PATIENT EDUCATION DAY

Creating community and sharing knowledge for people with migraine and other headache disorders and their loved ones.

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Up date on Treatment
Current and pipeline

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MILES FOR MIGRAINE

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*)

Preventive
(*Prophylactic*)

ALL MIGRAINE PATIENTS

SOME MIGRAINE PATIENTS

> 1 migraine/ week

MILES FOR MIGRAINE

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

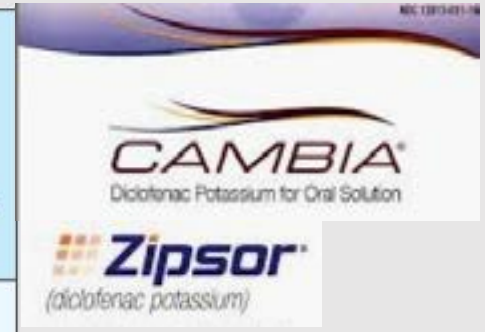
- **In the pipeline :**

- Intranasal (Vazegepant) by Biohaven Pharma (BHV-3500)

MILES FOR MIGRAINE

Non-Steroidal Anti-Inflammatory Drugs(NSAIDs)

Diclofenac potassium powder (Cambia)	Yes	Packets dissolved in water Available in boxes of 3 or 9 packets	50-mg packet every 2-4 h, maximum dose 150 mg/d	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.
Ibuprofen (Advil, Motrin, generic)	No	Liquid and oral tablet/ capsule	400-800 mg every 3 h; maximum dose 2,400 mg/d	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.
Naproxen (Anaprox, Aleve, generic)	No	Oral tablet and capsule	220 mg; usual dose, 500 mg, repeated in 1 h and again in 3-4 h; maximum dose 1,000 mg/d	Useful in younger patients; occasionally helpful for menstrual migraine. Nonsedating, 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.
Ketorolac (Toradol, generic; Sprix nasal spray)	Oral, IM, nasal spray	Injection: 60 mg/2 mL; repeat in 4 h if needed. Maximum dose, 2 injections/d Oral: 2 tablets/d, at most	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.	



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.

Drug Name (Brand)	Formulations	Usual Dosage	Comments
Almotriptan (Axert)	Oral tablet	12.5 mg every 3-4 h; limit to 25 mg/d	Similar to other triptans, almotriptan combines good efficacy with excellent tolerability. In 2009, almotriptan gained an official FDA indication for use in adolescents with migraine.
Eletriptan (Relpax)	Oral tablet	40 mg every 4 h; limit to 80 mg/d	Effective and well tolerated; minimal side effects include nausea, pressure in the throat, dizziness, and tiredness or weakness.
Frovatriptan (Frova)	Oral tablet	2.5 mg every 4 h; limit to 5 mg/d	Useful for slower-onset moderate or moderate to severe migraines; effective for preventing menstrual migraines. Long (26 h) half-life advantageous for patients with prolonged migraines. Mean maximal blood concentrations are seen approximately 2-4 h after a dose.
Naratriptan (Amerge, generic)	Oral tablet	1 tablet every 3-4 h; maximum 2 doses/d	Milder, longer-acting triptan. A generic form is available.
Rizatriptan (Maxalt, generic)	Oral tablet and rapidly disintegrating tablet	10 mg every 4 h; maximum 3 doses/d	Similar to sumatriptan (see below). Maxalt MLT (rapidly disintegrating tablets) are placed on the tongue; tablets have a pleasant taste and may be taken without water. Approved for use in children and adolescents. Side effects are similar to those of sumatriptan. A generic form is available.
Sumatriptan (Imitrex, generic; Onzetra Xsail nasal spray)	Oral tablet and nasal spray	Oral: 50 and 100 mg tablet every 2-3 h; maximum 200 mg/d Nasal spray: maximum daily dose 40 mg	More than 100 million people have used sumatriptan over the past 20 years. The generic form of sumatriptan is the least expensive triptan available.
Sumatriptan (Imitrex STAT dose, Sumavel DosePro, Alsuma, or generic prefilled syringes)	Subcutaneous injection	Injection: 4 and 6 mg every 3-4 h as needed; maximum dosing: twice daily	Although the usual dose had been 6 mg, the 4 mg STAT dose often is effective. A generic STAT form is available. Sumavel is a good "needle-free" option. Alsuma is a new EpiPen-type device containing 6 mg/0.5 mL of sumatriptan. A generic form is available. There are also generic, easy-to-use prefilled syringes of 6 mg sumatriptan.
Sumatriptan plus naproxen (Treximet)	Oral tablet	85 mg sumatriptan and 500 mg naproxen sodium. Dosage: 1 tablet every 3-4 h; maximum daily dose: 2 tablets	Treximet is an excellent combination drug that helps prevent recurrence of headache. The addition of naproxen may cause stomach pain or nausea.
Zolmitriptan (Zomig, generic tablets; Zomig 5 mg nasal spray)	Dissolvable tablet and nasal spray	Oral: 2.5 or 5 mg; usual dose 5 mg every 3-4 h as needed; maximum 10 mg/d Nasal spray: 2.5 or 5 mg	Zolmitriptan ZMT, 5 mg, is a pleasant-tasting, dissolvable tablet. Like Maxalt MLT, it provides an alternative to the oral tablets. A generic ZMT form is available. The nasal spray is very effective and works quickly.

