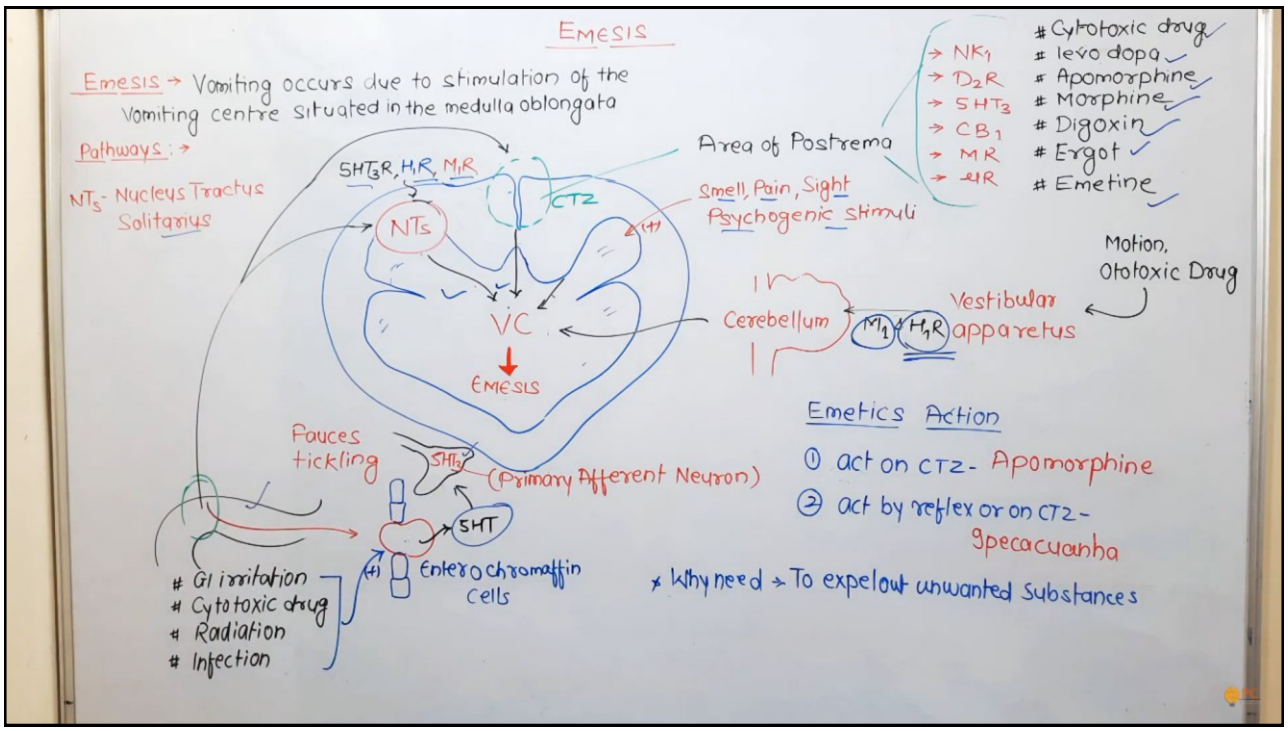
Emetics and Antiemetic Drugs

Website

Videos

Pharmacology 3 | U 2



Emesis

1) Apomorphine → on CTZ
- # Semisynthetic derivative of morphine
- # Dopaminergic agonist (+D_2R) on CTZ
- # dose = 6 mg, im/sc, → onset (5 min)
- # Not used orally because riquired large dose
- # Not used in Res. depression condition because it is a CNS & resp. depressant.

2) Ipecacuanha - by reflex & CTZ
- # Roots - "Cephaelis ipecacuanha"
- # active constituents - Emetin
- # Syrup - 15-30 ml - adult
  10-15 ml Children

Contraindication
- # Corrosive poisoning - alkali, acid
- # CNS stimulant drug poisoning - may convulsion
- # Kerosine poisoning - chance to aspiration
- # Unconscious patient
- # Morphine or phenothiazine poisoning
  ↳ Ineffective

