Chapter-4

Appetite Stimulants and Suppressant

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ABSTRACT

Appetite stimulants and suppressants are medications used to manage weight-related conditions by either increasing or decreasing appetite. Appetite stimulants, such as megestrol acetate and cyproheptadine, are often used in patients experiencing significant weight loss due to chronic illnesses like cancer or HIV/AIDS. These drugs work by interacting with hormones and neurotransmitters that regulate hunger, helping to improve nutritional intake and body weight. On the other hand, appetite suppressants, like phentermine and liraglutide, are used to aid weight loss in obese patients. These medications act on the central nervous system to reduce hunger signals, promoting a feeling of fullness and decreasing caloric intake. Both types of drugs play vital roles in managing weight but must be used cautiously due to potential side effects. Stimulants can cause edema and hormonal imbalances, while suppressants may lead to increased heart rate, insomnia, and gastrointestinal issues. Understanding the pharmacology of these agents is essential for their safe and effective use in treating appetite and weight disorders, ensuring that the benefits outweigh the risks for each patient.

Appetite Stimulants

1. **Megestrol Acetate (Megace):** A synthetic progestin used to stimulate appetite and weight gain in individuals with involuntary weight loss.

2. **Dronabinol (Marinol):** It contains synthetic cannabinoids and is used to stimulate appetite, particularly in patients with cancer or AIDS-related anorexia.

3. **Mirtazapine (Remeron):** An antidepressant that can increase appetite as a side effect and may be prescribed to individuals with depression and poor appetite.

Appetite Suppressants

1. **Phentermine (Adipex-P, Suprenza):** A central nervous system stimulant that reduces appetite and is used for short-term weight loss.

2. **Orlistat (Alli, Xenical):** This medication inhibits the absorption of dietary fats and is used to promote weight loss by reducing calorie intake.

3. **Lorcaserin (Belviq):** A serotonin receptor agonist that helps control appetite and is used for weight management in obese or overweight individuals. Please note that lorcaserin was voluntarily withdrawn from the market in February 2020 due to safety concerns.

Appetite Stimulants

Appetite stimulants are medications used to increase appetite and promote weight gain in individuals experiencing significant weight loss or poor appetite due to medical conditions such as cancer, HIV/AIDS, chronic illnesses, or certain psychological disorders. These medications help enhance the desire to eat and can improve nutritional intake and overall health.

Classification of Appetite Stimulants

1. **Hormonal Agents**
   - Megestrol Acetate
   - Corticosteroids
2. **Antihistamines**
   - Cyproheptadine
3. **Antidepressants**
   - Mirtazapine
4. **Cannabinoids**
   - Dronabinol
5. **Other Agents**
   - Anabolic Steroids

Pharmacology of Appetite Stimulants

1. **Hormonal Agents**

   Megestrol Acetate

   - Mechanism of Action: Megestrol acetate is a synthetic progestin that increases appetite through its effects on the hypothalamus and its potential to modulate various hormones involved in appetite regulation.
   - Uses: Treatment of anorexia, cachexia, and significant weight loss in patients with cancer or HIV/AIDS.
   - Side Effects: Weight gain, edema, thromboembolic events, and hormonal imbalances.

   Corticosteroids

   - Examples: Prednisone, Dexamethasone

- Mechanism of Action: Corticosteroids increase appetite by reducing inflammation and modulating the hypothalamic-pituitary-adrenal (HPA) axis, which can influence hunger signals.
- Uses: Short-term appetite stimulation in patients with cancer or chronic inflammatory diseases.
- Side Effects: Hyperglycemia, osteoporosis, hypertension, and increased risk of infection.

2. Antihistamines

Cyproheptadine

- Mechanism of Action: Cyproheptadine is a first-generation antihistamine with antiserotonergic properties. It increases appetite by antagonizing serotonin receptors that suppress hunger.
- Uses: Appetite stimulation in patients with anorexia or weight loss due to chronic illness.
- Side Effects: Sedation, dry mouth, dizziness, and weight gain.

