Drugs Used in Headache

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Headache : Causes

PRIMARY	SECONDARY	FACIAL PAIN
Migraine	Increased intracranial pressure	Temporal arteritis
Tension Headache		
Cluster Headache		

Sinus
pain is behind browbone and/or cheekbone.

Cluster
pain is in and around one eye.

Tension
pain is like a band squeezing the head.

Migraine
pain, nausea and visual changes are typical of classic form.

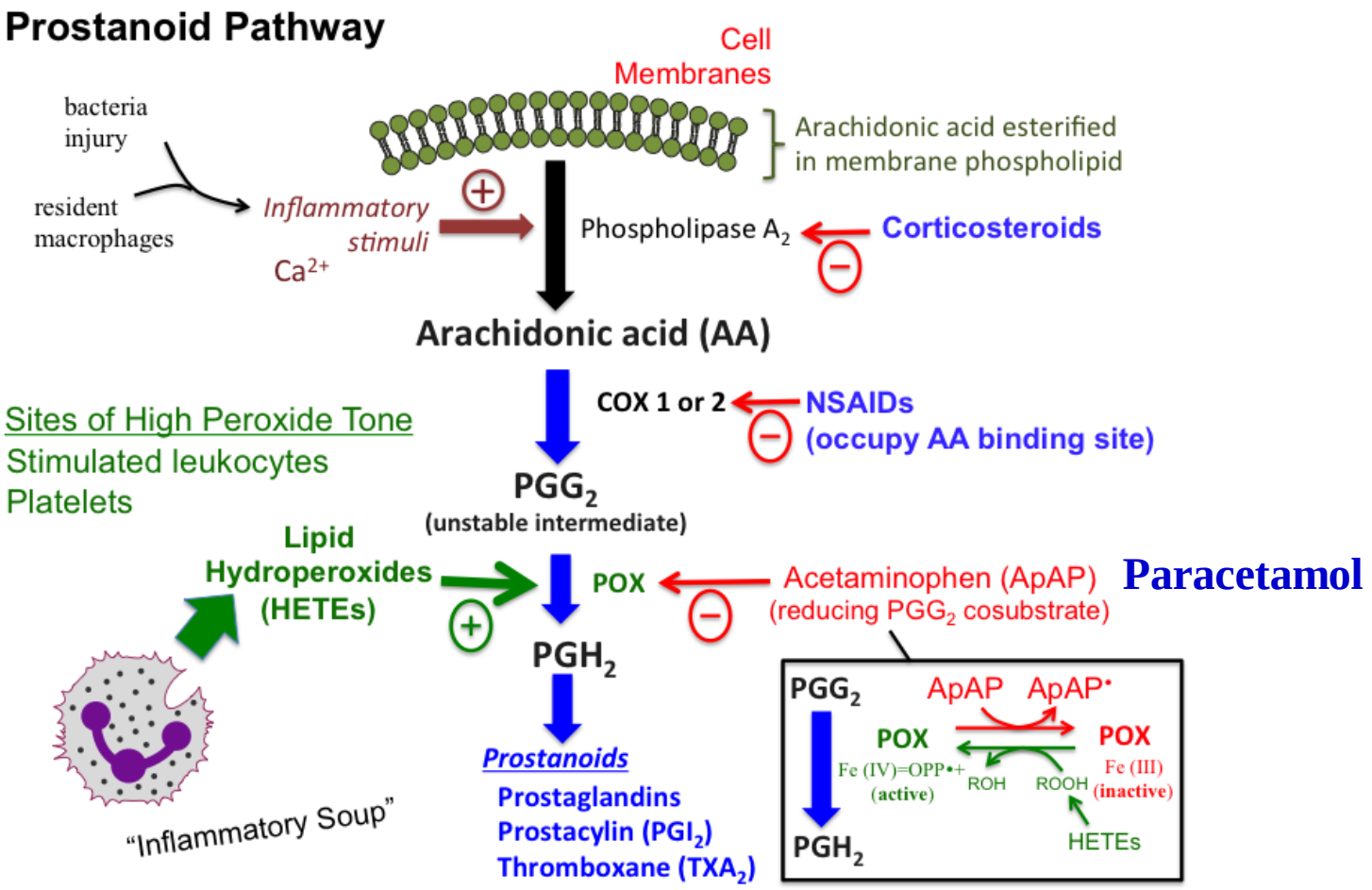
- General management : Analgesics
- Specific management : depends on aetiology

