Are Stimulants Appropriate in the Elderly?

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Disclosure/Conflict of Interest

• I, Cherry W. Jackson, have not actual or potential conflict of interest in relation to this program.
• Programming offered by Auburn University Harrison School of Pharmacy shall exhibit balance, providing the audience information of different perspectives from which to develop an informed professional opinion

Objectives

• Describe indications for the use of stimulants in the elderly
• Discuss prescribing limitations for stimulants in the elderly population
• Identify comorbid medical conditions that warrant concern when using stimulants
• Specify possible drug interactions that should be monitored for in patients taking stimulants
Question 1

• Which of the following are unapproved but accepted reasons for using stimulants in elderly patients?
  A. Schizophrenia
  B. Anxiety
  C. Apathy
  D. Insomnia

Question 2 and 3

• Mr. Z. is admitted to the hospital post stroke. He has depression and apathy and he is not eating or drinking currently and he will not be able to go to rehab until he is able to eat on his own. His other illnesses include ventricular arrhythmia, myocardial infarction, and chronic renal failure. His current height is 6 foot, weight is 142 pounds, blood pressure is 180/100, heart rate is 110, respiratory rate is 22. Current medications are: digoxin, warfarin, lisinopril, losartan, lasix, and sertraline. Mr. Z’s physician would like to initiate methylphenidate 2.5 mg so that the patient can be moved to rehab.

Question 2 (cont.)

• Which of the following medical conditions warrant concern when using stimulants?
  A. Stroke
  B. Depression
  C. Apathy
  D. Ventricular arrhythmia
  E. Chronic Renal failure
Question 3

• If a stimulant were initiated in Mr. Z. which of the following might you be concerned about causing a drug interaction?
  • A. Digoxin
  • B. Warfarin
  • C. Lisinopril
  • D. Losartan
  • E. Lasix
  • F. Sertraline

Stimulants

• Stimulants release dopamine from the brain
• Methylphenidate increases dopamine transport
• Dextroamphetamine binds the dopamine transporter.
• Stimulant effect occurs in 30-45 minutes
• Increased alertness, insomnia, euphoria, decreased appetite

Use of Stimulants in the Elderly

• Stimulants in the elderly:
  – Promote wakefulness
  – Increase energy
  – Improve attention
• Pharmacists should be aware of possible side effects/safety concerns
Use of Stimulants in the Elderly

• The elderly patient’s changing physiology presents treatment challenges
• Decreased response to antidepressants
• Stimulants may benefit the medically ill


Stimulants

• Starting doses in older adults
  – Methylphenidate 5 mg/day
  – Dextroamphetamine 5 mg/day
• Peak 2-4 hours
• Vital signs evaluated 2-4 hours after dose
• “Failed trial” no response after 20 mg/day
• Response that wanes can be repeated


Use of Stimulants in the Elderly

• Stimulants are used to treat:
  – Attention Deficit Hyperactivity Disorder (ADHD)
  – Apathy
  – Fatigue
  – Falls
  – Depression

Indications for Stimulants

• Attention Deficit Hyperactivity Disorder (ADHD)
  – 8% of children, 4% of adults
  – Characterized by impulsivity, motor restlessness, inattention
  – Societal burden
  – Lack of data on ADHD in older adults

Lazare J. ADHD in Older Adults. Todays Geriatric Medicine. 2014

Indications for Stimulants

• Attention Deficit Hyperactivity Disorder
  – Stimulants are first line treatments for ADHD
  – Improvement in symptoms compared to placebo.
  – Benefits of treatment often outweigh risks
  – Screen carefully

Lazare J. ADHD in Older Adults. Todays Geriatric Medicine. 2014

Forgetfulness or ADHD?

• Mr. A., age 68 is an attorney who presents for evaluation after he identified common features in friends that have attention-deficit/hyperactivity disorder (ADHD). In grade school, Mr. A’s teacher told him that he employed very little effort and was not meeting his potential, although he performed exceptionally well. He reports similar experiences throughout his education and says he was careful to select classes that were interesting, but did not required demanding projects or burdensome homework.
Forgetfulness or ADHD?

• In law school, he felt academically challenged for the first time but realized he had limited study skills. Mr. A. graduated in the top 26th percentile of his class using “an unbelievable amount of effort compared with other students.”
• Mr. A. describes significant impairment in organizational skills and ability to keep track of time, procrastination, completion of tasks, and substantial distractibility during conferences. He says he has difficulty reading briefs depending on his emotional connection to the subject matter.

Forgetfulness or ADHD?

