Appetite & Apothecary: Drug Interventions and Misadventures in Frailty

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Disclosures

- I have no conflicts of interest with regard to the pharmaceutical products discussed in this presentation.

- I will be discussing off-label use of certain drug products.
Objectives

Upon completion the learner will be able to:

1. List the common medications causing loss of appetite
2. Describe the common medications used for anorexia (indications, side effects and benefits)
3. Discuss pharmaceutical issues and strategies in patients with unintentional weight loss
Patient Case

- 85 y/o female
- CC: dry mouth, depressed, little energy
- WT: 102; 10# loss/6mos; BMI 19.9
- Diet: low fat, low Na; decreased appetite
- Social: lives alone; little family contact
- EtoH: 2-4 glasses wine/d
Patient Case (con’t)

- PMH: stage 3 CHF, depression, loose dentures
- Medications:
  - Lisinopril 20mg/d (ACE inhibitor; CHF)
  - Digoxin 0.125mg/d (+ inotrope; CHF)
  - Furosemide 40mg/d (loop diuretic; CHF)
  - Nortriptyline 50mg/d (TCA; depression)
Introduction

- Unintentional weight loss is estimated to have a drug etiology in:
  - 2-9% of outpatients
  - 14% of LTC patients

Mechanisms of Drug-Induced Weight Loss

- Anorexia
- Dysgeusia
- Dysphagia
- Nausea/vomiting

## Selected Drugs Causing Anorexia

<table>
<thead>
<tr>
<th>Agent</th>
<th>Agent</th>
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<tbody>
<tr>
<td>amantadine</td>
<td>decongestants</td>
<td>nicotine</td>
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<tr>
<td>antibiotics</td>
<td>digoxin</td>
<td>opiates</td>
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<tr>
<td>anticonvulsants</td>
<td>levodopa</td>
<td>SSRIs</td>
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<td>benzodiazepines</td>
<td>metformin</td>
<td>theophylline</td>
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## Selected Drugs Causing Dysgeusia

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<tr>
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<tbody>
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<tr>
<td>allopurinol</td>
<td>dopamine agonists</td>
<td>nitroglycerin</td>
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<td>ACE inhibitors</td>
<td>iron supplements</td>
<td>phenytoin</td>
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<tr>
<td>antibiotics</td>
<td>levodopa</td>
<td>statins</td>
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<td>anticholinergics</td>
<td>metformin</td>
<td>TCAs</td>
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<td>antihistamines</td>
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### Selected Drugs Causing Dysphagia

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<tbody>
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<td>anticholinergics</td>
<td>levodopa</td>
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<tr>
<td>bisphosphonates</td>
<td>NSAIDs</td>
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<tr>
<td>clonidine</td>
<td>potassium</td>
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<td>corticosteroids</td>
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# Selected Drugs Causing Nausea/Vomiting

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<th>Agent</th>
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</thead>
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<td>dopamine agonists</td>
<td>nitroglycerin</td>
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<tr>
<td>alendronate</td>
<td>hormonal agents</td>
<td>NSAIDs</td>
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<tr>
<td>allopurinol</td>
<td>iron supplements</td>
<td>opioid analgesics</td>
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<td>amantadine</td>
<td>levodopa</td>
<td>phenytoin</td>
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<tr>
<td>antibiotics</td>
<td>lipid lowering drugs</td>
<td>potassium</td>
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<tr>
<td>benzodiazepines</td>
<td>metformin</td>
<td>SSRIs</td>
</tr>
<tr>
<td>digoxin</td>
<td>metronidazole</td>
<td>theophylline</td>
</tr>
</tbody>
</table>

Patient Case

- Medications contributing to weight loss:
  - Lisinoril (dysgeusia)
  - Digoxin (anorexia, nausea/vomiting)
  - Furosemide (dehydration)
  - Nortriptyline (dysgeusia, dysphagia)
  - EtoH (empty calories)
Pharmacologic Approach to Unintentional Weight Loss

- Discontinue contributing medications
- Treat underlying problems:
  - Mood disorders
  - Behavioral symptoms of dementia
  - Pain
  - Nausea and vomiting
- Non-pharmacologic interventions
- Orexigenic agents
Depression

- Treatment of depression may result in weight gain
- SSRIs and newer agents preferred due to increased safety and tolerability vs. TCAs
  - Trials in elderly do not link SSRIs to substantial weight loss
  - Patients at or below IBW or significant GI adverse effects may be susceptible to weight loss early in treatment

Depression

- **Mirtazapine**
  - Both noradrenergic and serotonergic
  - Increased appetite, weight gain, less N/V vs. SSRIs in controlled geriatric depression trials
  - Safety and efficacy as orexigenic agent in non-depressed elderly is unknown