Sumatriptan(IMITREX)

MILES FOR MIGRAINE

TRIPTANs in the pipeline

- **Qtrypta :** Zolmitriptan **inter-cutaneous *miscroneedle*** 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

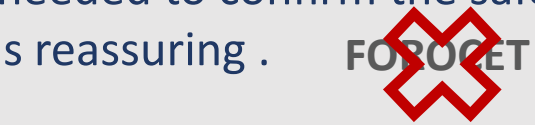
10-20 % , it is **not** allergy , can use other triptan (AXETRT and AMERGE)

- **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

Pregnancy : Contraindicated

- 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 24hour period

In the pipeline

Nasal powder formulation :

STS101- Satsuma Pharma

Upper nasal formulation using a proprietary Precision Olfactory Delivery (POD) :

INP104 – Impel Neuropharma

MILES FOR MIGRAINE

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)

Miscellaneous: off-label

▪ Antiemetic Medications

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

- Adding to NSAIDs , Triptan or Gpant is very helpful

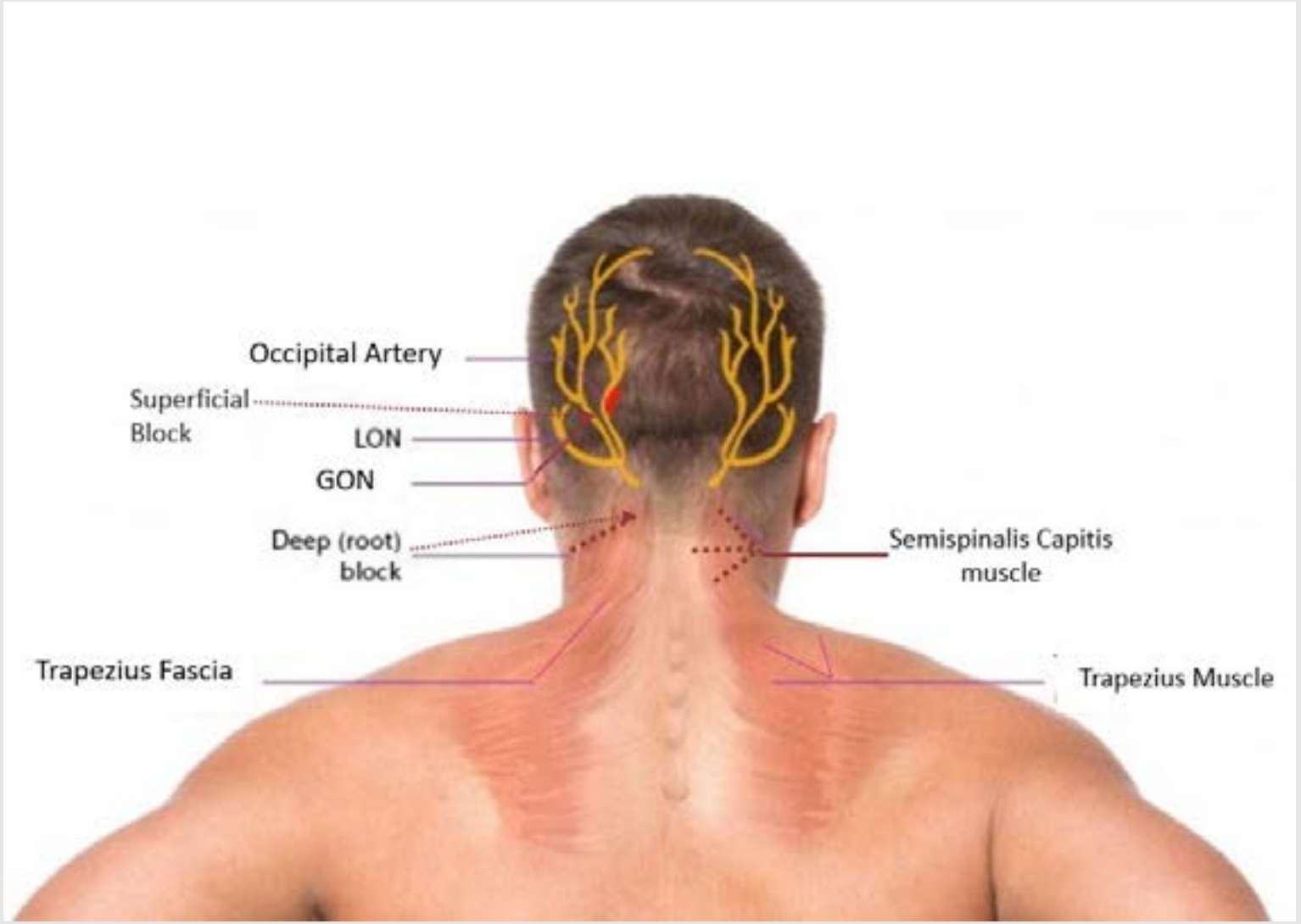
Drug Name (Brand)	Formulations/Dosage	Comments
Promethazine (Phenergan)	Available as tablets, suppositories, and oral lozenges	Mild but effective for most patients. Very sedating with a low incidence of serious side effects. Used for children and adults. Oral lozenges are formulated by compounding pharmacists.
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 prn)	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

