Migraine

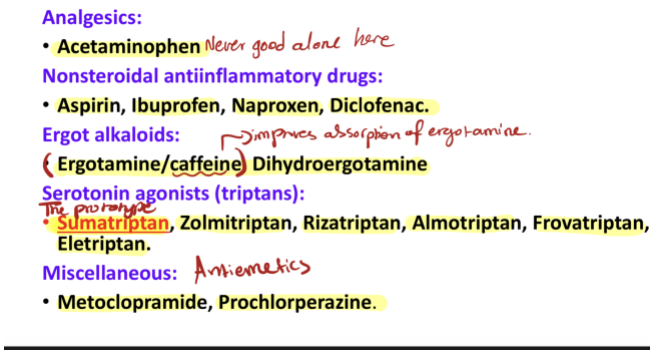
- Pathophysiology:
  - Vasodilation of intracranial extracerebral blood vessels ——>activation of the perivascular trigeminal nerves that release vasoactive neuropeptides———>interact with dural blood vessels to promote vasodilation and dural plasma extravasation —— —> neurogenic inflammation.
  - Activation of central pain transmission and Other brainstem nuclei results in associated symptoms (nausea, vomiting, photophobia, and phonophobia).

- Specific antimigraine drugs (ergot alkaloids and triptans) are agonists at vascular and neuronal 5-HT1 receptor subtypes;
  - vasoconstriction of meningeal blood vessels
  - inhibition of vasoactive neuropeptide release and pain signal transmission.
- Triggers of Migraine:
  - A. Food;
    - Alcohol
    - Caffeine/caffeine withdrawal
    - Chocolate
    - Fermented and pickled foods
    - Monosodium glutamate
    - Nitrate-containing foods
    - Saccharin/aspartame
    - Tyramine-containing foods
  - B. Environmental;
    - Glare or flickering lights
    - High altitude
    - Loud noises
    - Strong smells and fumes
    - Tobacco smoke
    - Weather changes
  - C. Hormonal:
    - Drop in estrogen.
  - D. Behavioral/physiological;
    - Excess or insufficient sleep
    - Fatigue
    - Menstruation, menopause
    - Sexual activity
    - Skipped meals
    - Strenuous physical activity (prolonged overexertion)
    - Stress or post-stress

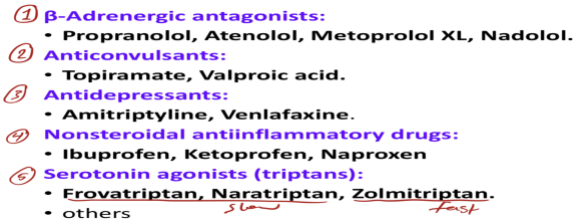
- Goals of acute therapy:
  - Terminate attack rapidly
  - Reduce recurrence
  - Restore ptn normal life
  - Cause minimal to no SE

- Goals of long term:
  - Reduce frequency, severity and disability.
  - Avoid escalation of headache-medication use. (prevent medication-induced headache)
  - Prevent headache
  - Educate ptn
  - Improve quality of life

- General info:
  - Drug therapy is the main stay.
  - Treatment divided into :
    - **abortive(acute):**
      - ✓ migraine specific;
        - ergots+triptans
        - Advised for severe attacks
      - ✓ non-specific ;
        - NSAID, anti-emetics, steroids
        - Advised for mild to moderate attack
      - ✓ Effective at onset of the attack.
      - ✓ Limit use to <10 times per month to avoid overuse headache.



    - **Preventative;**
      - ✓ administered on a daily basis to reduce the frequency, severity, and duration of attacks and improve responsiveness to symptomatic migraine therapies.
      - ✓ Start with low dose, Titrate the dose up.
      - ✓ Examples:
        - BB
        - Anticonvulsant
        - Antidepressant
        - NSAID
        - Triptans



      - ✓ Only **propranolol, timolol, divalproex sodium, and topiramate** have established efficacy.
      - ✓ 2-3 months need to achieve clinical benefit, 6 months for max benefit.

