Chapter-6

Emetics and Anti-Emetics

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ABSTRACT

Emetics and antiemetics are two classes of medications that serve opposite purposes in managing nausea and vomiting. Emetics, such as ipecac syrup, induce vomiting and are used primarily in certain poisoning cases to expel ingested toxins from the stomach. However, their use has declined due to the potential risks and the availability of more effective treatments. Antiemetics, on the other hand, are used to prevent or alleviate nausea and vomiting associated with various conditions, including chemotherapy, postoperative recovery, and motion sickness. These medications are classified based on their mechanisms of action, including serotonin (5-HT3) receptor antagonists like ondansetron, dopamine antagonists like metoclopramide, antihistamines like diphenhydramine, and anticholinergics like scopolamine. Each class targets different pathways involved in the vomiting reflex, providing comprehensive management options for different causes of nausea. Understanding the pharmacology, therapeutic uses, and potential side effects of emetics and antiemetics is essential for effective and safe treatment of nausea and vomiting, enhancing patient comfort and outcomes in various clinical scenarios.

Intoduction

Emetics are substances or medications that induce vomiting in individuals. They are typically used to help remove ingested toxins or irritants from the stomach by triggering the body's natural reflex to expel the contents of the stomach through the mouth. Emetics are sometimes administered in cases of accidental poisoning or overdose.

Anti-emetics, on the other hand, are medications or treatments designed to prevent or alleviate nausea and vomiting. They are often used in various clinical settings, such as to manage side effects of chemotherapy, control motion sickness, or relieve nausea associated with pregnancy (morning sickness) or post-operative recovery. Anti-emetics work by blocking or reducing the signals that trigger the vomiting reflex in the body, helping individuals feel more comfortable and avoid vomiting.

Emetics

Definition

Emetics are medications that induce vomiting. They are used in certain medical situations to empty the stomach contents, such as in cases of specific types of poisoning or overdose. The

use of emetics has become less common with the advent of safer and more effective treatments for poisoning.

Classification of Emetics

1. **Central Acting Emetics**
   - Apomorphine
2. **Peripheral Acting Emetics**
   - Ipecac Syrup

Pharmacology of Emetics

1. **Central Acting Emetics**

   Apomorphine

   - **Mechanism of Action:** Apomorphine is a dopamine agonist that stimulates the dopamine receptors in the chemoreceptor trigger zone (CTZ) of the brain, leading to the induction of vomiting.
   - **Uses:** Induction of vomiting in cases of poisoning when the patient is conscious and alert.
   - **Side Effects:** Respiratory depression, hypotension, sedation, and potential for abuse. It is typically administered via injection and should be used under medical supervision.
   - **Contraindications:** Not recommended for use in patients with impaired consciousness, respiratory distress, or those who have ingested corrosive substances or hydrocarbons.

2. **Peripheral Acting Emetics**

   Ipecac Syrup

   - **Mechanism of Action:** Ipecac syrup contains emetine and cephaeline, which irritate the gastric mucosa and stimulate the vomiting center in the brain. The combined effect induces vomiting.
   - **Uses**: Historically used to induce vomiting in cases of certain poisonings.
   - **Side Effects:** Diarrhea, abdominal cramps, prolonged vomiting, and potential for cardiac toxicity with excessive use. It is generally considered outdated and is rarely recommended in modern clinical practice.
   - **Contraindications:** Should not be used in patients who are unconscious, have ingested corrosive substances or hydrocarbons, or in cases where vomiting is contraindicated (e.g., risk of aspiration).

Antiemetics

Definition

Antiemetics are medications used to prevent or alleviate nausea and vomiting. These symptoms can be caused by various conditions, including motion sickness, chemotherapy, postoperative recovery, gastrointestinal disorders, and more. Antiemetics work through different mechanisms to target the pathways involved in the vomiting reflex.

Classification of Antiemetics

1. **Serotonin (5-HT3) Receptor Antagonists**
    - Ondansetron
    - Granisetron
    - Palonosetron
2. **Dopamine Antagonists**
    - Metoclopramide
    - Prochlorperazine
    - Domperidone
3. **Antihistamines (H1 Receptor Antagonists)**
    - Diphenhydramine
    - Meclizine
    - Dimenhydrinate
4. **Anticholinergics**
    - Scopolamine
5. **Neurokinin-1 (NK1) Receptor Antagonists**
    - Aprepitant
    - Fosaprepitant
6. **Cannabinoids**
    - Dronabinol
    - Nabilone
7. **Corticosteroids**
    - Dexamethasone
8. **Benzodiazepines**
    - Lorazepam

Pharmacology of Antiemetics

1. Serotonin (5-HT3) Receptor Antagonists

Ondansetron

- **Mechanism of Action:** Ondansetron blocks the serotonin 5-HT3 receptors in the central nervous system and the gastrointestinal tract, preventing nausea and vomiting.
- **Uses:** Prevention and treatment of chemotherapy-induced nausea and vomiting (CINV), postoperative nausea and vomiting (PONV), and radiation-induced nausea and vomiting.
- **Side Effects:** Headache, constipation, dizziness, and QT prolongation.

