

ACUTE TREATMENT OF MIGRAINES

Bridget Keller, M.D.
Assistant Professor of Neurology
Lake Erie College of Medicine
Bradenton, FL
bkeller@lecom.edu

LEARNING OBJECTIVES

- Understand the cost-effective patient-centered approach to treatment of migraines - Stratified care
- Know the evidenced based treatment options currently available for aborting migraine.
- Describe strategies for improving treatment response

WHAT IS A MIGRAINE HEADACHE?

International Classification of Headache Disorders

- ≥ 5 Headaches lasting 4-72hrs (untreated or unsuccessfully treated)
- **H/A has at least 2 of the 4**
 - Unilateral – can vary side to side
 - Pulsating quality
 - Moderate/severe intensity
 - Aggravated by routine activity (walking or climbing stairs)
- **During the H/A at least 1 of the 2**
 - Photophobia and Phonophobia
 - Nausea and/or vomiting

TREATMENT SUCCESS

- Medication Selection
- Dosing
- Route of Administration
- Timing of Administration
- Safety
- Tolerability
- Whether treatment addresses patient's definition of effectiveness

MODELS OF ACUTE TREATMENT

- **Step care across attacks** – usually inexpensive nonspecific analgesic medication. If unsuccessful return to provider for different medication along step-wise pattern.
 - Drawback – if unsuccessful it may lead to suboptimal and delayed treatment as patients wait for f/up appointments.
- **Step care within attacks** - patient counseled to initiate txt with low cost nonspecific analgesic med and if unsuccessful, can advance themselves to more migraine specific txt option along stepwise pattern within the attack.
 - Drawback – can still lead to suboptimal efficacy of txt as many migraine-specific treatments (ie. triptans) are best taken early in attack

MODELS OF ACUTE TREATMENT CONT'D

- **Stratified Care**- patient is entrusted with determining which attacks will respond to various treatments and is given autonomy to make appropriate treatment decision based on his/her personal experiences and preferences.
- **Stratified Care** best considers individual variance in headache severity and associated features (nausea,vomiting).
- **Stratified Care** is associated with higher patient satisfaction and also with decreased health care costs.

EXAMPLE OF STRATIFIED CARE

- 45-year-old man presents for evaluation of frequently occurring episodic migraine. Reports 6 headache days/month.
 - 2 days/month – severe, incapacitating, responsive to triptan
 - 4 days/month – mild-moderate, able to work through it with mild impairment in ability to function. Takes nonsteroidal anti-inflammatory
- Patient prefers two prescriptions – triptan for severe headaches, Motrin 600mg for less severe headaches because feels triptan is 'overkill'
- Encourage patient to treat with medication commensurate to his attack severity and degree of disability.
- Monitor for overuse.

AMERICAN HEADACHE SOCIETY ACUTE TREATMENT OF MIGRAINE GUIDELINES

- Level A evidence (established as effective for acute migraine treatment)
 - All triptans
 - OTC analgesics and NSAIDS (APAP, Ibuprofen, naproxen)
 - Dihydroergotamine (DHE) nasal spray
 - Diclofenac
- Level B evidence (probably effective)
 - Ketorolac, Ketoprofen
 - Codeine/acetaminophen
- Level C evidence (possibly effective)
 - Butalbital/APAP/caffeine
 - Parenteral opiates

