AD/HD: PEARLS FOR THE PRIMARY CARE PROVIDER

4th annual Pediatric Mental Health Update: Equipping the Primary Care Provider
March 5th, 2021
Daniel Nicoli, DO
DISCLOSURES
01 Review the evidenced based treatments for AD/HD

02 Discuss the role of the primary care provider in the treatment of AD/HD

03 Discuss pearls relevant to the primary care providers treating patients with AD/HD
ASSESS AND DIAGNOSIS AD/HD!
• AD/HD more frequently goes unrecognized in girls
• Historians (e.g., teachers and parents):
  • Great at recognizing kids that are loud, hyperactive, or aggressive (boys often present this way)
  • Do not always notice kids without externalizing symptoms who instead have more subtle signs such as drifting attention, poor organizational skills, making careless mistakes, losing things, and others
• Ask (and observe) if the parents have AD/HD (do they always show up late?)
SLIDE 1

Pre- and Perinatal Risk Factors for ADHD

Results from Logistic Regression Model

- Cigarette Exposure
- Alcohol Exposure
- Drug Exposure
- Low Birth Weight
- Psychosocial Adversity
- Socioeconomic Status
- Age at Birth
- Parental IQ
- Parental ADHD
- Parental Conduct Disorder

Odds Ratio (ADHD vs Control)
Worldwide Prevalence of ADHD in Children

Spain
New Zealand
Canada
Ireland
United Kingdom
Israel
Switzerland
Netherlands/Belgium
Germany
Ukraine
Brazil
Japan
New Zealand
Netherlands
United States
Canada
India

Prevalence of ADHD (%)

Prevalence of ADHD (%)

AD/HD

- Oppositional defiant disorder (60%)
- Conduct disorder (20%)
- Learning disorders (at least 25-30%)
- Anxiety disorders (30%)
- Depressive disorders (10-30%)
- Mania/mood lability (16%)
TREATMENT
• We must educate families on the pros and cons so that they can make an informed decision
• After providing education and recommendations, they typically consent to a trial of medication
WHAT’S THE BIG DEAL IF MY KID DAYDREAMS? I’D RATHER NOT PUT HIM ON MEDICATIONS!
THE AAP SAYS IT’S IMPORTANT

• High prevalence of AD/HD
• Severity of Consequences of AD/HD
• Effective treatments for AD/HD
“Under-achievement can lead to poor self-esteem, which can become the real enemy for those who are struggling to succeed.”

Dr. Edward Hallowell
Psychiatrist with AD/HD & Dyslexia
Author of the book “Driven to Distraction”
TALKING POINTS

Disruptive behavior
• Troublemakers
• Bad sportsmanship
• Excessive talking
• Cannot sit still
• Unfocused, not responsive to others
• Impulsive aggression

Immaturity and impulsiveness
• Center of attention
• Breaks the rules
• Blurting out answers
• Peer rejection

Adolescents continue to demonstrate social problems
• Poor participation in group activities
• Few friends
• Vulnerable to antisocial groups, drug abuse
MEDICATIONS
Findings MTA Study

(MTA Cooperative Group, 1999)

Hyperactive Impulsive Symptoms
(Teacher Reports)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Improvement at 14 Months (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediation Management</td>
<td>58%</td>
</tr>
<tr>
<td>Combination Therapy</td>
<td>60%</td>
</tr>
<tr>
<td>Behavioral Treatment</td>
<td>46%</td>
</tr>
<tr>
<td>Community-based Treatment</td>
<td>38%</td>
</tr>
</tbody>
</table>
YES, WE CAN!
ADHD Medication Treatment Algorithm
Based on AACAP Guidelines, 2007 and HEDIS 2010 Performance Measurements

Select Stimulant Agent
- Methylphenidate or Amphetamine
  - Long-Acting Kids / Adults

Or

- Methylphenidate or Amphetamine
  - Short-Acting
    - Small kids <16kg/35lbs
    - (low dose is not available in long-acting)

