Up date on Treatment
Current and pipeline

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Migraine Treatment

• Age of patient
• Frequency of migraine
• Severity of headaches
• Severity of associated symptoms (MBS)
• Other comorbid condition(s)
• Other medical/health condition(s)
• Patients’ education
Migraine Treatment

Abortive (As needed)

All Migraine Patients

Preventive (Prophylactic)

Some Migraine Patients

> 1 migraine/week
Abortive Migraine Treatment

- **Simple analgesics**: Acetaminophen
- **Non-Steroidal Anti-Inflammatory Drugs**: OTC & Prescription
- **Triptans**: Gold standard, every migraine patient MUST have it, unless contraindication
- **Ergots**: Migranal Nasal spray, Cafergot, DHE injection, 2 new formulation on pipeline
- **Gpants**: UBRELVY, NURTEC
- **Ditans**: REYVOW
- **Devices**: NERIVIO, Cefaley, Spring TMS, Gamma core

Butalbital-containing analgesics (Fioricet/Fiorinal) and Opioids (including Tramadol) are not migraine medication.
DITANs and GPANTs

- In market: 2020
- In the pipeline:
  - Intranasal (Vazegepant) by Biohaven Pharma (BHV-3500)
## Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulations</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac potassium powder</td>
<td>Yes</td>
<td>50-mg packet every 2-4 h, maximum dose 150 mg/d</td>
<td>Excellent new migraine abortive. Useful in younger patients and in older individuals who can tolerate NSAIDs. Typical side effects of NSAIDs, primarily GI, may occur. May be combined with triptans; caffeine may be added to increase efficacy.</td>
</tr>
<tr>
<td>(Cambia)</td>
<td></td>
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<tr>
<td>Ibuprofen (Advil, Motrin,</td>
<td>No</td>
<td>400-800 mg every 3 h; maximum dose 2,400 mg/d</td>
<td>Available OTC and approved for children; occasionally useful in treating menstrual migraine. GI side effects are common. May be used with triptans; caffeine increases efficacy.</td>
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<tr>
<td>generic)</td>
<td></td>
<td></td>
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<tr>
<td>Naproxen (Anaprox, Aleve,</td>
<td>No</td>
<td>220 mg; usual dose, 500 mg, repeated in 1 h and again in 3-4 h;</td>
<td>Useful in younger patients; occasionally helpful for menstrual migraine. Non-sedating, but patients frequently report GI upset. First/usual dose is taken with food or a Tums; may be repeated in 1 h if no severe nausea is present, and again in 3-4 h. May be used with triptans; caffeine increases efficacy.</td>
</tr>
<tr>
<td>generic)</td>
<td></td>
<td>maximum dose 1,000 mg/d</td>
<td></td>
</tr>
<tr>
<td>Ketorolac (Toradol, generic;</td>
<td>Oral, IM, nasal spray</td>
<td>Injection: 60 mg/2 mL; repeat in 4 h if needed. Maximum dose,</td>
<td>Ketorolac intramuscular (IM) injections, which can be administered at home, are much more effective than tablets. Nausea or GI pain may occur. Ketorolac is nonaddicting and does not usually cause sedation. Limit to 3 injections/wk due to possible nephrotoxicity. IV ketorolac is very effective. There is a nasal spray form of ketorolac (Sprix), which may produce a burning feeling in the throat. Sprix is more effective than tablets but not as effective as IM.</td>
</tr>
<tr>
<td>Sprix nasal spray)</td>
<td></td>
<td>2 injections/d</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Oral: 2 tablets/d, at most</td>
<td></td>
</tr>
</tbody>
</table>
TRIPTANs

- Must be given unless contraindication
- In market since early 90s
- There are 7 types → there are NOT ALL the same plus certain patients tolerate one of the triptans better than another, therefore it is worthwhile to try several in an individual patient.
- The most effective way to use triptans is to take them early in the headache (the earlier a patient takes these agents, the better the effect)