  - Chronic illnesses can limit the use of some drugs.
  - During acute attack, gastric stasis and severe nausea and vomiting might limit absorption of oral drugs. (Give anti-emetic 15-30 min before or use non oral migraine drugs)
  - Excessive use of acute migraine treatment can result in medication-overuse headache:
    - headache returns as the medication is eliminated, leading to use of more drug for relief.
    - daily or near-daily headache with superimposed episodic migraine attacks
    - Management:
      - discontinuation of the drug, headache return to it original characteristics.
      - Hospitalization might be necessary.
      - Detoxification can be accomplished on an outpatient basis.

- **Abortive therapy:**
  - **Analgesics and NSAIDs:**
    - Mild to moderate migraine
    - Acetaminophen alone not effective.
    - NSAIDs prevent inflammation in the trigeminovascular system.
    - suppository analgesic preparations are an option when nausea and vomiting are severe.
  - **Antiemetics:**
    - increases the absorption of analgesics and alleviate migraine-related nausea and vomiting.
    - successfully as monotherapy for the treatment of i**ntractable headache**, or treatment of **refractory migraine.**
    - **has a risk for QT prolongation.**
  - **Miscellaneous Nonspecific Medications:**
    - Corticosteroids can be considered as rescue therapy for status migrainous
    - Valproate and. Magnesium sulfate
  - **Ergot Alkaloids:**
    - Ergotamine tartrate and dihydroergotamine.
    - Oral and rectal preparations contain caffeine to enhance absorption and potentiate analgesia.
    - SE: same as triptans
  - **Triptans:**
    - Divided into:
      - **fast onset/high efficacy**: used in acute onset
      - **slower onset/lower efficacy:** used for prevention (nara/frovatriptan)
    - First member of this class, sumatriptan(ultra rapid acting)
    - triptans are appropriate first-line therapy for patients with mild to severe migraine.
    - the second-prototype generation agents zolmitriptan, rizatriptan, almotriptan.
    - individual responses cannot be predicted, and if one triptan fails, a patient can be switched successfully to another triptan.
    - Contraindication: IHD, pregnancy, hemiplagic and basilar migraine.
    - Drug interaction:
      - **Don't give** within 24 h with ergotamine
      - **Don't give** within 2 weeks of MAOIs
      - **Don't give** with SSRI, SNRI due to risk of serotonin syndrome.
    - SE:
      - Local site reaction , paresthesia, flushing and warmth.
      - Triptans sensation: tightness in chest and neck
      - Taste perversion.
      - Medication overuse headache.

- **Preventative therapy:**
  - When to use?
    - Recurrence migraine with significant disability.
    - Frequent attack >2 a week
    - Uncommon migraine variant (hemiplegic migraine, basilar migraine, and migraine with prolonged aura).
    - when headaches recur in a predictable pattern (exercise- induced migraine or menstrual migraine).
    - Ptn preference.

  - Overuse of acute headache medications will interfere with the effects of preventive treatment.
  - Categories of treatment:
    - ✓ **BB:**
      - most widely used drugs for migraine prophylaxis.
      - Metoprolol, propranolol, and timolol reduce the frequency of attacks by 50% in greater than 50% of patients.
    - ✓ **Antidepressant**:
      - beneficial effects of antidepressants in migraine are more independent of their antidepressant activity
      - The tricyclic antidepressant (TCA) amitriptyline and SNRI, venlafaxine are classified as probably effective for migraine
    - ✓ **Anti-convulsant:**
      - valproate, divalproex, and topiramate established efficacy
      - Topiramate most studied one with benefits as early as 2 weeks.
    - ✓ **Triptans:**
      - Frovatriptan, naratriptan useful for the prevention of menstrual migraine
      - started 1 - 2 days before attack and continued through the attack
      - Frovatriptan has established efficacy.

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