A REVIEW OF STIMULANTS FOR ADHD
FOR THE PRIMARY CARE PROVIDER

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OVERVIEW

- Review Stimulant Treatment for ADHD
STIMULANTS

- They are an approved indication for the treatment of ADHD in children
- Well documented 300+ controlled trials
- 70% or better improvement in individuals with true ADHD
STIMULANTS

• Have been shown to decrease interrupting and fidgetiness in the classroom and increase on-task behavior in the classroom.

• Improve parent-child relationships in the home as well as compliance and on-task behavior.

• Also improves other social interactions.
STIMULANTS

• Block the reuptake of DA and NE into the presynaptic neuron

• Increase the release of these into the extraneuronal space, but...

• Methylphenidate(s) and amphetamines have different mechanisms on release of DA
HOW I THINK ABOUT TYPE OF STIMULANTS FOR TREATING ADHD...

• TWO groups:
  • ‘The Amphetamines’
    • Dexedrine, Adderall, Vyvanse etc.
  • ‘The Methylphenidates’
    • Ritalin, Metadate, Concerta etc.

• The short half-life of stimulants has always been the problem.

• The science is in how the newer preparations deliver the old drug.
SOME NUTS AND BOLTS ABOUT STIMULANTS

• Some need higher doses

• Official limit is a guide, if there is a good response without side effects you could increase

• On the other hand, avoid heroic dosing

• There is evidence to support that if one stimulant fails try a different one before going to non-stimulants
MORE NUTS AND BOLTS ABOUT STIMULANTS

• Be careful what parents mean by non-response – this can vary!

• How are you measuring response?

• Use rating scales (a lot of good ones for free)
  • Child Behavior Checklist, Conners, Vanderbilt
  • No Gold Standard
  • Different measures of drug response do not correlate with each other

• Treat mood and anxiety disorders first, then ADHD
EVEN MORE NUTS AND BOLTS...

• How I remember it –
  • **Methelyphenidate:**
    • Heavy dose is 1.5 mg/kg/day
    • Medium dose is 1.0 mg/kg/day
    • Light dose is 0.5 mg/kg/day
    • Range is 0.3 to 2.0 mg/kg/day

• **Dexedrine** and **Focalin** are twice as potent so use half as much

• **NOT AN ABSOLUTE STANDARD**

• Use recommended starting doses from reliable Rx guide and go up or down as clinically indicated
  • I use Epocrates
AND A COUPLE MORE...

• Diagnosis demands that “several inattentive or hyperactive-impulsive symptoms were present prior to 12 years of age
  • What my thoughts are

• They do get misused/abused. People without ADHD can have improvement with rote-learning tasks but do not increase IQ. They can cause euphoria but with dangerous consequences
THE AMPHETAMINES

• Amphetamine has one chiral center, producing both dextro and levo isomers

• D isomer was felt to have more potent effects, but later found that L isomer was what some people would only respond to

• Started combining the isomers i.e. Adderall
SOME AMPHETAMINE PREPARATIONS

- **Dexedrine**
  - Dextroamphetamine sulfate

- **Dexedrine Spansule**
  - Dextroamphetamine in waxy capsule

- **Adderall, Adderall XR**
  - Mixed salts of amphetamine and dextroamphetamine

- **Vyvanse**
  - Lisdexamfetamine

- **Adzenys XR**
  - Amphetamine extended release orally disintegrating tablets

- **Dyanavel XR**
  - Amphetamine extended release oral suspension
ADDERALL XR - HOW'D THEY DO THAT?

- Capsule contains two types of beads, which together provide a “double pulsed” delivery of amphetamines.
- This is similar to BID dosing of regular Adderall.
VYVANSE
Lisdexamfetamine Dimemsylate

• The first stimulant to be offered as a Prodrug

• “Therapeutically inactive molecule” converted to active form after being absorbed by GI tract

• It is d-amphetamine and l-lysine

• Smoother onset and offset

• Supposedly “less likeable” to substance abusers
THE METHYLPHENIDATES

• Methylphenidate has two chiral centers, resulting in 4 isomers:
  • d-threo, d-erythro, l-threo, and l-erythro
SOME METHYLPHENIDATES

• **Ritalin**
  − Methylphenidate

• **Focalin**
  − Dexmethylphenidate

• **Daytrana**
  − Methyl-P transdermal

• **Concerta**
  − Methyl-P extended release capsule

• **Metadate CD**
  − Methyl-P extended release capsules

• **Quillivant XR**
  − Methyl-P extended release oral suspension

• **Quillichew ER**
  − Methyl-P extended release chewable tabs

• **Ritalin LA**
CONCERTA - HOW'D THEY DO THAT?

• Capsule is not digestible

• Methylphenidate is pumped out throughout the day

• 18mg = 5mg tid, 27mg = 7.5 tid 36mg = 10mg tid, 54 mg = 15mg tid

• “Backwards engineered”
CONCERTA...

This is a cartoon, but it gets the point across.
**CONCERTA...**

**Morning**
The MPH overcoat provides immediate release of 22% of the dose within 1 hour.

**1 hour later**
The push compartment expands, releasing MPH from MPH compartment #1 for the rest of the morning.

**Afternoon**
The push compartment continues to expand, releasing MPH from MPH compartment #2 during the afternoon. This extended delivery results in efficacy through 12 hours.
### METADATA-CD: EXAMPLE OF BEAD SYSTEM

#### Figure 1

<table>
<thead>
<tr>
<th>Rapid-release bead</th>
<th>Continuous-release bead</th>
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</thead>
<tbody>
<tr>
<td><img src="rapid-release-bead.png" alt="Diagram" /></td>
<td><img src="continuous-release-bead.png" alt="Diagram" /></td>
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</tbody>
</table>

- **Rapid-release bead**
  - Core
  - Methylphenidate HCl
  - Protective Membrane

- **Continuous-release bead**
  - Core
  - Methylphenidate HCl
  - Protective Coating
  - Release-control Membrane
METADATE CD

- Long-acting sustained release

- Mixture of long acting and short acting beads
  - 30% 6mg IR(immediate release), 70% 14mg SR(sustained release)

- Duration of action 8-12 hours
FOCALIN

- Purified d isomer methylphenidate
- 2x as potent so use half as much
- Peak effect is 1-4 hours
- Duration of action 2-5 hours
- Use BID

- Focalin XR same daily dose as Focalin but just once a day
TICS AND STIMULANTS

• Not an absolute contraindication

• Try different stimulants

• Weigh the cost of the tics with the cost of not successfully treating ADHD

• Some studies are suggesting stimulants decrease tics over time in kids with Tourette’s and ADHD
  • Strattera
QUESTIONS?