After you have taken the first dose:

- If the triptan worked to relieve your headache but then the headache returned later, you can repeat the dose after 2-4 hours.
- Each triptan has a maximum daily dose that you should not exceed.
TRIPTANs in the pipeline

• Qtrypta: Zolmitriptan inter-cutaneous *microneedle* system – by Zosano pharma

• AXS-07: oral, consisting of MoSEIC *meloxicam* and *rizatriptan* – by Axsome therapeutic
TRIPTANs: side effect and contraindication

- **SIDE EFFECTs** (*Triptan sensation*): nausea; jaw, neck, or chest tightness, pressure or squeezing; feeling of throat swelling, rapid heart rate; fatigue; numbness-tingling (especially involving the face); or a burning sensation over the skin, sensation of warmth. 10-20%, it is **not** allergy, can use other triptan (AXETRT and AMERGE).

- **CONTRAINDICATIONs**
  - Coronary artery disease
  - History of stroke or TIA
  - Uncontrolled high blood pressure

> ALL triptan should be limited to **no more than 10 days** of use per month to avoid Rebound Headache.

**Triptan During Pregnancy**

- The accumulated evidence from *sumatriptan’s pregnancy registry* and other studies suggest that this drug is a **safe** therapeutic option for the treatment of migraine attacks in pregnant women. More studies are needed to confirm the safety of the other triptans in pregnancy; however, evidence to date is reassuring.
ERGOTs

- They were the first anti-migraine drugs available
- They have more side effects: Nausea / Vomiting / Dizziness

**Dihydroergotamine (DHE):** is the safest ergot derivative:
- DHE is primarily a “venoconstrictor,” with little arterial effects. This renders it very unlikely to cause cardiac problems. *(Indeed, since its introduction in 1945, DHE has been remarkably safe)*
- **Intravenous** DHE is a very effective migraine-abortive agent administered in the office or emergency room/hospital (*DHE infusion 3-5 days*)
- **Nasal** *(Migranal Nasal Spray)* have been found to be safe and effective as well.
- Sublingual Tablets(*Ergomar®*): 1 tab at the onset of headache, Another tablet should be taken at half-hour intervals; dosage must not exceed three tablets in any 24-hour period

**In the pipeline**

- Nasal powder formulation: *STS101- Satsuma Pharma*
- Upper nasal formulation using a proprietary Precision Olfactory Delivery (POD): *JNP104 – Impel Neuropharma*
DEVICES (Neuro-Stimulators)

- Supraorbital and supratrochlear nerve simulation (Cefaly device)
- Single-pulse Transcranial Magnetic Stimulation (sTMS)
- Vagus Nerve stimulator: gammaCore® (nVNS)
- Non-invasive remote electrical stimulation (Nerivio)
## Antiemetic Medications

- > 70% of migraine patients has nausea
- Even the one that does not have nausea, might have gastric stasis
- Compazine and Reglan has highest evidence, even some anti-migraine effect
- Droperidol uses less often now

### Drug Name (Brand)  |  Formulations/Dosage  |  Comments
---|---|---
Promethazine (Phenergan)  |  Available as tablets, suppositories, and oral lozenges  |  Mild but effective for most patients. Very sedating with a low incidence of serious side effects. Used for children and adults. Oral lozenges are formulated by compounding pharmacists.
Prochlorperazine (Compazine)  |  IV, tablets, long-acting spansules, and suppositories  |  Very effective but there is a high incidence of extrapyramidal side effects. Anxiety, sedation, and agitation are common. When given IV, it may stop the migraine pain as well as the nausea.
Metoclopramide (Reglan)  |  Oral, IM, and IV; dose: 5-10 mg  |  Mild, but well tolerated; commonly used prior to IV DHE. Fatigue or anxiety do occur, but usually are not severe. It is Pregnancy Category B (relatively safe).
Trimethobenzamide (Tigan)  |  Tablets, oral lozenges, and suppositories  |  Well tolerated, useful in children and adults. Oral lozenges are formulated by compounding pharmacists.
Ondansetron (Zofran, generic)  |  Oral tablets and disintegrating tablets; dose: 4 or 8 mg (usually 8 mg every 3 to 4 h pm)  |  A very effective antiemetic with few side effects but expensive. It is not sedating. Zofran is extremely useful for patients who need to keep functioning and not be sedated with an antiemetic. It is Pregnancy Category B (relatively safe).

