Pharmacologic Intervention for Weight Loss: Does it Really Work?

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Learning Objectives

1. State the medications currently approved for medical weight loss.
2. Formulate a plan to approach pharmacologic weight loss systematically.
3. Recognize the side effects of the commonly used medications for weight loss.

AES Question 1

What assessments should be conducted for a patient who may be a candidate for weight loss therapy?

A. Body fat percentage, BMI, upper arm circumference
B. Abdominal circumference, thigh circumference, height
C. BMI, chest circumference, body fat percentage
D. BMI, abdominal circumference, waist to hip ratio

Review of Candidates

- Comorbid conditions
  - HTN
  - DM
  - CAD
  - Sleep apnea
  - OA leading to ambulation limitations
- Waist circumference
  - Women >35 inches
  - Men >40 inches
- BMI
  - >25% overweight
  - >27% treatment considered if comorbid conditions
  - >30% class I obesity
  - >35% class II obesity

Before Medications

- Multifaceted plan to incorporate all aspects
- May be on other medications that promote weight gain
- Review realistic expectations
- Address diet via a nutrition expert if you don’t have the skills
- Create activity plan that is reasonable or refer to wellness center with trained professionals
- Discuss benchmarks to measure success
- Then discuss medications as the add-on to the overall plan

Nutrition

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USDA Food Pattern

- Every 5 years, the U.S. Department of Agriculture (USDA) and U.S Department of Health and Human Services (HHS) develop *Guidelines* based on the latest nutrition research
  - Designed to provide authoritative advice on dietary habits to promote good health and healthy weight and to reduce risk for major chronic diseases
  - Provide Americans, ages 2 and older, food and beverage recommendations developed in consideration of evidence-based recommendation

Nutrition Tips

- Before prescribing a medication have patient keep a food journal for a minimum of 3 months
- Review journal monthly and discuss obvious poor choices
- Discuss substitutes for poor choices within your comfort zone
- Very few can change diet quickly. This is more of an exercise so they can see areas for improvement
- Consider diet/nutrition consult or referral to a program
  - 1,200 to 1,500 kcal/day for women
  - 1,500 to 1,800 kcal/day for men

Physical Activity

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AES Question 2

Which of the following is defined as moderate activity?

A. Strolling with friends around the block
B. Waiting tables
C. Light gardening
D. Gaming with the kids

Minimum Physical Activity

- Patient needs activity tracker for a minimum of 3 months prior to any medication
- Average goal for AEROBIC activity
  - –30 minutes 5 x a week above their day-to-day activities
  - –Can be 25 minutes 3x a week if vigorous activity
- To see ≥5% weight loss from baseline need approximately 300 minutes per week total
- Encourage patient to start slow
- Discuss activities that work for them, such as mall-walking or riding a bike

Definition of Activity

- Moderate
  -Increase in respiratory and HR
  -Light snow shoveling
  -Actively playing with children
  -Brisk walking
  -Water aerobics
  -Casual biking
  -Tennis
  -Ballroom dancing
  -Light gardening

- Vigorous
  -Breathing too hard or quickly to hold a conversation
  -Rollerblading at a quick pace
  -Cross country skiing
  -Competitive sports (soccer, football, etc.)
  -Racewalking/jogging/running
  -Swimming laps
  -Aerobic dancing
  -Jumping rope
  -Hiking

Calories Used per Hour in Common Physical Activities		
Moderate Physical Activity	**Approximate Calories/30 Minutes for a 154 lb Person[1]**	**Approximate Calories/Hr for a 154 lb Person[1]**
Hiking	185	370
Light gardening/yard work	165	330
Dancing	165	330
Golf (walking and carrying clubs)	165	330
Bicycling (<10 mph)	145	290
Walking (3.5 mph)	140	280
Weight lifting (general light workout)	110	220
Stretching	90	180
Vigorous Physical Activity	**Approximate Calories/30 Minutes for a 154 lb Person[1]**	**Approximate Calories/Hr for a 154 lb Person[1]**
Running/jogging (5 mph)	295	590
Bicycling (>10 mph)	295	590
Swimming (slow freestyle laps)	255	510
Aerobics	240	480
Walking (4.5 mph)	230	460
Heavy yard work (chopping wood)	220	440
Weight lifting (vigorous effort)	220	440
Basketball (vigorous)	220	440

[1] Calories burned per hour will be higher for persons who weigh more than 154 lbs (70 kg) and lower for persons who weigh less.
Source: Adapted from Dietary Guidelines for Americans 2005, page 16, Table 4.

Measure of Success

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AES Question 3

How long should nonpharmacologic therapy continue before adding a medication?

