

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

فَاِنَّ مَعَ الْعُسْرِ يُسْرًا

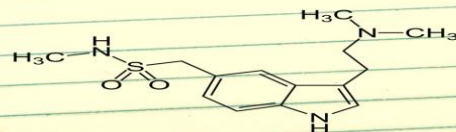
For indeed, with hardship [will be] ease.

94:5

# Treatment of migraine

## **Migraine**

- Pharmacology -



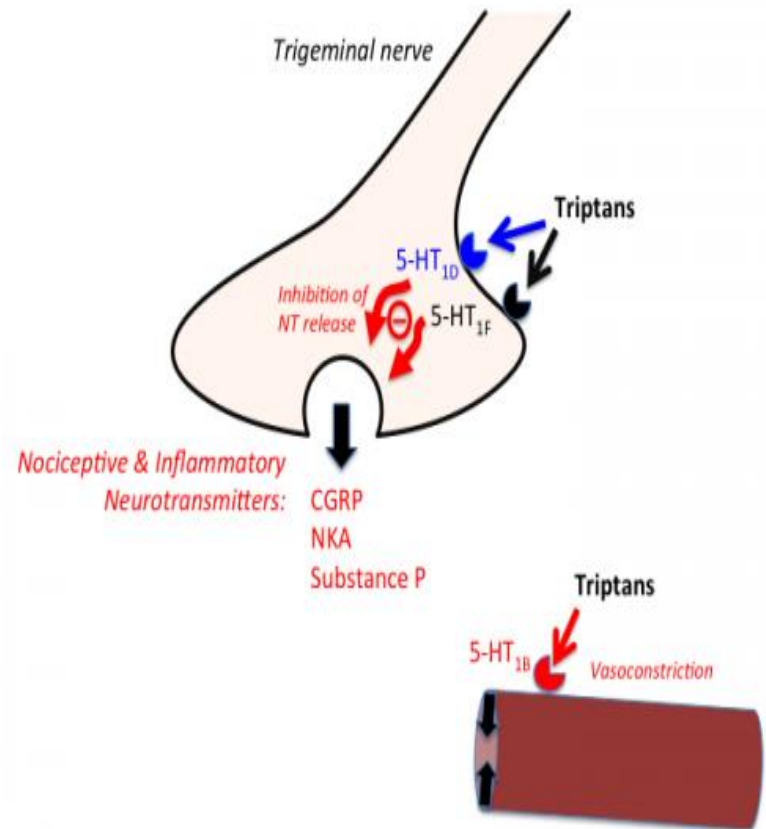
# Triptans;

- **First line treatment** for acute severe attack.
- Not useful for prophylaxis.
  - **Sumatriptan,**
  - **Zolmitriptan,**
  - Rizatriptan,
  - Eletriptan,
  - Almotriptan,
  - Frovatriptan,
  - Naratriptan.

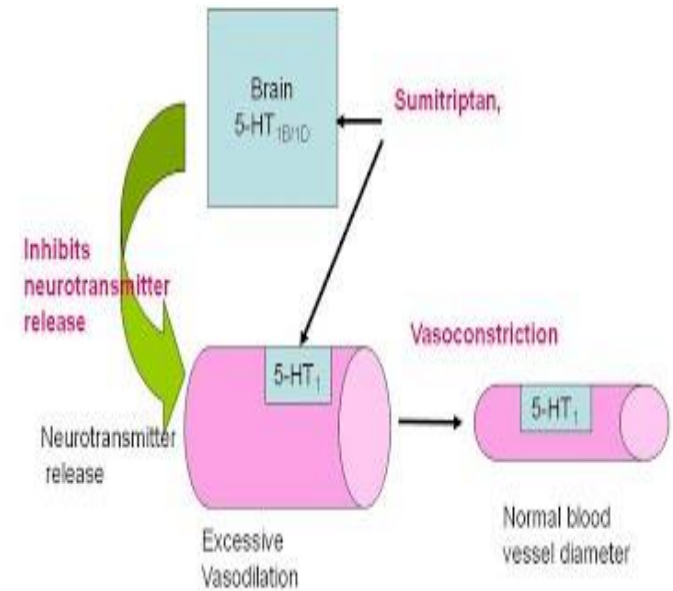
Triptans are Selective agonists for **presynaptic (inhibitory) 5-HT<sub>1D</sub> & 5-HT<sub>1B</sub> receptors.**

Activates **5-HT<sub>1D/1B</sub>** receptors on presynaptic trigeminal nerve endings to inhibit the release of vasodilating peptides.

Proposed Mechanisms for Triptan Effect on Migraine



- 5-HT<sub>1D</sub> receptor agonist activity results in **vasoconstriction** of dilated cerebral vessels.
- Rapidly & effectively **abort** or markedly ↓ the severity of migraine in about **75 %** of patients.
- **Sumatriptan --- oral, nasal, S/C or rectal.**
- **Zolmitriptan --- oral & nasal.**
- All other agents are taken **orally.**
- **Onset**--Parenteral – 20 minutes.  
Orally 1 to 2 hours.



