Management of Obesity

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Objectives

- Background
- Control of Energy Homeostasis
- Approach to Diet and Exercise
- Medications
- FDA Approved Endoscopic Therapies

Overweight and Obesity

Background

- Defined by BMI
  - Measure of weight (kg) per height (m²)
- Overweight
  - BMI – 25-29.9 kg/m²
- Obese (by BMI category)
  - Class 1 – 30-34.9 kg/m²
  - Class 2 – 35-39.9 kg/m²
  - Class 3 (severe) – ≥ 40 kg/m²

https://www.cdc.gov/obesity/adult/defining.html
National and Local Data - 2017

- Ohio specifics:
  - 33.8% obesity prevalence
  - #11 nationally
  - Indiana – 12th
  - Kentucky – 8th
  - WV – 1st

Impact of Obesity

- According to CDC:
  - 2015-2016 estimated prevalence of adults who are obese is 39.8%.
  - The estimated annual medical cost of obesity in the U.S. was $147 billion in 2008 U.S. dollars.
  - The per capita medical costs for people who are obese were $1,429 higher than those of normal weight.

Prevalence of Self-Reported Obesity Among Non-Hispanic Black Adults, by State and Territory, BRFSS, 2014-2016
Population data


Pathophysiology

• Food is a basic need.
• Caloric restriction leads to decreased metabolic rate.
• Overfeeding leads to a temporary increase in metabolic rate.
• The body will defend a higher set point (overweight) – patients often refer to this as yo-yo dieting.

Physiology

• Food is a basic need.
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Control of Energy Homeostasis


Pathophysiology

- Leptin
- Insulin
- GLP-1
- CCK
- PYY
- Gut Bacteria
  - SCFAs
- Inflammation


Management of Obesity

- Multiple modes of therapy
  - Dietary – Medical Nutrition Therapy
  - Exercise/Activity
  - Behavioral therapy
  - Combination Therapy
  - Pharmacotherapy
  - Endoscopic Therapy
  - Surgery

Nutrition

- Low calorie diet
  - Men 1500-1800 kcal/day
  - Women 1200-1500 kcal/day
- 500 kcal/day deficit should produce roughly 1 lb per week of weight loss
- No one diet is most effective – rather go with patient preference
- Maintain appropriate balance of nutrients
- Dietary intake should not be lower than 800 calories per day
- Initial goal of 10% decrease in body weight


Activity

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Activity Description</th>
<th>Approximate Duration in Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Walking, moderate pace (3 mph, 1.5 miles/hour)</td>
<td>30</td>
</tr>
<tr>
<td>Moderate</td>
<td>Walking, fast pace (4 mph, 2.5 miles/hour)</td>
<td>32</td>
</tr>
<tr>
<td>Moderate</td>
<td>Table tennis</td>
<td>35</td>
</tr>
<tr>
<td>Moderate</td>
<td>Biking</td>
<td>32</td>
</tr>
<tr>
<td>Moderate</td>
<td>Social dancing</td>
<td>29</td>
</tr>
<tr>
<td>Moderate</td>
<td>Lawn tennis (served and returned)</td>
<td>29</td>
</tr>
<tr>
<td>Hard</td>
<td>Jogging (5 mph, 2.5 miles/hour)</td>
<td>18</td>
</tr>
<tr>
<td>Hard</td>
<td>Field hockey</td>
<td>16</td>
</tr>
<tr>
<td>Very Hard</td>
<td>Running (5 mph, 3 miles/hour)</td>
<td>13</td>
</tr>
</tbody>
</table>


Activity – a caveat

- Exercise (especially at higher intensity) leads to calorie expenditure
- As the body perceives the calorie loss, hunger signals increase
- In fact, it is possible for people to gain weight while increasing exercise due to overeating in response
- A survey-study performed in 1997 of 784 people who were able to maintain 30 lbs of weight loss for > 1 year, only 1% achieved this with exercise alone


Motivational Interviewing

- Directive – patient centered counseling that helps explore and resolve issues related to complex behaviors.
- Initially developed for addictive behaviors
- Main difference between motivational interviewing and education sessions is that the motivation is elicited FROM the patient, rather than imparted from the healthcare provider

