MANAGEMENT OF ASTHMA AND OBESITY INCLUDING USE OF APPETITE SUPPRESSANTS

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Link Between Obesity and Asthma

- Obesity is major risk factor for asthma
- Obesity increases severity in asthmatic patients
- Endocrine regulation of airway nerves likely contribute to airway hyperactivity in obese states
- Obese patients with asthma may represent unique phenotype less responsive to ICS
- Modest weight reduction can improve clinical manifestations and asthma outcomes
Obesity Guidelines

- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) Consensus Conference on Obesity: Building and Evidence Base for Comprehensive Action
- AACE and ACE Position Statement on the 2014 Advanced Framework for a New Diagnosis of Obesity as a Chronic Disease

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Framework for New Diagnosis of Obesity

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Anthropometric Component</th>
<th>Clinical Component</th>
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</thead>
<tbody>
<tr>
<td>Overweight</td>
<td>BMI 25-29.9</td>
<td>No obesity related complications</td>
</tr>
<tr>
<td>Obesity</td>
<td>BMI ≥30</td>
<td>No obesity related complications</td>
</tr>
<tr>
<td>Obesity Stage 1</td>
<td>BMI ≥ 25</td>
<td>Presence of 1 or more mild to moderate obesity related complications</td>
</tr>
<tr>
<td>Obesity Stage 2</td>
<td>BMI ≥ 25</td>
<td>Presence of 1 or more severe obesity related complications</td>
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</tbody>
</table>
Obesity Related Complications

- Metabolic syndrome
- Pre-diabetes
- Type 2 DM
- Dyslipidemia
- Hypertension
- Abnormal liver function
- PCOS
- OSA
- Osteoarthritis
- Urinary stress incontinence
- Disability/immobility

Monitor

- Blood pressure
- Waist circumference
- Fasting glucose
- Fasting lipid panel (Total Chol, LDL, HDL, triglicerides)
- Creatinine
- Hepatic transaminases

- Above in addition to assessment of:
  - Diet
  - Meal pattern preferences
  - Physical activity
Steps in Weight Loss Recommendations

- Weight loss less likely if emphasis in on physical activity vs. behavioral and healthy eating strategies
- Pharmacologic interventions should be considered only after 3-6 months if no change achieved with lifestyle interventions
- First confirm patient is not taking drugs that might produce weight gain
  - Some diabetes medications
  - Antidepressants
  - Anti-epileptics
  - Steroids

OTC Products

- Not controlled by FDA if marketed as supplement
- Limited studies in humans
- Existing studies have small sample sizes
- Most sponsored by industry
### OTC Products

- **Garcinia Cambogia**
  - MOA: might inhibit fat-producing enzyme and increase levels of serotonin
  - May cause modest weight loss however the effects are small

- **Caffeine**
  - MOA: boosts metabolism and increases fat burning
  - SE: anxiety, insomnia, jitteriness, irritability, etc.
  - Can have short term benefits but tolerance develops quickly

- **Hydroxycut**
  - MOA: contains "plant extracts and caffeine-action probably related to caffeine"
  - Few studies, no data on long-term effectiveness, can help with weight loss

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### OTC Products

- **Orlistat (Alli OTC, Xenical by rx)**
  - MOA: inhibits breakdown of fat in the gut
  - Effect: can increase wt. loss by 6 lbs.
  - SE: digestive SE

- **Raspberry Ketones**
  - MOA: in rats increase breakdown of fat and increase levels of adiponectin
  - No human studies, massive doses used in rat studies

- **Green Coffee Bean Extract**
  - MOA: caffeine increases fat burning Cholorgenic acid (CA) can slow breakdown of carbs in the gut
  - SE: caffeine related SE and CA can cause diarrhea
  - May cause modest weight loss
OTC Products

- **Glucomannan**
  - MOA-from fibrous plant, increases feelings of fullness
  - Three human studies showed 8-10 lb. loss in 5 weeks when used with a healthy diet
  - Can lower BS, chol and trigs and helps constipation
  - SE-bloating, flatulence and soft stool
  - Can interfere with some oral meds if taken at the same time

- **Meratrim**
  - MOA-combination of two plant extract that may change metabolism of fat cells
  - Modest weight loss but only 1 study
  - SE-none reported

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**OTC Products**

- **Green Tea Extract**
  - MOA-can increase fat burning especially in the abdominal area, contains some caffeine

- **Conjugated Linoleic Acid (CLA)**
  - MOA- may reduce appetite and boost metabolism
  - Effectiveness-caused wt. loss of about 0.2 lbs./week for up to 6 months
  - SE-digestive side effects and may have harmful long term effects contributing to fatty liver, insulin resistance and increased inflammation
OTC Products

• Forskolin
  • MOA-raises level of cAMP which may stimulate fat burning
  • Effectiveness-One study showing some benefit another no benefit
  • SE-very limited data. Recommendation to avoid this supplement until more research is done
• Bitter Orange/Synephrine
  • MOA-contains synephrine which is related to ephedrine which has been banned. Reduces appetite and increases fat burning
  • SE-cardiac effects and may be addictive

Prescription Drugs -- Short-term Use

• Approved for less than 12 weeks
• Controlled substances with potential for abuse
• Not recommended if patient has:
  • Heart disease
  • High blood pressure
  • Hyperthyroidism
Didrex (benzphetamine)

- For short term use (< 12 weeks) in patients 12 and up
- Drug class-amphetamine
- MOA-decreases appetite, increases feeling of fullness
- Dosing-25-50 mg 1-3 times a day
- Possible SE
  - Increased BP and HR
  - Nervousness
  - Insomnia
  - Dry mouth
  - Constipation