Antiemetics

1. Anticholinergic Drug → Block M_1R
   - Hyoscine → Motion Sickness
   - Dicyclomine → Motion & Morning Sickness
2. Antihistamines → Block H_1R Centrally & M_1R
   - Promethazine
   - Diphenhydramine
   - Dimenhydrinate
   - # Protect from motion sickness (4-6 h)
   - # Sedative & Anticholinergic
   - # Reduce Extrapyramidal side effect of metoclopramide
   - # In combinat° - chemo-induce vomitting
   - Doxylamine - # Sedative anti Hist. & anticholinergic
   - # Along with pyridoxime → Morning Sickness, Early pregnancy but some report → Interfere Folate metabolism & Teratogenic
   - Meclozine → Less sedative - Sea Sickness
3. Neuroleptics → Centrally D_2R Antagonist
   - Chlorpromazine, Triflupromazine, Prochlorperazine
   - # Also having M_1R & H_1R blocking activity
   - # Broad spectrum antiemetic drugs
     - ↳ Morning Sickness, Radio/chemo-induced vomitting
     - ↳ Disease (Gastritis, Uremia, migraine) induced
     - ↳ Drug & Postanesthesia induced
   - * Prochlorperazine - Labyrinthine Supressant, Anti vertigo, Antiemetic
4. Prokinetics - Promot GI transit & speedup gastric emptying by enhancing co-ordinative propulsive motility
   - Metoclopramide → D_2 & $5HT_3R$ antagonist & $5HT_4$ Agonist
   - Domperidone → D_2 antagonist
   - Cisapride, Mosapride, itopride, Levosulpride
     - ↳ $5HT_4$ Agonist, weak $5HT_3$ antagonist
5. $5HT_3$ Antagonist
   - Ondansetron, Granisetron, Palonosetron, Ramosetron
6. NK_1 Receptor Antagonist (Neurokinin Receptor)
   - * chemo → Sub-P → (+) NK_1R → Vomitting
   - Aprepitant - also have D_2 & $5HT_3$ blocking act°
   - (Ap. 120 mg + Ondan 80 mg + Dexamethasone 80 mg)
   - Fosaprepitant (prodrug - perenterally used)
7. Adjuvants
   - Dexamethasone, Benzodiazepines, Dronabinol

PROKINETIC ANTIEMETICS

PROKINETIC - Promote the GI transit & G. emptying

1. METOCLOPRAMIDE

Procainamide derv. introduce in 1970 as "Gastric hurrying" agent

MOA – # D_2 antagonism (CTZ) ↳ ↑ Gastric emptying
↳ ↑ lower esophegal Sphincter (LES) tone

SHT_4 Agonism → ↑ Ach release from myentric motor neuron in GIT → ↑ G. hurrying & LES tone
↳ These effect ↑ by Bethenachol & ↓ by Atropine *

SHT_3 Antagonism (at high dose) - * SHT_3 (CTZ)

P'kinetics → Orally absorbed, Cross BBB & plecenta
$t_{1/2}$ = 1h, duration: 4-5h, onset - 10 min (orally)

ADR – Sedatn, Dizziness, and Loose stool

• Long term → EPS, Galactorrhoea, Gynomastia

Interaction – Abolish therapeutic effect of L-Dopa

Uses – # Antiemetic – drug/disease/Radio/chemo induced
Gastrokinetic
Dyspepsia
GERD

2. DOMPERIDONE

D_2R antagonist chemically related to "Haloperidol" but pharmacology related to Metoclopramide
Lesser antiemetic & prokinetic
Prokinetic action is related to D_2 blocking *
Poorly cross BBB so extrapyramidal motor side effect is rare
It produce Hyperprolactinemia

P'kinetic - orally absorbed but only 15% BA due to first pass metabolism

Interactn – Administered with L-dopa, it counteract their dose limiting emetic action without affect in parkinson

ADR - Dry mouth, loose stool, headach, Galactorrhoea, Cardiac arrhythmia - developed when iv adm.

Use – Antiemetic in many condition

ANTIEMETICS

CISAPRIDE

MOA – 5HT_4 Agonist mainly (Prokinetic action)
Weak SHT_3 Antagonism
↳ ↑ G. emptying & LES tone
↳ ↑ Esophagal Peristalisis
↳ Also ↑ Colon transit

No Extrapyramidal motor side effects

P'kinetic - Orally absorbed, 33% BA, $t_{1/2}$ = 10h
metabolized in Liver, dose should ↓ in hepatic disorder.

ADR → Abdominal Cramp, Diarrhoea, "Torsades De point (Arrhythmia)

Interactn – Along with Azoles antifungal, Macrolide antibiotics, Antidepressant, HIV Protease Inhibitor [CyP Enz. Inhibitors] → ↑ Arrhythmic action

Uses - GERD, Dyspepsia, Constipation

MOSAPRIDE – Similar actn as Cisapride but NO arrhythmic action

ONDANSETRON

MOA – SHT_3 Antagonist
↳ Developed to control radio/chemo induced emesis & later also used in post operative nausea & vomiting
↳ It blocks the depolarizing actn of SHT on CTZ & NT_S
↳ It has minor SHT_3 antagonism activity but no dopaminergic action
↳ Not used in morning & motion sickness
↳ For better effective take along with promethazine / Dexamethasone / BZDs

P'kinetics - Orally absorbed (60-70% BA), Metabolised by Liver (Glucuronic & Sulfate Conjugation), excreted through urine & Faeces.
$t_{1/2}$ = 3-5h

ADR - Headach, Dizziness, Mild constipation, abdominal discomfort

Use – Antiemetics