Analgesics

- Paracetamol

- NSAIDs

Mechanism of action



Paracetamol

Mechanism of action

- Paracetamol : Inhibits prostaglandin synthesis

  only in brain

Adverse Effects

- Usually well tolerated
  - ✓ Allergic reactions - sometimes
  - ✓ Analgesic nephropathy – chronic use

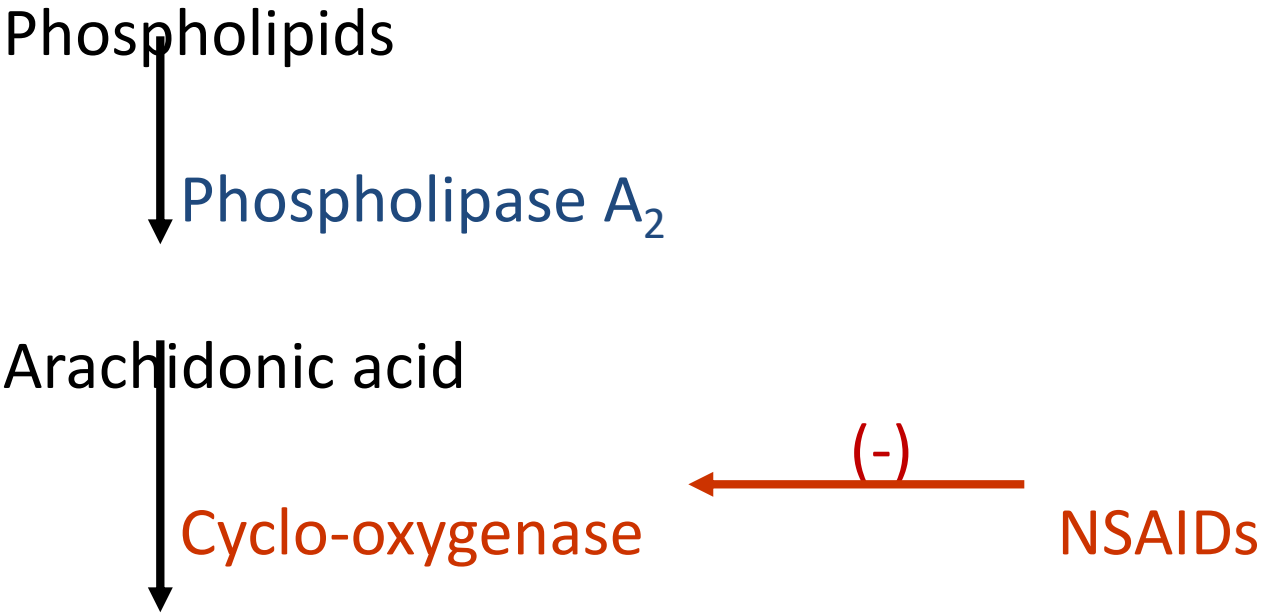
NSAIDs


ASPIRIN
Ibuprofen 400
NAPROXEN
Tablets BP 500mg
28
Tablets

Mechanism of Action

NSAIDs : Inhibit prostaglandin synthesis

central and peripheral



Types

→ Cox-2 selective

- Celecoxib
- Meloxicam

→ Non-cox-2 selective

- Aspirin
- Ibuprofen
- Diclofenac
- Indomethacin
- Mefenamic acid (premenstrual headache)