Medication and Dose	American Headache Society Evidence Assessment*	Canadian Headache Society Quality of Evidence	Canadian Headache Society Recommendation
Analgesics			
Acetaminophen 1000 mg	Level A	High	Strong
Nonsteroidal anti-inflammatory drugs			
Acetylsalicylic acid 500 mg	Level A	High	Strong
Diclofenac 50 mg, 100 mg	Level A	High	Strong
Ibuprofen 200 mg, 400 mg	Level A	High	Strong
Naproxen 500 mg, 550 mg	Level A	High	Strong
Triptans			
Almotriptan 12.5 mg	Level A	High	Strong
Eletriptan 20 mg, 40 mg, 80 mg	Level A	High	Strong
Frovatriptan 2.5 mg	Level A	High	Strong
Naratriptan 1 mg, 2.5 mg	Level A	High	Strong
Rizatriptan 5 mg, 10 mg	Level A	High	Strong
Sumatriptan (oral) 25 mg, 50 mg, 100 mg	Level A	High	Strong
Sumatriptan (intranasal) 10 mg, 30 mg	Level A	High	Strong
Sumatriptan (subcutaneous) 4 mg, 6 mg	Level A	High	Strong
Zolmitriptan (oral) 2.5 mg, 5 mg	Level A	High	Strong
Zolmitriptan (subcutaneous) 2.5 mg, 5 mg	Level A	High	Strong
Ergots			
Dihydroergotamine (intranasal) 2 mg	Level A	Moderate	Weak
Dihydroergotamine (subcutaneous) 1 mg	Level B	Moderate	Weak
Dihydroergotamine (IV, IM) 1 mg	Level B	N/A	N/A
Combinations			
Sumatriptan/naproxen 85 mg/500 mg	Level A	High	Strong
Acetaminophen/acetylsalicylic acid/caffeine 500 mg/500 mg/130 mg	Level A	N/A	N/A
Recommendation for Nonsedative Use in Episodic Migraine			
Oral opioid and tramadol combinations			
Tramadol/acetaminophen 75 mg/650 mg	Level B	Moderate	Weak
Codine/acetaminophen 25 mg/400 mg	Level B	Low	Weak
Codine 30 mg	Level C	Low	Weak
Ergots			
Ergotamine 1-2 mg	Level C	Moderate	Weak
Recommendation Against Use in Episodic Migraine Except Under Unusual Circumstances			
Opioids			
Butorphanol (intranasal) 1 mg	Level A	Low	Strong
Butabital-containing medications			
Butabital/acetaminophen/caffeine 50 mg/325 mg/40 mg	Level C	Low	Strong
Butabital/acetaminophen/caffeine/codine 50 mg/325 mg/40 mg/30 mg	Level C	Low	Strong

*0 = intramuscular; NS = intravenous; N/A = not applicable.
*Data from Marmura MJ, et al. Headache.⁷ and Worthington I, et al. Can J Neurol Sci.⁸
Level A = medications are established as effective for acute migraine treatment based on available evidence; Level B = medications are probably effective based on available evidence; Level C = medications are possibly effective based on available evidence.

ACUTE MEDICATIONS WITH LEVEL A EVIDENCE

Class	Drug	Dose
Analgesic	Acetaminophen	1,000 mg PO (for non-incapacitating attacks)
Ergots	Dihydroergotamine	2 mg NS 1 mg pulmonary inhaler
NSAIDs	Aspirin	500 mg PO
	Diclofenac	50 mg or 100 mg PO
	Ibuprofen	200 mg or 400 mg PO
	Naproxen	500 mg or 550 mg PO
Opioids	Butorphanol	1 mg NS
Triptans	Almotriptan	12.5 mg PO
	Eletriptan	20 mg, 40 mg, or 80 mg PO
	Frovatriptan	2.5 mg PO
	Naratriptan	1 mg or 2.5 mg PO
	Rizatriptan	5 mg or 10 mg PO
	Sumatriptan	25 mg, 50 mg, or 100 mg PO 10 mg or 20 mg NS 4 mg or 6 mg SC
	Zolmitriptan	2.5 mg or 5 mg PO or NS
Combinations	Acetaminophen/aspirin/caffeine	500 mg/500 mg/130 mg PO
	Sumatriptan/naproxen	85 mg/500 mg PO

Abbreviations: NS, nasal spray; NSAIDs, nonsteroidal anti-inflammatory drugs; PO, oral medication; SC, subcutaneous injection.