Granisetron

- **Mechanism of Action:** Similar to ondansetron, granisetron blocks 5-HT3 receptors.
- **Uses:** CINV, PONV, and radiation-induced nausea and vomiting.
- **Side Effects:** Headache, constipation, and potential QT prolongation.

Palonosetron

- **Mechanism of Action:** A newer 5-HT3 receptor antagonist with a longer half-life, it effectively blocks serotonin receptors.
- **Uses:** CINV, PONV.
- **Side Effects:** Headache, constipation, and less potential for QT prolongation compared to older 5-HT3 antagonists.

2. Dopamine Antagonists

Metoclopramide

- **Mechanism of Action:** Blocks dopamine D2 receptors in the chemoreceptor trigger zone (CTZ) and enhances gastrointestinal motility.
- **Uses:** PONV, CINV, gastroparesis, and GERD.
- **Side Effects:** Extrapyramidal symptoms (EPS), drowsiness, fatigue, and diarrhea.

Prochlorperazine

- **Mechanism of Action:** Blocks dopamine D2 receptors in the CTZ.
- **Uses:** Severe nausea and vomiting, migraine-associated nausea.
- **Side Effects:** EPS, sedation, hypotension, and anticholinergic effects.

Domperidone

- **Mechanism of Action:** Blocks peripheral dopamine receptors and increases gastrointestinal motility.
- **Uses:** Nausea and vomiting associated with gastroparesis and other gastrointestinal disorders.
- **Side Effects:** QT prolongation, dry mouth, and abdominal cramps.

3. **Antihistamines (H1 Receptor Antagonists)**

Diphenhydramine

- **Mechanism of Action:** Blocks H1 receptors in the vestibular system and the CTZ, providing antiemetic effects.
- **Uses:** Motion sickness, vertigo, and PONV.
- **Side Effects:** Sedation, dry mouth, blurred vision, and urinary retention.

Meclizine

- **Mechanism of Action:** Similar to diphenhydramine, it blocks H1 receptors.
- **Uses:** Motion sickness, vertigo.
- **Side Effects:** Drowsiness, dry mouth, and dizziness.

Dimenhydrinate

- **Mechanism of Action:** Combines diphenhydramine and theophylline, blocking H1 receptors.
- **Uses:** Motion sickness, nausea, and vomiting.
- **Side Effects:** Drowsiness, dry mouth, and blurred vision.

4. **Anticholinergics**

Scopolamine

- **Mechanism of Action:** Blocks muscarinic receptors in the vestibular system and the CTZ, preventing motion sickness.
- **Uses:** Motion sickness, PONV.
- **Side Effects:** Dry mouth, blurred vision, drowsiness, and urinary retention.

5. **Neurokinin-1 (NK1) Receptor Antagonists**

Aprepitant

- **Mechanism of Action:** Blocks NK1 receptors in the brain, preventing nausea and vomiting.
- **Uses:** CINV, PONV.
- **Side Effects:** Fatigue, hiccups, dizziness, and potential drug interactions.

Fosaprepitant

- **Mechanism of Action:** Prodrug of aprepitant, blocks NK1 receptors.
- **Uses:** CINV, PONV.
- **Side Effects:** Similar to aprepitant, with infusion-related reactions.

6. **Cannabinoids**

Dronabinol

- **Mechanism of Action:** Activates cannabinoid receptors in the brain, reducing nausea and increasing appetite.

- **Uses:** CINV, anorexia in patients with AIDS.
- **Side Effects:** Euphoria, dizziness, confusion, and potential for abuse.

Nabilone

- **Mechanism of Action:** Synthetic cannabinoid, similar to dronabinol.
- **Uses:** CINV, anorexia.
- **Side Effects:** Similar to dronabinol.

7. **Corticosteroids**

Dexamethasone

- **Mechanism of Action:** Reduces inflammation and has antiemetic properties, although the exact mechanism is not fully understood.
- **Uses:** CINV, PONV, and as an adjunct to other antiemetics.
- **Side Effects:** Insomnia, increased blood sugar, increased risk of infection, and adrenal suppression with long-term use.

8. **Benzodiazepines**

Lorazepam

- **Mechanism of Action:** Enhances the inhibitory effects of GABA in the central nervous system, providing anxiolytic and antiemetic effects.
- **Uses:** Anticipatory nausea and vomiting associated with chemotherapy.
- **Side Effects:** Sedation, dizziness, respiratory depression, and potential for dependence.

Dexamethasone

1. **Pharmacological Class**: Dexamethasone is a synthetic corticosteroid and belongs to the class of glucocorticoids.

2. **Mechanism of Action:** Dexamethasone exerts its antiemetic effects through multiple mechanisms. It reduces inflammation and suppresses the immune response, particularly in the central nervous system. This anti-inflammatory and immunosuppressive action can help prevent nausea and vomiting caused by chemotherapy.