Behavioral Symptoms of Dementia

- Few studies of antipsychotics in frail elderly with dementia have shown clinically significant weight gain
  - Olanzapine reported to increase appetite anecdotally
- Atypical antipsychotics may produce weight gain when appropriately used to treat psychosis or behavioral disturbances in dementia patients

Orexigenic Agents: Overview

- Evidence to support use limited to small uncontrolled trials
- Benefit limited to small amount of weight gain without evidence of decreased morbidity/mortality, improved function, or increased quality of life
- Many agents have significant ADEs which limit usefulness
Orexigenic Agents

- Megestrol
- Cyproheptadine
- Dronabinol
- Anabolic agents: HGH, testosterone
- Eicosapentanoic acid (EPA)
Megestrol

- Synthetic progesterone
- Shown to improve appetite and weight gain in AIDS and cancer cachexia
  - Mean weight gain 3.5-4.2kg
  - Dose 80mg TID to 800mg/d
- ADEs: thromboembolism, diabetes, adrenal suppression, edema, constipation, delerium

Megestrol in Elderly
Yeh et al.

- Benefit of megestrol in frail LTC residents with protein-energy undernutrition
- 69 mostly male VA NH residents (mean 76y)
- Megestrol 800mg/d vs. placebo
- Statistically significant improvement in appetite, GDS, and enjoyment
- No significant difference in weight gain or other nutritional parameters

Megestrol and DVT

- Bolen et al reported 32% of NH residents treated with megestrol developed DVT
- Unclear risk vs. benefit
  - A-fib, DVT, immobility

Cyproheptadine

- Antihistamine and serotonin antagonist
- Adult dose: 8-16mg/d
- Weight gain: 1-2kg
- No studies in geriatric or dementia populations
- ADEs: anticholinergic effects, tachycardia, delerium
- Interaction with SSRIs

Dronabinol

- Synthetic $\Delta^9$-tetrahydrocannabinol
- Shown to decrease nausea and improve appetite and weight gain in HIV patients
- Dose: 2.5mg BID before lunch & supper
- ADEs: (dose dependent) delerium, somnolence, dizziness, confusion, euphoria, paranoia, “high” feeling, ataxia, hallucinations, functional impairment
- ADEs and high cost are prohibitive for many elderly

Dronabinol in the Elderly
Volicer et al.

- Placebo-controlled crossover study of dronabinol in 11 patients with probable AD
- Body weight increased more during dronabinol treatment (2.5-7lbs) vs. placebo periods (1.5-4.5lbs)

Human Growth Hormone

- Recombinant HGH (somatotropin) may increase lean body mass
- Dose: 20mcg/kg SQ TIW
- ADEs: carpal tunnel syndrome, edema, gynecomastia, glucose intolerance diabetes, arthralgia, myalgias, headache
- ADEs and very high cost limit use

HGH in the Frail Elderly
Kaiser et al.

- Double-blind placebo controlled study in 10 frail elderly men
- HGH 100mcg/kg IM daily x3 weeks
- Increased middle arm circumference
- Mean weight gain: 2.2 kg
- No side effects noted (N=5)

HGH and Mortality
Takala et al.

- HGH may attenuate catabolic response to injury, surgery, and sepsis
- Study in adults in ICU setting showed increased mortality with use of HGH therapy at 0.1mg/kg/day
- Also increased LOS and duration of mechanical ventilation

Testosterone

- TST decreases with age, chronic illness, and malnutrition
- TST increases muscle mass in AIDs wasting
- Oral oxandrolone FDA approved for cachexia
  - Dose: 2.5mg BID-QID (up to 20mg/d)
- Effect on appetite not studied
- ADEs: prostate growth, increased HCT, fluid retention, hepatotoxicity, prostate cancer

Testosterone in the Elderly
Sih et al.

- RCT of TST in 35 hypogonadal older men
- TST 200mg IM BIW vs. placebo x12 months
- **Results**: increased lean body mass and exercise performance
- Weight gain and appetite not measured

Testosterone in the Elderly
Bakhshi et al.

- RCT of TST in 15 medically ill older men on a geriatric evaluation unit
- TST 100mg weekly
- Results: improvement in functional status and grip strength
- Weight gain and appetite not measured

Eicosapentaenoic Acid

- EPA studied for anti-cachectic effect in cancer patients
- Cochran Database meta-analysis
  - Studies have not shown significant weight gain vs. placebo or matched active treatment control in cancer cachexia
  - Insufficient data to establish benefit vs. placebo
- ADEs: abdominal discomfort, diarrhea, n/v
- Not studied for weight loss in the elderly

Key Concepts

- Effectiveness of medications to treat anorexia and weight loss is difficult to demonstrate in frail elderly populations.
- Frail elderly are at high risk for ADEs.
- Risk vs. benefit and potential ADEs should be weighed carefully before treatment.
- Screening and treatment of depression and dementia should not be overlooked.
Questions

It's QUESTION TIME!!