Treating ADHD in Special Populations: Early Childhood, Autism, Epilepsy, & Prenatal Exposure

Douglas Russell, MD

WY PAL Webinar | April 27, 2020
Objectives

• Review standard ADHD stimulant titration strategies
• Appreciate how age and comorbidities complicate diagnosis and treatment
• Learn how to adjust treatment strategies in special populations.
Disclosures

- No financial or personal conflicts of interest.
- I will be discussing off-label indications for certain medications.
ADHD Statistics

- Prevalence: 7.8%-11.0%
- Boys>Girls
- Median age at diagnosis: 6

ADHD Statistics

Currently take medication 69.3%

Do not currently take medication 30.7%

ADHD: Standard Methylphenidate Titration

- **Ritalin**
  - 5 mg TID = 15 mg/day
  - 10 mg TID = 30 mg/day
  - 15 mg TID = 45 mg/day

- **Concerta**
  - 18 mg daily x 5d
  - 36 mg daily x 5d
  - 54 mg daily x 5d

**Booster**
## ADHD: Stimulant Titrations

<table>
<thead>
<tr>
<th>Methylphenidate</th>
<th>Amphetamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerta: 18mg → 36mg → 54mg</td>
<td>Adderall XR: 10mg → 20mg → 30mg</td>
</tr>
<tr>
<td>Focalin XR: 10mg → 15mg → 20mg</td>
<td>Vyvanse: 30mg → 50mg → 70mg</td>
</tr>
</tbody>
</table>
ADHD in Preschool
Social-emotional Milestones

- Seeks to please friends
- Engages in fantasy play
- More likely to agree to rules
- Enjoys singing/dancing/acting
- More independent
Emotional and Behavioral Impairments

- Attention-deficit/Hyperactivity Disorder
- Autism Spectrum Disorder
- Oppositional Defiant Disorder
- Posttraumatic Stress Disorder
- Major Depressive Disorder
- Anxiety Disorders
- Sleep Disorders

ADHD in Preschool: Assessment

- Clinical suspicion
- Detailed history of symptoms
- Collateral from 2+ contexts
  - Strengths and Difficulties Questionnaire (SDQ)
- IMPAIRMENT
ADHD in Preschool: Behavioral Treatments

- Dyadic and behavioral treatments are first line
  - Behavioral Parent Training
  - Parent-child Interaction Therapy (PCIT)
Positive Parenting

- Positive reinforcement for positive behaviors
- Avoidance of positive attention for negative behaviors
- Appropriate consequences for behaviors that cannot be ignored.
More Non-medication Treatment Options

- Regular physical exercise
- Time in nature
- Diet
- Sleep hygiene
More Non-medicatiion Treatment Options
ADHD in Preschool: PATS

- NIMH multi-center randomized crossover efficacy trial
- 3-5.5 y/o with severe ADHD unresponsive to 10 week psychosocial intervention
- 37/279 patient parents said behavioral treatment resulted in satisfactory improvement

Greenhill et al. JAACAP 2006.
ADHD in Preschool: PATS

- Stimulants are generally effective
  - ES = 0.4-0.7
  - Lower doses provided better balance of benefits and side effects

- Lower response rates compared to older children
  - ES in MTA Study (7-9 y/o) = 0.5-1.3

- Higher rate of side effects
  - 11% attrition vs <1% in MTA

Greenhill et al. JAACAP 2006.
# Preschool vs School Age

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Agent</th>
<th>Effect Size</th>
<th>Attrition due to SEs</th>
<th>Avg optimum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATS (3-5 y/o)</td>
<td>MPH IR</td>
<td>0.35-0.66</td>
<td>11%</td>
<td>0.7 +/- 0.4 mg/kg/day</td>
</tr>
<tr>
<td>MTA (7-9 y/o)</td>
<td>MPH IR</td>
<td>0.52-1.31</td>
<td>&lt;1%</td>
<td>1.0 +/- 0.5 mg/kg/day</td>
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Greenhill et al. JAACAP 2006.  
Wigal et al. JAACAP 2006.  
ADHD in Preschool: MPH titration

MPH IR 2.5 mg PO BID x7d

MPH IR 5 mg PO BID x7d

If effective AND well-tolerated, consider switch to once daily formulation, NTE 10mg/day
ADHD in Preschool: Guanfacine titration

Guanfacine IR 0.25mg PO BID x2 weeks

→

Guanfacine IR 0.5mg PO BID
ADHD and Autism

Data Courtesy of CDC

<table>
<thead>
<tr>
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<th>Prevalence</th>
<th>Percent</th>
<th>About 1 in every &quot;x&quot; children</th>
</tr>
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<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>16.8 per 1,000</td>
<td>1.7%</td>
<td>1 in 59</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Boys</td>
<td>26.6 per 1,000</td>
<td>2.7%</td>
<td>1 in 38</td>
</tr>
<tr>
<td>Girls</td>
<td>6.6 per 1,000</td>
<td>0.7%</td>
<td>1 in 152</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
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<tr>
<td>White</td>
<td>17.2 per 1,000</td>
<td>1.7%</td>
<td>1 in 58</td>
</tr>
<tr>
<td>Black</td>
<td>16.0 per 1,000</td>
<td>1.6%</td>
<td>1 in 63</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>13.5 per 1,000</td>
<td>1.4%</td>
<td>1 in 74</td>
</tr>
<tr>
<td>Hispanic*</td>
<td>14.0 per 1,000</td>
<td>1.4%</td>
<td>1 in 71</td>
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ADHD and Autism

ADHD
- Inattention
- Hyperactivity

ASD
- Communication
- RRBI

Social
ADHD and Autism

• In prior version of DSM, ASD was an exclusion criterion for ADHD. Not so in DSM-5.