**Motivational Interviewing**

- **Examples:**
  - “What have you found to be helpful so far?”
    - Is it keeping a journal? Has it been engaging a friend/coworker?
    - This can be a good jumping off point to set short term goals.
  - “How many days have you been able to add in activity?”
    - If a person truly has limited time during the week, suggest focusing more on the weekends for leisure activity
  - “Have you noticed any changes since you’ve started exercising?”
    - Hopefully the answer is yes – then reflect on things like stamina, better energy, sleep quality, and potentially better blood pressure

**Pharmacotherapy**

**Phentermine - Adipex**

- Phentermine works via release of norepinephrine
- Prescribed as intermittent therapy based on this trial from 1968
- Definition of intermittent varies, but in Ohio this is 3 months on 6 months off.
- Caution with glaucoma, MAOIs, cardiac disease, hyperthyroidism.

**Use of medications**

- Medications do not work on their own; they must be part of a comprehensive approach
- Candidates:
  - BMI > 27 with comorbid conditions
  - BMI > 30
  - History of unsuccessful attempts at weight loss OR inability to maintain weight loss
- Comorbid conditions include
  - DM II, HTN, Hyperlipidemia, and OSA
- Guideline states that medications may amplify adherence to diet and exercise
  - Potentially help to make exercise easier after initial weight loss

*J Clin Endocrinol Metab, February 2015, 100(2):342–362*
Orlistat – Xenical (Rx), Alli (OTC)

- Pancreatic lipase inhibitor, reduces absorption of dietary fats, must be taken three times a day with meals.
- Available in prescription (120mg) and OTC (60mg) doses.
- Mean weight loss after 1 year on full dose compared with placebo about 3%.
- Approved for long term use.
- Significant GI side effects.
- May be a good option for patients with prior cardiac disease.


Lorcaserin - Belviq

- 5HT2-C serotonin receptor agonist
- Central effect on the hypothalamus to reduce appetite
- 10mg twice daily, or 20mg XR daily
- Caution use with SSRIs, SNRIs, St. John’s Wort, Dextromethorphan, triptans, and bupropion
- Contraindicated in Pregnancy

Phentermine/Topiramate - Qsymia

- Phentermine acts centrally via norepinephrine, topiramate works via GABA receptors
- Can titrate dose based on response

Lancet 2011; 377: 1341–52

Phentermine/Topiramate

- Caution use in patients with uncontrolled hyperthyroidism, cardiac disease, kidney stones, glaucoma, or if on MAOIs
- Contraindicated in pregnancy – topiramate is teratogenic
- Renal dose adjustment, not to increase above 7.5/46mg dose
**Bupropion/Naltrexone - Contrave**

- Bupropion has combined effects on appetite (mild) and cravings. Naltrexone acts centrally on hypothalamus to potentiate appetite reduction.
- Dose is titrated weekly until week 4 (final dose is 2 pills twice a day)
- Caution in patients with history of seizure, substance use (alcohol or opioids), anorexia or bulimia, uncontrolled HTN, glaucoma or on MAOIs

**Liraglutide - Saxenda**

- GLP-1RA – works in the gut to slow gastric emptying and centrally to reduce appetite
- Dose needs to be titrated by 0.6mg per week
- Contraindicated in patients with family history of MEN-2, personal or family history of medullary thyroid cancer, and pregnancy

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**Pharmacotherapy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight Loss Above Placebo</th>
<th>Pluses</th>
<th>Minuses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>3.6 kg (7.9 lbs) in 2-24 weeks</td>
<td>Inexpensive, greater weight loss</td>
<td>No long term data, side effects</td>
</tr>
<tr>
<td>Orlistat</td>
<td>2.9-3.4% (6.5-7.5 lbs) - 1 year</td>
<td>Non-systemic, long term data, inexpensive OTC</td>
<td>Side effects, less weight loss</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>3.65kg (8 lbs) - 1 year</td>
<td>Side effect profile, long term data</td>
<td>Cost</td>
</tr>
<tr>
<td>Phen/Top</td>
<td>14.5 lbs (low dose) 18.9 lbs (high dose) - 1 year</td>
<td>Robust weight loss, long term data</td>
<td>Teratogenic, cost</td>
</tr>
<tr>
<td>Bup/Nal</td>
<td>6.3kg (~13 lbs) – 1 year</td>
<td>Greater weight loss, food addiction(?)</td>
<td>Side effect profile, cost</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>1.6kg (12.3 lbs) – 1 year</td>
<td>Side effect profile, long term data, cardiovascular(?)</td>
<td>Injectable, cost</td>
</tr>
</tbody>
</table>

