots should be avoided in pregnancy, breastfeeding, uncontrolled hypertension, cardiovascular/cerebrovascular or peripheral artery disease, or recent triptan use. Its cost, limited accessibility, and side-effect profile have limited uptake in the ED, though there are data to support single doses of dihydroergotamine in this setting.[92,93]

Adjunctive Medications for Refractory Migraine

Adjuncts can be considered to treat migraine or alleviate associated symptoms to reduce functional impairment.

Magnesium sulfate. Magnesium sulfate 1 g intravenously infused over 15 minutes is a safe option for migraine treatment in the ED.[94,95] Overall, study conclusions have been mixed on the effectiveness of magnesium compared with alternative therapies.[96,97] Magnesium sulfate may be more effective in migraine with aura than in migraine without aura,[67,98] and further benefit might be derived from its role in treating associated symptoms of migraine (eg, photophobia and phonophobia).[98] Potential side effects include hypotension, and it is contraindicated in patients with neuromuscular disease.

Valproic acid. Two meta-analyses showed that valproic acid was not superior to comparative treatments for acute migraine.[99,100] Importantly, both meta-analyses evaluated valproic acid against strong comparators: dopamine antagonists,[99,100] NSAIDs,[99] or triptans.[99] Consequently, although valproic acid should not replace treatments with higher levels of evidence for first-line use, a loading dose of 800 to 1,000 mg of intravenous valproic acid (if available) is a reasonable adjunct after other agents have been ineffective, and pregnancy has been excluded.

Novel Therapies: Gepants and Ditans

Gepants and ditans are 2 novel categories of acute migraine treatment. Gepants are calcitonin gene-related peptide (CGRP) receptor antagonists,[101] and ditans are selective 5-HT_{1F} receptor antagonists targeting the trigeminal system.[68,102] Both of these medication classes have favorable efficacy and safety profiles.[103-108] A systematic review of 64 randomized controlled trials comparing gepants, ditans, and triptans found that 1) gepants and ditans had higher odds of achieving pain relief at 2 hours than placebo but lower odds of achieving pain relief at 2 hours than triptans, and 2) gepants had the lowest odds of adverse events among the 3 drug categories.[109] Preclinical data suggest gepants might not be associated with the development of medication-overuse headache.[110] They may eventually carve a larger role in

treating migraine attacks in the ED, should evidence emerge for their use in this setting.

Gepants. Four gepants have been shown to effectively treat migraine so far: ubrogepant, rimegepant, atogepant, and zavegepant. Ubrogepant and zavegepant are indicated for acute migraine treatment, rimegepant for acute or preventive, and atogepant for preventive. Currently, ubrogepant and atogepant have been approved both in Canada and USA, and rimegepant and zavegepant in the USA.

Ubrogepant can be dosed at 50 mg or 100 mg orally daily as needed; a second dose can be repeated after 2 hours.[111] Zavegepant is given intranasally 10 mg once/24-hour period as needed.[112] Rimegepant is dosed 75 mg orally once daily as needed for acute therapy.[113] Gepants should be avoided in patients taking strong CYP3A4 inhibitors. Unlike triptans, gepants are not vasoconstrictors and are not contraindicated in patients with uncontrolled hypertension, cardiovascular/cerebrovascular or peripheral artery disease. Still, they do prevent vasodilation, and mice models suggest increased brain infarcts when gepants are administered with experimentally occluded middle cerebral arteries; therefore, they are prudent to be avoided in those at very high risk of stroke.[114,115]

Ditans. Lasmiditan has been approved for acute migraine attacks in the USA. Like triptans, ditans act on the trigeminovascular system; however, because of their specificity for 5-HT_{1B} receptors, they are unlikely to result in vasoconstriction and appear to be safe in those with vascular risk factors.[102,116] Lasmiditan is dosed at 50 mg, 100 mg, or 200 mg orally daily as needed. After taking lasmiditan, patients must avoid driving and operating heavy machinery, given its sedating effects.

