Medications in the Treatment of Obesity

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Diplomate of American Board of Obesity Medicine
NO DISCLOSURES
**Classification of Obesity**

<table>
<thead>
<tr>
<th>BMI (Body Mass Index)</th>
<th>Weight Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5 – 24.9</td>
<td>“Normal”</td>
</tr>
<tr>
<td>25 – 29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30 – 34.9</td>
<td>Obesity Class I</td>
</tr>
<tr>
<td>35 – 39.9</td>
<td>Obesity Class II</td>
</tr>
<tr>
<td>40 or more</td>
<td>Obesity Class III</td>
</tr>
</tbody>
</table>

**BMI>23 is considered overweight for South, Southeast and East Asians**
## Medication Review

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug Class</th>
<th>Weight Gain</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric agents</td>
<td>Antipsychotic</td>
<td>Clozapine, risperidone, olanzapine, quetiapine, haloperidol, perphenazine</td>
<td>Ziprasidone, aripiprazole</td>
</tr>
<tr>
<td></td>
<td>Antidepressants/mood stabilizers: tricyclic antidepressants</td>
<td>Amytriptyline, doxepin, imipramine, nortriptyline, trimipramine, mirtazapine</td>
<td>Bupropion(^a), nefazodone, fluoxetine (short term), sertraline (&lt;1 year)</td>
</tr>
<tr>
<td></td>
<td>Antidepressants/mood stabilizers: SSRIs</td>
<td>Fluoxetine(^?), sertraline(^?), paroxetine, fluvoxamine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antidepressants/mood stabilizers: MAOIs</td>
<td>Phenylzine, tranylcypromine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lithium</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Neurologic agents</td>
<td>Anticonvulsants</td>
<td>Carbamazepine, gabapentin, valproate</td>
<td>Lamotrigine(^?), topiramate(^a), zonisamide(^a)</td>
</tr>
<tr>
<td>Endocrinologic agents</td>
<td>Diabetes drugs</td>
<td>Insulin (weight gain differs with type and regimen used), sulfonylureas, thiazolidinediones, sitagliptin(^?), metiglinide</td>
<td>Metformin(^a), acarbose(^a), miglitol(^a), pramlintide(^a), edenatide(^a), liraglutide(^a)</td>
</tr>
</tbody>
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Apovian CM et al. *J Clin Endocrinol Metab.* 2015;100:342-362
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<th>Drug Class</th>
<th>Weight Gain</th>
<th>Alternatives</th>
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</thead>
<tbody>
<tr>
<td>Gynecologic agents</td>
<td>Oral contraceptives</td>
<td>Progestational steroids, hormonal contraceptives containing progestational steroids</td>
<td>Barrier methods, IUDs</td>
</tr>
<tr>
<td></td>
<td>Endometriosis treatment</td>
<td>Depot leuprolide acetate</td>
<td>Surgical methods</td>
</tr>
<tr>
<td>Cardiologic agents</td>
<td>Antihypertensives</td>
<td>α-blocker?, β-blocker?</td>
<td>ACE inhibitors?, calcium channel blockers?, angiotensin-2 receptor antagonists</td>
</tr>
<tr>
<td>Infectious disease agents</td>
<td>Antiretroviral therapy</td>
<td>Protease inhibitors</td>
<td>—</td>
</tr>
<tr>
<td>General</td>
<td>Steroid hormones</td>
<td>Corticosteroids, progestational steroids</td>
<td>NSAIDs</td>
</tr>
<tr>
<td></td>
<td>Antihistamines/anticholinergics</td>
<td>Diphenhydramine?, doxepin?, cyproheptadine?</td>
<td>Decongestants, steroid inhalers</td>
</tr>
</tbody>
</table>

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Treatment Pillars

- Nutrition
- Physical Activity
- Behavior Therapy
- Pharmacotherapy
- Bariatric Surgery