3. Antidepressants

Mirtazapine

- Mechanism of Action: Mirtazapine is a tetracyclic antidepressant that increases appetite by antagonizing central presynaptic alpha-2 adrenergic receptors, serotonin receptors (5-HT2 and 5-HT3), and histamine receptors.
- Uses: Treatment of depression with concurrent appetite stimulation and weight gain.
- Side Effects: Sedation, increased appetite, weight gain, and dry mouth.

4. Cannabinoids

Dronabinol

- Mechanism of Action: Dronabinol is a synthetic form of delta-9-tetrahydrocannabinol (THC), the active component of cannabis. It stimulates appetite by activating cannabinoid receptors in the brain.
- Uses: Appetite stimulation in patients with AIDS-related anorexia and chemotherapy-induced nausea and vomiting.
- Side Effects: Euphoria, dizziness, paranoia, and potential for abuse.

5. Other Agents

Anabolic Steroids

- Examples: Oxandrolone
- Mechanism of Action: Anabolic steroids promote muscle growth and weight gain by increasing protein synthesis and muscle mass.
- Uses: Treatment of severe weight loss and muscle wasting in patients with chronic diseases.
- Side Effects: Liver toxicity, hormonal imbalances, and potential for abuse.

Appetite Suppressants

Appetite suppressants are medications or substances that reduce hunger, decrease food intake, and aid in weight loss. These agents are commonly used as part of a comprehensive weight management program for individuals with obesity or overweight conditions. Appetite suppressants work by influencing the central nervous system to decrease appetite or increase feelings of fullness.

Classification of Appetite Suppressants

1. **Central Nervous System Stimulants**
   - Sympathomimetic Amines
   - Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
2. **Serotonin Agonists**
   - Selective Serotonin 5-HT2C Receptor Agonists
3. **Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists**
   - GLP-1 Agonists
4. **Combination Drugs**
   - Combination of Central Nervous System Stimulants and Other Agents

Pharmacology of Appetite Suppressants

1. **Central Nervous System Stimulants**

   Sympathomimetic Amines

   Examples: Phentermine, Diethylpropion

   Mechanism of Action: These drugs stimulate the release of norepinephrine and dopamine in the hypothalamus, leading to reduced appetite and increased energy expenditure by activating the "fight or flight" response.

   Uses: Short-term treatment of obesity.

   Side Effects: Increased heart rate, elevated blood pressure, insomnia, nervousness, and potential for abuse and dependence.

   Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

   Example: Sibutramine (withdrawn from the market due to cardiovascular risks)

   Mechanism of Action: These drugs inhibit the reuptake of serotonin and norepinephrine, increasing their levels in the brain and promoting a feeling of satiety.

   Uses: (Previously used) Treatment of obesity.

   Side Effects: Increased heart rate, elevated blood pressure, dry mouth, constipation, and insomnia.

2. Serotonin Agonists

Selective Serotonin 5-HT2C Receptor Agonists

Example: Lorcaserin (withdrawn from the market due to cancer risk concerns)

Mechanism of Action: Lorcaserin selectively activates serotonin 5-HT2C receptors in the brain, which helps increase feelings of fullness and reduce food intake.

Uses: (Previously used) Treatment of obesity.

Side Effects: Headache, dizziness, fatigue, nausea, and potential psychiatric effects.

3. Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

GLP-1 Agonists

Examples: Liraglutide, Semaglutide

Mechanism of Action: These drugs mimic the action of GLP-1, a hormone that promotes insulin secretion, slows gastric emptying, and increases feelings of fullness, thereby reducing appetite.

Uses: Treatment of obesity and type 2 diabetes.

Side Effects: Nausea, vomiting, diarrhea, constipation, and potential risk of pancreatitis.

4. Combination Drugs

Examples: Phentermine/Topiramate (Qsymia), Bupropion/Naltrexone (Contrave)

Mechanism of Action: Combination drugs use multiple mechanisms to reduce appetite and promote weight loss. For example:

- Phentermine/Topiramate: Combines the appetite-suppressing effects of phentermine with the anticonvulsant and weight-loss-promoting effects of topiramate.
- Bupropion/Naltrexone: Combines bupropion's effects on dopamine and norepinephrine with naltrexone's effects on the opioid system, both contributing to appetite suppression and weight loss.