Singh R, et al. Migraine Acute Therapies. Practical Neurology. 2019;18(4):63-67.

TRIPTANS

- Serotonin agonists that bind 5-hydroxytryptamine 5-HT_{1B/1D} receptors.
- All triptan and triptan combination meds have strong evidence for effectiveness for acute treatment of migraine at standard doses.
 - 42%-76% of patients experience pain relief at 2 hrs. (vs. 27% with placebo).
 - 18-50% of patients pain free at 2 hrs (vs 11% with placebo)
 - 29%-50% of patients experience pain relief at 24 hrs (vs. 17% with placebo).
 - 18-33% of patients pain free at 24hrs (vs 10% with placebo)

Cameron C, Kelly S et al Triptans in the acute treatment of migraine: a systematic review and network meta-analysis. *Headache* 2015;55(Suppl 4):221-235

TRIPTAN COMBINATION TXT

- Several studies have shown combination of sumatriptan and naproxen (85mg/500mg) to be effective for acute txt of migraine vs placebo.
- Some studies showing statistical superiority to sumatriptan or naproxen monotherapy.
- Large, multicenter, randomized, double-blind, placebo controlled 4-arm study with endpoint of 24hr sustained pain-free response:
 - Combo sumatriptan + naproxen - 46% pain free
 - Sumatriptan monotherapy - 29% pain free
 - Naproxen monotherapy- 25% pain free
 - Placebo - 17% pain free

Smith TR, Sunshine A et al. Sumatriptan and naproxen sodium for the acute treatment of migraine. *Headache* 2005;45(8):983-991

TRIPTAN SIDE EFFECTS AND CONTRAINDICATIONS

- Contraindications
 - History of stroke or MI
 - Coronary Artery Disease (CAD)
 - Hemiplegic migraine
 - Migraine with brainstem aura
 - Uncontrolled Hypertension
 - Peripheral vascular disease (PWD)
- Common Side effects
 - Tingling
 - Warmth
 - Flushing
 - Chest discomfort
 - Dizziness
 - Drowsiness
- Warn patients ahead of time.

WHICH TRIPtan TO USE?

Category	Usage	Triptan
Immediate acting/ultra fast injectable	Quick onset, severe pain	Sumatriptan subcutaneous
Fast acting	Moderate onset, moderate pain	Sumatriptan oral/nasal, Eletriptan, Rizatriptan (oral/melt) Zolmitriptan (oral/melt/nasal) , Almotriptan
Slow onset, long acting	Slow onset, long duration, menstrual; prodrome	Frovatriptan, Naratriptan

NONSPECIFIC ANALGESICS

- Acetylsalicylic Acid
- Acetaminophen
- Ibuprofen
- Naproxen
- Diclofenac
- All efficacious compared to placebo in acute treatment of migraine
- Potentially useful options for treating mild to moderate headache (stratified care model)
- Performed only slightly less effectively than triptans when compared to placebo
- Generally well-tolerated

ACETYLSALICYLIC ACID

- Acetylsalicylic acid – 1000mg similar efficacy to sumatriptan. Superior to placebo in several studies.
 - Combine with metoclopramide 10mg if patient has nausea
 - Effervescent formulation preferred by some patients
 - BC powder Original = 845mg aspirin/65mg caffeine
 - BC powder Arthritis Pain = 1000mg aspirin/65mg caffeine

NAPROXEN/IBUPROFEN

- Naproxen – meta-analysis included 4 randomized, double blind, placebo controlled studies showed naproxen sodium superior to placebo with regard to:
 - 2 hour pain relief
 - 2 hour pain freedom
 - 2 hour relief associated with nausea, photophobia and phonophobia.
- Ibuprofen – large, multicenter, double blind placebo controlled study of 660 subjects showed ibuprofen 200mg and 400mg more effective for acute migraine not requiring bedrest or associated with nausea >20% of time.
 - 400mg outperformed 200mg dose.

