The Use of ADHD Medication in the Pediatric Population

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Objectives

- Discuss the importance of treatment with medications in children with attention deficit hyperactivity disorder (ADHD)
- Compare and contrast efficacy, adverse effects and formulations between medication classes in the treatment of ADHD in children
- Describe appropriate patient education points and management of side effects

ADHD Facts

- Hyperactivity, impulsivity, and/or inattention
- Estimated prevalence ~ 11%
- More common in boys (4:1 ratio)
- Comorbid psychiatric disorders are frequent
Pathophysiology

- Not clearly elucidated
- Genetic factors
- Physiologic changes
  - Catecholamine imbalance
  - Decreased cerebral volume
- Environmental influences
  - Dietary
  - Prenatal medications

Clinical Presentation

Hyperactivity/Impulsivity
- Present by Age 4
- Present by Age 8-9
- Impaired function present

Inattention

Core Symptoms

**Hyperactivity and impulsivity**
- Excessive fidgetiness
- Difficulty remaining seated
- Feelings of restlessness
- Difficulty playing quietly
- Difficulty to keep up with
- Excessive talking
- Difficulty waiting turns
- Blunting out answers too quickly
- Interruption or intrusion of others

**Inattention**
- Failure to provide close attention to detail
- Difficulty maintaining attention in play
- Seems not to listen
- Fails to follow through
- Difficulty organizing tasks
- Avoids tasks that require consistent mental effort
- Loses objects required for tasks or activities
- Easily distracted by irrelevant stimuli
- Forgetfulness in routine activities
DSM-V Criteria

- For children <17 years
  - ≥6 symptoms of hyperactivity and impulsivity
  - or ≥6 symptoms of inattention
- Symptoms must
  - Occur often
  - Be present in more than one setting
  - Persist for at least 6 months
  - Be present before the age of 12
  - Impair function in academic, social, or occupational activities
  - Be excessive for the developmental level of the child

Practice guidelines

- Stage 1 – Stimulants
- Stage 2 – Stimulant class not used in stage 1
- Stage 3 – Atomoxetine
- Stage 4 – Buproprion or Tricyclics
- Stage 5 – Drug class not used in stage 4
- Stage 6 – Alpha₂ agonists

Stimulant Medications
Stimulants

- Methylphenidate and amphetamines
- Increase dopamine and norepinephrine
- Fast onset of action
- Short and long-acting formulations
- Long record of safety and efficacy
- Response rate of ~ 70-90%

Methylphenidate Products

<table>
<thead>
<tr>
<th>Brand</th>
<th>Duration</th>
<th>SIG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritalin, Methylin</td>
<td>Short</td>
<td>5-20 mg two-three times daily</td>
</tr>
<tr>
<td>Ritalin SR, Methylin SR, Methylin ER, Metadate ER</td>
<td>Intermediate</td>
<td>20-40 mg one-two times daily</td>
</tr>
<tr>
<td>Concerta, Metadate CD, Ritalin LA</td>
<td>Long 8-12 hours</td>
<td>18-72 mg once daily 20 mg once daily 20-40 daily</td>
</tr>
</tbody>
</table>

SR = sustained release; ER = extended release; CD = controlled delivery; LA = long acting
Methylphenidate Products

- Quilivant XR - oral suspension
  - Combined PK characteristics of both IR and ER formulations
  - Maybe useful for children not able to swallow pills

Image from: https://healthy.kaiserpermanente.org/health/consumer/Methylphenidate_Products