Didrex (benzphetamine)

- Possible interactions
  - MAO inhibitors within 14 days may precipitate hypertensive crisis
  - Decrease the hypotensive effect of antihypertensives
  - May enhance the effect of tricyclic antidepressants
Tenuate (diethylpropion)

• For short term use (< 12 weeks) in patients 16 and up
• Drug class-monoamines
• MOA decreases appetite, increases feeling of fullness
• Dosing 25 mg po tid ac or 75 mg once a day in midmorning
• Possible SE
  • Headache
  • Increase BP and HR
  • Nervousness
  • Insomnia
  • Dry Mouth
  • Constipation

Tenuate (diethylpropion)

• Possible interactions
  • Antidabetic drug requirements may be altered
  • Concurrent use with general anesthesia may result in arrhythmias
  • Pressor effects may be increased when used with other drugs
  • May interfere with antihypertensives

• Not recommended in patients who used any anorectic agents within the prior year.
Adipex-P, Suprenza (phentermine)

- For short term use (< 12 weeks) in patients 16 and up
- MOA
  - Decreases appetite, increases feeling of fullness
- Dosing 18.75-37.5 mg po daily
- Possible SE
  - Primary pulmonary HTN
  - Headache
  - Increase BP and HR
  - Nervousness
  - Insomnia
  - Dry Mouth
  - Constipation

Adipex-P, Suprenza (phentermine)

- Possible interactions
  - Phentermine has serious interactions with at least 42 different drugs
  - Phentermine has moderate interactions with at least 172 different drugs
Prescription Drugs -- Long-Term Use

- The following drugs are approved for long term use

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Belviq (lorcaserin)

- Indicated in patients 18 and up
- MOA: Serotonin agonist
  - Decreases appetite, increases feeling of fullness
- Dosing 10 mg po bid
- Possible SE
  - Headache
  - Nausea
  - Dry Mouth
  - Dizziness
  - Fatigue
  - Constipation
Belviq (lorcaserin)

- Possible interactions
  - Drugs that may affect the serotonergic neurotransmitter systems (triptans, MOA, etc.)
  - SSRIs
  - Dexomethorphan
  - Tricyclic antidepressants
  - Cytochrome P450 substrates
  - Use with caution in drugs that are CYP 2D6 substrates

Contrave (naltrexone & bupropion* ER)

- MOA
  - Decreases appetite, increases feeling of fullness
- Dosing-increasing doses for first 4 weeks (8/90mg)
  - Week 1—1 tab in AM
  - Week 2—1 tab AM and PM
  - Week 2—2 tab AM 1 PM
  - Week 4 and beyond 2 tab AM and PM
- Possible SE
  - Nausea
  - Constipation
  - Headache
  - Vomiting
  - Dizziness

* Can increase risk of suicidal thoughts and behaviors
Contrave (naltrexone & bupropion* ER)

• Possible interactions
  • MAOs
  • CYP 2P D6
    • SSRI antidepressants
    • antipsychotics
    • Phenobarbital
    • Many others
  • digoxin
  • dopamine
  • anti-virals
  • beta blockers
  • Drugs that lower seizure threshold

Phendimetrazine

• MOA-Decreases appetite, increases feeling of fullness
• Indicated in patients 17 and up
• Dosing-ER 105 mg po daily 30-60 min before AM meal, immediate release 35 mg 2-3 times a day 1 hour before meals
• Possible SE
  • Increase BP and HR
  • Nervousness
  • Insomnia
  • Dry Mouth
  • Constipation
**Phendimetrazine**

- Possible interactions
  - MAO
  - ETOH
  - Caffeine
- Side effects
  - Nervousness
  - Palpations
  - Elevated BP
  - Nausea or vomiting

**Xenical (orlistat)**

- MOA-Blocks absorption of fat
- Approved for 12 and up
- Dosing-120 mg po tid with meals
- Possible SE
  - Decreased absorption of fat-soluble vitamins
  - Oily spotting
  - Intestinal cramps
  - Gas with discharge
  - Diarrhea
  - Fecal urgency
  - Incontinence
Xenical (orlistat)

- Possible interactions
  - Fat soluble vitamins
  - Cyclosporine
  - Levothyroxine
  - Anticoagulants
  - Amiodarone
  - Anti-epileptics
  - Anti-retrovirals

Qsymia (phentermine* & topiramate ER)

- MOA
  - Decreases appetite, increases feeling of fullness
  - Increased risk of birth defects
- Dosing
  - 3.75/23 po in AM for 2 weeks
  - Then 7.5/46 If no wt loss in 2 weeks d/c
  - If wt loss continues can increase to 11.25/69
  - 15/92 dose for increase wt loss
- Possible SE
  - Insomnia
  - Dry Mouth
  - Dizziness
  - Constipation
  - Pins and needles feeling
  - Changes in sense of taste or smell

* Potential for abuse
Qsymia (phentermine* & topiramate ER)

- Possible interactions
  - Same as those for phentermine

Saxenda (liraglutide)

- MOA
  - Slows gastric emptying, increases feeling of fullness
  - Administered by injection (SQ) once daily
- Dosing
  - Start with 0.6 mg qd then increase weekly by 0.6 mg until 3 mg dose reached
- Possible SE
  - Nausea
  - Vomiting
  - Pancreatitis
  - Hypoglycemia

- Boxed warning thyroid gland tumors in animal studies
Saxenda (liraglutide)

- Contraindications
  - Personal or family history of medulary thyroid carcinoma
  - Multiple endocrine neoplasms syndrome type 2

- Interactions
  - Monitor for increased side effects association with oral medications due to delayed gastric emptying