Update on the Recent Advances in Obesity Management

Benjamin O’Donnell, MD – Oct 5th, 2018
Objectives

• Background
• Control of Energy Homeostasis
• Approach to Diet and Exercise
• Medications
• Recently Approved Endoscopic Therapies
Background
Adult Obesity Rate by State, 2017

Select years with the slider to see historical data. Hover over states for more information. Click a state to lock the selection. Click again to unlock.

Percent of obese adults (Body Mass Index of 30+)

- 0 - 9.9%
- 10 - 14.9%
- 15 - 19.9%
- 20 - 24.9%
- 25 - 29.9%
- 30 - 34.9%
- 35%+

Ohio, 2017

Adult Obesity Rate: 33.8%
State Rank: 11
95% Confidence Interval +/- 1.3%

https://stateofobesity.org/adult-obesity/
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.

http://www.cdc.gov/obesity/data/adult.html#Groups
Prevalence of Obesity

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

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Figure 1. Prevalence of obesity among adults aged 20 years and over, by poverty income ratio, sex, and race and ethnicity: United States 2005–2008

- Men
  - Total: 32.9% (PIR≥350%), 34.6% (130%≤PIR<350%), 29.2% (PIR<130%)
  - Non-Hispanic white: 32.2% (PIR≥350%), 34.8% (130%≤PIR<350%), 30.1% (PIR<130%)
  - Non-Hispanic black: 44.5% (PIR≥350%), 35.5% (130%≤PIR<350%), 28.5% (PIR<130%)
  - Mexican American: 40.8% (PIR≥350%), 30.5% (130%≤PIR<350%), 29.9% (PIR<130%)

- Women
  - Total: 29.0% (PIR≥350%), 39.0% (130%≤PIR<350%), 42.0% (PIR<130%)
  - Non-Hispanic white: 27.5% (PIR≥350%), 38.1% (130%≤PIR<350%), 39.2% (PIR<130%)
  - Non-Hispanic black: 47.6% (PIR≥350%), 51.6% (130%≤PIR<350%), 54.7% (PIR<130%)
  - Mexican American: 40.8% (PIR≥350%), 34.5% (130%≤PIR<350%), 44.9% (PIR<130%)

*Significant trend.

NOTES: PIR is poverty income ratio. Persons of other race and ethnicity included in total.


Population data

Figure 3. Prevalence of obesity among adults aged 20 years and over, by education, sex, and race and ethnicity: United States 2005–2008

Pathophysiology
Pathophysiology

“Obesity, by definition, results from ingesting calories in excess of ongoing requirements.”¹

Pathophysiology

- Food is necessary for life.
- Caloric restriction leads to decreased metabolic rate.
- The body defends the higher set point; patients often refer to this as yo-yo dieting.


Control of Energy Homeostasis

*Central nervous system control of food intake and body weight.* Vol 443: 21 September 2006. doi:10.1038/nature05026
Pathophysiology

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

Management of Obesity
Treatment

• 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 lbs per week of weight loss
- No one diet is most effective – rather go with patient preference
- Maintain appropriate balance of nutrients
- Diet should not be lower than 800 calories per day
- Initial goal of 10% decrease in body weight

### TABLE IV-5:

**DURATION OF VARIOUS ACTIVITIES TO EXPEND 150 KILOCALORIES FOR AN AVERAGE 70 KG (154 LB) ADULT**

<table>
<thead>
<tr>
<th>Intensity</th>
<th>Activity</th>
<th>Approximate duration in minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Volleyball, noncompetitive</td>
<td>43</td>
</tr>
<tr>
<td>Moderate</td>
<td>Walking, moderate pace (3mph, 20 min/mile)</td>
<td>37</td>
</tr>
<tr>
<td>Moderate</td>
<td>Walking, brisk pace (4mph, 15 min/mile)</td>
<td>32</td>
</tr>
<tr>
<td>Moderate</td>
<td>Table tennis</td>
<td>32</td>
</tr>
<tr>
<td>Moderate</td>
<td>Raking leaves</td>
<td>32</td>
</tr>
<tr>
<td>Moderate</td>
<td>Social dancing</td>
<td>29</td>
</tr>
<tr>
<td>Moderate</td>
<td>Lawn mowing (powered push mower)</td>
<td>29</td>
</tr>
<tr>
<td>Hard</td>
<td>Jogging (5 mph, 12 min/mile)</td>
<td>18</td>
</tr>
<tr>
<td>Hard</td>
<td>Field hockey</td>
<td>16</td>
</tr>
<tr>
<td>Very Hard</td>
<td>Running (6 mph, 10 min/mile)</td>
<td>13</td>
</tr>
</tbody>
</table>

Source: Surgeon General's Report on Physical Activity and Health
Activity – a caveat

Pharmacotherapy
Use of medications

- Medications do not work on their own, 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*
Phentermine - Adipex

Comparison of Continuous and Intermittent Anorectic Therapy in Obesity

J. F. MUNRO,* M.B., M.R.C.P.ED. ; A. C. MacCUISH,* M.B., CH.B.
ELIZABETH M. WILSON,* S.R.D. ; L. J. P. DUNCAN,* M.B., B.SC., F.R.C.P.ED.