Goal 5-10% weight loss
<table>
<thead>
<tr>
<th>Condition</th>
<th>% weight loss for therapeutic benefit</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Prevention</td>
<td>3% to 10%</td>
<td>DPP (Lancet, 2009) SEQUEL (Garvey et al, 2013)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5% to &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3% to &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>HbA1c</td>
<td>3% to &gt;15%</td>
<td>Look AHEAD (Wing, 2011)</td>
</tr>
<tr>
<td>NAFLD</td>
<td>10%</td>
<td>Assy et al, 2007; Dixon et al, 2004; Anish et al, 2009</td>
</tr>
<tr>
<td>Sleep Apnea</td>
<td>10%</td>
<td>Sleep AHEAD (Foster, 2009) Winslow et al, 2012</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>5-10%</td>
<td>Christensen et al, 2007; Felson et al, 1992; Aaboe et al, 2011</td>
</tr>
<tr>
<td>Stress Incontinence</td>
<td>5-10%</td>
<td>Burgio et al, 2007 Leslee et al, 2009</td>
</tr>
<tr>
<td>GERD</td>
<td>5-10% (women) 10% (men)</td>
<td>Singh et al, 2013 Tutujian R, 2011</td>
</tr>
<tr>
<td>PCOS</td>
<td>5-15% (&gt;10% optimal)</td>
<td>Panidis D et al, 2008; Norman et al, 2002; Moran et al, 2013</td>
</tr>
</tbody>
</table>
Pathophysicsiology

Pathophysiology of Eating and Weight Regulation

↑ Appetite ↓

Ghrelin
CCK
GLP-1
OXM
PYY
Insulin
Amylin
Leptin

↑ Energy Expenditure ↓

Stomach
Small Intestine
Large Intestine
Pancreas
Fat Cells
We “under” prescribe

2% of adults with OBESITY received pharmacotherapy

86% of adults with T2DM received pharmacotherapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of Action</th>
<th>Mean Weight Loss&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Study Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine resin</td>
<td>Norepinephrine-releasing agent</td>
<td>3.6 kg</td>
<td>2 to 24 weeks</td>
</tr>
<tr>
<td>Diethylpropion</td>
<td>Norepinephrine-releasing agents</td>
<td>3.0 kg</td>
<td>6 to 52 weeks</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Pancreatic and gastric lipase inhibitor</td>
<td>2.9 to 3.4 kg, 2.9% to 3.4%</td>
<td>1 year</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>5HT&lt;sub&gt;2c&lt;/sub&gt; receptor agonist</td>
<td>3.6 kg, 3.6%</td>
<td>1 year</td>
</tr>
<tr>
<td>Phentermine/topiramate</td>
<td>GABA receptor modulation (topiramate) plus norepinephrine-releasing agent (phentermine)</td>
<td>6.6 kg (recommended dose), 6.6%; 8.6 kg (high dose), 8.6%</td>
<td>1 year</td>
</tr>
<tr>
<td>Naltrexone bupropion</td>
<td>Reuptake inhibitor of dopamine and norepinephrine (bupropion) and opioid antagonist (naltrexone)</td>
<td>4.8%</td>
<td>1 year</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>GLP-1 agonist</td>
<td>5.8 kg</td>
<td>1 year</td>
</tr>
</tbody>
</table>

<sup>a</sup> Savings as percentage of initial body weight or mean kg weight loss.

