PHARMACOLOGIC TREATMENT OPTIONS FOR OBESITY

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Goals

• Discuss the burden of obesity
• Identify how much weight loss is necessary to improve health outcomes
• Determine advantages and disadvantages of pharmacologic therapies for obesity
• Review the history of obesity medications in the US

Disclosures

• I have nothing to disclose

Pre-Test

1. What percentage of the population meets criteria for overweight or obesity?
   a) 2/3 of US adults
   b) 1/2 of US adults

2. How much weight loss is necessary to improve health outcomes?
   a) 10%
   b) 3-5%

3. True or False: All currently approved pharmacologic treatments for obesity must be discontinued after 12 weeks of treatment.

Classification of Overweight and Obesity

National Heart, Lung, and Blood Institute. Obes Res. 1998;6(suppl)1:S15
Overweight and Obesity Prevalence Increasing Among U.S. Adults

Prevalence (%)

http://www.cdc.gov/nchs/data/hus/hus13.pdf#064

CDC/NCHS, Health, United States, 2013, Figure 11. Data from the National Health and Nutrition Examination Survey.

Patient Scenario

• DM is a 48 year old Alaska Native Male with type 2 diabetes, hyperlipidemia, hypertension and obesity
  • Current Weight 334 lbs
  • Current Height 6'2"
  • Current BMI 43.05 kg/m²

Patient Scenario

• What is DM's classification of overweight or obesity?

Patient Scenario

• What is DM's classification of overweight or obesity?

Patient Scenario

• What is DM's classification of overweight or obesity? Current BMI 43.05 kg/m²

Patient Scenario

How would your advice to DM change if you learned his weight history?

<table>
<thead>
<tr>
<th>Date</th>
<th>7-29-13</th>
<th>1-8-14</th>
<th>3-21-14</th>
<th>8-1-14</th>
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<td>345.2</td>
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<td>-56.1</td>
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<td>Change in %</td>
<td>-1%</td>
<td>-11%</td>
<td>-14%</td>
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What recommendations would you give DM?
How much weight loss is necessary to improve health outcomes?

**MODEST SUSTAINED WEIGHT LOSS OF 3-5% HAS BEEN ASSOCIATED WITH BETTER HEALTH OUTCOMES**

**Specific benefits of 3-5% weight loss**

- **Blood glucose**
  - patients with T2DM weight loss of 2%-5% lowers A1C by 0.2%-0.3%
- **Cholesterol**
  - 3 kg lowers TG by 15 mg/dL.
  - 5- to 8-kg loss decreases LDL-C ~5 mg/dL and increases HDL-C ~2–3 mg/dL.
- **Blood pressure**
  - 5% weight loss is associated with a 3 mmHg reduction in systolic and 2 mmHg in diastolic.


**Medical Complications of Obesity**

- Pulmonary disease
- Obstructive sleep apnea
- Hypoxemia
- Coronary heart disease
- Diabetes
- Hypertension
- Severe pancreatitis
- Cancer
- Breast, uterus, cervix
- Colon, esophagus, pancreas
- Kidney, prostate
- Phlebitis
- Venous stasis
- Severe pancreatitis
- Gout
- Nonalcoholic fatty liver disease
- Gall bladder disease
- Gynecologic abnormalities
- Infertility
- Polycystic ovarian syndrome
- Osteoarthritis
- Idiopathic intracranial hypertension
- Cataracts
- Cataracts
- Retinopathy
- Diabetic nephropathy
- Nephrotic syndrome
- Nephritic syndrome

**Redefining Success**

>5% weight loss in 3 months is considered successful

Celebrate the small victories!