Uses

- Symptomatic relief of headache of any cause

  ❖Cluster headache : poor response to analgesics

Adverse Effects

- **Gastrointestinal – mucosal damage**
  - **dyspepsia, gastritis, peptic ulcers, GI bleeding**
- **Renal**
  - **acute tubular necrosis → renal failure**
  - **acute interstitial nephritis**
  - **glomerulonephritis**
  - renal papillary necrosis → **analgesic nephropathy**
- **Sodium and fluid retention**
- **Hypersensitivity reactions**
- **precipitation of asthma**
- **thrombocytopenia**

Migraine

Introduction

- Migraine is common and very unpleasant;
  lot of disability

- Classical migraine
  - ✓ initial aura
  - ✓ a severe throbbing headache, often unilateralassociated with photophobia, nausea, vomiting

Pathophysiology

- Controversial
  - ? Primarily vascular
  - ? Primarily neural
  - ❖ Probably multi-factorial

- 5-HT (Serotonin) plays a central role

Vascular hypothesis

- **Aura** is due to;
  - ✓ Ischemia induced by **intracranial vasoconstriction**

- **Headache** is due to;
  - ✓ Subsequent rebound **extra cranial vasodilation** and activation of perivascular nociceptive nerves

Cortical spreading depression(CSD)

CSD-Neuronal depolarization followed by depressed activity slowly spreading anteriorly across the cortex from occipital depression

↓

Reduced metabolism/High extracellular [K^+]

↓

Reduced blood flow (Oligaemia)

↓

AURA

Inflammation hypothesis

Activation of the trigemino vascular system

↓

Stimulates nociceptive neurons in meninges and extra cranial blood vessels

↓

Release plasma proteins and pain-generating substances such as calcitonin gene-related peptide, substance P, vasoactive intestinal peptide, and neurokinin A

↓

Sterile inflammation

↓

Vasodilation

↓

Pain

Serotonin

- 5-HT (Serotonin) plays a central role in migraine
  - Activity of serotonin on

trigeminal sensory neurons (5-HT1D receptors)

smooth muscle cells in meningeal vessels

(5-HT1B receptors)

Block neurotransmission

Vasoconstriction

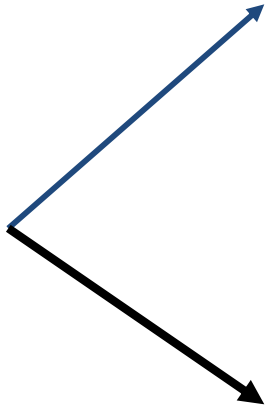
Serotonin

- **Serotonin**(5-HT) concentrations in blood **increase** during the **aura** phase-**Vasoconstriction**
- **Decrease** to subnormal levels in the **headache** phase-**Vasodilatation**

- How does vomiting lessen migraine headache?

Drugs Used In Migraine

- Two basic groups;



Acute attack treatment

✓Migraine specific Rx

✓Migraine non-specific Rx

Prophylactic treatment

Drugs Used In Migraine…….

Acute attack treatment	Prophylactic treatment
Migraine non-specific Rx • Analgesics PCM, NSAIDS, • Antiemetics Domperidone Metoclopramide Migraine specific Rx • 5-HT agonists Triptans	• Beta-blockers Propranolol, Metoprolol • Ca-channel blockers Verapamil Flunarizine • Antiepileptics Topiramate Na valproate • Antidepressants Amitriptyline • 5-HT antagonists Pizotifen

Acute Attack Treatment…..

- To relieve the symptoms after onset of attack

Disease non-specific treatment

- paracetamol
- NSAIDS
- anti-emetics (domperidone, metoclopramide)

Disease specific treatment

- triptans (Sumatriptan)

Acute Attack Treatment…..

- Treatment should be started early in the attack
- Disease specific treatment

  - when simple measures fail
  - when more aggressive therapy is indicated

- Addition of anti-emetics is helpful

  - enhance gastric emptying
  - enhance absorption of drugs
  - relieve nausea & vomiting

Acute Attack Treatment…..