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<tr>
<th>Anti-Obesity Drugs</th>
<th>Why Choose this drug?</th>
<th>Why NOT choose this drug?</th>
</tr>
</thead>
</table>
| Phentermine        | Inexpensive, time tested | • Stimulant side effects – anxiety, irritability  
                  |                       | • Schedule IV controlled substance  
                  |                       | • Known active cardiac disease  |
| Topiramate         | **Double Benefits:** Migraines, Seizures, Binge eating, Bipolar  
                  | • May help insomnia, reduce soda intake, excessive carb intake? Inexpensive | • “Dopamax” – cognitive, word finding difficulty  
                  |                       | • Teratogenic effect (planning to be pregnant)  |
| Phentermine/Topiramate Cr (Qsymia) | Same as above. Highly effective | • Stimulant effect, **teratogenic effect**, $$$, hx of kidney stones or glaucoma  
                                |                       | • Higher doses greater cost  |
| Liraglutide (Saxenda) | **Double Benefits:** Diabetes, prediabetes  
                      | • Improves BP, cardiovascular data, lack of central side effects, high efficacy | • Gastroparesis, history of MTC, hx of pancreatitis, $$$  |
| Lorcaserin (Belviq) | **Double Benefits:** Diabetes improvement  
                      | • Less central side effects  
                      |                       | • Less effective  
                      | • Evening eating  
                      | • Potential interaction with SSRI  
                      |                       | • $$/Schedule IV controlled substance  |
| Naltrexone/Bupropion XR (Contrave) | **Double Benefits:** Alcohol cessation(Nal), Smoking, Depression(Bup) Diabetes improvement  
                                    | • Excessive cravings, hedonistic food drive | • Stimulant side effects, nausea (Naltrexone), $$  
                                    |                       | • Hx of seizures, uncontrolled HTN, active bulimia  
                                    |                       | • Less effective  |
| Orlistat (Xenical, Alli) | Hypertriglyceridemia  
                        | No central side effect profile | • Less effective  
                        |                       | • GI Side effect profile, B12 deficiency, $  |
| Metformin          | **Double Benefits:** PCOS, Diabetes, Pregnancy, Atypical Antipsych Meds  
                  | Inexpensive | • GI Side effect profile, B12 deficiency  |
Monitoring

- Start medication
- 1 month follow up for side effects
- 3 month follow up for weight loss effect
- <5% weight loss increase the dose or try a new medication
Case 1: 60yo Female

Weight 210lb
BMI 37-class 2 obesity
Goal at 6 months is 10% down or 189lb
Exercises 3-5 days a week (tennis)

PMH: hypertension and hyperlipidemia
Medications: Hydrochlorothiazide 25mg daily

Labs:
HgbA1c 6.1%

Lipids:
Total cholesterol 268
Trig 95
HDL 80
LDL 169
What medication for obesity would you use in this patient?

A. Phentermine/Topiramate (Qsymia)
B. Naltrexone/Bupropion (Contrave)
C. Metformin
D. Liraglutide (Saxenda)
Weight Loss

Weight (lb) vs. BMI

- Weight (lb)
- BMI

- Started Saxenda

Graph showing weight loss and BMI change over time.
Case 2: 59yo Female

Weight 198lb
BMI 31-Class 1 obesity
Hungry all the time, late night cravings, difficulty with portion control

PMH: CPPD, knee osteoarthritis

Medications: Plaquenil, Celecoxib, Glucosamine-Chondroitin

Labs:
HgbA1C-5.5%
Lipids:
Total chol-224
Trig-112
HDL-67
LDL-135
What medication for obesity would you use in this patient?

A. Phentermine/Topiramate (Qsymia)
B. Naltrexone/Bupropion (Contrave)
C. Orlistat
D. Liraglutide (Saxenda)
Case 3: 54yo Male

Weight: 294lb
BMI 37
Rarely hungry, emotional eating

PMH: Hypertension, Obstructive sleep apnea
Medications: Benazepril 10mg

Labs:
HgbA1C: 6%
AST: 38
ALT: 65
Total Cholesterol: 214
Triglycerides: 184
HDL: 48
LDL: 129
What medication for obesity would you use in this patient?

A. Phentermine/Topiramate (Qsymia)
B. Naltrexone/Bupropion (Contrave)
C. Orlistat
D. Liraglutide (Saxenda)
Weight loss

**Weight (lb)**

- Started Contrave
- Started Saxenda

**BMI**

- Started Contrave
- Started Saxenda

Weight (lb):
- 260
- 265
- 270
- 275
- 280
- 285
- 290
- 295
- 300

BMI:
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
Take Home Points

Stage the patient’s obesity and discuss it as a disease process that it is

Review and adjust current medications that may be contributing to weight gain

Start an anti-obesity medication at the same time as providing lifestyle interventions

Recommend frequent follow up for monitoring of efficacy, side effects and adherence
Questions?