Nerve Blocks

Cranio-facial nerve blocks are frequently used to treat migraine in the outpatient setting. In the ED, sphenopalatine ganglion and occipital nerve blocks are increasingly used to treat primary headache disorders.[117] At present, evidence for their ED use supports safety, but it is unclear whether they are superior to existing first-line interventions or sham blocks.[118-121] Limited but emerging evidence suggests benefit from supratrochlear, supraorbital, and auriculotemporal nerve blocks, though they have not been specifically studied in the ED.[122,123] Incorporating nerve blocks in acute migraine care should be tailored on an individual basis. High-quality evidence guiding nerve block selection is lacking; we recommend prioritizing sphenopalatine ganglion and occipital nerve blocks because of their stronger supporting evidence and considering the accompanying nerve blocks based on the headache location. It remains unknown whether nerve blocks might supplant some established medical therapies or serve as adjuncts for refractory symptoms or cases where there are contraindications to migraine-specific medications. The injection sites for nerve blocks for migraine are shown in Figure 4 and the accompanying Video E1 (available at http://www.annemergmed.com).

Sphenopalatine ganglion nerve block. The sphenopalatine ganglion is a collection of neuronal bodies behind the middle nasal turbinate linked to the trigeminovascular system and implicated in various primary headache disorders.[124,125] Multiple methods have been described to block the sphenopalatine ganglion. The *method of Barre* consists of applying anesthesia intranasally with a cotton-tipped applicator more than 30 seconds to each nare. Patients should be supine with the neck extended and the head rotated 30 to 45 degrees toward the affected side.[126] The "Tx360 targeted device" is an alternative intranasal anesthetic applicator.[127] From our experience, using an angiocatheter to drip the anesthetic intranasally is an effective way of performing the sphenopalatine ganglion block, or it can be similarly achieved with viscous lidocaine and a syringe.[128] Lastly, another practical method is to use an atomizer to deliver 4% lidocaine topically.[129] It is unclear which method is most effective.

Occipital nerve block. The greater occipital nerve is a sensory branch of C2 that carries information to the brain through a relay in the spinal trigeminal nucleus to where primary trigeminal afferents also carry incoming migraine pain signals. Most commonly, the greater occipital nerve branch is blocked; however, the lesser occipital nerve can also be targeted.[130] The greater occipital nerve injection site is one third of the distance between the occipital protuberance and the mastoid process, and the lesser occipital nerve site is two thirds the distance of this same line. Lidocaine or bupivacaine, with or without corticosteroids, can be used. Data are lacking regarding which anesthetic is most effective. Generally, the inclusion of corticosteroids in the blocks is not advised because of the lack of evidence and higher side-effect potential.[131]

Nerve blocks with emerging evidence: supratrochlear, supraorbital, and auriculotemporal nerve blocks. In addition to sphenopalatine ganglion and occipital nerve blocks, other nerve blocks have gained attention in treating migraine.[132] Supraorbital and supratrochlear nerve blocks may prevent attacks in patients with chronic migraine.[133,134] A recent randomized controlled trial carried out in the ED found supraorbital nerve blocks to be safe and more effective than placebo in treating acute migraine attacks; however, they are less effective than

occipital nerve blocks when performed in isolation.[135] Supratrochlear and auriculotemporal nerve blocks have not been evaluated in randomized controlled trials for treating acute migraine attacks in the ED.