Methylphenidate Products

- Daytrana – transdermal delivery system
  - Apply on the hip for up to 9 hours

- Dexmethylphenidate – Focalin, Focalin XR

Image from: http://daytranasideeffects.com

Amphetamine Products

<table>
<thead>
<tr>
<th>Duration of agents (Brand)</th>
<th>Dosing (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short acting: 3-5 hrs</td>
<td></td>
</tr>
<tr>
<td>Dextroamphetamine (Dexedrine, Dextrostat)</td>
<td>&lt;25 kg: 2.5-10 daily &gt;25 kg: 5-10 two-three times per day</td>
</tr>
<tr>
<td>Interm. acting: 5-8 hrs</td>
<td></td>
</tr>
<tr>
<td>Dextroamphetamine (Dexedrine spansule) Mixed salts (Adderall)</td>
<td>5-15 twice daily ~ 0.5 mg/kg/day</td>
</tr>
<tr>
<td>Long acting: 8-12 hrs</td>
<td></td>
</tr>
<tr>
<td>Mixed salts (Adderall XR)</td>
<td>10-30 daily</td>
</tr>
<tr>
<td>Lisdexamphetamine (Vyvanse)</td>
<td>30-70 daily</td>
</tr>
</tbody>
</table>
Stimulant Considerations
- Abuse potential
- Adverse events
- Growth complications
  - Studies show average 1 cm/yr in the first 1-3 years
  - Drug holiday may be recommended
- Black Box Warning
  - Risk of sudden death

Non-Stimulant Treatment Options

Pharmacological Action of ADHD drugs:
- Dopamine
- Noradrenaline
- Serotonin
- Norepinephrine
- Serotonin
- Norepinephrine

Adapted from: http://www.sec.gov/Archives/edgar/data/1566049/000114420413020453/v340623_f1a.htm
Strattera® (atomoxetine)
- Selective norepinephrine reuptake inhibitor
- Therapeutic effect seen in 2-4 weeks
- Dose must be titrated
  - ≤70kg: start at 0.5mg/kg for min of 3 days, then 1.2mg/kg
  - >70kg: start at 40mg for a min of 3 days, then 80mg for 2-4 weeks, then may titrate to max dose of 100mg
- AE: decreased appetite, increase BP

Tricyclic Antidepressants (TCAs)
- Most common: Nortriptylline, imipramine, desipramine
- Increase in norepinephrine
- Useful if comorbidity of
  - Obsessive compulsive disorder
  - Depression, anxiety
  - Tics
- Higher adverse effect profile

Wellbutrin® (buproprion)
- Increases DA and NE function
- Limited efficacy studies in children
- Dosing: 3-6 mg/kg/day titrated over 2 weeks
- Safer cardiovascular profile
- Delayed onset of action
- May exacerbate tics
**Alpha<sub>2</sub> Agonists**
- Clonidine and guanfacine
- Inhibits norepinephrine
- Clonidine transdermal patch
  - Lasts 5 days in children (7 days in adults)
  - Must titrate with oral dose first
- AE: Bradycardia, depression, rebound hypertension

**SNRI’s**
- Venlafaxine and Duloxetine
- Selective norepinephrine reuptake inhibitors
- May be considered as an alternative agent in patients who fail conventional treatment options
- Limited data in children

**Drug Selection**
- Stimulants considered first-line agent
- Atomoxetine: alternative if non-stimulant is preferred
  - Comorbid tic or anxiety disorder
- Alpha<sub>2</sub> agonists: tic disorder, hyperactivity, or aggressiveness
- TCAs: comorbid depression or anxiety
Complementary and Alternative Therapy

- Herbals
  - Kava kava, valerian root – for insomnia
  - Ginkgo biloba, ginseng – improve cognition
  - Evening primrose
  - Focus ADDult, BrightSpark ADD – combination herbal products

Non-pharmacologic Treatment Options

- Behavioral interventions
- Psychotherapy interventions
- Dietary interventions
  - Elimination diets
  - Food dyes
  - Essential fatty acid supplementation
Counseling Points

- Side effects are to be expected
- Discuss time to efficacy and titrating to efficacy
  - Efficacy ~ 35-50% improvement from baseline
- Explain use of different formulations
- Educate on abuse potential
  - Children with ADHD may be at higher risk for substance use

Test your knowledge

- True or False: Alpha-2-adrenergic agonists are not recommended for adolescents with a history of illicit substance use.

Test your knowledge

- True or False: Decreased appetite is a common side effect among all medication types used for ADHD
Test your knowledge

- True or False: Parents should be educated to closely monitor for unusual changes in behavior and suicidal ideation in pediatric patients during initiation of atomoxetine therapy.

Questions?

References