

Emetics & Antiemetics



List of Drugs induce vomiting

- Anticancer drugs
- Amiodarone
- Apomorphine
- Chloroquine, quinine
- Diltiazem
- Emetine
- Ergot derivatives
- Erythromycin, tetracyclines
- Fluroquinolones
- Metronidazole



Antiemetics

Classification:

1. Anticholinergics:

Hyoscine, Dicyclomine

2. H₁ antihistaminics:

*Promethazine, Diphenhydramine, Cyclizine,
Meclozine, Cinnarizine*

3. Neuroleptics:

*Chlorpromazine, Prochlorperazine, Haloperidol,
etc.*

4. Prokinetic drugs:

*Metoclopramide, Domperidone, Cisapride,
Mosapride*

5. 5HT₃-Antagonists:

Ondansetron, Granisetron, Dolasetron

6. Adjuvant antiemetics:

Corticosteroids, Benzodiazepines, Cannabinoids



Anticholinergics

Hyoscine:

- Most effective for motion sickness
- 0.2 -0.4mg oral, i.m
- Brief duration of action
- Produces sedation and other anticholinergic side effects
- Suitable for short brisk journeys
- Transdermal patch 1.5mg applied behind the pinna – to be delivered over 3 days –suppresses motion sickness while producing only mild side effects



Anticholinergics

Cont...

Dicyclomine:

- 10-20mg oral
- Used for prophylaxis of motion sickness and for morning sickness
- It has been cleared of teratogenic potential



H₁ antihistaminics

- Some antihistaminics are antiemetic
- They are useful mainly in motion sickness and lesser extent in morning sickness, postoperative and some other forms of vomiting
- Their antiemetic effect appears to be based on anticholinergic, antihistaminic and sedative properties
- Drugs available
 1. Meclizine
 2. Cyclizine
 3. Dimenhydrinate
 4. Diphenhydramine
 5. Promethazine – *Used in pregnancy, used by NASA for space motionsickness*



H₁ antihistaminics

Cont..

- All antihistaminic drugs are more effective when taken ½-1 hr before commencing journey
- Once sickness has started, it is more difficult to control



Neuroleptics

- ❑ Potent antiemetics
- ❑ Act by *blocking D_2 receptors in the CTZ*
- ❑ Antagonize apomorphine induced vomiting
- ❑ Antiemetic dose is much lower than antipsychotic doses
- ❑ These agents should not be administered until the cause of vomiting has been diagnosed



Neuroleptics

Cont...

- Broad spectrum antiemetic , effective in;
 - Drug induced and postanesthetic nausea and vomiting
 - Disease induced vomiting
 - Chemotherapy induced (mildly emetogenic)
 - Morning sickness: should not be used except in hyperemesis gravidarum



