ADHD Treatment Update

Kyle Benner, M D
Child and Adolescent Psychiatrist
Medical Director, Ambulatory Behavioral Health
Swedish Medical Group
Disclosures

• None. No financial relationships.
• You will see brand-name pharmaceuticals, as this presentation will review newer medications, which are not yet available in generic formulation.
What’s not included:

• Diagnostic Review
• Evidence-base for stimulants
• Medications prior to 2012
  • Non-stimulants
What to Expect

• Review of Medications since 2012
• Psychotherapy update
• New data on why you should treat ADHD and long-term outcomes of ADHD treatment (the good and the bad)
Medications
Since Quillavant XR (methylphenidate) 2012:

- Short-acting Stimulant (<6 hours):
  - Zenzedi (dextroamphetamine sulfate) 2013
- Long-acting Stimulant (>6 hours):
  - Evekeo (amphetamine sulfate) 2012
  - Contempla XR ODT (methylphenidate) 2014
  - Aptensio XR (methylphenidate) 2015
  - Dynavel XR (amphetamine) 2015
  - Adzenys XR (amphetamine) 2016
  - Mydais (dextroamphetamine/amphetamine) 2017
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Age</th>
<th>Duration of Action</th>
<th>Dose</th>
<th>Form</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zenzedi d-AMPH</td>
<td>3-16yo</td>
<td>4-6 hrs</td>
<td>5-40mg qd-tid</td>
<td>tablet</td>
<td>2.5mg starting dose for 3-5yo 2.5mg and 7.5mg tablet</td>
</tr>
<tr>
<td>Evekeo AMPH</td>
<td>3yo +</td>
<td>6 hrs</td>
<td>5-40mg, qd-tid</td>
<td>tablet</td>
<td>DoA, 2.5mg starting dose for 3-5yo</td>
</tr>
<tr>
<td>Dynavel XR AMPH</td>
<td>6yo +</td>
<td>8-12 hrs</td>
<td>2.5-20mg qam</td>
<td>liquid</td>
<td>AM PH Quillavant XR</td>
</tr>
<tr>
<td>Adzenys XR AMPH</td>
<td>• 6-12yo</td>
<td>• 9-10 hrs</td>
<td>• 6.3-18.8mg qam</td>
<td>ODT</td>
<td>50%IR/50%ER Children metabolize faster Orange-flavored</td>
</tr>
<tr>
<td></td>
<td>• 13yo +</td>
<td>• 11 hrs</td>
<td>• 6.3-12.5mg qam</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mydais d-AMPH/AMPH</td>
<td>13yo +</td>
<td>12-16hr</td>
<td>12.5-25mg qam</td>
<td>capsule</td>
<td>Three pH sensitive layers</td>
</tr>
<tr>
<td>Contempla XR ODT MPH</td>
<td>6-17yo</td>
<td>8-12hr</td>
<td>17.3-51.8mg qam</td>
<td>ODT</td>
<td>25%IR/75%ER Grape-flavored</td>
</tr>
<tr>
<td>Aptensio XR MPH</td>
<td>6yo +</td>
<td>10-12hr</td>
<td>10-60mg qam</td>
<td>capsule</td>
<td>40%IR/60%ER</td>
</tr>
</tbody>
</table>
Zenzedi (2013)

- d-AM PH
- Ages 3-16
- Duration of Action: 4-6 hours
- Tablet, 5mg-40mg qday-tid
  - For 3-5yo, starting dose of 2.5mg
- **Only immediate release dextroamphentamine**
- 2.5mg doses and 7.5mg doses
  - Younger children
Evekeo (2012)

- AM PH
- 3yo +
- Duration of action 6 hours
- Tablet, 5mg-40mg qday-tid
  - For 3-5yo, starting dose of 2.5mg
Dynavel XR (2015)

- AM PH
- Ages 6yo +
- Duration of Action 8-12 hours
- Liquid, 2.5-20mg qam
Adzenys XR (2016)

• AM PH

• Ages 6yo +
  • 6-12yo
    • Duration of Action 9-10 hours
    • ODT, 6.3-18.8mg qam
  • 13yo +
    • Duration of Action 11 hours
    • ODT, 6.3-12.5mg, qam

• 50% Immediate Release + 50% Extended Release

• Orange flavored
M ydais (2017)

• d-AM PH/AM PH
• Ages 13yo +
• Duration of Action 12-16 hours
• Capsule, 12.5-25mg qam
Contempla XR ODT (2014)

- M PH
- Ages 6-17 yo
- Duration of Action 8-12 hours
- ODT, 17.3-51.8mg qam
- 25% Immediate Release + 75% Extended Release
- Grape flavored
Aptensio XR (2015)

- M PH
- Ages 6yo +
- Duration of Action 10-12 hours
- Capsule, 10-60mg qam
- 40% Immediate Release + 60% Extended Release
Psychotherapy

- CBT, JAACAP July 2018

  - Cool Kids, individual + parent therapy
  - 842 Children ages 5-18yo, Sydney, Australia
  - Concurrently treated with medication
  - Improvement in anxiety symptoms
  - Remission sustained at 3 and 6 months
  - Monitored with Structured Clinical Interview
  - Improvement in ADHD severity ratings
Psychotherapy

