Overweight and Obesity

Pharmacist Objectives

1. Describe behavioral skills and techniques used in cognitive behavior therapy (CBT) to help clients modify eating and activity habits.
2. Understand the current criteria for anti-obesity pharmacotherapy use.
3. Given a patient case identify the appropriate anti-obesity pharmacotherapy option(s).

Pharmacy Technician Objectives

1. Identify the multiple factors that contribute to obesity
2. Identify resources available to help patients with weight loss
3. Differentiate patients who are potential candidates for anti-obesity pharmacotherapy.

Patient Case

Wanda is a 30-year-old female who is 5' 4" and weighs 180 lbs (BMI 30.9 kg/m²). She has struggled with her weight throughout her life. About 10 years ago she injured herself during a college track meet. Unfortunately, she could not maintain her previous lifestyle after the injury and is now the heaviest she has ever been. She wants to try a pharmacologic agent to assist with weight loss before pursuing bariatric surgery. Her main motivation for losing weight is to help with ongoing fertility issues.

PMH: pancreatitis in 2003, type 2 diabetes
Medications: metformin 1000mg BID, glimepiride 4mg daily

1. Does Wanda qualify for pharmacologic weight loss medications?
   A. Yes
   B. No

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3. What is Wanda’s goal weight after 6 months?
   A. 144 lbs
   B. 153 lbs
   C. 167 lbs
   D. 173 lbs

2. Which agent would you start to assist with Wanda’s weight loss journey?
   A. Liraglutide
   B. Orlistat
   C. Phentermine/topiramate
   D. Naltrexone/bupropion
Prevalence

- In 2015-2016, estimated to be:
  - ~40% in US adults (≥ 20 years of age)
  - ~19% of youths (2-19 years of age)

Complications of Obesity

- Associated with CHD
  - HTN, dyslipidemia, coronary artery disease, arrhythmias
- Increased risk of cerebrovascular disease
- Hemorrhagic and ischemic stroke
- Obesity increases risk of DM, gallbladder dx, sleep apnea, osteoarthritis, cancer, disorders of female reproduction, ESRD and psoriasis

Clinical Indicators

- Overweight = BMI 25-29.9
- Obese = BMI 30 or >
- Metabolic syndrome (3 or more of the following)
  - Waist circumference >40” (men), >35” (women)
  - TGL >150 mg/dl
  - HDL <40 mg/dl (men), <50 mg/dl (women)
  - BP >130/85 mm Hg
  - Fasting glucose >100 mg/dl

Guidelines

- The Endocrine Society Guidelines - 2015
- 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults
- Obesity Medicine Association – updated annually
Management

- Weight loss goals set by individuals are usually done for cosmetic reasons rather than health reasons.
- Weight loss of 5-10% has been shown to have positive benefits for individuals with HTN and DM.
- NHLBI guidelines state 10% weight loss in 6 months.
  - If this is achieved, further weight loss can be attempted.
  - The 10% loss carries the most health benefit and is easiest to attain.
- Weight loss is indicated for patients with health problems (i.e., HTN, sleep apnea, OA, type 2 DM).

Approaches to Obesity

- Adoption of a healthy lifestyle (i.e., diet and exercise habits).
- Pharmacologic therapy (nonprescription and prescription medications, dietary supplements).
  - BMI ≥ 30 or BMI ≥ 27 with comorbidities.
- Bariatric surgery.
  - BMI ≥ 40 or ≥ 35 with comorbidities.

Obesity Algorithm

- A Lifelong Challenge
  - Successful weight loss and maintenance of loss require significant behavioral modification.
  - OTC agents should be only a short-term measure unless a primary care provider (PCP) supervises therapy.
  - Prescription products available.
  - Pharmacologic treatment often results in modest weight loss.
  - Regain possible when therapy stopped.

Treatment Goals

1. Improvement in comorbid condition and chronic diseases associated with overweight and obesity, such as type 2 diabetes and CVD.
2. Improvement in psychological health and feelings of well-being.
3. Cosmetic benefit.

Goals

- Reduce body weight by about 5%-10% over 6 months.
Nonpharmacologic Therapy (Lifestyle Modification)

- **Dietary Change**
  - Most used strategy
  - Changes in proportions of fat, protein, and carbohydrates
  - Use of macronutrient substitutes (sugar and fat substitutes)
  - Changes in timing or frequency of meals

- **Physical activity**
  - Less effective in producing weight loss initially but is important in maintaining weight loss and improving overall fitness

Caloric Restriction

- Allowances for moderately active adults vary with age, gender, and body weight
- U.S. suffers from “portion distortion” - need to relearn appropriate portion sizes based on age and activity levels
- Calorie deficit of 500 kcal/day or more
  - Low-calorie diet (LCD) of about 1200-1800 kcal/day usually results in a weight loss of 1-2 lbs per week
  - Very low-calorie diet (VLCD) of 800 calories or less should be conducted under supervision of physician
  - Faster initial weight loss but long-term results no better