Sumatriptan

The preferred disease specific Rx

- 5-HT agonist ⟶ vasoconstriction
- Poor oral absorption
- High 1st pass metabolism
- Delayed response
- Does not cross blood brain barrier
- Routes & doses: Oral/Nasal spray /Subcutaneous

Acute Attack Treatment…..

Sumatriptan…..

SE;

- nausea & vomiting, general malaise
- dizziness, vertigo, sedation
- altered sensation
- transient increase in BP
- Coronary vasoconstriction-may precipitate angina
- Dysrrhythmias

CI;

- Ischaemic heart disease
- PVD
- Uncontrolled hypertension

Acute Attack Treatment…..

Ergotamine

- Partial agonist at alfa adreno receptors and serotonin receptors
- Vasoconstrictor
- Blocks trigeminal nerve transmission
- Pharmacokinetics
- Poorly absorbed (Inhalation/Suppository)
- Duration of action 12-24 hrs

Side Effects;

- Nausea, Vomiting
- Peripheral vasoconstriction including coronary vassels-Ischaemia (Over dose-gangrene formation)
- Powerful oxytotic-dangerous in pregnancy
- Increase pre & after load-Precipitate angina

Prophylactic Treatment

- Frequent attacks → marked disability

- Frequent intake of acute attack medication may aggravate headache frequency

  (refractory daily or near daily headache)

Prophylactic treatment

Prophylactic Treatment

- Depends on;
  - frequency of attacks
  - tolerability of attacks
    - ✓severity
    - ✓response to acute attack Rx
    - ✓individual factors

Prophylactic Treatment…..

- Beta-blockers: propranolol, metoprolol
- Ca channel blockers: flunarizine, verapamil
- Antiepileptics: topiramate, sodium valproate
- Tricyclic antidepressants: amitriptyline
- 5-HT antagonists: pizotifen

Prophylactic Treatment…..

Beta blockers

Propranolol, metoprolol,

- Mechanism - ? modulation of central neurotransmitters
  not its beta-blocking action

- AE: bradycardia, hypotension,
  peripheral vasoconstriction
  bronchospasm
  fatigue, loss of energy, sleep disturbances

- CI: bronchial asthma, severe bradycardia, PVD

Prophylactic Treatment…..

Calcium channel blockers

Flunarizine

- Cerebro-selective Ca channel blocker
- Prevents mechanical contraction of the muscle wall of the artery
- antihistamine activity
- Given orally

- AE: weight gain
  tiredness
  depression

Prophylactic Treatment…..

Antiepileptcs

Topiramate

- AE: weight loss, GI disturbances, dizziness, drowsiness, mood changes, myalgia,glaucoma

Sodium valproate

- AE: drowsiness, weight gain, hair loss, liver toxicity, teratogenicity

Prophylactic Treatment.....

5HT antagonists

Pizotifen

- A 5-HT antagonist ⟶ vasodilatation

- AE: increased appetite & weight gain
  drowsiness
  anti-muscarinic effects
  enhances the action of alcohol on brain

Other 5HT antagonists- Cyproheptadine, Methysergide

Prophylactic Treatment…..

Antidepressants

Amitriptyline

- A tricyclic anti-depressant
- Effective even if patient is not depressed
- AE : dry mouth, blurred vision, constipation, sedation, urine retention, arrhythmias, confusion

Non-Pharmacological Aspects

Explaining to the patient

- It is not curable but it can be controlled
- It takes time
- It is not a life-threatening condition

Life style modification

- Identification & avoidance of precipitants
- Regular habits

CLUSTER HEADACHE

Cluster Headache

Acute attack treatment

- Analgesics : not helpful
- Rx: triptans

  O_2 inhalation

Prophylactic treatment

- Drugs used in migraine prophylaxis: not useful
- Rx : Lithium

  Verapamil

  Topiramate

Tension Headache

Tension Headache

- Analgesics +/- antidepressants

Thank you