• 22-83% of children with ASD meet criteria for ADHD

• Shared heritability:
  • 50-72% of contributing genetic factors overlap

Sokolova E. J Autism Dev Disord. 2017
ADHD and Autism: RUPP

- Double-blind, placebo controlled, crossover trial with open label continuation using MPH in children with moderate to severe hyperactivity
- N=72, ages 5 to 14.
- 49% responded with ES = 0.2-0.54
- SEs led to 18% attrition.

RUPP Autism Network. JAMA 2005
# ADHD and Autism

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<tr>
<td>RUPP (5-14 y/o)</td>
<td>MPH IR</td>
<td>0.20-0.54</td>
<td>18%</td>
<td>Not reported</td>
</tr>
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RUPP Autism Network. JAMA 2005
ADHD in Autism: MPH titration

MPH IR 2.5 mg PO BID x7d

MPH IR 5 mg PO BID x7d

Consider switch to long acting, proceed with caution
ADHD and Epilepsy
ADHD and Epilepsy

- ADHD in epilepsy: ~30%
  - Boys = Girls
  - Inattentive > Hyperactive
- Epilepsy in ADHD: 2.3% (0.5% gen pop)

Besag et al. Epileptic Disord 2016
Socanski et al. 2013. Epilepsy Behav 2010
ADHD in Epilepsy: Assessment

• Clinical suspicion
• Detailed history of symptoms
• Collateral from 2+ contexts
  ▪ Vanderbilt
• Neuropsychological testing
• IMPAIRMENT
ADHD in Epilepsy: Safety of standard treatments

• Methylphenidate:
  ▪ Multiple studies since 1997 show neutral effect on seizure exacerbation. One showed EEG improvements.

• Atomoxetine:
  ▪ 4 studies since 2007 imply no effect on seizures

• (Risperidone)
  ▪ Small study 2004 implied no effect on seizures

Besag et al. Epileptic Disord 2016
ADHD in Epilepsy: Stimulant Titration

Concerta 18mg x7d → Concerta 36mg x7d
ADHD and Prenatal Drug Exposure
ADHD and prenatal drug exposure

• Substances typically used in combination
• Direct effects of drug exposure AND environmental factors both impact fetus
ADHD and prenatal alcohol exposure

- FAS: 0.3 to 9 per 1000 children with FAS
- FASD: 1-5% in US

ADHD and prenatal alcohol exposure

Weighted Prevalence Estimates of Any Alcohol Use* Among Women Aged 18-44 Years – BRFSS 2016

- 29.2% — 47.6%
- 47.9% — 55.6%
- 55.6% — 58.1%
- 59.8% — 68.3%
ADHD and prenatal alcohol exposure
ADHD and prenatal alcohol exposure

Williams et al. Pediatrics 2015
ADHD and prenatal alcohol exposure

Williams et al. Pediatrics 2015
FASD: Neurodevelopmental

- Cognitive/Learning
- Visual/Spatial
- Memory
- Executive functioning
- Attention
FASD: Neurodevelopmental

Mattson et al. Neuropsychol Rev. 2011
ADHD and prenatal exposure: Optimal arousal theory

Kable J. Seattle Children’s Psychiatry Grand Rounds 1/10/20. Used with permission. Do not duplicate.
# ADHD and Prenatal exposure

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Dysfunction</th>
<th>Differences</th>
<th>Stimulus changes needed</th>
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<tbody>
<tr>
<td>Autism</td>
<td>Easily over aroused</td>
<td>Downward shift in need for central stimulation or reduced ability to modulate or habituate stimulus input</td>
<td>Reduce sensory input</td>
</tr>
<tr>
<td>ADHD</td>
<td>Under aroused</td>
<td>Shift in level of central stimulation found to be optimal from inadequate neurotransmission of incoming stimulation</td>
<td>Respond to stimulant medications and increases in arousal</td>
</tr>
<tr>
<td>FAS</td>
<td>Arousal dysfunction</td>
<td>Slower gating of incoming stimulation and reduced capacity to inhibit attending to distracting stimuli</td>
<td>Respond to simplification of sensory input (fewer distracters and slower presentation)</td>
</tr>
<tr>
<td>Cocaine Exposure</td>
<td>Heightened arousal responses</td>
<td>Over aroused by stimulation and difficulties returning to baseline levels. Also has difficulties with maintaining inhibitory control</td>
<td>Monitoring of arousal level so stimulus input can be modified when too high. Longer periods allowed for recovery of functioning</td>
</tr>
</tbody>
</table>
ADHD and prenatal exposure: Titration

- Modify expectations based on type of PE
- Monitor closely for SEs, esp irritability/activation
- Lower threshold to transition to non-stimulants
Any Questions?