Prokinetic drugs

- Promote GI transit and speed gastric emptying
- Drugs available

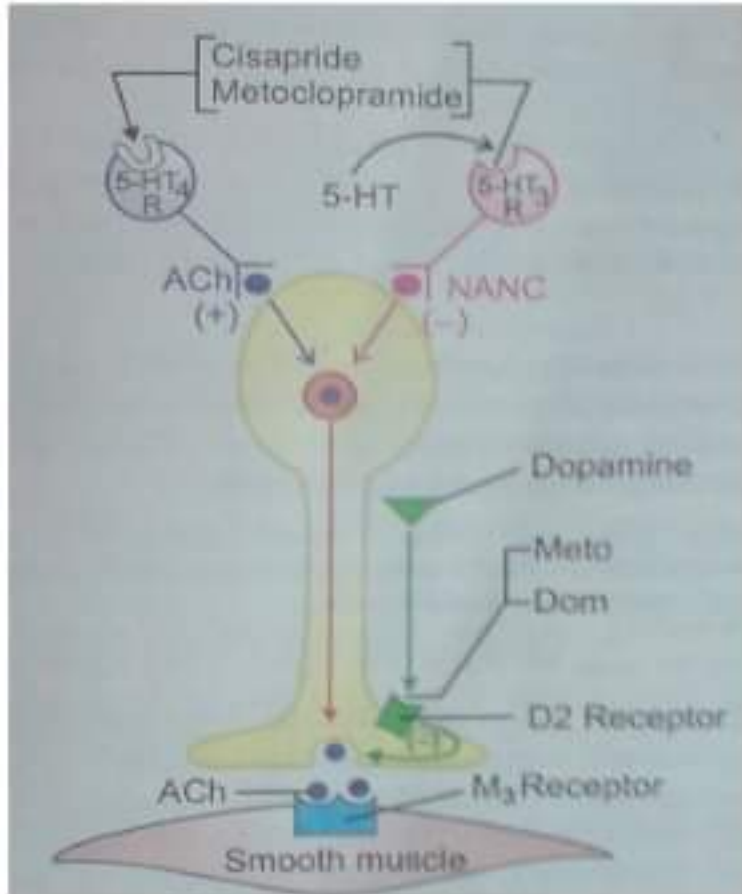
Metoclopramide

Domperidone

Cisapride



Mechanism of action of Prokinetic Drugs



- D₂ antagonism
- 5-HT₄ agonism
- 5-HT₃ antagonism



Emesis

- Is a protective mechanism which serves to eliminate harmful substances from the stomach and duodenum
- Occurs due to stimulation of the emetic center situated in the medulla oblongata
- Multiple pathways can elicit vomiting
- CTZ and NTS are the most important relay areas for afferent impulses arising from GIT, throat and other viscera
- CTZ is also accessible to blood borne drugs, mediators, hormones, toxins etc.,



Prokinetic drugs

Cont...

- Metoclopramide
 - Introduced in early 1970s as a 'gastric hurrying agent'
 - Widely used antiemetic

• *Actions:*

GIT CNS



Prokinetic drugs

Cont...

Interactions:

- Hastens absorption of many drugs:
 - Aspirin,
 - Diazepam etc. by facilitating the gastric emptying
- Reduces absorption of digoxin



Prokinetic drugs

Cont...

Adverse effects:

- Well tolerated
- Sedation, dizziness, diarrhoea, muscle dystonias
- Long term use can cause parkinsonism, galactorrhoea and gynaecomastia

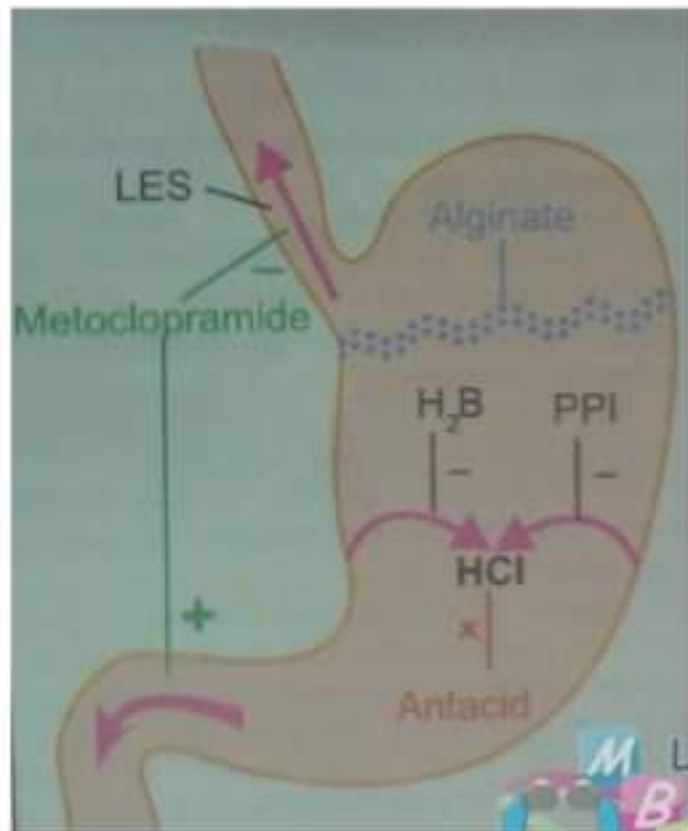


Prokinetic drugs

Cont...