Altered Proportions of Food Groups

- Dietary Guidelines for Americans recommend a diet with no more than 35% of total calories come from fat
  - No more than 10% from saturated fat
  - Very low-fat vegetarian diets
  - Dietary fat must be chosen carefully to prevent essential fatty acid deficiency
  - These diets can increase TG levels and lower HDLs in the short term because of the high carbohydrate content
  - Many popular high-protein, higher-fat, and low-carb diets

Very-low Carbohydrate Diets

1. Prevent elevated insulin levels, promote storage of body fat
2. Weight loss likely due to caloric decrease
3. Initial weight loss partially due to diuretic effect and glycogen depletion

Type of Low-Carb Diets

- Atkins/Keto - Very low carb → 5%-15% of total calories from carbohydrates
- Ketogenic focuses on high fat content as well
- Zone diet - Moderate carbs → 35%-50% of calories from carbohydrates

Meal Replacement Therapy

- Typically geared toward replacing up to two meals a day with:
  - Liquid drink
  - Snack bar
  - Measured frozen meal
- Dieter is encouraged to eat a “reasonable” third meal each day
- One advantage is portion control
- Typically contain 200-300 kcal per serving
- Caution use of protein bars
  - Pt. may consume only protein bars; can lead to ↑ in protein levels
- Early weight loss from these products can give a psychological boost to dieter

Benefits/risks of certain diets

- Low-carbohydrate diets generally have more favorable effects on triglycerides and HDL cholesterol levels, whereas low-fat diets have more favorable effects on LDL and total cholesterol
- High-protein foods consumed in large quantities on these diets could increase uric acid levels and precipitate gout
- Restriction of fruits, vegetables, whole grains, and milk products could increase an individual’s risk of various cancers by depleting essential vitamins, minerals, and fiber and can also lead to constipation.
Commercial Weight Loss Programs

- Structured programs popular in U.S.
- More women than men enroll in these programs
- Systematic review showed that results are suboptimal
- Controlled trials are needed before efficacy and cost-effectiveness can be touted
- Large component of success is support groups and periodic meetings of groups of dieters
- Good short-term results, but...
  - Limited long-term efficacy
  - Patients typically lose 5% of body weight over first 6 months, then return to baseline weight by 12-24 months
- High dropout rates

Physical Activity

<table>
<thead>
<tr>
<th>Physical Activity Recommendations and Caloric Expenditure Rates</th>
<th>60 min most days of the week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (for reduction of chronic disease)</td>
<td>Aerobic: 150 minutes of moderate aerobic activity or 75 minutes of vigorous physical activity a week, performed in 3-10 minute episodes</td>
</tr>
<tr>
<td>Adults (for prevention of body weight gain over time)</td>
<td>60 minutes of moderate-vigorous activities most days of the week</td>
</tr>
<tr>
<td>Adults (for sustaining weight loss)</td>
<td>60-90 minutes of moderate intensity exercise daily</td>
</tr>
</tbody>
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Behavioral Therapy

- Environmental modification
  - Do not have high-calorie foods readily available
- Modifying thinking patterns
  - Set reasonable, specific, proximate goals; identify and plan for potential obstacles to the goals
- Self-efficacy
  - Maintain an optimistic and positive approach
- Social support
  - Rely on family, friends and health care practitioners

Pharmacologic Therapy

- Generally, not recommended as first-line treatment
- FDA recommends that if they are used, they be used singly (not in combination) and at the lowest effective dose
- If used, should be used concomitantly with lifestyle modifications
- Usually started at BMIs > 30 or > 27 with comorbidities

Phentermine - Schedule IV

Mechanism of action: sympathomimetic amine and stimulates hypothalamus to release norepinephrine

- Efficacy
  - 5% body weight in 12 weeks
- Dosing
  - Phentermine HCl = 37.5 mg (or 18.75 mg) once per morning
  - Phentermine resin = 30 mg (or 15 mg) once per morning
  - Phentermine HCl = 8 mg (or 4 mg) three times a day before meal
- Most common Adverse Reactions
  - Headache
  - High blood pressure
  - Rapid/Irregular HR
  - Insomnia
  - Tremor
- Contraindications
  - Hypersensitivity & Pregnancy / Nursing
  - History of cardiovascular disease (coronary artery disease, stroke, arrhythmias, congestive heart failure, uncontrolled hypertension)
  - Administration during or within 14 days following the administration of monoamine oxidase inhibitors
  - Hyperthyroidism
  - Hypersensitivity
  - Seizures
  - Kidney & liver disease
  - History of drug abuse