A. 1 month
B. 3 months
C. 6 months
D. 12 months

How to Measure Success

- Degree of weight loss and improvement in associated risk factors
- Timeline is variable but need monthly office visits:
  - First month
    - Loss should exceed 2 kg or about a pound a week
  - Third month
    - Loss should be between 3-5% using nonpharmacologic methods
    - Can initiate medication therapy after first month but not recommended
    - Same benchmarks are used for success
  - Sixth month
    - Loss should be 3-5% secondary to the addition of medications
    - If not achieved then medication should be D/Ced
  - Twelve months
    - Loss of 10-15% is considered very good
    - Loss exceeding 15% is considered excellent

Pharmacologic Agents

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AES Question 4

Which of following patient characteristics has the greatest impact on medication selection?

A. Comorbid diseases
B. Renal function
C. Age
D. Insurance coverage

Orlistat

- Two versions:
  - Xenical dosed at 120 mg TID with each main meal containing fat
  - Alli dosed at 60 mg up to TID with meals containing 15 g of fat
- Actions:
  - Inhibits GI lipase and reduces the absorption of fat by 30%
- Efficacy:
  - 1-year trial showed an average of 8% weight loss
  - 4-year trial showed an average of 3% weight loss
  - Large percentage of improvement in BS and BP indices
- Safety:
  - Flatus, oily spotting, fecal incontinence, cramps
  - Increases with % of fat in each meal
  - Loss of fat soluble vitamins, so supplementation is needed
- Cost:
  - Xenical is about $480/month
  - Alli is $45/month

Liraglutide (Saxenda)

- Actions:
  - GLP1 receptor agonist that reduces appetite and energy intake
- Efficacy:
  - 1 year trial showed a loss of 3.9-5.2 kg more than placebo
  - 44 to 62% reached goal of 5% or greater within a year
  - Evaluate wt loss at 16 weeks and must achieve a 4% loss
- Dose:
  - Titration dose starting at 0.6 mg/d increased weekly 0.6 mg to target dose of 3 mg/d by week 5
  - Done to minimize GI upset

Liraglutide (Saxenda)

- Safety:
  - Nausea, GI upset, vomiting, low BS in DM pts
  - Consider dose adjusting other DM meds by 50%
  - Insulin dose should be reduced by 20%
  - One of every 18 pts stopped due to ADRs
- Cost:
  - Approximately $2000/month
- Population Considerations:
  - DM patients on high doses of insulin
  - Borderline hyperglycemia
  - Pts on atypical antipsychotics
  - DM patients as first-line therapy?

Lorcaserin (Belviq)

- Actions:
  - $5\text{-}HT_{2C}$ > $5\text{-}HT_{2B}$ agonist that causes appetite suppression
- Efficacy:
  - 1 year showed a loss of 3.3 kg more than placebo
  - Must achieve 5% weight loss by week 12
  - <50% reached the weight loss goal of 5% within 1 year
- Safety:
  - Data with $5\text{-}HT_{2B}$ agonist causing valvular disease
  - Psychiatric effects were common
  - HA was most common
  - Hypoglycemia in DM pts
  - Caution with serotonin syndrome if used with other serotonergic agents
  - 1 in 53 stopped drug secondary to ADR

Lorcaserin (Belviq)

- Dose:
  - 10 mg BID with no titration required
- Cost:
  - $265/month
- Population Considerations:
  - C-IV
  - Drug interactions with other 5-HT agents
  - CHF
  - H/O priapism
  - DM
  - Operate heavy machinery

AES Question 5

Why are phentermine and diethylpropion indicated for short-term use?

A. Tolerance occurs, drug dependence may occur, and long-term safety data is unavailable
B. They are classified as schedule II drugs with high abuse potential
C. Their effect on weight loss is dangerously rapid and a recovery period is recommended
D. Psychosis is common following 3-4 weeks of use

Phentermine (Adipex-P)

- Actions:
  - Sympathomimetic stimulant
- Efficacy:
  - 6-month trials showed a loss of 3.6 kg more than placebo
  - Trials are much shorter in duration
  - Dosing varies in trials
- Dose:
  - 18.75 mg to 37.5 mg taken before breakfast
  - 18.75 mg BID
  - 15-30 mg taken 2 hours after breakfast
  - Usually no more than 3-6 months of use

Phentermine (Adipex-P)

- Safety:
  - Pulmonary HTN
  - Valvular heart disease
  - Dependence
  - Tachycardia and increased BP
  - C-IV
- Cost:
  - $45/month
- Population Considerations:
  - CV disease and/or valvular insufficiency/murmur
  - HF and/or LVH
  - Addictive personality
  - H/O CVA, MI, afib,

