Migraine

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Migraine

- Severe recurrent, throbbing headache affecting only one side of the head.
- Females are 3-fold more affected than males.

Types of migraine headache

1. *Migraine without aura* (85% of patients)

severe, unilateral, pulsating headache that typically lasts from 2 to 72 hours. These are aggravated by physical activity and are accompanied by nausea, vomiting, photophobia, and phonophobia.

2. *Migraine with aura* (15% of patients)

neurologic symptoms precede the headache, which can be visual, sensory, and/or cause speech or motor disturbances

AURA

Due to V.C. induced by released 5-HT by platelets

ACUTE ATTACK

Due to Vasodilation, inflammation and edema as a result of accumulated metabolites and inflammatory mediators e.g. prostaglandins

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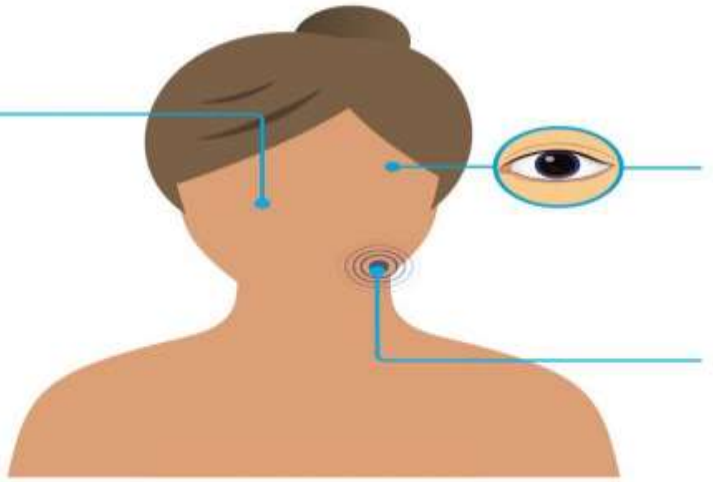
Migraine Phases

Aura Phase

Motor auras:
- slurred or jumbled speech
- difficulty understanding what others say
- difficulty writing
- problems thinking clearly



Visual auras:
- flashing lights
- zig-zagging lines
- blurred vision
- blind spots that expand over time

Sensory auras:
- numbness or tingling

The biological basis of migraine headache

- Aura is caused by reduced blood flow (*hypoperfusion*) in the posterior part of the cerebral hemisphere, which then gradually spreads forward.
- In the headache phase, *hyperperfusion* occurs.
- Pain may be due to extracranial and intracranial arterial dilatation with subsequent release of neuroactive substances such as substance P.

Drug therapy for acute migraine

I- Triptans

These agents rapidly and effectively abort or markedly reduce the severity of migraine headaches in about 70% of patients.

Members: sumatriptan, naratriptan, rizatriptan, eletriptan & zolmitriptan.

Mechanism of action:

-It is a serotonin agonist at ***5-HT_{1D} receptors***.

-This subtype of serotonin receptors is found on small peripheral nerves that innervate the intracranial vasculature.

-Their activation suppresses the release of sensory neuropeptides as substance P.

Uses

Sumatriptan is given orally, S.C. or intranasally.

Side effects:

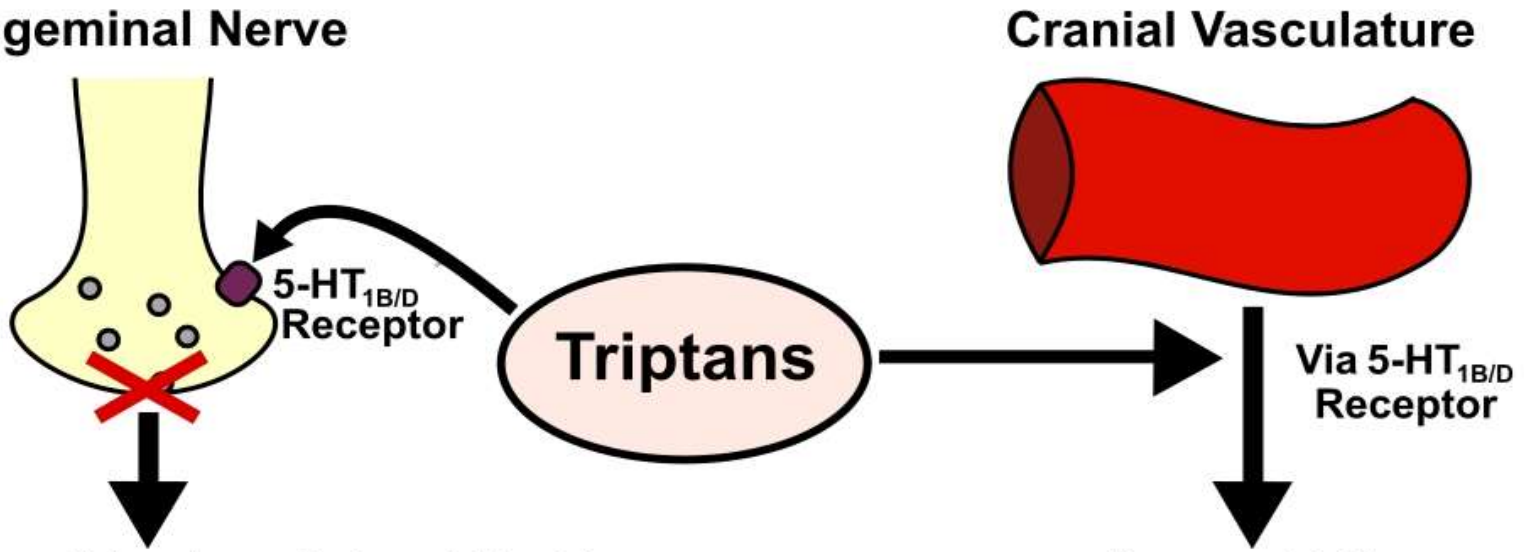
Nausea & vomiting.