- Parent Management Training, JAACAP August 2018
- Parent Training for Preschool ADHD in Routine, Specialist Care: A Randomized Controlled Trial, Lange, et al

- New Forest Parenting Programme, children present for 3 of 8 sessions
- 164 Children age 3-7, Denmark
- No medication
- Improvement in Parent rating scales
- Remission sustained at 3 months
- But not teachers (not unusual for PT)
- Family Strain Parent self-efficacy
MTA updates

• BRIEF Review
• Multimodal Treatment Study of Children with ADHD
  • December 1999, published
  • 579 children, ages 7-9 over 14 months
  • 7 sites- diverse, generalizable sample
  • Four groups:
    • Intensive medication management alone
    • Intensive behavioral treatment alone
    • Combination of both
    • Routine community care (the control group)
  • Findings:
    • Medication Management and Combination Treatment > Behavioral Treatment alone or Routine Care
    • Combination Treatment helps best with specific symptoms of anxiety, academic performance, parent-child relations, and social skills
      • Less medication prescribed with Combination Treatment
MTA Updates

• Follow-up, JAACAP, November 2016
• Functional Adult Outcomes 16 Years After Childhood Diagnosis of Attention-Deficit/Hyperactivity Disorder: MTA Results, Hechtman, et al
  • After concluding treatment, MTA becomes a naturalistic study
  • Follow-ups at 2, 3, 6, 8, 10, 12, 14, and 16 years post-baseline
  • Compare ADHD Group to Local Normative Comparison Group
  • Reviewing 12-16yr follow-up (adults)
  • 476 participants from ADHD group and 214 age/sex-matched classmates
  • Those in ADHD Group lost to follow-up had significantly lower family income, younger maternal age, less maternal and paternal education, more paternal mental health problems, lower IQs, and higher teacher-rated ADHD and oppositional defiant disorder.
  • So, things presented on the next slides might be worse...
MTA Updates

• Education
  • Majority of ADHD Group (61.7%) had a high school degree or less
  • Majority of LNCG participants completed at least some college (60.8%)
MTA Updates

• Occupational Outcomes
  • ADHD Group significantly:
    • more likely to be fired/quit a job (0.61 vs 0.32)
    • lower income in last year
    • utilize public assistance (16% vs 3.2%)

• Sexual Behavior Outcomes
  • ADHD Group significantly associated with:
    • younger age at first intercourse (16.3 vs 17.2)
    • more sexual partners (15.7 vs 9.45)
    • greater number of offspring by age 18 years (0.298 vs 0.113)
MTA Updates

• Substance Use, JAACAP, October 2017
• Substance Use Among Children With and Without Attention-Deficit/Hyperactivity Disorder Followed Prospectively Into Early Adulthood in the MTA, Mitchell, et al
  • Increased risk for weekly marijuana and daily tobacco use into young adulthood
  • At age 21, marijuana (32.8% vs. 21.3%), tobacco (39.5 % vs 17.5%)
  • Increased risk for heavy drinking up to age 25
  • No differences between ADHD Group and LNCG for:
  • Nonmarijuana illicit drug use
  • Prescription drug misuse (<2%)
MTA Updates

• ADHD and Growth, The Journal of Child Psychology and Psychiatry, March 2017
  • Young adult outcomes in the follow-up of the multimodal treatment study of attention-deficit/hyperactivity disorder: symptom persistence, source discrepancy, and height suppression, Swanson, et al
    • ADHD group was $1.29 \pm 0.55$ cm ($p < 0.1$) shorter than LNCG
    • Consistent/Inconsistent use had shorter height than Negligible use
      • $2.55 \pm 0.73$ cm ($p < 0.0005$) shorter
      • Consistent use shorter than Inconsistent use
        • $2.36 \pm 1.13$ cm ($p < 0.4$)

• Not consistent with previous long-term follow-up studies
• Stimulants have been used at higher doses for longer periods of time in subsequent decades
  • 1960s, 34,350 mg vs 1990s, 66,003 mg
• Risk of growth suppression depends on timing of treatment administration and duration of treatment
• Combining Behavioral Interventions to lower total dosing
ADHD and STIs

- Sexually Transmitted Infection Among Adolescents and Young Adults With Attention-Deficit/Hyperactivity Disorder: A Nationwide Longitudinal Study, Chen, et al, JAACAP January 2018
  - 17,898 adolescents and young adults with ADHD vs 71,592 age-matched peers
  - Taiwan, National Health Insurance
  - ADHD diagnosed by board-certified psychiatrist
  - ADHD Group had:
    - STIs at younger age (20.51 vs 21.90)
    - Higher incidence of STIs (1.2% vs 0.5%)
    - Higher incidence of SUD (2.5% vs 0.9%)
    - ADHD treatment decreases STI risk in men
References


Sexually Transmitted Infection Among Adolescents and Young Adults With Attention-Deficit/Hyperactivity Disorder: A Nationwide Longitudinal Study. Chen, Mu-Hong et al. Journal of the American Academy of Child & Adolescent Psychiatry, Volume 57, Issue 1, 48 – 53