**Activation of 5-HT<sub>1D</sub> receptors** leads either to **vasoconstriction** or to **inhibition of the release of proinflammatory neuropeptides.**

# Adverse effects;

- **Nausea & vomiting** much less than ergot derivatives.
- **Other adverse effects** include **altered sensation** (tingling, warmth), **dizziness**, **muscle weakness**, **neck pain**, **injection site reaction**.
- **A slight increase in BP, coronary vasospasm (1-5% of patients) and risk of MI.**



## Contraindications of triptans;

- **Coronary artery disease and angina** -----5-HT<sub>1B</sub> activity in the coronaries --- cause coronary vasospasm.
- **Naratriptan & Eletriptan** --- severe hepatic, renal impairment & peripheral vascular syndrome.
- **Frovatriptan** --- peripheral vascular disease.
- **Zolmitriptan** --- Wolff-Parkinson-White (WPW) syndrome.

## Disadvantages of triptans;

- **Duration of action** shorter than the duration of the headache----elimination t<sub>1/2</sub> is 2 hrs.
  - **Several doses** required during prolonged migraine
  - Adverse effects limit the maximum safe daily dose
- **Extremely expensive drugs.**

## **Ergot derivatives** for acute attack of migraine; (Ergotamine tartrate & Dihydro-ergometrine)

- **Highly specific for migraine pain; not analgesic for any other condition.**
- Effective during **prodrome** & during the attack ----- progressively less effective if delayed.
- As **compared** to sumatriptan
  - **Efficacy similar.**
  - **Nausea is more common.**
- Oral, S/L, I/M, rectal suppository, intranasal & inhaler (I/V for intractable migraine).



# Ergotamine is given in combination with caffeine, why?

- Combines with caffeine (100 mg caffeine for each 1 mg ergotamine tartrate) to **facilitate absorption of ergot alkaloid.**
- **Not > 6 mg** to be taken for each attack and no more than **10 mg per week.**
- Cumulation and prolong vasoconstriction.

## **Contraindications of ergotamine;**

- Pregnancy,
- 1st and 2nd stages of labour,
- Peripheral vascular diseases,
- Coronary Artery disease.

## Agents used to treat an acute attack

### Agents used in prophylaxis

Several classes of drugs are effective in reducing the frequency and severity of migraine attacks:

- $\beta$ -Blockers: *Propranolol* and *timolol*.
- Tricyclic antidepressant: *Amitriptyline*
- Anticonvulsant: *Divalproex*
- Calcium channel blocker: *Verapamil*

### TRIPTANS

- Triptans rapidly and effectively abort or markedly reduce the severity of migraine headaches in about 80 percent of patients.
- Triptans are serotonin agonists, acting at 5-HT<sub>1D</sub> receptors.

### DIHYDRO-ERGOTAMINE

- *Dihydroergotamine* is a vasoconstrictor.
- Most effective when given during the prodromal phase.
- Contraindicated in pregnancy, and in patients with peripheral vascular disease or coronary artery disease.

### ANALGESICS

- Anti-inflammatory drugs, such as *aspirin*, *naproxen*, and *meclofenamate*, are useful in relieving migraine attacks.
- Severe pain may require administration of opioids, such as *codeine sulfate* or *meperidine*.

Time

### Asymptomatic phase

- Between attacks, no symptoms or pathologic features are evident.

Start of attack

### Prodromal phase

- Visual disturbances that precede the actual headache
- Associated with arterial vasoconstriction, and release of serotonin

### Headache phase

- Pain, nausea and vomiting
- Associated with cerebral vasodilation and lower-than-normal levels of serotonin

# Indications of Prophylaxis of migraine

- Attacks  $\geq 2$  / month.
- If the headache is **severe** or accompanied by serious **neurological symptoms**.
- Patient grossly **incapacitated** during the attack.
- **Analgesics/NSAIDs** usually do **not** afford adequate relief.
- Specific drugs like ergot alkaloids/ **triptans** + anti-emetics have to be prescribed.
- Prophylactic regimens lasting **6 months or more** are recommended.

# Drugs used for prophylaxis of migraine;

(no value in treatment of acute attack)

- **$\beta$ -blockers;**

- **Propranolol** is the drug of choice.

- ❖ Reduce frequency as well as severity of attack in up to 70 % of patients. **Dose;** 40 mg BD --- 160 mg BD.

- ❖ Effect seen in 4 weeks and is sustained.

- Nadolol is also effective.

- **$\beta$  blockers with ISM activity are ineffective e.g., pindolol.**

- **CCB; --- Flunarizine** (a relatively weak CCB that also inhibit  $\text{Na}^+$  channel). It is claimed to be **cerebro-selective CCB**. **Verapamil** is also effective.