• Family history revealed that his mother likely had undiagnosed ADHD. He recently married and his wife encouraged him to seek treatment for “forgetfulness”. Mr. A. maintains a busy, successful law practice but has become increasingly frustrated by his inability to follow through on simple tasks that could help grow the practice and generate revenue.
• Mr. A. has an elevated score on the ADHD Symptom Rating Scale. He is referred to his primary care physician to evaluate his general health before beginning medication. At follow-up, Mr. A was started on lisdexamfetamine 20 mg/d titrated to 40mg/d.

Forgetfulness or ADHD?

• On subsequent visits he reports improved symptoms without side effects. His vital signs are normal and he reports feeling more productive in his work and achieving significant improvement in the day-to-day operations of his practice.
ADHD and Stimulants

• Patients tend to be:
  – High functioning
  – Professional success
  – Academic success
  – Inefficient learning
  – Distraction


ADHD and Stimulants

• Diagnosis and treatment of ADHD improves
  – Functional impairment
  – Quality of life


Indications for Stimulants

• Apathy
  – Apathy is a loss of motivation, interest, or initiative
  – Common in dementia of Alzheimer’s type (DAT)
  – Impairment in activities of daily living
  – Increased burden for caregiver

Apathy vs. Depression

- Apathy is not depression
- Apathy and depression symptoms overlap
- Significant decrease in glucose metabolism with apathy
- Depression was associated with hypometabolism


Apathy vs. Depression

- Apathy may be more prominent in the elderly
- Treatment with SSRI’s may lead to apathy
- Symptoms include:
  - Fatigue, inattentiveness, forgetfulness, word-finding difficulty, mental slowing


No Interest in Life

- Mr. B., age 76, has dementia of the Alzheimer’s type. His family brings him to a psychiatrist because Mr. B. exhibits a generalized loss of interest. His history reveals a gradual onset of memory problems with a steady decline. Current deficits include problems with forgetfulness, misplacing items, increasing difficulty with names, occasional repetitiveness, and mild word finding difficulty. His family complains that Mr. B does not take care of himself, sits all day long, is not interested in his favorite TV shows, is indifferent to his physical health, is not interested in catching up with friends and has been doing very little from day to day.
No Interest in Life

• He does not seek food but cleans his plate when served. His family became concerned when Mr. B showed no excitement in going to his grandson’s baseball games, which he had previously enjoyed. Mr. B. denies any concerns and scores a 3 out of 15 on the Geriatric Depression Scale. Mr. B’s family rated him 4 on the same scale.

• On the Apathy Evaluation Scale (AES), he scores 46 (moderate severity). We start methylphenidate, 5 mg administered in the morning and early evening (5 pm). Subsequent conversations 2 weeks later with Mr. B’s family reveals Mr. B’s interest levels have improved and reported no side effects.

No Interest in Life

• Methylphenidate increased to 10 mg twice a day. Mr. B has remarkably improved hygiene one month later and is more engaged in the interview. He scored a 32 (mild severity) on the AES and the family notes that he is interested in watching his grandson play baseball. During this treatment, we did not change Mr. B’s other medications-donepezil, 10 mg/day, and bupropion, 150 mg/day.

Apathy and Stimulants

• Open label study of patients with DAT
  – Methylphenidate 10 – 20 mg/day
  – Improvement in AES Scores
• Hermann et al.
  – Methylphenidate 20 mg/day vs placebo
  – Improvements in AES scores
• Double-blind, placebo-controlled crossover study
  – Dextroamphetamine 20 mg/day
  – Improvement in NPI- apathy subscales

Stimulants and Depression

• Depression
  – Affects more than 6.5 million Americans over age 65
  – Treat depression acutely
  – Rapidly acting
  – Medically ill/medically fragile


Stimulants and Depression

• Monoamine hypothesis—depression results from decreased norepinephrine and serotonin.
• Increasing these neurotransmitters in the prefrontal cortex could improve depressive symptoms


Depression in the Medically Ill

• Mr. C. is a 71 year old man with a history of chronic obstructive pulmonary disease (COPD), hypertension, and hypercholesterolemia who was admitted to the hospital for the treatment of a COPD exacerbation. When his symptoms of COPD worsened on the third day of hospitalization, he was transferred to the intensive care unit and intubated. He remained intubated for 6 years, and his respiratory function improved enough to allow for extubation.
Depression in the Medically Ill

• Mr. C slowly recovered, but by the fifth day of hospitalization, he appeared withdrawn, apathetic, and dysphoric. His appetite had waned, as had his participation in his daily regimen of chest physical. Psychiatric consultation was requested for evaluation of depression. Finding symptoms of major depressive disorder, poor oral intake, and limited participation in his medical and rehabilitative care, the consultant psychiatrist considered prescribing a psychostimulant.