Drugs to Avoid: Opioids and Barbiturates

The American College of Emergency Physicians holds a Level A recommendation to avoid opioids in treating headache.[136] The use of opioids and barbiturates in migraine has been associated with medication-overuse headache, progression to chronic migraine, poorer quality of life, higher headache-related burden, headache recurrence following an ED visit, and exposure to addictive potential.[137-142]

With the multitude of drugs available, the lack of benefit from opioids and barbiturates compared with other agents, and the demonstrated harm of these agents, there is no role for opioids or barbiturates in treating acute migraine attacks in the ED.[66,67,143]

Experimental and Controversial Treatments

Propofol. Currently, the evidence supporting the use of propofol in treating migraine has been mixed and limited to small, randomized trials or observational studies.[144-147] In addition to establishing the magnitude of the benefit of propofol in treating migraine, its safety profile needs to be further examined to better understand its role in treating migraine in the ED.[148,149]

Ketamine. Ketamine (intranasal, intravenous, and subcutaneous) has been studied in randomized controlled trials evaluating its efficacy in treating migraine.[150-155] Studies have not consistently demonstrated a benefit with ketamine compared with placebo or alternative therapies. High heterogeneity between the studies, small sample sizes, and high risk of bias limit their generalizability.[156] The lack of demonstrated benefit and side-effect profile (eg. vomiting, derealization, emergence reaction) limit the role of ketamine in treating migraine in the ED.

Intravenous lidocaine. Small studies have shown pain reduction with intravenous lidocaine in migraine attacks; however, they have not demonstrated sustained benefit beyond 30 minutes.[157,158] There is insufficient evidence to recommend intravenous lidocaine for treating acute migraine attacks.

Special Populations

Pregnancy and lactation. Most migraine therapies lack data demonstrating safety or harm for use during pregnancy and lactation. Acetaminophen and metoclopramide are both first-line for most pregnant or lactating women.[159] Nonsteroid anti-inflammatory drugs (NSAIDs) are contraindicated in the third trimester, controversial in the second trimester, and should be deprioritized compared with acetaminophen, metoclopramide, sumatriptan, magnesium sulfate, and nerve blocks.[159,160] Concerns around triptans causing teratogenicity are likely overestimated: a systematic review of 8 studies with a total of 13,097 patients found little evidence linking triptans with fetal abnormalities; however, one study found a possible association between triptan use during pregnancy and increased child emotionality.[161] Nerve blocks can be offered in pregnancy and lactation.[162,163]

Pediatric. The approach to treating acute migraine attacks in the pediatric population is similar to adults, save for a few considerations. First, some migraine-specific treatments lack high-quality pediatric ED evidence; their use is supported by inference from either the adult ED or pediatric outpatient setting. Second, adolescents might be at higher risk of opioid misuse and overdose compared with older adults.[164,165] Pediatric-specific reviews have been published on the evaluation and treatment of pediatric migraine attacks in the ED.[166-169]

Post-traumatic headache. High-quality evidence to inform post-traumatic headache management is lacking. In practice, after excluding serious secondary causes, post-traumatic headache is treated in accordance with headache semiology (eg, migraine, tension-type headache, cervicogenic headache). A recent randomized controlled trial found that metoclopramide with diphenhydramine was effective at treating post-traumatic headache in the ED; however, the proportion with migraine semiology was not reported.[170] Pending future data to inform otherwise, we recommend ED patients with post-traumatic headache of migraine semiology be treated with migraine-specific therapy with specific consideration of metoclopramide with diphenhydramine.

PREVENTION OF RECURRENT MIGRAINE ATTACKS

Aside from treating migraine attacks to resolution, ED practices that may prevent recurrence include administering corticosteroids, recommending migraine nutraceuticals, and prescribing daily preventive medications where indicated.