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**Medications that Can Cause Weight Gain**

- **Anti-depressants**
  - Avoid paroxetine, amitriptyline, nortriptyline, venlafaxine, and duloxetine
  - Better choices are bupropion, fluoxetine, sertraline, citalopram, or escitalopram
- **Anti-epileptics**
  - Avoid valproate and gabapentin
  - Better choice is carbamazepine
- **Anti-psychotics**
  - Choose aripiprazole or ziprasidone
  - Set expectations with patient, decision to initiate medicine should be shared between doctor and patient.
- **Diabetes medicines**
  - Insulin, Sulfonylureas, TZDs, glinides
  - Recommend concomitant use of Metformin, pramlintide, or GLP-1 agonists/analogues
  - Recommend use of ACE-inh, ARBs, and Calcium Channel Blockers over Beta-blockers (non-selective) for HTN
  - Choose NSAIDs and DMARDs over glucocorticoids in patients with arthritis.
  - Average weight gain with glucocorticoids approximately 4-8%
A note on schedule IV in Ohio

- Phentermine, Lorcaserin, and the combination phentermine/topiramate fall under schedule IV
- Prescribing laws exist when it comes to weight loss medications and differ between short term and long term anorexiants
- Prescribers should be familiar with these prescribing laws – which impact timing of prescriptions, follow-up visits, and potential for refills


Endoscopic Therapy

Intragastric Balloons

- Approved for use in patients with BMI 30-40

- Orbera – two RCT (194 pts), using the IGB for 6 months achieved weight loss of 14.2% vs. 4.8% in the control. In long term follow-up, weight regain reduces total weight loss by about 50%.

- ReShape Duo (dual balloon system) – REDUCE trial (326 subjects - 264 opted for balloon placement). Those with IGB lost 7.6% vs 3.6% in the control group. Approved for use up to 6 months.

- Obalon (ingestible) – can place up to 3 balloons prior to removal (after 3-6 months later). Initial study only 17 subjects treated for 12 weeks – lost median 5kg (no control).


Intragastric Balloons

- Contraindicated in patients with documented history of reflux esophagitis, those taking blood thinners, or prior bariatric surgery.

- Most common side effects:
  - Nausea
  - Vomiting
  - Abdominal pain

- Rare side effects:
  - Gastric ulcers
  - Duodenal blockage
  - Pancreatitis

**Duodenal jejunal bypass sleeve**
- Investigational only currently - endoscopically placed sleeve that is deployed with an anchor at the duodenal bulb.
- Bile and pancreatic enzymes pass round the sleeve and nutrients then mix and are digested further down similar to a gastric bypass.
- Small studies show 10-12 kg weight loss at 12-24 weeks
- Significant decreases in A1C
- Increases in GLP-1
- Side effects (3-5%):  
  - Pain  
  - Nausea/vomiting  
  - Potential for migration  
  - GI bleeding  
  - Sleeve obstruction
- Rare side effects (all < 0.5%):  
  - Cholangitis  
  - Liver abscesses*  
  - Acute cholecystitis  
  - Esophageal perforation


**Aspiration Therapy (AT)**
- Instill 150-200 ml of water and repeat until no food particles are retrieved
- Trial leading to FDA approval included 207 subjects followed for 52 weeks  
  - 58.6% of the AT group vs 15.3% of lifestyle group reached >25% excess weight loss (preset goal)


**Take home points**
- Weight loss (meaningful) is a LONG TERM process and requires a multidisciplinary approach.
- Lifestyle modifications are the basis of any successful weight loss program.
- Medications are available to help patients adhere to a diet and exercise program.
- Several non-surgical options have recently been approved.
- Bariatric surgery remains most effective therapy in terms of weight loss and sustainability.
- Good resource: http://obesity.aace.com/obesity-algorithm#/start