- Phentermine is a sympathomimetic anorexiant, primarily works through release of norepinephrine
- Prescribed as intermittent therapy based on this early trial from 1968 – definition of intermittent varies, but in Ohio this is 12 weeks on 6 months off.
- Caution with glaucoma, MAOIs, cardiac disease, hyperthyroidism.
Orlistat –Xenical, 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
- Comes in several doses.

*Phentermine/Topiramate* - *Qsymia*

*Lancet* 2011; 377: 1341–52
Phentermine/Topiramate

- Caution use in patients with uncontrolled hyperthyroidism, uncontrolled cardiac disease, kidney stones, glaucoma, or on MAOIs
- Contraindicated in pregnancy
- Renal dose adjustment, not to increase above 7.5/46mg dose

Dose titration

- 3.75/23mg daily for 14 days
- 7.5/46mg daily for 12 weeks
  - If ≥ 3% weight loss, continue
  - If < 3% weight loss, adjust dose
    - 11.25/69mg or 15/92 mg daily for 12 weeks
      - If ≤ 5% weight loss on 15/92mg dose, taper off.
- If < 5% weight loss, continue
Bupropion/Naltrexone - Contrave

- Bupropion has NE effect, plus modulates dopamine to decrease 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

Saxenda prescribing information, © 2014-2015 Novo Nordisk
# 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>5.6kg (12.3 lbs) – 1 year</td>
<td>Side effect profile, long term data, cardiovascular(?)</td>
<td>Injectable, cost</td>
</tr>
</tbody>
</table>
Rohan Khera, MD; Mohammad Hassan Murad, MD, MPH et al. Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events; A Systematic Review and Meta-Analysis. *JAMA*. 2016;315(22):2424-2434
Endoscopic Therapy
Intragastric Balloons

Table 1. Comparison of Intragastric Balloons Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Orbera</th>
<th>ReShape</th>
<th>Spatz</th>
<th>Obalon</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of balloons</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>Up to 3</td>
</tr>
<tr>
<td>Balloons filled with ...</td>
<td>Saline and methylene blue</td>
<td>Saline and methylene blue</td>
<td>Saline</td>
<td>Nitrogen gas</td>
</tr>
<tr>
<td>Fill volume per balloon, mL</td>
<td>500–750</td>
<td>450</td>
<td>Adjustable</td>
<td>250</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30–40</td>
<td>30–40</td>
<td>27+</td>
<td>30–40</td>
</tr>
<tr>
<td>Insertion method</td>
<td>Endoscopic</td>
<td>Endoscopic</td>
<td>Endoscopic</td>
<td>Oral capsule device</td>
</tr>
<tr>
<td>Removal method</td>
<td>Endoscopic</td>
<td>Endoscopic</td>
<td>Endoscopic</td>
<td>Endoscopic</td>
</tr>
<tr>
<td>Time until removal, mo</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>FDA approved</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

BMI, body mass index; FDA, Food and Drug Administration.
Intragastric Balloons

- **Orbera** – in two RCT (66 & 128 enrollees), patients using the IGB for 6 months achieved 14.2% vs. 4.8% in the control (18.2 kg vs 6 kg in the control). In long term follow-up, mean weight regain was about half of the initial weight lost.

- **ReShape Duo** (dual balloon system) – REDUCE trial enrolled 326 subjects, of those eventually 264 opted for balloon placement. Early retrieval occurred in 9.1%. Those with IGB lost 7.6% vs 3.6% in the control group.

- **Obalon** (ingestible balloon) – can place up to 3 balloons prior to removal. Initial study with 17 subjects with a mean BMI of 31 (44 attempted balloons), 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

- Endoscopically placed device consisting of the sleeve that is deployed and an anchor that sits 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)

- Endoscopically placed gastrostomy tube – siphon assembly allows for aspiration of gastric contents 20 minutes post-meal
- Instill 150-200 ml of water and repeat until no food particles are retrieved
- Trial leading to FDA approval included 207 subjects, BMI 35-55 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
Thank you!

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