Suthisang CC et al. Meta-analysis of the efficacy and safety of naproxen sodium in the acute treatment of migraine. Headache 2010;50(5):808-818.

Suthisang C et al. Efficacy of low dose ibuprofen in acute migraine treatment: systematic review and meta-analysis. Ann Pharmacother 2007;41(11):1782-1791

DICLOFENAC

- Several randomized, double-blind, placebo-controlled studies and a Cochrane Review have shown efficacy of diclofenac for acute treatment of migraine vs placebo.
 - Oral tablet- 50mg
 - Powder dissolved in 1-2 ounces water.
 - Diclofenac with potassium bicarbonate buffer that allows diclofenac to remain in solution as it enters the stomach.
 - Once mixed with water the buffered preparation becomes ionized. In acidic stomach the ionized diclofenac is protonated, facilitating faster absorption in small intestine → faster peak plasma concentration.

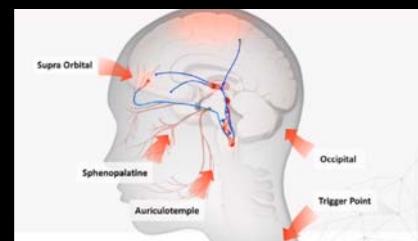
Diener HC et al. Efficacy and tolerability of diclofenac potassium sachets in migraine: a randomized, double blind, cross-over study in comparison with diclofenac potassium tablets and placebo. Cephalgia 2006;26(5):537-547

PARENTERAL TREATMENTS FOR ACUTE MIGRAINE ATTACK

- No meds having level A evidence identified by American Headache Society
- Level B evidence (probably effective)
 - Chlorpromazine 12.5mg (25mg/ml), Droperidol 2.75mg, Metoclopramide 10mg, prochlorperazine 10mg (also given IM)
 - Dihydroergotamine 1mg (also SC, IM)
 - Ketorlac 30mg-60mg (also IM)
 - Magnesium sulfate 1g -2g (migraine with aura)
- Level C (possibly effective)
 - Valproate 400mg-1000mg
 - Tramadol 100mg
 - Dexamethasone 4mg – 16mg

NERVE BLOCKS

- Few Retrospective & Non-controlled prospective studies have shown efficacy for
 - Greater occipital
 - Suprartochlear
 - Supraorbital
 - Sphenopalatine ganglion nerve blocks
- Reported to provide long-term improvement lasting weeks as well as resolution of allodynia
- Despite relative lack of evidence, nerve blocks generally accepted as safe/well tolerated
- Well designed studies will be necessary to better delineate efficacy and cost-effectiveness of these treatments for migraine.



NEUROMODULATION TO ABORT MIGRAINE

- Neuromodulation - functional modification of neural circuits with electromagnetic current, delivered noninvasively or via implanted devices.
- Advantages:
 - High tolerability
 - Minimal contraindication
 - No risk of medication overuse
 - Potential efficacy
- Disadvantages:
 - Cost
 - Lack of insurance coverage
- 4 noninvasive devices available for clinical use

TRANSCRANIAL MAGNETIC STIMULATION

- In 2014, FDA approved Single pulse transcranial magnetic stimulation for acute treatment of migraine with aura.
 - Pain free response at 2 hrs - 39% (vs 22% sham stimulation)
 - Sustained pain free response at 24 hrs – 29% (vs 16% placebo)
 - Sustained pain free response at 48 hrs – 27% (vs 13% placebo)



Rental – \$150/month
for first 3 months;
\$200/month for the
first year thereafter

VAGAL NERVE STIMULATION

- Vagal nerve stimulation: used for both abortive and preventative therapy.
 - In 1 open label study for acute self treatment of 3 migraine attacks in 3 week period 64% subjects had pain relief within 2 hrs. 39% reported freedom from pain.
 - Randomized sham-controlled study nVNS superior to sham for acute treatment as early as 30 and 60minutes after onset
 - No difference 120minutes after pain onset.
 - Minimal adverse events, more often reported in Sham group
 - Lip or face pulling
 - Dizziness, neck pain, burning, soreness