Uses:

- Antiemetic
- Gastrokinetic
- Dyspepsia
- Gastroesophageal reflux disease



Prokinetic drugs

Cont...

Domperidone:

- D₂ antagonist
- Chemically related to haloperidol but pharmacologically related to metoclopramide
- Has lower ceiling antiemetic and prokinetic actions
- Poorly crosses BBB
- Rare extra pyramidal side effects
- Given with levodopa or bromocriptine to counteract their dose limiting emetic action



Prokinetic drugs

Cont...

- ❑ Absorbed orally, but bioavailability is only 15% due to first pass metabolism
- ❑ Completely metabolized and excreted in urine
- ❑ $t_{1/2}$ is 7.5hr
- ❑ Side effects are less than with metoclopramide
 - ❑ *Dry mouth,*
 - ❑ *Loose stools*
 - ❑ *Headache*
 - ❑ *Rashes*
 - ❑ *Galactorrhoea*
 - ❑ *Cardiac arrhythmias on rapid i.v. injection*



Prokinetic drugs

Cont...

Which is a better antiemetic – Metoclopramide or Domperidone ?

- As CTZ is outside BBB both have antiemetic effects.
- But as metoclopramide crosses BBB it has adverse effects like extrapyramidal side effects..
- Domperidone is well tolerated



Prokinetic drugs

Cont...

Cisapride:

- Prokinetic drug with little antiemetic property, because it lacks D2 receptor antagonism
- Gastric emptying is accelerated
- LES tone is improved, esophageal peristalsis augmented
- Devoid of action on CTZ and does not produce extrapyramidal symptoms
- Primary indication of cisapride has been GERD*



5-HT₃ antagonists

- ❑ Potent antiemetics
- ❑ Even though 5-HT₃ receptors are present in vomiting centre & CTZ, the antiemetic action is restricted to emesis caused by vagal stimulation.
- ❑ High first pass metabolism
- ❑ Excreted by liver & kidney
- ❑ No dose reduction in renal insufficiency but needed in hepatic insufficiency
- ❑ Given once or twice daily – orally or intravenously.



5-HT₃ antagonists

Cont...