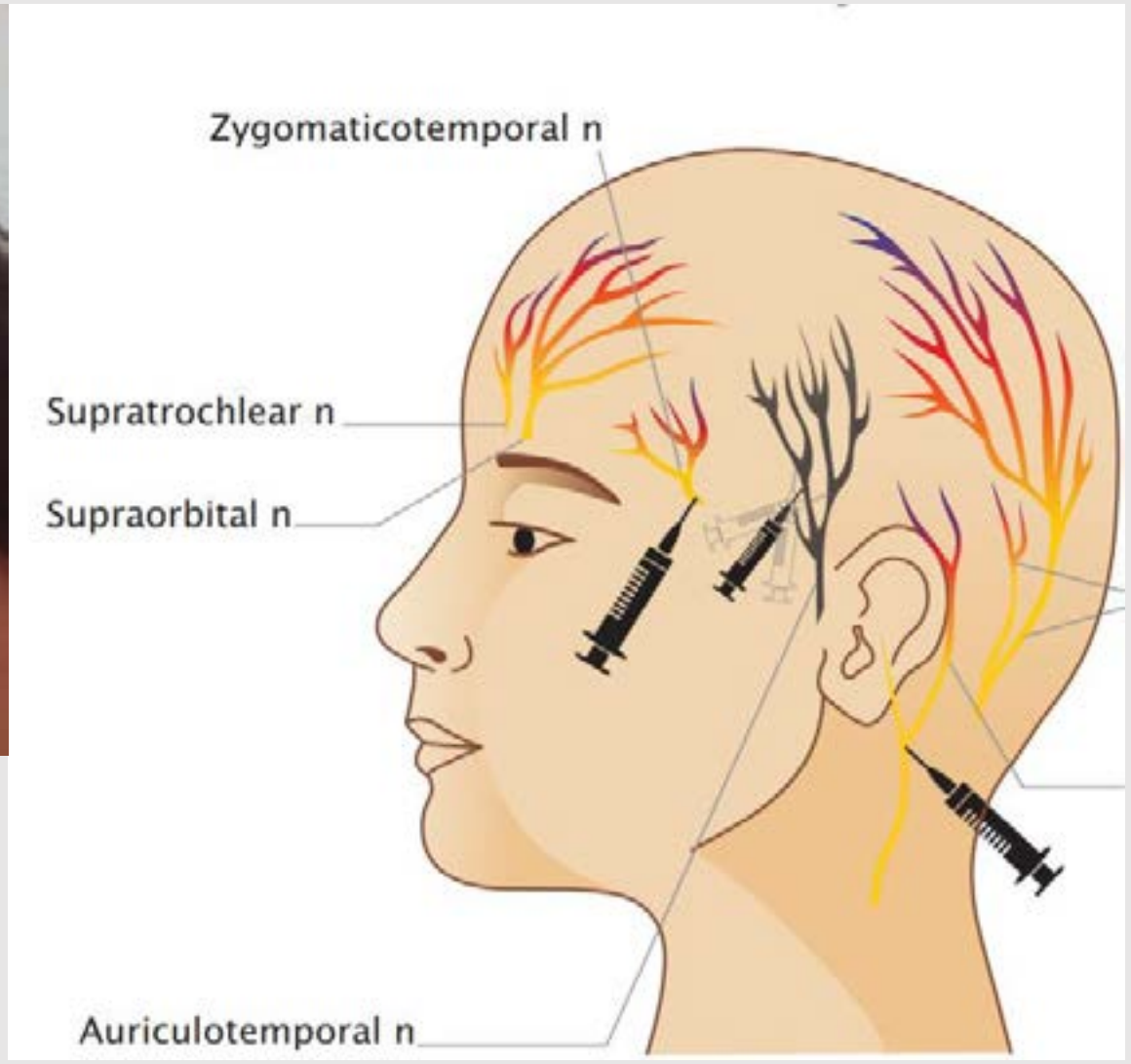
Interventional Treatment (*Nerve Blocks*)