Tassorelli C et al. Noninvasive vagus nerve stimulation as acute therapy for migraine: The randomized PRESTO study. *Neurology* 2018;91:e364-e373

VAGAL NERVE STIMULATOR FOR H/A TREATMENT

gammaCore



- First noninvasive hand held VNS applied at the neck.
- FDA approved April 2017 for acute tx of episodic cluster headache
- FDA approved January 2018 for tx of migraine

EXTERNAL TRIGEMINAL NERVE STIMULATION

- Transcutaneous eTNS is delivered with a device worn over the forehead, designed to stimulate the bilateral supratrochlear and supraorbital nerves.
- For acute migraine treatment, 1 hr of eTNS within 3 hours of migraine onset = 57% pain reduction.
- In 24 hrs after used ~35% reported decreased use of rescue medication
- Most frequently reported Adverse Event:
 - Paresthesias



PERIPHERAL ELECTRICAL STIMULATION (PES)

- Electrode placed on upper arm generates a non-painful electric stimulus thought to exert a generalized analgesic effect through conditioned pain modulation (CPM) via activation of inhibitory pathways.
 - Randomized sham controlled trial (n=71), 64% pts who had 20minutes of PES soon after migraine attack onset had at least 50% ↓ pain in > ½ their treated attacks vs 26% (sham stimulation).
 - Prospective randomized sham-controlled multicenter trial (n=252). Pts treated h/a attack within 1 hr of onset. Results shown on next slide.
 - Adverse effects: discomfort, no serious AEs reported.

Yamitsky D, Volokh L et al. Nonpainful remote electrical stimulation alleviates episodic migraine pain. Neurology. 2017;88:1250-5.

REMOTE ELECTRICAL NEUROMODULATION



Nerivio Migra

- FDA Approved 5/2019
- Smart phone controlled wireless device
- 30-45minutes
- Electrical stimulation perceptible but not painful.

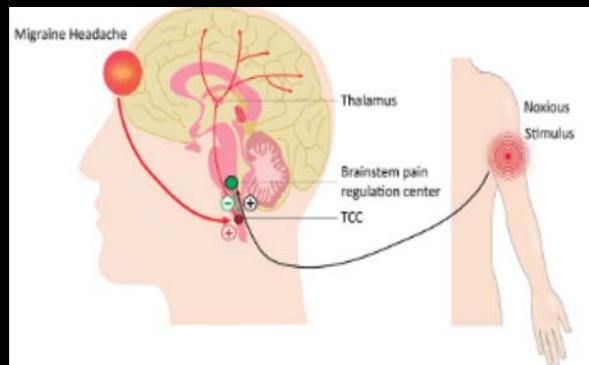
Prospective randomized sham-controlled multicenter trial (n=252)

	Active	Sham
2hrs ↓ h/a pain	66.7%	38.8%
Resolution of h/a at 2hrs	37.4%	18.4%
↓ Most bothersome sx(mbs)	46.3%	22.2%
↓ in combo of h/a and mbs	40%	15.2%

Yarnitsky D, Dodick D et al. Remote Electrical Neuromodulation (REN) Relieves Acute Migraine: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. *Headache*. 2019

REMOTE ELECTRICAL NEUROMODULATION

- Stimulation of C and A δ noxious sensory fibers in upper arm
- Ascending pain pathway to brainstem (black)
- Activation of descending pain inhibitory pathway (green)
- Release of serotonin and noradrenalin which inhibit incoming messages of pain in the trigeminal cervical complex (TCC) that occur during a migraine attack (red)



Yarnitsky D, Dodick D, et al. Remote Electrical Neuromodulation (REN) Relieves Acute Migraine: A Randomized Double-Blind, Placebo-Controlled, Multicenter Trial. *Headache*. 2019.