Dexamethasone

Three meta-analyses demonstrated that dexamethasone is safe and effective at reducing headache recurrence from migraine.[171-173] For moderate-severe migraine attacks in the ED, dexamethasone 10 mg intravenously should be

offered in the absence of contraindications (American Headache Society Level B recommendation).[70] Adverse effects from a single dose of dexamethasone are rare and generally mild (eg, flushing, nausea, and paresthesias).[174,175]

Preventive Medications: Migraine Nutraceuticals and Daily Prescription Medications

The benefit of migraine preventives is well established, and they have been shown to decrease ED usage.[176] A systematic review and meta-analysis, including 66 randomized controlled trials, found that migraine preventives are associated with a more than 50% reduction in headache frequency.[177] Still, only a minority of eligible patients are prescribed preventive medications.[2] Given that migraine is associated with a high burden of disability and significant ED usage, all eligible patients should be offered preventive medications in the ED or promptly by their primary care provider (Table 4). Indications to consider preventive agents include:[178]

1. High frequency of attacks: 8 or more headache days/month, or 4 or more headache days/month not responding reliably to acute therapy;
2. At risk of medication-overuse headache;
3. Contraindications to acute therapy;
4. Severe attacks with significant functional impairment (eg, hemiplegic migraine attacks).

The Canadian Headache Society strongly recommends nutraceuticals for patients with migraine who meet the criteria for preventive interventions.[178] A limited number of trials have shown benefit from nutraceuticals in reducing migraine severity and frequency, while having minimal side effects and excellent tolerability.[179] One or more of magnesium citrate, coenzyme Q10, and riboflavin can be prescribed safely in the ED (Table 4).

In choosing a preventive medication, patient preference, comorbidities, side-effect profile, and drug-drug interactions should be considered. The 3 medications with the highest level of evidence for efficacy and strongest recommendations from the American Academy of Neurology (AAN) and Canadian Headache Society include metoprolol (or propranolol), topiramate, and amitriptyline.[178,180] Other medications from different drug classes that could be considered include gabapentin, candesartan, venlafaxine, and valproic acid.

Patients started on preventive therapy should follow up with their primary care provider, and those who have failed preventive medications should be referred to a neurologist for consideration of medication optimization, botulinum toxin-A injection, or preventive CGRP-pathway antagonist therapy.[178,180-182]

DISCHARGING PATIENTS: INSTRUCTIONS AND COUNSELING

The primary goal of treating acute migraine attacks in the ED is to achieve full resolution of symptoms (or as close as possible)[69,70] and, in turn, decrease attack recurrence, reduce persistent debilitating symptoms, and lower the risk of developing chronic migraine from incomplete treatment.[12,183,184] Although this is ideal, for some patients achieving a modest relief of symptoms after a reasonable attempt with multiple agents can be sufficient.[185] Providing patients with a prescription for an acute medication equips them with a treatment they can use at home to avoid ED visits. Lastly, counseling patients on trigger avoidance and cautious medication use can help reduce migraine morbidity.

Lifestyle Modifications

Lifestyle modifications that may decrease migraine attack frequency and severity include reducing alcohol consumption, avoiding dehydration, safeguarding against hunger by meal planning, increasing physical activity, improving sleep hygiene, and limiting caffeine to fewer than 2 days/week.[181,186-188] Additionally, patients should keep a headache diary to identify their own triggers and protective factors. Large high-quality studies are still needed to support many of these common recommendations. A patient handout with discharge recommendations can be found in Figure 5.

Use of Acute Therapy

Acute medications are most effective when used as soon as a migraine attack is recognized. Patients should be encouraged to treat all migraine attacks to avoid prolonged exposure and central sensitization. The use of acute medications should be limited to 10 days/month (15 if acetaminophen or NSAID monotherapy only) to avoid medication-overuse headache; patients at risk of medication-overuse headache should be considered for initiation of preventive therapy and referred to neurology.

CONCLUSIONS

Migraine is a leading reason for patients to visit the ED and a significant driver of global morbidity. The primary goal of treating acute migraine attacks in the ED is symptom resolution with evidence-based migraine treatments. There is no role for opioids in treating migraine in the ED. Eligible patients should be offered daily preventive therapy to reduce

the frequency and severity of migraine attacks. There is an emerging role for the integration of nerve blocks for treating migraine attacks in the ED, though further research in this area is required. Gepants and ditans are promising categories of medications to effectively treat migraine attacks, though they have not yet been studied in the ED setting.

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