- Only FDA approved over-the-counter weight loss aid
- Encourage patients to take multivitamin
- Efficacy
  - Moderately effective in helping mildly to moderately overweight patients lose weight
  - 391 mildly to moderately overweight patients were randomized to orlistat 60 mg TID vs. placebo x 16 weeks
  - Mean weight loss from baseline 3.05 kg (6.7 lbs) with orlistat vs. 1.9 kg (4.2 lbs) with placebo (p < 0.001)
- Cost ~ $50-70
Phentermine/topiramate (Qsymia)

Mechanism of action:
• Phentermine: appetite suppression and satiety enhancement through blocking neuronal voltage-dependent sodium channels, enhances GABAergic activity, antagonizes AMPA/kainate glutamate receptors
• Topiramate: reduces neuronal excitability

Efficacy
• 5-10% of body weight

Dosing
• Starting = 3.75 mg/23 mg (phentermine/topiramate ER)
• After 14-day intervals, and as clinically indicated, escalate doses to:
  • Recommended dose = 7.5 mg/46 mg
  • Titration dose = 11.25 mg/69 mg
  • Max dose = 15 mg/92 mg
• Gradually wean dose from the top dose (15 mg/92 mg) to help avoid potential seizures

Side Effects
• Paresthesia, dizziness, constipation, dysgeusia (taste distortion), dry mouth, insomnia

Monitor:
• Metabolic acidosis
• Elevated creatinine
• Lowering of glucose levels

Contraindications
• Pregnancy
• Glaucoma
• Hyperthyroidism
• During or within 14 days of taking MAOIs

Liraglutide (Saxenda)

Mechanism of action: GLP-1 receptor agonist

Efficacy
• 5-10% of body weight

Dosing
• Week 1 = 0.6 mg per day
• Week 2 = 1.2 mg per day
• Week 3 = 1.8 mg per day
• Week 4 = 2.4 mg per day
• Week 5 on = 3.0 mg per day

Side Effects
• Nausea/vomiting, decreased appetite, diarrhea, constipation, abdominal pain, headache, fatigue, increased lipase

Contraindications
• Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2
• Pancreatitis
• Pregnancy

Naltrexone/bupropion (Contrave)

MECHANISM OF ACTION (MOA) of Contrave: exact neurochemical effects leading to weight loss are not fully understood. May be due to the regulation of food intake: the hypothalamus (appetite regulatory center) and the mesolimbic dopamine circuit (reward system).

Efficacy
• >5-10% of body weight

Dosing
• Week 1 = 1 tablet in AM
• Week 2 = 1 tablet in AM + 1 tablet in PM
• Week 3 = 2 tablets in AM + 1 tablet in PM
• Week 4 and beyond = 2 tablets in AM, 2 tablets in PM

Side Effects
• Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea, and acute closure glaucoma

Contraindications
• Uncontrolled hypertension
• Seizure disorders, anorexia nervosa or bulimia, or undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs
• Use of other products containing bupropion
• Chronic opioid use
• During or within 14 days of taking monoamine oxidase inhibitors
• Pregnancy category X

Complementary Therapy

Stimulants, Energy Boosters, Thermogenic Aids
• Bitter orange - i.e., HTN, MI, seizures, stroke
• Caffeine, cola, nut - i.e., issues, nausea, anxiety, insomnia

Fat and Carbohydrate Modulators
• Chromium - well tolerated
• Green Tea - increased heart rate, GI issues, headache
• Licorice - pseudosaldosteronism, HTN, hypokalemia
• Garcinia, brindleberry - i.e., issues, not rec. in patients with DM or dementia

Appetite suppressants
• Plantain or psyllium - i.e., HTN, GI issues, N/V
• Hoodia - no risks reported yet

Fat absorption blockers
• Chitosan - i.e., HTN, fasting, N/V, constipation

Carbohydrate Absorption Blockers
• Ginseng - i.e., HTN, fasting, N/V, constipation

Pre/Probiotics - may promote microbiome conducive to weight loss
Complementary Therapy

- Laxatives and Diuretics
  - Safety/efficacy not proven for long-term weight loss
  - Cascara sagrada → abdominal pain, diarrhea, muscle weakness
  - Dandelion → contraindicated in pts with gallbladder or bile duct obstruction

Ephedra

- 2004
  - FDA declared dietary supplements containing ephedrine alkaloids (ephedra) adulterated because such supplements present an unreasonable risk of illness or injury
    - 37 cases of patients using Ma Huang resulted in
      - stroke
      - myocardial infarction
      - sudden death

Ephedra-free products

- Not Recommended
  - 140 AE’s related to dietary supplements containing ephedrine alkaloids (aka Ma Huang, usually combined with caffeine) were reviewed
    - 31% were considered definitely or probably related
    - 31% considered possibly related
  - AE’s included HTN, palpitations, tachycardia, stroke, seizures, and resulted in death or permanent disability in 26% of these potentially related cases

Cornerstones of Weight Loss and Management

- All three must occur for long-term success
  - Lifestyle Changes
  - Increased exercise
  - Dietary modifications

Questions?