NONINVASIVE NEUROMODULATION DEVICES FOR TREATMENT OF MIGRAINE

Mode	Device/ Manufacturer	FDA- Approved	Migraine indication	CH indication	Evidence
nVNS	gammaCore/ electroCore	YES	Acute treat- ment in adults age 18 and up	Acute treat- ment and adjunctive preventive treatment for adults > age 18	Adjunctive treatment reduced frequency of CH and provided benefit for acute treatment of ECH For CM or high-frequency EM, 64% had pain relief with 40% of those achieving freedom from pain For EM, nVNS superior to sham at 30 or 60 minutes, although not statistically different at 120 minutes
sTMS	sTMSMini/ eNeura	YES	Acute and preventive treatment in adults and adolescents > age 12 years		In pivotal trial, 39% given active stimulation had pain relief vs 22% with sham stimulation; at 24 and 48 hours, 29% and 27% of people who had active stimulation, respectively, had continued relief vs 16% and 13% with sham stimulation Active stimulation using a preventive protocol resulted in 2.75 fewer mean headache days per month
eTNS	Multiple/ Cefaly	YES	Acute and preventive treatment of migraine in adults age 18 and up		Active stimulation (20 minutes daily for 3 months) reduced mean number of headache days/month; the 50% responder rate for active vs sham treatment was 38.1% vs 12.1% In prospective open-label study, 1 hour of treatment within 3 hours of treatment reduced pain by 57.1%. 2 hours of treatment reduced pain by 52.8%, and only 34.6% used rescue medication for following 24 hours
PES	Nervio Migra/ Theranica	NO YES	Acute treat- ment in adults age 18 and up		Active stimulation for 20 minutes, soon after the migraine attack onset, resulted in 64% of the treated patients to have at least 50% pain reduction in more than half of their treated attacks, compared to only 26% of the participants in the sham group

Abbreviations: CH, cluster headache; CM, chronic migraine; EM, episodic migraine; eTNS, external trigeminal nerve stimulation; nVNS, noninvasive vagus nerve stimulation; PES, peripheral electrical stimulation; sTMS, single-pulse transcranial magnetic stimulation.

Najib, U; Frey, J et al. Neuromodulation Therapies for Headache. *Practical Neurology*. 2019;18(4):80-84

MANIPULATIVE MEDICINE AND MIGRAINE

- Osteopathic Manipulative Treatment – Nonpharmacologic, noninvasive manual medicine
- Osteopathic providers use a wide variety of therapeutic manual techniques to improve physiological function and help restore homeostasis altered by somatic dysfunction.
- Cranial treatments to abort migraine:
 - Occipitoatlantal decompression
 - Venous sinus drainage
 - Compression of the Fourth Ventricle (CV-4 technique)

CALCITONIN GENE RELATED PEPTIDE

- Neuropeptide belonging to the calcitonin family
- Potent vasodilator of cerebral arteries
- Released into jugular venous system during migraine
- Serum CGRP levels are elevated in patients with chronic migraine
- CGRP infusion evokes migraine
- Small molecule CGRP-receptor antagonists (gepants) effectively **abort migraine attacks** and are being studied for migraine prevention.
- Large molecule anti-CGRP and anti-CGRP receptor monoclonal antibodies(mAbs) prevent episodic and chronic migraine

CALCITONIN GENE-RELATED PEPTIDE ANTAGONISTS

- Small molecules (Gepants)
 - 1st anti-CGRP medications developed. 6 have been tested in acute treatment, 3 in active investigation
 - Block CGRP from vasodilating
 - Do not cause vessels to constrict
 - Viable treatment option in patients with cardiovascular risk factors who are unable to take triptans or ergotamines.
- **Ubrogепант , rimegeپант, atogepант**
- Gepants show ~20-25% pain free rate at 2 hours (vs placebo) and no serious adverse SEs.