Uses: Treatment of obesity.

Side Effects: Depends on the individual components but may include increased heart rate, elevated blood pressure, insomnia, dry mouth, dizziness, and gastrointestinal disturbances.

Appetite Stimulants

Megestrol Acetate

1. Mechanism of Action

- Megestrol acetate is a synthetic progestin, a type of hormone related to progesterone.
- It binds to and activates progesterone receptors in the body, influencing various physiological processes.

2. Effect on Appetite and Weight Gain

- One of the primary uses of megestrol acetate is as an appetite stimulant.

- It is thought to work by increasing appetite and promoting weight gain, particularly in individuals with involuntary weight loss, such as those with cancer or HIV/AIDS.

3. Clinical Indications

- Megestrol acetate is prescribed to stimulate appetite and facilitate weight gain in patients with conditions leading to cachexia (severe muscle wasting) or anorexia.

Dronabinol

1. Mechanism of Action

- Dronabinol is a synthetic form of delta-9-tetrahydrocannabinol (THC), the active compound found in cannabis.
- It acts on cannabinoid receptors in the central nervous system.

2. Effect on Appetite and Nausea

- Dronabinol has appetite-stimulating properties and can alleviate nausea.
- It is used to boost appetite and reduce nausea and vomiting in patients undergoing chemotherapy or experiencing weight loss associated with conditions like AIDS.

3. Clinical Indications

- Dronabinol is primarily prescribed for the management of chemotherapy-**induced** nausea and vomiting, as well as for stimulating appetite in HIV/AIDS patients with associated weight loss.

Mirtazapine

1. Mechanism of Action

- Mirtazapine is an atypical antidepressant that affects various neurotransmitter systems in the brain.
- It enhances the release of norepinephrine and serotonin while blocking certain serotonin receptors.

2. Effect on Appetite

- One of the side effects of mirtazapine is an increase in appetite.
- This medication can cause weight gain due to its influence on appetite and metabolism.

3. Clinical Indications

- Mirtazapine is primarily used to treat depression and other mood disorders. Its appetite-stimulating side effect may be useful for individuals with depression who have reduced appetite and weight loss.

Appetite Suppressants

Phentermine

1. **Mechanism of Action**
   - Phentermine is a sympathomimetic amine that acts as an appetite suppressant.
   - It primarily works by stimulating the release of norepinephrine in the brain, which leads to decreased appetite and increased feelings of fullness.

2. **Effect on Appetite and Weight Loss**
   - Phentermine reduces appetite and promotes weight loss by influencing the central nervous system to decrease hunger and food intake.
   - It may also increase energy expenditure by its sympathomimetic actions.

3. **Clinical Indications**
   - Phentermine is prescribed for short-term weight management in individuals with obesity as part of a comprehensive weight loss program, typically for a few weeks to a few months.

Orlistat

1. **Mechanism of Action**
   - Orlistat is a lipase inhibitor.
   - It works by inhibiting pancreatic lipase, an enzyme that breaks down dietary fat in the digestive tract, thus reducing fat absorption.

2. **Effect on Fat Absorption and Weight Loss**
   - Orlistat decreases the absorption of dietary fats, leading to a reduced caloric intake from fat.
   - This leads to weight loss and may also result in improvements in lipid profiles.

3. **Clinical Indications**
   - Orlistat is used for long-term weight management in individuals with obesity. It is intended for use in conjunction with a reduced-calorie diet and a comprehensive weight loss plan.

Lorcaserin

1. **Mechanism of Action**
   - Lorcaserin is a selective serotonin 5-HT2C receptor agonist.
   - It specifically activates the 5-HT2C receptors in the brain, which play a role in appetite control and satiety.

2. **Effect on Appetite and Weight Loss**
   - Lorcaserin works by enhancing the feeling of fullness and reducing hunger.

- It helps individuals consume fewer calories by moderating their appetite, thus promoting weight loss.

3. Clinical Indications

- Lorcaserin was used to treat obesity as an adjunct to diet and exercise. However, it was voluntarily withdrawn from the market in February 2020 due to safety concerns.