Phentermine/Topiramate (Qsymia)

- Actions:
  - Phentermine is a sympathomimetic stimulant
  - Topiramate enhances GABA, antagonizes glutamate receptors, inhibits carbonic anhydrase leading to decreased appetite and early satiety
- Efficacy
  - 1 year showed a loss of 9 kg more than placebo
  - About 70% in clinical trials met the goal of 5% loss
  - Goal is 3% loss by week 12 or 5% by week 24, if not achieved increase dose or D/C
- Dose
  - Titration schedule
  - Initiate at 3.75 mg/23 mg daily x 14 days
  - Increase to 7.5 mg/46 mg daily x 10 weeks (goal 3%)
  - If needed, increase to 11.25 mg/69 mg daily x 14 days
  - Increase to 15 mg/92 mg daily x 10 weeks
  - Must achieve 5% loss by then, if not D/C

Phentermine/Topiramate (Qsymia)

- Safety:
  - C-IV
  - REMS required
  - Too many ADRs to list
  - 1 in every 12 stopped due to ADR
- Cost:
  - $230/month
- Population Considerations:
  - Uncontrolled HTN, afib, tachycardia, Valvular disease
  - CI in Pregnancy - test at baseline and monthly
  - H/O suicide attempt or ideation
  - ETOH abuse/CNS depressants
  - Liver impairment

Diethylpropion

- Action:
  - Sympathomimetic stimulant
- Efficacy:
  - Pooled data showed a loss of 3 kg more than placebo
  - D/C after 4 weeks if not lost at least 1.8 kg
- Safety:
  - Pulmonary HTN
  - Valvular heart disease (consider baseline EKG and ECHO pre and post)
  - Dependence
  - Tachycardia and increased BP
  - C-IV

Diethylpropion

- Dose:
  - IR 25 mg TID to QID taken 1 hour before a meal and mid-evening
  - SR 75 mg daily taken mid-morning
- Cost:
  - $30/month
- Population Considerations:
  - CV disease and/or valvular insufficiency/murmur
  - HF and/or LVH
  - Addictive personality
  - H/O CVA, MI, afib,

Naltrexone/Bupropion (Contrave)

- Actions:
  - Bupropion is a DA and NE reuptake inhibitor working to suppress appetite, similar structure to diethylpropion
  - Naltrexone is a competitive inhibitor of opioid receptors with possible effect on hypothalamic system impacting the pleasure/reward pathways.
- Efficacy:
  - 1 year showed a loss of 2.77 kg more than placebo
  - Pooled analysis of three studies
  - Must achieve a 5% weight loss by week 12 of maintenance dosing
- Dose:
  - Naltrexone 8 mg/Bupropion 90 mg tablets with titration schedule to minimize side effects
  - Initiate at 1 tablet daily x 1 week then increase to 1 tablet BID x 1 week
  - Increased to 2 tablets in AM and 1 tablet in PM x 1 week then 2 tablets BID

Naltrexone/Bupropion (Contrave)

- Safety:
  - Increase BP and HR so unsure of CV effects
  - 50% dropped out of trials secondary to side effects such as nausea, HA, and constipation
  - Concerns about insomnia, suicidal ideation, anorexia
- Cost:
  - $250/month
- Population Considerations:
  - Seizures
  - Uncontrolled BP and/or HR
  - ETOH abusers
  - Eating disorders
  - Chronic opioid users

Final Thoughts

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Best Practice Recommendations

- Do not try to fix obesity at the first visit
- Emphasis on patient and lifestyle choices, not medications
- Refer to experts if you are uncomfortable with nutrition or activity recommendations
- Be a cheerleader
- Incorporate medications as ADJUNCT therapy
- Choose medication based on patient's characteristics

Barriers Are Huge

- Patients have unrealistic expectations
- Obesity management is multifaceted
- Certain maintenance medications cause weight gain, ie psych meds
- Many physicians do not have the training to develop a comprehensive weight loss plan
- Gyms, activity centers, etc., cost money for membership
- Eating healthy is difficult on a budget
- Non-pharmacologic management only has one monitoring parameter – weight loss
- Medications are not benign or inexpensive

Best Practice Recommendations

- Set realistic expectations
- Engage experts to join the team
- Use non-pharmacologic management for 3 months to gauge commitment of the patient
- Pharmacologic management is ADJUNCT to the non-pharmacologic components
- Not everyone will be a candidate for medications
- See patients monthly to assess progress and evaluate for side effects
- Positive enforcement is crucial
- However, playing bad parent is also required to push patients to excel each time even if they are on track, such as increasing exercise time

Questions