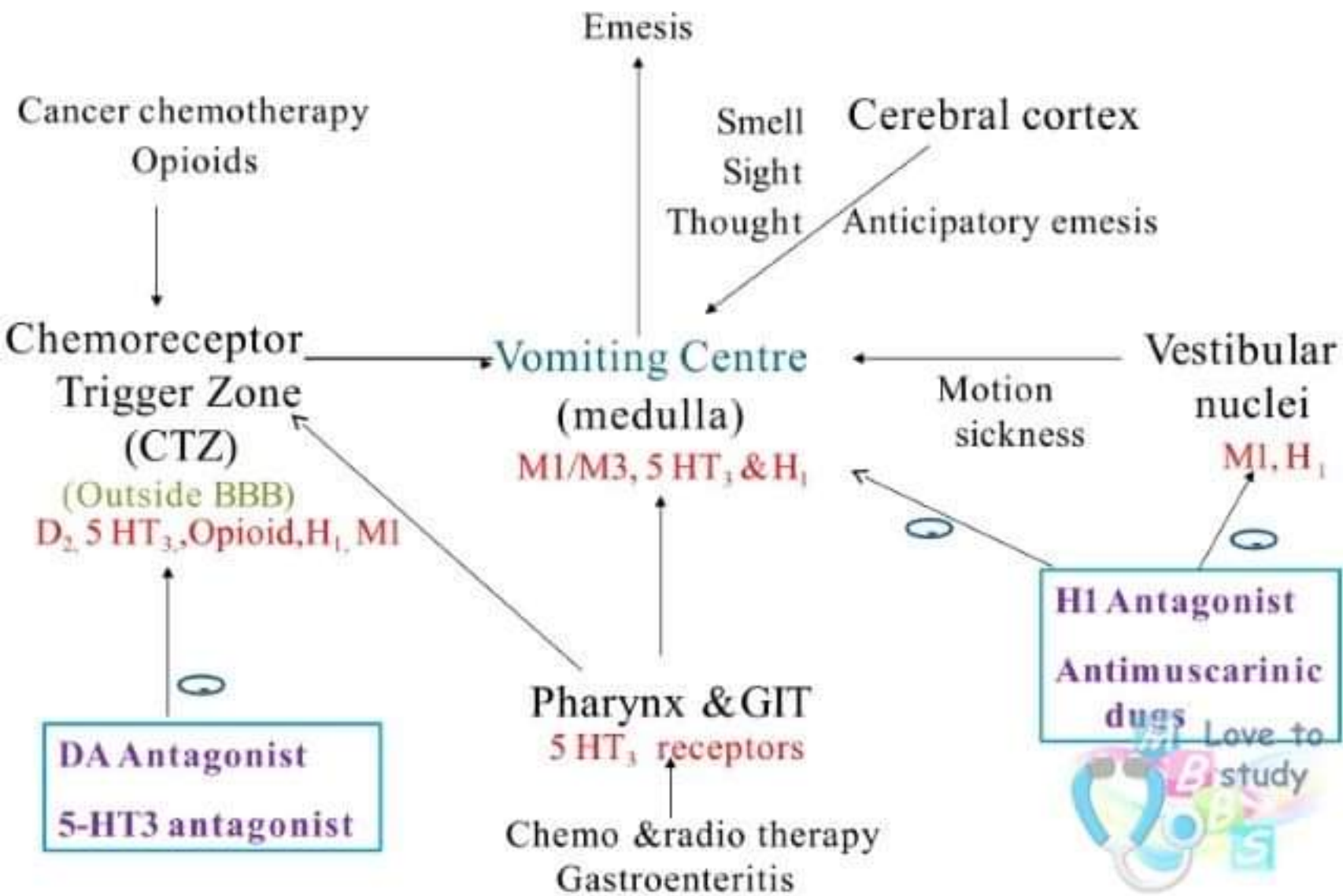
- Ondansetron 32 mg / day
- Granisetron 10 µg / kg / day
- Dolasetron 1.8 mg / kg / day

Indications

- Chemotherapy induced nausea & vomiting – given 30 min. before chemotherapy.
- Postoperative & postradiation nausea & vomiting



Pathophysiology of Emesis



5-HT₃ antagonists

Cont...

Adverse Effects

- Excellent safety profile
- Headache & constipation (common side effect)
- All three drugs cause prolongation of QT interval, but more pronounced with dolasetron.



Emetics

According to site of action:

- a. Centrally acting: *Apomorphine & Morphine*
- b. Peripherally acting: *Mustard, Potassium tartrate (tartar emetic) and hypertonic sodium chloride*
- c. Both: *Ipecacuanha*



Emetics—centrally acting

Apomorphine:

- Given SC/IM-6mg
- Causes vomiting within 15 min
- In hypersensitive individuals, however, even a subtherapeutic dose may elicit severe emesis and collapse
- Vomiting is often accompanied by sedation
- It should not be used if respiration is depressed
- Large doses often produce restlessness, tremors, occasionally convulsions
- Sometimes may cause hypotension, syncope and coma



Emetics—peripherally acting

Mustard:

- Volatile oil
- Formed as a result of a reaction between a glycoside and an enzyme in the presence of water
- It is safe and easily available
- Dose -1 tp in water

Sodium chloride:

- Given orally
- Withdraws fluid from the cells lining the stomach thus causes irritation which causes reflex emesis



Emetics—both

Ipecacuanha (Emetine):

- Acts by irritating gastric mucosa as well as through CTZ
- Dried root of *Cephalis ipecacuanha* contains emetine
- Used as *syrup ipecac* (15-20ml adults, 10-15ml children, 5ml in infants) for inducing vomiting
- Takes 15 min or more for the effect



- Although *apomorphine* is highly effective emetic, syrup *ipecac* is safer



Emetics—contraindication

All emetics contraindicated in;

- Corrosive (alkali, acid) poisoning
- CNS stimulant drug poisoning
- Kerosine (petroleum) poisoning
- Unconscious patient