Or

- Strattera® (Atomoxetine)
  - Use for ADHD with co-morbid anxiety or tic disorder
  - Use with decreased appetite, and / or decreased sleep from other ADHD meds, or with substance abuse problems

Initial Dose
- Select starting dose and times of administration
  - Once daily dosing is helpful for kids in school and prevents the need to send a medication supply to the school nurse
  - Twice daily dosing is helpful in kids with late evening behavior episodes

Titrated Dose
- Titrate dose upward every one to three weeks until maximum dose is achieved or side effects preclude further dose increase

Achievement Goals
- ADHD Symptoms remit
- No side effects
- For students, teacher & parent rating scales are helpful as dose is increased.

Initial Follow Up Visit
- Initial follow up should be within 30 days or less of therapy initiation

- Determine if response is appropriate
  - 41% will respond to either stimulant medication
  - 44% will respond better to one medication than another
  - Strattera may take up to 6 weeks to see effect

- Assess for side effects
  - Headache
  - Insomnia
  - Decreased appetite or weight loss
  - Tics
  - Emotional lability / irritability
  - If side effect is burden to patient:
    - Adjust dose, change medication or wait as many side effects are transient and will resolve

- If optimal results have not been achieved:
  - Review Diagnosis and assess for any undetected co-morbidities
  - If ADHD diagnosis is reconfirmed, consider behavioral therapy next before adding a non-FDA approved medication

Adding or Stopping Medications
- At least 2 or more visits during the next 9 month period

- If maximum dose of Methylphenidate, amphetamine or atomoxetine has been achieved, continue & monitor for side effects

Adding Another Medication
- Add-on meds:
  - Bupropion, tricyclic antidepressant, clonidine or guanfacine

Often necessary when:
- Patient has co-morbid aggression
- Necessary to reduce side effects of tics or insomnia

Discontinuing a Medication
- If an add on medication is ineffective, titrate dose downward over a 1-2 week period to avoid sudden drops in blood pressure
<table>
<thead>
<tr>
<th>Medicine</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>0.92</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>0.80</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>0.73</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.58</td>
</tr>
<tr>
<td>Modafinil</td>
<td>0.49</td>
</tr>
<tr>
<td>Bupropion</td>
<td>0.32</td>
</tr>
<tr>
<td>Omega Threes</td>
<td>0.21-0.3</td>
</tr>
</tbody>
</table>
• First line  →  Stimulants
• Second line  →  Stimulants
• Third line  →  Consider stimulants with or without adjuncts first, if not an option, then atomoxetine
• Fourth line  →  Alpha-2-AgonistsGuanfacine, clonidine
Methamphetamine Hydrochloride

Dosing/Administration

Pediatric Dosing

Important Note
- Methamphetamine has a high potential for abuse. The drug should be prescribed or dispensed sparingly and patients should be warned of the dangers of misuse. Special attention should be paid to the possibility of subjects obtaining methamphetamine for non-therapeutic use or distribution to others.

Attention deficit hyperactivity disorder
- (6 y and older) initial, 5 mg ORALLY once or twice daily; may increase by 5 mg weekly; usual effective dose, 20-30 mg ORALLY daily; may be given in two divided doses daily [1]

Simple obesity
- 12 years and older: 5 mg ORALLY 30 minutes before each meal [1]
I DON’T RECOMMEND PRESCRIBING METHAMPHETAMINE; THAT WAS A JOKE, AND HOPEFULLY IT WAS FUNNY
Best Response (percent) vs. Stimulant

- Dextroamphetamine
- Methylphenidate
- Equal response to either Stimulant

6 studies
N=274

Spencer et al. Arch of Gen Psych 2001
ALPHA-2A AGONISTS

- Central actions on postsynaptic alpha-2A receptors in the prefrontal cortex leads to mediation of norepinephrine actions
- Can be used, alone or in combination with a stimulant, to treat comorbid AD/HD and:
  - Hyperactivity
  - Anxiety
  - Aggression
  - Tics
IS MY KID TOO YOUNG FOR MEDICATIONS?
Effect Sizes:

3-5 yo: 0.5-0.6
6-12 yo: 0.8-1.2
13-17 yo: 0.94
Adults: 0.9

70 + years of study, >250 trials, >6,000 subjects
Monitor

- Weight, Height, BMI
- Pulse
- Tics
- Blood Pressure
- Vitamin D
2008 study showed that treatment with stimulant medication led to statistically significant delays in height and weight.