- **Anticonvulsant;**

- Valproic acid, Topiramate ---- suppress excessive firing of the nerve endings.

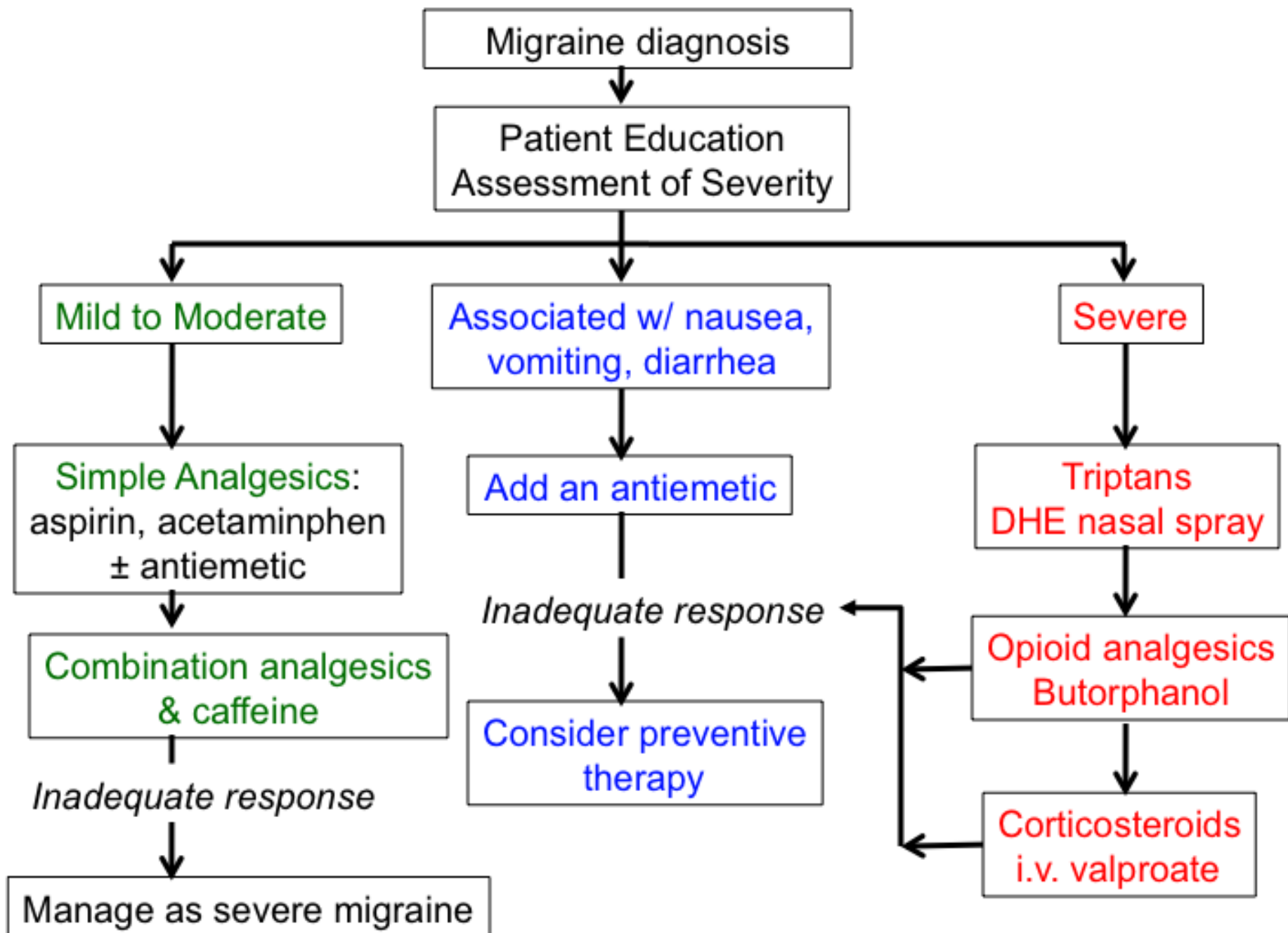
- **Antidepressants;**

- TCA; e.g., Amitriptyline, Nortriptyline.

- **Obsolete drugs;** --- Ergonovine & Methysergide.

- ❖ **Methysergide is ineffective in acute episodes of migraine.**

- ❖ It has been used in the prophylaxis of migraine but its chronic use may induce **retroperitoneal fibroplasia and sub-endocardial fibrosis.**



A landscape photograph featuring rolling green hills in the foreground and middle ground. The foreground is dominated by a field of bright yellow wildflowers. The sky is a deep blue, filled with soft, white, wispy clouds. The overall scene is bright and cheerful.

**Thank You**