Occipital Nerve Block



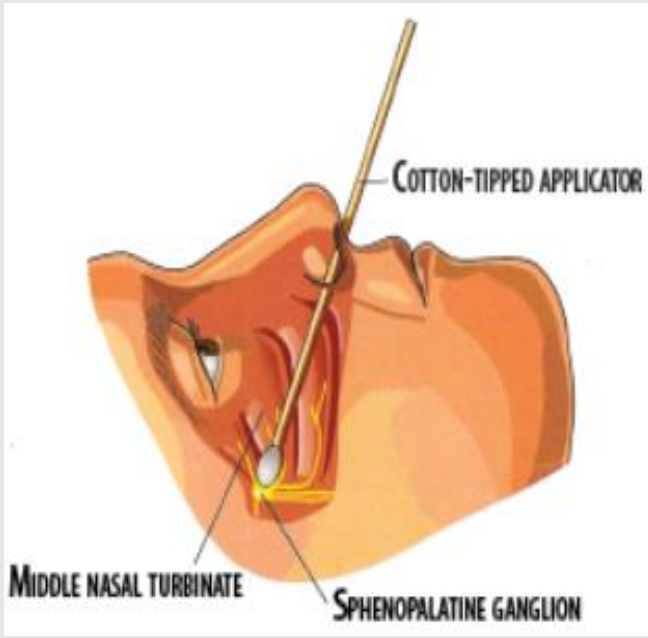
Interventional Treatment (*Nerve Blocks*)

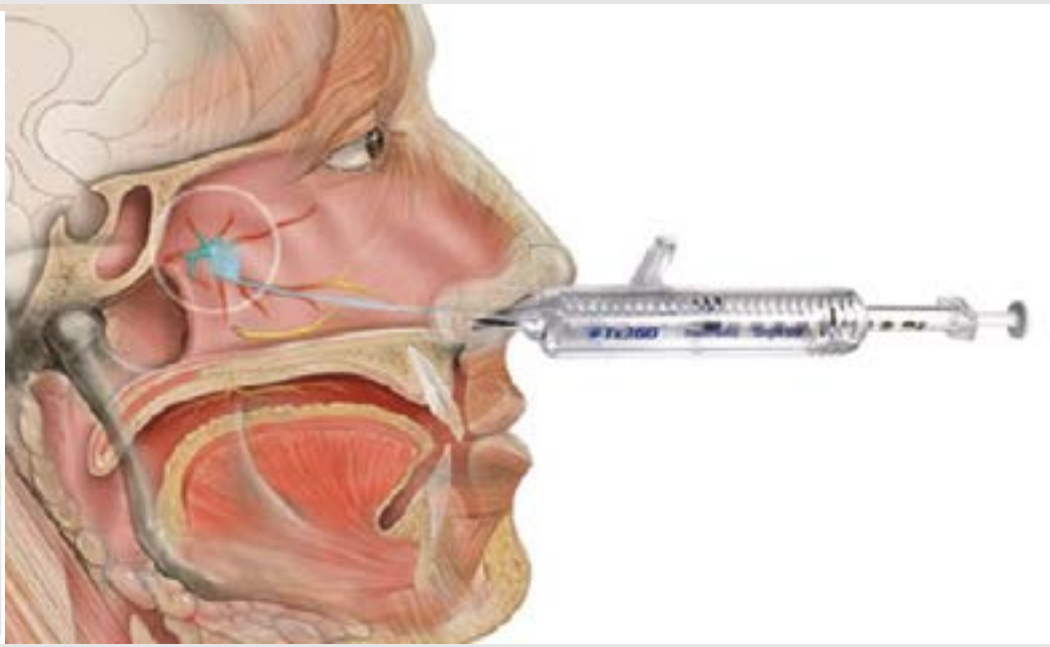
Trigeminal Nerve Branches Block



Interventional Treatment (*Nerve Blocks*)