Harvard AD/HD team found statistically significant evidence of attenuation of these deficits over time.

The qualitative review suggested that growth deficits may be dose dependent, deficits may not differ between methylphenidate and amphetamine.

Treatment cessation may lead to normalization of growth, and further research should assess the idea that attention-deficit/hyperactivity disorder itself may be associated with dysregulated growth.
BONE DENSITY

• 6,489 NHANES participants aged 8 to 20 years, of whom 159 were receiving stimulants (primarily amphetamines or amphetamine analogs) for AD/HD. After adjustment for confounders, those using the medications had a total 3.9% lower bone density at the lumbar spine and 3.7% lower bone density at the femoral neck compared with nonusers.

• Recommend:
  • Calcium intake of 800 to 1,300 mg daily
  • 60 minutes of weight-bearing exercise or activity every day
  • Monitor vitamin D levels
FOR KIDS < 5 YEARS OLD

• Medication not first line unless significant concerns
• First line:
  • Behavioral Parent Training (behavioral modification applied for use in the home)
  • Behavioral classroom management (behavioral modification techniques given to teachers)
  • Organizational skills training
• Consider referral to child psychiatry for complex or severe case in this age group
RESOURCES FOR PARENTS

- Parent Child Interaction Therapy (PCIT)
- Kazdin Behavior Management Training
- Parent Management Training – Oregon Model (PMTO)
- Collaborative Problem Solving
- Russell Barkley
- Rex Forehand
- Love & Logic
MY KID IS NOT EATING AND LOST ONE POUND!
DO NOT GIVE UP TOO QUICKLY ON STIMULANTS!
ADVICE FOR BAD EATERS

- Get them some nutrition in the afternoon
- Big breakfast and big dinner, late night snacking is okay
- Nutrition shakes
THE FAMILY HAS A HISTORY OF SUDDEN CARDIAC DEATH!
April 2008 AHA released policy statement that all youth on stimulants should receive EKG

May 16, 2008, the AHA and AAP, and AACAP, jointly issued a news release clarifying that obtaining an ECG before starting medication was “reasonable” but not mandatory.

The risk of cardiac arrest from stimulants is no greater than sudden cardiac arrest in the general pediatric population—Gould et al., 2009
WILL IT GIVE MY KID A TIC?
NO!
• To date, research has not established a “definitive and causal” relationship of the emergence of tics with stimulant use.
• Though some studies have indicated that transient tics may occur more often in a population of AD/HD patients (with and without a history of tic disorders) treated with stimulants, this data remains controversial...Pidosny & Virani—2006
• Researchers studied 136 children aged 7 to 14 years with AD/HD and a chronic tic disorder taking MPH.
• Throughout the 4-month study, researchers found improvement in all of the children who received medication.
• "Not only did tics not worsen during treatment, the severity of tics actually decreased in all treatment groups," writes study author Roger Kurlan, MD, of the University of Rochester Medical Center in New York
WILL MY KID BECOME DEPENDENT ON THIS MEDICATION?
Unadjusted Total Cerebral Brain Volume for Unmedicated and Medicated Children and Adolescents with ADHD and Controls'

10-year NIMH Study, subjects age 5-18 years at baseline

*P=.001 by 2-way ANOVA (group [medicated vs. unmedicated vs. control] by sex).
DON’T KIDS ABUSE STIMULANTS?
WELL, ACTUALLY YES, BUT SO DO ADULTS! WAIT, THAT DOESN’T HELP; SCRATCH THAT AND LOOK AT THIS...
Substance Abuse in AD/HD Youth
Growing Up: Effect of Pharmacotherapy

(Biederman, Wilens, Mick et al., Pediatrics 1999)
GOOD NEWS FOR PARENTS WORRIED ABOUT DRUG USE!