3. **Clinical Uses:** Dexamethasone is commonly used as part of a combination regimen to prevent and treat chemotherapy-induced nausea and vomiting. It is often administered along with other antiemetic medications, such as serotonin (5-HT3) receptor antagonists (e.g., ondansetron) and NK1 receptor antagonists (e.g., aprepitant).

4. **Adverse Effects:** Common side effects of dexamethasone can include increased appetite, weight gain, fluid retention, mood changes, and increased risk of infection. Prolonged or high-dose use of corticosteroids like dexamethasone can lead to various side effects, including immune suppression and metabolic changes.

Aprepitant

1. **Pharmacological Class:** Aprepitant is a neurokinin-1 (NK1) receptor antagonist.

2. **Mechanism of Action:** Aprepitant works by blocking the action of substance P, a neurotransmitter involved in the emetic (vomiting) reflex. By antagonizing NK1 receptors in the central nervous system, it helps prevent nausea and vomiting, particularly during the delayed phase after chemotherapy.

3. **Clinical Uses:** Aprepitant is used in combination with other antiemetic medications to prevent both acute and delayed chemotherapy-induced nausea and vomiting, especially for highly emetogenic chemotherapy regimens.

4. **Adverse Effects:** Common side effects of aprepitant can include fatigue, hiccups, and changes in liver enzyme levels. It can also interact with various medications, so it's important for healthcare providers to consider potential drug interactions when prescribing it.

Lorazepam

1. **Pharmacological Class:** Lorazepam is a benzodiazepine, which acts as a central nervous system depressant.

2. **Mechanism of Action:** Lorazepam enhances the inhibitory action of gamma-aminobutyric acid (GABA), a neurotransmitter that reduces neuronal excitability. By binding to GABA receptors in the brain, lorazepam increases the calming and sedating effects of GABA, resulting in reduced anxiety and muscle relaxation.

3. **Clinical Uses:** Lorazepam is primarily used for its anxiolytic (anxiety-reducing) and sedative properties. It is commonly prescribed to manage anxiety disorders, acute panic attacks, and as a preoperative or perioperative medication to reduce anxiety and induce relaxation. It may also be used as an anti-emetic in some cases, particularly for nausea and vomiting related to anxiety.

4. **Adverse Effects:** Common side effects of lorazepam can include drowsiness, dizziness, confusion, and impaired coordination. It may also cause a risk of tolerance, dependence, and withdrawal if used over an extended period or in higher doses.

Dronabinol (THC)

1. **Pharmacological Class:** Dronabinol is a synthetic form of tetrahydrocannabinol (THC), the active component in cannabis (marijuana).

2. **Mechanism of Action:** Dronabinol, like natural THC, acts on the endocannabinoid system. It binds to cannabinoid receptors, primarily CB1 receptors in the central nervous system. By activating these receptors, it can have various effects, including reducing nausea and vomiting and increasing appetite.

3. **Clinical Uses:** Dronabinol is used to manage chemotherapy-induced nausea and vomiting, particularly when other anti-emetic treatments have proven ineffective. It can

also be used to stimulate appetite in individuals with AIDS-related anorexia and for managing chronic pain and muscle spasticity in certain medical conditions.

4. **Adverse Effects:** Common side effects of dronabinol can include dizziness, euphoria, confusion, and alterations in mood and perception. It may also cause increased heart rate, dry mouth, and in some cases, anxiety or paranoia. As with natural THC, it can have psychotropic effects, and its use may be subject to regulatory restrictions in many regions.

Ginger

1. **Active Compounds:** The active compounds in ginger include gingerol and shogaol, which are responsible for its medicinal properties.

2. **Mechanism of Action:** Ginger has several pharmacological actions, including antiemetic (anti-nausea and vomiting), anti-inflammatory, and prokinetic effects on the gastrointestinal tract. It is thought to exert its antiemetic properties by acting on serotonin receptors (specifically the 5-HT3 receptor) and by reducing gut spasms. The exact mechanisms are not fully understood.

3. **Clinical Uses:** Ginger is commonly used to manage nausea and vomiting associated with various conditions, including pregnancy (morning sickness), motion sickness, and chemotherapy-induced nausea. It can also help alleviate digestive discomfort and reduce inflammation.

4. **Adverse Effects:** Ginger is generally well-tolerated, and side effects are rare. Some individuals may experience mild gastrointestinal symptoms such as heartburn, gas, or diarrhea.

Peppermint

1. **Active Compounds:** Peppermint contains menthol, the primary active compound responsible for its medicinal properties.

2. **Mechanism of Action:** Peppermint has several pharmacological effects, including muscle relaxation and the reduction of spasms in the gastrointestinal tract. Menthol can act as a smooth muscle relaxant and may help reduce gastrointestinal discomfort.

3. **Clinical Uses:** Peppermint is used to manage various gastrointestinal symptoms, including indigestion, bloating, and irritable bowel syndrome (IBS). It can help relieve discomfort related to gas and spasms in the digestive tract.

4. **Adverse Effects:** Peppermint is generally well-tolerated, but it may cause heartburn or mild allergic reactions in some individuals. In some cases, concentrated peppermint oil can cause a burning sensation in the mouth or throat.