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MANAGEMENT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN ADOLESCENTS

Although attention-deficit/hyperactivity disorder (ADHD) is estimated to affect more than ten percent of adolescents, treatment guidelines are typically reflective of studies conducted in younger, preschool or grade school-aged, children. Adolescents are typically treated through extrapolation of these guidelines, which may or may not be appropriate. This issue of *CLIPs* briefly summarizes an article that reviews the most appropriate treatment options for adolescents with ADHD. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at (205) 726-2659.

Chan E, Fogler, JM, Hammerness PG. Treatment of attention-deficit/hyperactivity disorder in adolescents: a systematic review. *JAMA*. 10 May 2016;315(18): 1997-2008.

Introduction

- ADHD has a prevalence of about 12% in 12 to 17-year-old adolescents.
- The estimated societal cost of ADHD is between $143 billion and $266 billion annually.
- Adverse outcomes of ADHD (mental, physical, and psychosocial) may be mitigated with appropriate treatment.
- Approximately 45% of patients who are diagnosed take their prescribed medication each week.
- Current guidelines are largely based on studies that focus on preschool and grade school aged children or studies that have evaluated children and adolescents collectively.

Methods

- Studies were located by searching CINAHL Plus, MEDLINE, PsycINFO, ERIC, and the Cochrane Database of Systemic Reviews for English-language articles for peer-reviewed journal articles published between January 1, 1999, and January 31, 2016.
- To be included, studies were required to meet *diagnostic and statistical Manual of Mental Disorders* (4th Ed.) or *Diagnostic and Statistical Manual of Mental Disorders* (4th Ed, Text Revision), randomly assign participants to treatment groups, evaluate at least one valid outcome measure, and report results for adolescents separately.
- Efficacy was determined by the ADHD Rating scale total symptom scores (Range: 0-54, with 54 indicating most severe symptoms)
- Six double-blind, randomized control trials (RCTs) and one meta-analysis of pharmacological treatments were included as well as 10 RCTs of psychosocial treatments were included.

Methylphenidate

- The osmotic-release oral system (OROS; extended-release) was associated with a mean symptom score reduction of 14.93±10.72 points while placebo had a 9.58±9.73 point reduction after 6 weeks (P=0.001).
- Patients using the transdermal system had a mean difference of -9.96 points (95% CI; -13.39 to -6.53 points) compared to placebo after 7 weeks (P< 0.001).
- No studies were found that evaluated the effectiveness of dexmethylphenidate in adolescents.

Amphetamines

- Extended-release (ER) mixed amphetamines were associated with a total symptom score change of -17.8 points (-9.4 placebo; P<0.001) after 4 weeks; hyperactive-inattentive symptoms were most improved.
- Lisdexamphetamine is a prodrug that is converted to dexamphetamine following cleavage of the lysine residue in the bloodstream; in a meta-analysis, it was associated with ADHD total symptom score reductions of between 19.3 and 21.1 points (P<0.006).

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Atomoxetine

- Atomoxetine is classified as a norepinephrine reuptake inhibitor and is FDA-approved as ADHD monotherapy.
- Effectiveness is similar to methylphenidate and amphetamines: -13.99±12.97 points vs. -6.95±10.07 points placebo (P<0.001).
- Fast or slow titration schedules may be used (titration over 3 days versus 14-18 days), as there appears to be no difference in efficacy (-17.26±0.79 points and -16.48±0.81 points, respectively).
- A high maintenance dose (1.4 mg/kg/d) was associated with sustained symptom control, whereas, a low dose (0.8 mg/kg/d) was associated with a return of symptoms (mean increase in symptom score 1.93±1.05 points, P<0.07 and 3.80±1.05 points, P<0.001, respectively).

Alpha-2 Adrenergic Agonists

- This class is a good substitute for patients who are unable to take stimulants or for patients who found stimulants ineffective.
- Extended-release clonidine and guanfacine have both been approved by the FDA for the treatment of ADHD as either monotherapy or adjunctive therapy to stimulants.
- Guanfacine has been proven effective as monotherapy in adolescents, but evaluation of its effectiveness adjunctively is needed; clonidine also warrants investigation, both adjunctively and as monotherapy.

Tolerability of Medications

- Stimulants commonly cause gastrointestinal (GI) side effects (e.g., reduced appetite, nausea, and abdominal pain), headache, irritability, insomnia, and weight loss. The transdermal system can cause irritation of the skin.
- Atomoxetine and guanfacine can also cause GI adverse effects (reduced appetite, nausea, vomiting, and abdominal pain), as well as, dizziness, fatigue/drowsiness, and headache.
- Stimulants may cause slight increases in systolic and diastolic blood pressure. In contrast, extended-release guanfacine may decrease blood pressure and pulse; atomoxetine did not have any effect on vital signs.

Psychosocial Treatment

- There are 3 primary psychosocial treatment options for patients with ADHD:
    1. Behavioral therapy: rewards positive behaviors and ignores those that are undesired;
    2. Direct skills therapy: develops study skills, organizational ability, and time management; and
    3. Cognitive behavioral therapy (CBT): utilizes motivational interviewing, cognitive restructuring, and mindfulness to address problematic thought processes.
- In practice, the above techniques are typically used together in various combinations.
- The primary benefit seen with psychosocial treatment is improved functional outcomes, though slight reductions in impulsive, inattentive, and hyperactive symptoms were noted by parents.
- Some patients with emotional and behavioral symptoms may experience reductions in internalization symptoms, anxiety, depression, and oppositional-defiant symptoms, but these results were inconsistent.

Academic/Organizational Support

- There is some evidence to suggest that academic and organizational support can increase GPA.
- CBT with or without additional training has also been shown to increase executive function.
- However, the evidence supporting both of these claims is contradictory, and benefits were minimal.

Conclusions

- Pharmacotherapy is associated with the most robust reduction of adolescent ADHD symptoms compared to psychosocial treatment. Methylphenidate, ER amphetamines, and atomoxetine are particularly effective.
- Psychosocial treatment may be used to improve functional outcomes, but there is little evidence to support its use for ADHD total symptom management or for patients with combined emotional and behavioral symptoms.
- Aside from treatment, adherence should also be addressed; many adolescents are unaware of their need for treatment and do not understand the importance of regularly taking their medication. This, coupled with the increasing independence of adolescents, leads to inadequate treatment of ADHD in this population.
- Further research is warranted to evaluate appropriate dosing and further treatment options for adolescents with ADHD.