• According to a study in the Br J Psychiatry July 11, 2013, stimulant medications appear to lower the risk for substance abuse disorders in adolescents with AD/HD

• In a large, prospective, longitudinal study investigators from the SUNY found that adolescents with AD/HD who were not treated with a stimulant medication for their disorder had a 2-fold increased risk of developing an SUD compared with their counterparts who were treated.

• Untreated adolescents with AD/HD also had a 2.6-fold increased risk of developing an SUD compared with a healthy, age-matched control group.

• Multiple past studies show no connection.
WILL THEY HAVE TO TAKE THIS MEDICATION FOREVER?
THEY MIGHT CHOOSE TO...
<table>
<thead>
<tr>
<th>Study</th>
<th>Age of patients and follow-up</th>
<th>Findings at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barkley et al, 1990¹</td>
<td>6 years, follow-up at 14 years</td>
<td>72% with AD/HD</td>
</tr>
<tr>
<td>Biederman et al, 1996²</td>
<td>6 – 17 years, 4 year follow-up</td>
<td>85% with AD/HD</td>
</tr>
<tr>
<td>Gittelman et al, 1995³</td>
<td>16 – 23 years</td>
<td>68% with AD/HD in adolescence</td>
</tr>
<tr>
<td>Weiss et al, 1985⁴</td>
<td>5 – 12 years, 5, 10 and 15 year follow-up</td>
<td>66% with at least 1 core symptom of AD/HD by adulthood</td>
</tr>
</tbody>
</table>
SINCE STARTING THE MEDICATION, MY KID GETS SO MOODY AND HYPER IN THE EVENINGS!
ER Methylphenidate Formulations

*Data presented are intended for illustrative purposes only and are not derived from a single cross-over study. These pharmacokinetic profiles represent the superimposition of data generated in three previously published bioavailability studies of MPH dosage formulations at similar strengths administered to healthy adult volunteers.\textsuperscript{102,105,107}
DOES MY KID NEED TO TAKE IT EVERYDAY?
YES, OR NO, IT DEPENDS...
WILL THEY EVER GROW OUT OF THIS?
KIND OF, SOMEWHAT, AND PROBABLY...
ADHD is Characterized By a Delay in Cortical Maturation

DLPFC = dorsolateral prefrontal cortex; TOPJ = temporal-occipital-parietal junction.

WE PREFER A “NATURAL” APPROACH
IF YOU ARE NEW TO OREGON, BE PREPARED TO ANSWER THIS QUESTION, LIKE A LOT...
THESE DO NOT REPLACE A STIMULANT

- Psychoeducation
- AD/HD diet (INCA study), no artificial colors
- Structure/schedule, exercise, good sleep hygiene, sensory issues (OT eval)
- RLS in AD/HD kids: Ferrous sulfate, magnesium
- AD/HD Supplements: phosphatidylserine, Omega-3
- Sleep supplements: melatonin, magnesium
- Impulsivity/hyperactivity: Zinc, B6
- Cognitive: Vit. D levels (correct low levels)
- Balanced Nutritious Diet
- Raw foods vs processed foods
- High Omega 3 fatty acids
- Iron rich foods
- Minimize/Eliminate Junk Food
- Iron is critical in the synthesis of dopamine
- Iron is essential for the myelination of brain cells
- Some studies show that iron stores are low in up to 84% of AD/HD youth
- Ferritin levels <30 ng/ml need treatment
Several studies have shown that AD/HD youth have lower levels of omega 3 fatty acids.

Several studies have shown that AD/HD symptoms are improved with fish oil, flaxseed oil, and primrose oil.

More studies, continuing to learn more.
REFERENCES


• Book – Evidence-Based Psychotherapies for Children and Adolescents, 2nd Ed by John Weisz and Alan Kazdin, Guilford Press 2010
QUESTIONS