Sphenopalatine Ganglion Block





Preventive Migraine Treatment

Most Bothersome symptoms

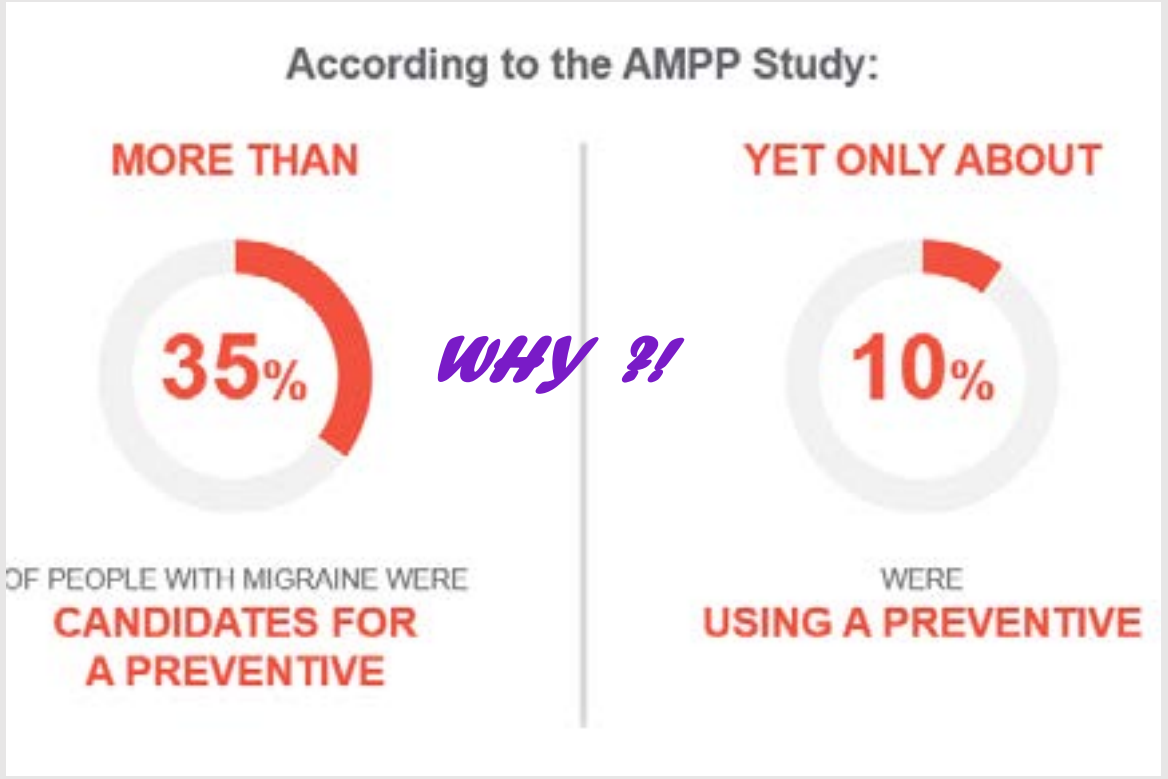
Quality of life and function

- HIT-6
- MIDAS

MILES FOR MIGRAINE

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.*



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

MILES FOR MIGRAINE

Preventive Migraine Treatment
2.Daily Oral medication (pills)