Voss T, Lipton RB et al A phase IIb randomized, double-blind, placebo-controlled trial of ubrogeпант for the acute treatment of migraine. Cephalgia 2016;36(9):887-898

5-HT_{1F} AGONISTS

- Early studies have shown agonism of the 5-HT_{1F} (serotonin) receptor to be effective for acute treatment of migraine
 - Anti-inflammatory effects
 - Does not produce vasoconstriction
- Lasmiditan – in phase 3 studies superior to placebo RE: 2-hr pain-free response at 100mg and 200mg (28% &32% vs 15%)
 - Most common adverse events- dizziness, paresthesias, somnolence, nausea, fatigue. Mild-moderate & self limited

ASSESS RESPONSE TO TREATMENT

- At follow up visits ask specific questions – EFFICACY , TOLERABILITY
- DON'T ASK – “Is it working?” This doesn't address:
 - Speed of onset
 - Degree of improvement (efficacy)
 - Recurrence of headache
 - Tolerability
- 30-40% of triptan users are dissatisfied with or respond suboptimally¹
- 4-Item Migraine Treatment Optimization Questionnaire (mTOQ-4)
 - Validated questionnaire that can help assess treatment optimization

1. Viana M, et al. Triptan nonresponders: do they exist and who are they? *Cephalgia* 2013;33(11):891-896

MIGRAINE TREATMENT OPTIMIZATION QUESTIONNAIRE (MTOQ-4)

Domain	Never/ Rarely	Less Than Half the Time	Half the Time or More
After taking your migraine medication, are you pain free within 2 hours of most attacks?	0	1	2
Does one dose of your migraine medication relieve your headache and keep it away for at least 24 hours?	0	1	2
Are you comfortable enough with your migraine medication to be able to plan your daily activities?	0	1	2
After taking your migraine medication, do you feel in control of your migraines enough so that you feel there will be no disruption to your daily activities?	0	1	2
Subtotal			Total of all columns ^b

^a Data from Lipton RB, et al, Cephalgia.⁵⁷
^b Scoring is as follows: 0 = very poor treatment efficacy; 1-5 = poor treatment efficacy; 6-7 = moderate treatment efficacy; 8 = maximum treatment efficacy.

Vargas, Bert B. Acute Treatment of Migraine
 CONTINUUM: Lifelong Learning in Neurology 24(4):1032-1051, August 2018.

CASE 1

- A 32-year-old woman with a hx of episodic migraine with aura was seen for a 3-month follow-up visit. Started on a new medication at her last visit.
- Current visit, she stated her response to treatment had been “good.”
- Answers to specific questions revealed she could fully abort each attack with her new medication when taken early, but she frequently delayed treatment or avoided treatment altogether because of the presence of medication SEs (nausea, chest tightness), which impaired her ability to function at work.
- When she delayed treatment, she often noted that her acute attacks improved but did not fully resolve. She had a total score of 5 on the four-item Migraine Treatment Optimization Questionnaire (mTOQ-4) administered in clinic.

CASE 2

- A 22-year-old woman presented for consultation regarding her 4-year history of episodic migraine without aura with a time to peak severity of under 1 hour and prominent nausea and vomiting with most attacks. She stated that her orally administered acute treatment was effective only if she took it immediately and only if she could avoid vomiting.
- 2 Barriers to Effective Treatment
 - Rapid onset of maximal pain
 - Difficulty taking oral medication
- Change to intranasal or injectable
 - Faster onset of action
 - Bypasses GI system