Depression in the Medically Ill

• Mr. C. would be a good candidate for psychostimulant treatment of his depressive symptoms based on the information presented. He had no obvious contraindications to the use of stimulants, and he would most likely have benefited from their rapid onset of action. This rapid effect would have been particularly important for him because his poor appetite and inability to participate in his care were contributing to a suboptimal medical outcome.

Depression in the Medically Ill

• He could have been started at either 2.5 or 5 mg of dextroamphetamine or methylphenidate. His vital signs should have been monitored closely (especially during the first few hours following a dose), given his medical fragility. Both the literature on psychostimulants and our experience suggest that he would have tolerated this treatment well and had an excellent chance of responding rapidly to treatment.
Stimulants and Depression

• Randomized placebo-controlled trial of methylphenidate in the elderly

• Three case studies of methylphenidate as an antidepressant in elderly patients - no significant side effects

• Case reports with adjunctive venlafaxine, mianserin, citalopram, and fluoxetine

Jansen IH. J Am Geriat 2001;149:474-76.

Stimulants and Depression

• Double-blind, placebo controlled trial of methylphenidate and citalopram

• 143 patients, average age 69.7 yo
  – Methylphenidate plus placebo (48)
  – Citalopram plus placebo (48)
  – Citalopram plus methylphenidate (47)

• Citalopram dose 20-60 mg; Methylphenidate 5-40 mg


Stimulants and Depression

![Graph depicting change in HAM-D scores over time](image)

Scale (HAM-D) Score Over Time, by Treatment Condition, Among Patients Receiving Citalopram, Methylphenidate, or Their Combination.

- Statistically significant differences between citalopram plus placebo and methylphenidate plus placebo: p < 0.05.
- Statistically significant differences between citalopram plus placebo and methylphenidate plus methylphenidate: p < 0.05.
- Statistically significant differences between citalopram plus methylphenidate and methylphenidate plus placebo: p < 0.05.

Lavretsky H. Am J Psychiatry 2015
Stimulants and Depression

- Patients who might benefit from stimulants
  - Terminal cancer and depression
  - Post-stroke depression
  - Bipolar depression
  - HIV
  - Poor weaning from mechanical ventilation
  - Medically fragile patients
  - Poor nutritional intake
  - When rapid recovery is needed


Indications for Stimulants

- Fatigue
  - Frequently seen in patients with medical illnesses
    - Mood disorders
    - Sleep disturbances
    - Side effect of interferon alpha
  - Rule out:
    - Hypothyroidism
    - Anemia
    - Electrolyte disturbances


Indications for Stimulants

- Falls
  - Decreased cognition
  - Decrease in gait stability
  - Double-blind placebo-controlled trial
    - Methylphenidate 20 mg/day
    - Improves executive function
    - Improves gait stability

Safety Concerns with Stimulants

• The FDA issued warnings in 2007 concerning cardiovascular effects
• Stimulants can increase heart rate and blood pressure
• The FDA reversed its warning in 2011


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<td>Schelleman</td>
<td>2012</td>
<td>Retrospective matched cohort/methylphenidate</td>
<td>Medicaid (5 states) and health insurance database (HealthCore)</td>
<td>18 years and older methylphenidate users (n=43,999) matched to nonusers (n=175,955)</td>
<td>1. Sudden death/ventricular arrhythmia 2. Stroke 3. MI 4. Stroke</td>
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**Side Effects**

- Less common side effects include:
  - Anxiety
  - Insomnia
  - Hallucinations
  - Anorexia
  - Delirium
  - Palpitations
  - Headache
  - Glaucoma


**Drug Interactions**

- Drug-drug interactions
  - MAOI: methylphenidate
  - Warfarin: methylphenidate
  - Tricyclic antidepressants: stimulants

Prescribing Limitations

- Stimulants are schedule II controlled substances
- DEA allows 90 day supply
- Prescription is for legitimate medical purpose
- Must provide written instructions
- Must indicate the earliest fill date
- Multiple prescriptions are permissible in state laws


Controversies

- Efficacy yesterday vs. today
- Interest in completing new research?
- Precautions
  - Stimulant misuse
  - Careful use
  - Balance of risks and benefits

Chukwujekwu CC. Geriatric Med. 2009 430-431

Controversies

- Low risk of misuse and dependence
- Drug dependence
  - 18-29 years 4.1%
  - 30-40 years 3.5%
  - 45-64 years 1.9%
  - 65 and over 0.2%

Chukwujekwu CC. Geriatric Med. 2009 430-431
Conclusion

• Use stimulants with care
• Balance risks and benefits

Chukwujekwu CC. Geriatric Med. 2009 430-431

Question 1

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Questions