### Muscle relaxants (carisoprodol, diazepam)

### Antipsychotic: Haloperidol
Interventional Treatment (Nerve Blocks)

Occipital Nerve Block
Interventional Treatment (Nerve Blocks)

Trigeminal Nerve Branches Block
Interventional Treatment (Nerve Blocks)

Sphenopalatine Ganglion Block
Preventive Migraine Treatment

Most Bothersome symptoms

Quality of life and function

Chronic Migraine

HIT-6

MIDAS
Preventive Migraine Treatment

- There is no algorithm to determine who is to go on preventive headache medication: The number of monthly headaches is one factor, along with comorbidities.
- Patients have to be willing to take daily medication (many do not want any daily meds). There is no absolute rule that applies to headache treatment.
- In using medication, a realistic goal is to decrease the headache frequency and severity not to completely eliminate the headaches.

- Patients should play an active role in medication choice: medications should be selected depending on the patient’s medical and psychological comorbidities, GI system, medication sensitivities, weight, sleep, family history of reaction to medications, finances, willingness to take daily meds, and many other factors.

According to the AMPP Study:

- More than 35% of people with migraine were candidates for a preventive
- Yet only about 10% were using a preventive

Why?!
Preventive Migraine Treatment

1. Supplements and Herbs

- **Feverfew**: Has anti-inflammatory effects, is a daisy-like perennial plant found commonly in gardens and along roadsides. Can cause a mild increased tendency toward bleeding, and should be discontinued two weeks prior to any surgery.

- **Petadolex (butterbur)**: is a purified form of the herb butterbur and is made of extracted plant certified by the German Health Authority.

- **Magnesium**: It has been shown that magnesium levels in the brains of migraine patients tend to be lower than normal. A dose of 400 or 500 mg per day can be used as a preventive.

- Miscellaneous herbs/supplements: vitamin B2; CoQ10 and fish oil hriboflavin, and feverfew.

The problem with many herbal supplements is quality control.
A. Blood pressure medication:
- Propranolol, Metoprolol, Nadolol, Tomolol
- Verapamil, Amlodipine, Flunarizine
- Candesartan

B. Anxiety/Depression medication:
- Amitriptyline (Elavil); nortriptyline (Pamelor)
- Venlafaxine (Effexor)

C. Anti-Seizure medication:
- Topiramate (Topamax, TROKENDI-XR, Qudexy-XR)
- Valproic acid (Depakote)

Off-Label: Gabapentin (Neurontin), Zonisamide (Zonegran), Memantine (Namenda), Cyproheptadine (Periactin), Cinnarizine, ...
Preventive Migraine Treatment

3. Botox injection

Only approved for Chronic Migraine (> 15 headache days/month)

Every 12 weeks

155-195 UNITS
Preventive Migraine Treatment

4. Monoclonal antibodies against CGRP

- Block the calcitonin gene-related peptide (CGRP)

- Blocking CGRP can reduce the migraine headache

- Sub-Q self injection
- IV infusion
- Monthly
- Quarterly
1 Injection - Once a month

First month 2 injection
After that 1 inj per month

1 injection – Once a month

3 injection – quarterly

Quarterly IV infusion (30 min)

**Side effects:** Hypersensitivity reaction (allergy), Injection site reaction, Constipation, increase blood pressure (so far with AIMOVIG)

**In the pipeline**

**Atogepant:** highly potent, orally-administered CGRP receptor antagonist