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**

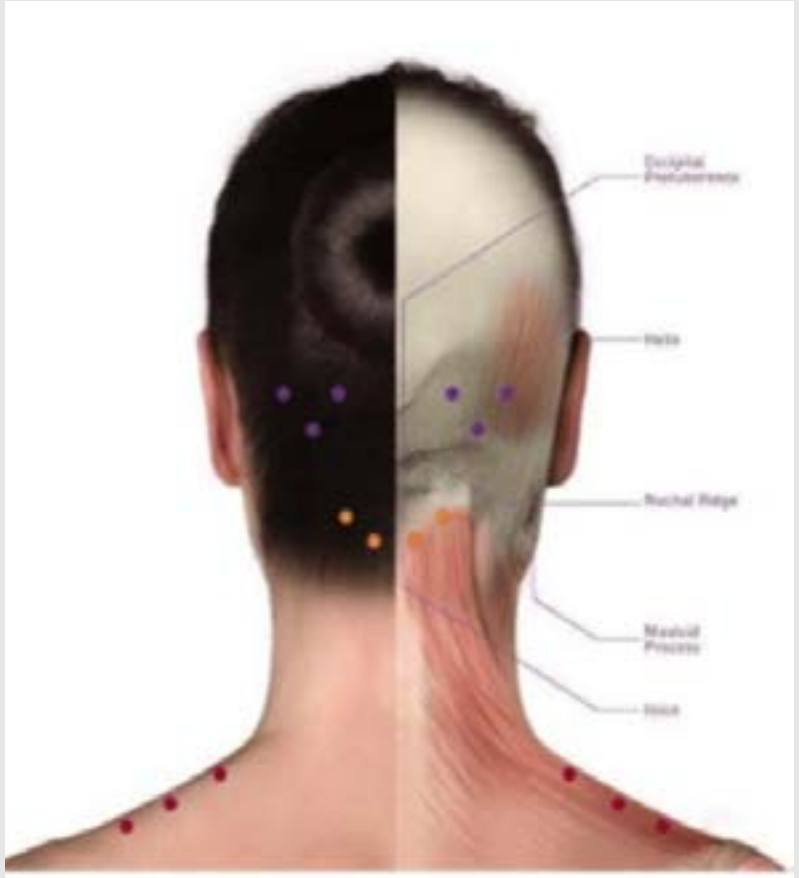
- Topiramate(Topamax , TROKENDI-XR , Qudexy –XR)
- Valproic acid (Depakote)

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)*

155-195
UNITS

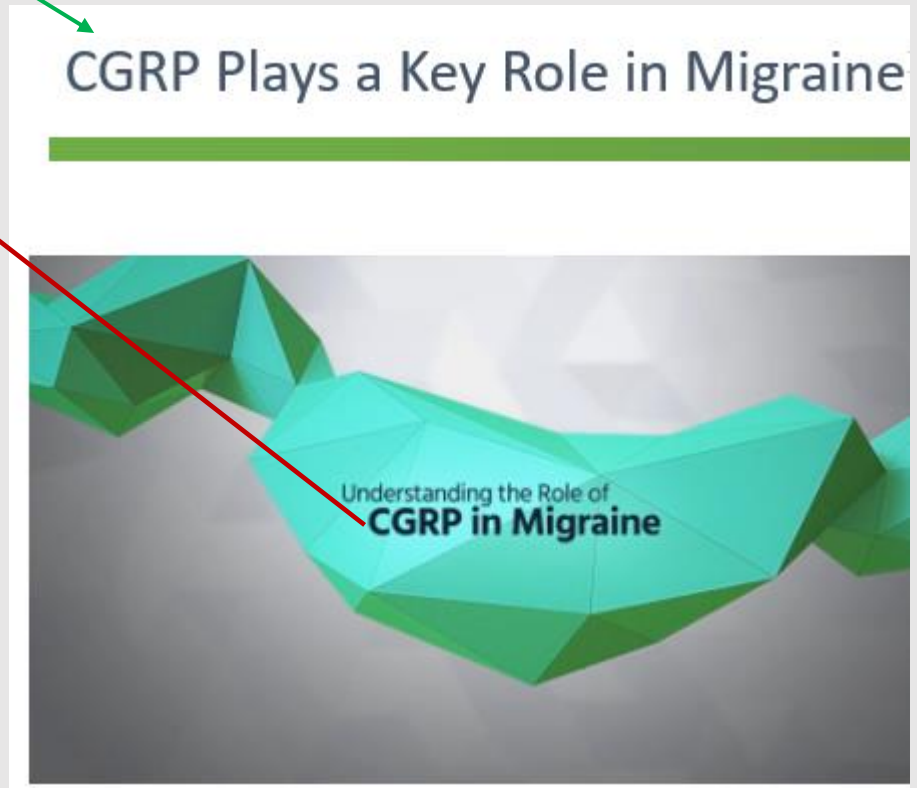


Every **12** weeks

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

MILES FOR MIGRAINE

70 mg

1 Injection - Once a month

OR

140 mg

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

MILES FOR MIGRAINE

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MILES FOR MIGRAINE