Parathesia.

Chest pain.

N.B. It is ***avoided in*** patients with ischemic heart diseases.

Proposed Triptan Mechanism of Action



Moises Dominguez

II- Ergotamine

Mechanism of action:
Ergotamine is α blocker with vasoconstrictor effect.
It has similar actions to triptans but with less selectivity at 5HT receptors.

Contraindications:

Peripheral vascular diseases.

Hypertension.

Angina.

Pregnancy.

Not given with triptans

Dihydroergotamine a derivative of ergotamine. It can be given intravenously

III- Analgesics

NSAIDs are often effective in mild to moderate migraine e.g. aspirin.

Drugs for migraine prophylaxis

Indications:

1- If the attack occurs two times or more per month.

2.If the headache is complicated by serious neurologic signs

1. ***Beta Blockers:*** propranolol & nadolol.
2. ***Methysergide*** (5-HT_2 antagonist and 5-HT_1 partial agonist).

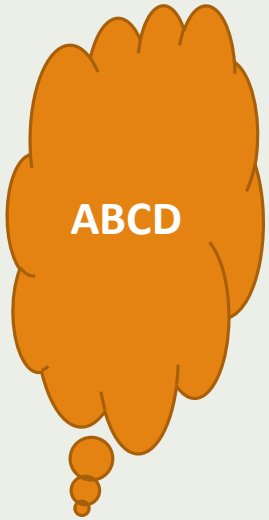
   -It <u>should not</u> be used for long periods as it causes **fibroplastic changes** in the retroperitoneal space, pleural cavity and endocardium. It also causes **hallucinations**.

3- Pizotifen (5-HT_2 antagonist is also used to stimulate appetite.

4.Flunarizine: Calcium channel blocker.

5.Clonidine.

Treatment	Prophylaxis
Mild Attack • Simple analgesics (Non-narcotic analgesics e.g. Aspirin 900 mg or Paracetamol 1g) •Antiemetic (e.g. metoclopramide) • Sedatives (e.g. diazepam)	•**A**lpha (α2- Agonists) >>> Clonidine •**A**nxiolytic >>>> Diazepam •**A**ntidepressants >>> TCA (Amitriptyline) •**A**nti-Serotonin drugs >>> Cyproheptadine Pizotifen • **M**ethysergide >>> Strong 5-HT antagonist •**B**- Blocker as Propranolol •**C**alcium channel blockers>>> Verapamil • **D**iuretics & low salt diet: In menstruation-associated migraine
Severe attack •Ergotamine + metoclopramide + caffeine + simple analgesics •Sumatriptan (5-HT Agonist).	



Neuropathic pain

Neuropathic pain is pain caused by damage or disease that affects the nervous system, such as diabetic peripheral neuropathy, postherpetic neuralgia, or spinal cord injury.

Drugs for Neuropathic pain:

Neuropathic pain is a common clinical presentation of many peripheral neuropathies such as painful diabetic neuropathy, HIV-associated neuropathy, chemotherapy-induced neuropathy, post-herpetic neuralgia (herpes zoster virus) and trigeminal neuralgia.

Guidelines offer consistent recommendations for treating neuropathic pain.

There is not much available evidence that supports specific combinations of medications. However, combination of gabapentin with an opioid were superior to monotherapy.

Effective therapies

1. Calcium channel α2-delta ligands: e.g. gabapentin, pregabalin.

- These medications are recommended as first-line therapy.

2. Tricyclic antidepressants (TCAs):e.g., Amitriptyline, Nortriptyline, Desipramine.

- However, TCAs cause possible cardiotoxicity. Therefore, caution should be taken in patients with cardiac disease.

3. Serotonin-norepinephrine reuptake inhibitors (SNRIs):e.g., duloxetine, venlafaxine.

4. Selective serotonin receptor inhibitors (SSRIs):e.g., fluoxetine, citalopram.

5. Opioid Analgesics: e.g., Tramadol, oxycodone, and morphine.

- These medications are recommended as second-line therapy because of concerns about abuse and opioid toxicity.

6. Antiepileptic drugs: e.g. carbamazepine. **It is one of the first-line therapies for trigeminal neuralgia.**

7. Central skeletal muscle relaxants: e.g., Baclofen.

8. Topical therapies: e.g., Capsaicin (8% patches), lidocaine (5% patches or gel), botulinum toxin type A (Subcutaneous injections).

- Topical therapies are recommended in patients with local neuropathy (e.g., postherpetic neuralgia and trigeminal neuralgia) and may be considered first-line therapies for elderly patients.
- The advantages of topical or local therapies include lower systemic drug levels, fewer adverse effects, and fewer drug interactions.

(Tramadol)

- Tramadol is a **centrally acting analgesic** whose mechanism of action is predominantly based on **blockade of serotonin reuptake.**
- It inhibits norepinephrine transporter function.
- It has weak μ receptor agonist.
- **Use:** chronic neuropathic pain.
- **Toxicity:** seizures- It is contraindicated in patient with history of epilepsy.


THANK YOU