

## **Antiemetic Drugs**

### **Definition:**

- A group of drugs which are used to control nausea and vomiting.
- Antiemetic are used to treat motion sickness and for the treatment and prevention of nausea and emesis associated with cancer chemotherapy.

### **Classification:**

#### **1. Histamine H<sub>1</sub> receptor antagonist:**

Cyclizine, Dimenhydrinate, Diphenhydramine, Meclizine.

#### **2. Muscarinic antagonist**

Hyoscine (Scopolamine).

#### **3. 5-HT<sub>3</sub> receptor antagonists**

Ondansetron, Granisetron, Palonosetron & Dolasetron

#### **4. D<sub>2</sub> Antagonists:**

##### **a. Substituted Benzamides**

Metoclopramide, Domperidone

##### **b. Butyrophenones**

Droperidol, Haloperidol

##### **a. Phenothiazines**

Prochlorperazine, Promethazine.

## **5. Benzodiazepines**

Alprazolam, Lorazepam

## **6. Corticosteroids**

Dexamethasone, Methylprednisolone

## **7. Neurokinin-1 receptor blocker**

Aprepitant

## **8. Cannabinoid receptor agonist**

Dronabinol

### **Dopamine receptor antagonist:**

- The D<sub>2</sub> antagonists have antiemetic effect and act mainly as antagonist of the dopamine D<sub>2</sub> receptors in the CTZ(chemoreceptor trigger zone).

### **Metoclopramide:**

#### **Mechanism of action:**

- It blocks D<sub>2</sub> receptor in chemoreceptor trigger zone.

#### **pharmacokinetics:**

- Rapidly absorbed from GIT after oral administration
- Undergoes a high degree first pass metabolism
- It is excreted in the urine and breast milk also.

#### **Indication:**

cytotoxic drug induced emesis

Migraine

Post-operatively and pre-operatively emesis

**Adverse effects:**

Extra pyramidal symptoms

Fatigue, Restlessness

Dystonia

Galactorrhoea

Dysmenorrhea

**Dose:**

10-20mg orally or IV every 6 hrs

**Domperidone:**

**Mechanism of action:**

It also blocks D<sub>2</sub> receptors in CTZ and does not cross blood brain barrier.

**Pharmacokinetics:**

- It is rapidly absorbed after oral administration and excreted in urine
- It is recommended that domperidone be taken 15 to 30 minutes before eating.

**Indication:**

Cytotoxic drug induced emesis

Gastrointestinal symptoms

**Adverse effects:**

Hyperprolactinemia

Galactorrhea

Menstrual irregularities

Abdominal cramps

**Prochlorperazine, Promethazine**

- Phenothiazines are antipsychotics with potent antiemetic property due to D<sub>2</sub> antagonism and anti-muscarinic properties
- Sedative property due to anti-histaminic property
- Promethazine is used for morning sickness of pregnancy.

**5HT<sub>3</sub> receptor antagonist:**

Ondansetron, Granisetron, Palonosetron & Dolasetron

**Mechanism of action:**

Act as anti-emetic by selectively blocking central 5HT<sub>3</sub> receptors in vomiting center & CTZ & mainly by blocking periphery 5HT<sub>3</sub> receptors on intestinal vagal and spinal afferent fibers.

**Pharmacokinetics:**

- These are well absorbed from GIT and are extensively metabolized from liver and excreted in urine.
- Ondansetron requires dosage adjustment in hepatic insufficiency.

**Indication:**

Chemotherapy induced nausea and vomiting

To prevent and treat post operative and post radiation nausea and vomiting.

**Adverse effects:**

Headache, dizziness, constipation and prolongation of QT interval.

**Dose:**

A single oral dose given 1 hour before chemotherapy may be equally effective in following regimen:

- Ondansetron 8mg twice daily or 24mg once, Granisetron 2mg, dolasetron 100mg.

**Histamine H<sub>1</sub> receptor antagonist:****Mechanism of action:**

- They have anticholinergic and H<sub>1</sub> antagonist sedating properties.
- They act on vestibular afferents and within brainstem and produce specific depression of conduction.

**Pharmacokinetics:**

They are well absorbed after oral administration with maximum serum level.

**Indication:**

Motion sickness, postoperative emesis

**Adverse effects:**

Dizziness, sedation

Cycloplegia

Urinary retention

Confusion, dry mouth

**Drug interaction:**

- Patients taking Monoamine oxidase inhibitors(MAOIs) should not take antihistamines because the MAOIs can exacerbate the anticholinergic effects of antihistamine.

**Dose:**

50mg PO taken 30 minutes before departure

**Muscarinic antagonist:**

It is used for prevention of motion sickness and have some activity in post-operative nausea and vomiting and have no effect in chemotherapy induced nausea.

**Adverse effect:**

Dry mouth

Blurred vision

Drowsiness

**Neurokinin-1 receptor blocker:**

Aprepitant

**Mechanism of action:**

- Act as antiemetic, selectively block NK<sub>1</sub> receptor in area postrema.
- No effect on serotonin, dopamine or corticosteroid receptors
- Block substance P from binding to NK<sub>1</sub> receptors.

**Pharmacokinetics:**

Oral bioavailability of aprepitant is 65% and is metabolized by liver.

**Indication:**

It is used in combination with 5HT<sub>3</sub> antagonists and corticosteroids for prevention of acute and chronic nausea and vomiting from cancer chemotherapy

**Adverse effects:**

Fatigue, dizziness, diarrhoea

**Cannabinoid receptor antagonist:**

Dronabinol

The exact mechanism of antiemetic action of dronabinol is unknown but probably relates to CB1 subtype of cannabinoid receptors on neurons in and around vomiting center.

**Dose:** Dronabinol is usually administered in dosage of 5mg/m<sup>2</sup> just prior to chemotherapy and every 2-4 hours as needed.

**Pharmacokinetics:**

It is readily absorbed after oral administration and undergoes first pass metabolism and excreted slowly in days to weeks in faeces and urine.

**Indication:**

It is used in cytotoxic drug induced emesis

Appetite stimulant

AIDS

**Adverse effects:**

Euphoria

Dysphoria

Sedation

Hallucination

Dry mouth

**Corticosteroids:**

Dexamethasone, Methylprednisolone

- Antiemetic MOA not clear
- Enhance action of 5HT3 antagonists in cancer chemotherapy induced nausea and vomiting.

**Dose:**

Dexamethasone 8-20mg intravenously before chemotherapy, followed by 8mg/d orally for 2-4 days is commonly administered.

**Benzodiazepines:**

- Used prior to cancer chemotherapy to reduce anticipatory vomiting.
- Vomiting caused by anxiety.