Treatment	Onset (Minutes)	T _{max} (Hours) ^a	Half-life (Hours)	Maximum Daily Dose
Triptans				
Alimoclitin	30-120	1.4-3.8	3.2-5.7	25 mg
Eltroclitin	30	1.0-2.0	3.6-5.5	80 mg
Frovatriptan	120-180	2.0-4.0	25	7.5 mg
Naratriptan	60-180	2.0-3.0	5.0-6.3	5 mg
Rizatriptan (tablet)	30-120	1.2	2.0-3.0	30 mg (15 mg if taking propranolol)
Rizatriptan (orally disintegrating tablet)	30-120	1.6-2.5	2.0-3.0	30 mg (15 mg if taking propranolol)
Sumatriptan (tablet)	20-30	2.5	2.0	200 mg
Sumatriptan (nasal spray)	15	1.0-1.5	2.0	40 mg
Sumatriptan (nasal powder)	15	0.75	3.0	44 mg
Sumatriptan (injection)	10-15	0.2	1.7-2.0	12 mg
Sumatriptan/naproxen	20-30	1.0 (sumatriptan)/5.0 (naproxen)	2.0 (sumatriptan)/19 (naproxen)	2 tablets
Zolmitriptan (tablet)	45	2.0	2.5-3.0	10 mg
Zolmitriptan (orally disintegrating tablet)	45	3.3	2.5-3.0	10 mg
Zolmitriptan (nasal spray)	15	3.0	3.0	10 mg
Ergots				
Dihydroergotamine (nasal spray)	30	0.75	10	4 mg (maximum weekly dose 12 mg)
Simple analgesics				
Acetaminophen	30	0.5-1.0	2.0	4000 mg
Acetylsalicylic acid (effervescent)		0.3-0.5	0.25	2600 mg
Acetylsalicylic acid (tablet)	30	1.0-2.0	2.0-4.5 (<250 mg) 15-30 (>4000 mg)	4000 mg
Ibuprofen (tablet)	60	1.0-2.0	2.0	2400 mg
Naproxen sodium	30	2.0	14	1375 mg
Diclofenac potassium (tablet)	60	<1.0	2.0	150 mg
Diclofenac potassium (powder)	15	0.25	2.0	Safety and efficacy of a second dose not established

^a T_{max} refers to time to maximum plasma concentration.

CONTINUUM: LIFELONG LEARNING IN NEUROLOGY

Pharmacology of Acute Migraine Treatments

TROUBLE SHOOTING SUBOPTIMAL RESPONSE

Patient Response	Treatment Considerations
No response	Increase dose, ensure treatment is early, consider a need to change route of administration, try a different medication after two adequate trials
Partial response	Increase dose, ensure treatment is early, ensure a second dose is taken
Recurrence	Ensure treatment is early, ensure a second dose is taken, consider a longer-acting medication (TABLE 4-2), consider adding a complementary medication such as a nonsteroidal anti-inflammatory drug or antiemetic
Inconsistent response	Increase dose, consider a need to change route of administration
Overuse	Establish use limits and plan of care with patient, limit number prescribed, add prophylactic treatment

^a Courtesy of David W. Dodick, MD.

CONTINUUM: LIFELONG LEARNING IN NEUROLOGY

CASE 3

- 19-year-old male with hx of migraine with aura.
- 3 years of inconsistent response to Sumatriptan 25mg which previously gave complete and consistent relief since age 10.
- No changes in health or migraine history
- Tolerated Sumatriptan 25mg well.
- Problem – inconsistent response may reflect suboptimal dosing that was previously effective
- Solution – treat with adult dose of Sumatriptan 50mg or 100mg.

SUMMARY

- Stratified approach allows patients to make autonomous decisions for their attacks
 - Under the guidance of provider who helps patient select treatments based on their unique needs.
- Triptans, intranasal DHE, non-specific analgesics remain mainstays of 1st line treatment. Newer drugs (CGRP antagonists, 5-HT_{1F} agonists) on horizon.
- Factors to consider when selecting optimal txt include
 - Onset of action, Tmax, half-life, route of administration, time to peak severity, recurrence of h/a and patient preference.
- Response to treatment and patient satisfaction with txt should be assessed regularly