

HEADACHE & MIGRAINE Drugs

| Drug | MOA | Pharmacokinetics | Uses | Adverse effect |
|--|---|---|--|--|
| <p>Drug used on :</p> <p>A) ACUTE ATTACK</p> <p>1. ABORTIVE THERAPY</p> <p>a. ERGOTS (Non-Selective)</p> <p>Ergotamine tartarate</p> <p>Dihydroergotamine</p> | <p>Agonism at 5HT₁. At presynaptic trigeminal nerve endings → ↓ release of vasodilating peptides ↓ excessive firing of these nerve endings.</p> <p>At blood vessels → ↓ vasodilation & stretching of the pain endings by ↓ transmitter release in the perivascular space</p> <p>Partial agonist effect on α-adrenoceptors → vasoconstriction</p> | <p>Ergotamine tartarate: Oral absorption → low bioavailability. Sublingual → Low bioavailability. Rectal suppository → Better bioavailability. Elimination → Extensive hepatic 1st pass metabolism. Excretion → 90% of metabolites in bile Traces unmetabolized → urine & feces.</p> | <p>T_{1/2} 2 hrs, BUT, vasoconstriction → 24 hr (↑ tissue binding). Present in all forms. Dihydroergotamine: More rapid hepatic clearance. Present in → nasal spray, inhaler & injections.</p> <p>Contraindications: Pregnancy & miscarriage. Heart disease. Hypertension. Liver and kidney diseases. Fever, sepsis. For prophylaxis of migraine. With TRIPTANES. With β-blocker.</p> | <p>N & V, abdominal pain & diarrhea. Feeling of cold and numbness of limbs, tingling Hallucination. Pericardial distress... Prolong use → rebound headache due to vasodilatation followed by vasoconstriction. Prolong use & high dose → paraesthesia & gangrene.</p> |
| <p>b. TRIPTANES (Selective)</p> <p>Sumatriptan → Nasal spray, & injectable</p> <p>Naratriptan → Orally</p> | <p>Agonism at 5HT₁. At presynaptic trigeminal nerve endings → ↓ release of vasodilating peptides ↓ excessive firing of these nerve endings</p> <p>At meningeal, dural, cerebral vessels → ↓ vasodilation & stretching of the pain endings.</p> | <p>Oral absorption → low bioavailability. Subcutaneously → high bioavailability 97% → peak plasma concentration → 2 min. → t_{1/2} 2 hrs Metabolized → liver Excretion → urine</p> | <p>Contraindications: With MAO Is, lithium, SSRIs, → (5HT) Heart diseases (see adverse effect) MonoAmine oxidase inhibitor (anti-depressant)</p> | <p>Same ERGOTS + In cluster headache</p> <p>Mild pain & burning sensation at the site of injection. Paraesthesia, tingling, warmth, heaviness. Flushing / Dizziness. Hypertension. Vasospasm Ischemic heart; Angina → M.I Arrhythmias</p> |

2. Rescue therapy

a. Analgesics
NSAIDs / Aspirin → **Acetaminophen.**
Non-opioid: m agonist; **tramadol** act on 5HT & NE receptor.
Sedatives; **butalbital.**
Opioid; **Butorphanol.**
b. Antiemetics

B) PREVENT RECURRENCE

Needs time to do its effect (6 month **course**), Uses:
 More than 2 migraine attacks occur per month.
 Single attacks that last longer than 24 hours.
 Acute symptomatic treatment is needed for > 2-3 times/week.
 Headaches impair the patient's lifestyle.
 Abortive therapy fails or is overused.

a. Antiepileptics:

Block Na channel & augment GABA at GABA-A receptors → **Gabapentin**

Topiramate; weight loss & dysthesia.

Valproic; weight gain, hair loss, polycystic ovary → **not** given to **young females**.

b. Antidepressants:

Pizotifen; Like TCA + 5HT₂ antagonist + mild antimuscarinic & antihistaminic activity. Drowsiness, ↑ appetite → weight gain.

Not given with other CNS depressants → sedation

Not given with MAO Is

TCA; Ami & nortriptyline → Dopamine antagonists

SSRIs: Selective serotonin reuptake inhibitor.

c. Antihypertensives:

β blockers; **Propranolol**, **atenolol**, **metoprolol**. Not in young & anxious nor in elderly & depressed, diabetic.

Ca Channel Blockers:

Cinnarazine, **flunarizine**, **verapamil**.

ACEIs: angiotensin converting enzyme inhibitor → **lisinopril**.

ARB: angiotensin II receptor blocker → **candesartan**.

d. Antispastic muscle relaxants:

Tizanidine

| Medication | T _{max} (h) | t _{1/2} (h) |
|----------------|----------------------|----------------------|
| DHE | 1 | 10 |
| Sumatriptan SQ | 0.25 | 2 |
| Rizatriptan | 1-1.5 | 2-3 |
| Zolmitriptan | 2.5 | 3 |
| Naratriptan | 2-3 | 6 |
| Eletriptan | 2.8 | 4 |
| Frovatriptan | 2-3 | 26 |

