Pharmacotherapy for Obesity: To Use or not to Use

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The Patient

- 55 year old female
- 5'5", 200 lbs, BMI 33.3
- BP 135/80, waist 100cm
- Past medical history: HTN, dyslipidemia, menopause age 50
- Social history: 2 children, ages 14, 16. Works full time, sedentary job. Walks 30 minutes 2x/week. No tobacco, occasional EtOH. Eats out about once/week
- Family history: parents and siblings obese, mother MI age 60
- Medications: HCTZ, simvastatin, MVI
- Labs: A1C 6%, LDL 100, TG 160
- Exam: no clinical features of cortisol excess or thyroid dysfunction

What are her options?

Obesity is a chronic disease

- It impairs normal functioning of some aspect of the body
- It has characteristic signs and symptoms
- It results in harm or morbidity to the affected individual

Obesity affects most systems

- NAFLD
gallstones
- Type 2 diabetes
insulin resistance
- Obstructive sleep apnea
CAD, HTN
- Plus increased risk
malignancies
osteoporosis
depression
### Metrics of Obesity

- BMI (kg/m²)
- Waist circumference
- Waist/hip ratio
- Body composition
  - Bioelectrical impedance analysis
  - DEXA
  - Skin fold measurement

### Our patient

- Postmenopausal female
- Central obesity
- BMI 33
- Comorbidities
- Increased CV risk
- No secondary causes

### Initial assessment

- Weight history
  - Including prior attempts at weight loss
- Current diet/24 food recall
- Comorbidities that increase CV risk
- Secondary causes for obesity?

### Weight history

- High school graduation: 140 lbs (BMI 23)
- College: gained about 10 lbs
- Pregnancy: gained 40 lbs
- 40s-50s: steady weight gain, about 3 lbs/year
- Formal programs: Weight Watchers 5 years ago, lost 20 lbs in about 6 months, regained + gained more
- No pharmacotherapy, no surgery

### Your initial recommendation is:

- A. Prescription weight loss medication
- B. Very low-carbohydrate diet, return to clinic in 3 months
- C. Hypocaloric diet, return to clinic in 1 month
- D. Referral for bariatric surgery
- E. Reassurance. Since she does not have diabetes or CAD, aggressive efforts at weight loss are not necessary at this time

### Obesity treatment options (nonsurgical)
The cornerstones of obesity treatment

Which diet do you recommend?

Adherence to any diet wanes over time

Weight loss correlates with adherence to diet

12 mos weight loss (kg)

1 = not adherent 10 = perfect adherence

Some studies show greater weight loss with a low-carbohydrate diet

Some diets may be better for maintaining weight loss

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Pharmacotherapy of Obesity: To Use or Not to Use?

Diets and weight loss: keep this in mind

Pharmacotherapy for the treatment of obesity

True or false

Only patients with BMI > 35 are candidates for obesity pharmacotherapy

Which medication(s) are approved for the treatment of obesity?

A. Sibutramine
B. Orlistat
C. GLP-1 agents (liraglutide, exenatide)
D. Phentermine
E. Topiramate
F. Metformin
G. Thyroid hormone

Pharmacotherapeutic options for ongoing treatment of obesity

• Orlistat
• Phentermine/Topiramate
• Lorcaserin

What is considered a successful response to pharmacotherapy for weight loss?

A. 10%
B. 20%
C. 3-5%
D. There is no absolute amount of weight loss that indicates successful treatment

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Orlistat: mechanism of action

- Lipase inhibitor
  - Blocks fat absorption from the duodenal mucosa

Orlistat: weight loss

- Low carbohydrate diet
  - no caloric restriction
- Orlistat + low fat diet
  - -500 to -1000 kcal/day
  - Yancy et al, 2010

Orlistat: side effects

- Flatulence +/- fecal discharge
- Fecal urgency
- Fecal incontinence
- Fatty stool, oily spotting
- Increased defecation

Phentermine/topiramate

- Phentermine: sympathomimetic anorectic
- Topiramate extended release: anti-epileptic, unclear mechanism of action for weight loss (GABA agonist)

Weight loss: phentermine/topiramate

- Gadde et al, Lancet 2011

Phentermine/topiramate side effects

- Paresthesia
- Dizziness
- Dysgeusia
- Insomnia
- Constipation
- Dry mouth
Phentermine/topiramate

contraindications and precautions

- PREGNANCY
  - Congenital malformations (cleft lip)
- Prescribed through a central pharmacy due to teratogenicity
  - www.QsymiaREMS.com

Phentermine/topiramate

practical information

- Dose titration
  - 3.75mg/23mg x 14 days
  - Increase to 7.5/46 mg
- 12 weeks, if < 3% weight loss, wean off OR titrate up again
- 24 weeks, if < 5% weight loss on 15/92mg dosing, wean off

Lorcaserin

- Approved in 2012 for BMI > 30 or > 27 with comorbidities
  - In conjunction with lifestyle intervention
- Not yet available in the US

Lorcaserin: mechanism of action

- Selective serotonin receptor agonist
  - 5HT₂C receptor
- Appetite/weight-reducing effects of serotonin mediated by the 5HT₂C receptor in the brain
  - 100-fold less affinity for the 5HT₂B receptor in the heart

Lorcaserin: weight loss

Lorcaserin: common side effects

- Headache
- Dizziness
- Nausea
- Fatigue
- Dry mouth
- Constipation
- URI/nasopharyngitis
**Lorcaserin: practical information**

- **Dosing:** 10mg bid
- **Assess response at 12 weeks**
  - If < 5%, **discontinue**
- **Contraindicated in pregnancy**
- **Drug interactions**
  - SSRIs, SSNRIs
- **Hepatic metabolism, renal clearance**

**Medications associated with weight loss**

- **Bupropion**
  - 2.8 kg at 6-12 months
- **Fluoxetine**
  - 3.15 kg at 12 months
- **Metformin**
  - Neutral to mild weight loss (up to -2.4 kg over 12 months in some studies)
- **Zonisamide**
  - 5% (compared to placebo) over 16 weeks
- **GLP-1 agents (exenatide and liraglutide)**
  - 3% over 30 weeks

**Weight loss with exenatide treatment in overweight and obese nondiabetic women**

- 2.5 kg

**Liraglutide and weight loss**

- Kaplan 2010

**True or false**

If weight loss occurs with pharmacotherapy, this treatment cannot be stopped or the weight will be regained

(Generally) True
Take home points: Obesity Pharmacotherapy

- Always used in combination with ongoing lifestyle intervention
- Sustained and typically greater weight loss than lifestyle monotherapy
- Assess efficacy at 12 weeks
  – Goal 3-5% weight loss
- Understand side effects, warnings
- Plan for frequent monitoring and followup

Back to our patient

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THANK YOU!