**Goals of Obesity Treatment**

- Setting achievable weight-loss goals is essential to sustained weight loss
- An appropriate weight-loss goal is 5%–10% from baseline within a 6-month period
- Patients should be reevaluated every 6 months to determine whether additional weight loss is appropriate
- Prevention of regain is often difficult; as a result, obesity should be treated as a chronic condition
A guide to selecting treatment for overweight and obesity

<table>
<thead>
<tr>
<th>BMI</th>
<th>Treatment</th>
<th>With co-morbidities</th>
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<tbody>
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<td>25-26.9</td>
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<tr>
<td>27-29.9</td>
<td>Drug therapy</td>
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</tr>
<tr>
<td>30-34.9</td>
<td>Bariatric surgery</td>
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</tr>
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<td>35-39.9</td>
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<tr>
<td>&gt;40</td>
<td>Bariatric surgery</td>
<td>+</td>
</tr>
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</table>

Medications Approved for Weight Loss in the US

- Short-Term Management
  - Phentermine
  - Diethylpropion
  - Benzphetamine

- Long-Term Management
  1. Orlistat
  2. Lorcaserin
  3. Phentermine-topiramate
  4. Naltrexone SR/Bupropion SR
  5. Liraglutide
Orlistat

- **Brand Name** - Xenical®, Alli (OTC)
- FDA approved 1999 for obesity management including weight loss and weight maintenance
- **Mechanism of Action (MOA)** - reversible inhibitor of gastric lipase → blocks fat absorption
- **Expected decrease in weight** - 7.6 lbs at one year

Orlistat

- **Dosing** - 120 mg three times a day with each meal containing fat
- **Advantages** - not a controlled substance
- **Disadvantages** - lots of GI side effects, must separate dose from certain other medications (cyclosporine and levothyroxine)
- **Noteworthy** - recommended to take a multivitamin containing fat-soluble vitamins

Lorcaserin (lor-KA-ser-in)

- **Brand Name** - Belviq®
- FDA approved 2012 as an adjunct to lifestyle modifications for chronic weight
- **Mechanism of Action (MOA)** - selective serotonin 2C receptor agonist → promotes satiety
- **Expected decrease in weight** - 7.24 lbs at one year

Lorcaserin (lor-KA-ser-in)

- **Dosing** - 10 mg twice a day +/- food
- **Advantages** - generally well tolerated
- **Disadvantages** - should not be used with most antidepressants, controlled substance
- **Noteworthy** - Discontinue if 5% weight loss is not achieved by week 12

Phenteramine/Topiramate

- **Brand Name** - Qsymia® kyoo-SIM-ee-uh
- FDA approved 2012 as an adjunct to a reduced-calorie diet and exercise for obesity
- **Mechanism of Action (MOA)** - sympathomimetic anorectic and anti-seizure medication → promotes satiety
- **Expected decrease in weight** - 20 lbs at one year

Phenteramine/Topiramate

- **Dosing** - take in the morning +/- food
- 3.75mg/23 mg in the morning for 14 days titrate based on response to a max dose of 15mg/92 mg
- **Advantages** - more weight loss
- **Disadvantages** - need to avoid abrupt withdrawal, controlled substance
- **Noteworthy** - D/C or escalate dose if 3% weight loss not achieved after 12 weeks on the 7.5mg/46 mg
Naltrexone SR/ Bupropion SR

**Brand Name**- Contrave®

- FDA approved September 10, 2014 as an adjunct to a reduced-calorie diet and exercise for obesity
- **Mechanism of Action (MOA)**- an opioid receptor antagonist and an antidepressant → appetite/craving reduction
- **Expected decrease in weight**- 9lbs at one year

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Liraglutide

**Brand Name**- Saxenda®

- FDA approved December 23, 2014 as an adjunct to a reduced-calorie diet and exercise for obesity, expected to be launched in the first half of 2015
- **Mechanism of Action (MOA)**- GLP-1 agonist, increase satiety, slows gastric emptying
- **Expected decrease in weight**- about 12lbs

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**Patient Scenario #2**

A 42 yo man who is 70 inches who weighs 242 pounds with no comorbidities starts lorcaserin and intense comprehensive lifestyle changes for weight loss.

Twelve weeks after starting lorcaserin he is disappointed with his weight loss.

His current weight is 235 pounds.

What is the best recommendation for this patient?
Patient Scenario #2

1. Continue lorcaserin and explain that this weight loss is typical
2. Continue lorcaserin for another 12 weeks, it requires 6 months for maximum effect
3. Discontinue lorcaserin and initiate phentermine/topiramate

Patient Scenario #2

1. Continue lorcaserin and explain that this weight loss is typical
2. Continue lorcaserin for another 12 weeks, it requires 6 months for maximum effect
3. Discontinue lorcaserin and initiate phentermine/topiramate

Patient Scenario #3

• PP is a 57 year old male with type 2 diabetes, hyperlipidemia, hypertension, hypothyroidism and obesity
  • Current Weight 264 pounds
  • Current Height 67 inches (5'7'')
  • Current BMI 41.51 kg/m²

Patient Scenario #3

• What is DM’s classification of overweight or obesity?

- Underweight (<18.5)
- Normal (18.5–24.9)
- Overweight (25.0–29.9)
- Obesity (30.0–34.9)
- Extreme obesity (>40.0)
Patient Scenario #3

What is DM’s classification of overweight or obesity? Current BMI 43.05 kg/m²

What additional information would you need?

Patient Scenario #3

• Weight history

<table>
<thead>
<tr>
<th>Date</th>
<th>12-20-11</th>
<th>8-30-12</th>
<th>4-5-13</th>
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<tr>
<td>Weight in lbs</td>
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<td>311</td>
<td>325</td>
<td>265</td>
<td>244</td>
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<tr>
<td>BMI Kg/m²</td>
<td>50.7</td>
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<td>41.5</td>
<td>38.4</td>
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<tr>
<td>Change in %</td>
<td>+28%</td>
<td>+33%</td>
<td>-18%</td>
<td>-25%</td>
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</tr>
</tbody>
</table>

Patient Scenario #3

What advice would you give PP?

Patient Scenario #3

• PP medications include
  - Aspirin 81 mg daily
  - Vitamin D 2000 units daily
  - Levothyroxine 88 mcg daily
  - Losartan 50 mg daily
  - Metformin 2000 mg daily
  - Simvastatin 40 mg daily

PP wants to keep his weight loss momentum going, he has researched prescriptions medications on the internet and is asking about a prescription for orlistat

Let’s review…

Which one of the following interventions is likely to produce the highest percentage of weight loss?

1. Orlistat 120mg three times a day
2. Lorcaserin 10mg twice a day
3. Phentermine/topiramate 7.5/46 mg once daily

Patient Scenario #3

What does PP need to know about orlistat prior to beginning therapy?

1. PP should follow a nutritionally balanced, reduced-calorie diet that contains approximately 30% of calories from fat
2. PP should administer levothyroxine and orlistat at least 4 hours apart
3. GI side effects may increase when orlistat is taken with a diet high in fat (>30% total daily calories from fat)
4. PP should take a multivitamin containing fat-soluble vitamins
WHAT ARE THE BARRIERS TO USING WEIGHT LOSE MEDICATIONS?

Patient Scenario #4

• TS is a 62 year old woman
• Diagnosed with T2DM 3 years ago
• A1C has increased from 7.0% to 7.8%
• Weight has increased steadily over the past 3 years
  • Patient priority #1 = loss weight
  • Patient priority #2 = feel better
  • Patient priority #3 = improve A1C

Patient Scenario #4

• TS Current Medications
  • Metformin 1,000 mg twice a daily
  • Insulin glargine 20 units nightly
  • Pioglitazone 15 mg daily
  • HCTZ 25 mg daily
  • Lisinopril 10 mg daily
  • Aspirin 81 mg daily
  • Atorvastatin 80 mg daily

Patient Scenario #4

• TS’s 3 year weight history

Patient Scenario #4

• Given TS’s case what thoughts or recommendations would you have?
• What diabetes medications are associated with weight gain?
• What diabetes medications are associated with weight loss?
Key Take Away Points

- Trend weight overtime, celebrate 3-5% weight loss
- Set realistic goals
- Prevent additional weight gain!
- Support patients as they cycle from one approach to another and never forget the importance of lifestyle change in achieving targets

Key Take Away Points

- Losing weight is hard, maintaining weight lose is even harder
- Pharmacotherapy for obesity may have greatest benefit for maintenance of weight loss
- Consider using weight loss medications chronically, in same manner as medications for other chronic conditions

Post-Test

1. What percentage of the population meets criteria for overweight or obesity?
   a) 2/3 of US adults
   b) 1/2 of US adults

2. How much weight loss is necessary to improve health outcomes?
   a) 10%
   b) 3-5%

3. True or False: All currently approved pharmacologic treatments for obesity must be discontinued after 12 weeks of treatment.
   a) True
   b) False

THANK YOU!

Questions?