## Management of ADHD

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## Comorbidity of psychiatric disorders with ADHD LD ODD/CD Depressive Bipola disorders disord ers ADHD

## Common Comorbid Disorders Associated with ADHD

Disorder	Estimated % Associated with ADHD
Oppositional defiant	• 50%
disorder or Conduct disorder	
Learning disabilities	• 40%
Anxiety disorder	• 30%
Major Depression	• 30%
Bipolar disorder	• 10% - 20%

## CASE

• A 7 year old girl has been referred to a psychiatrist by her teacher because she displays inattention, distractibility, and poor concentration and because her academic performance resulted in falling grades. Her parents describe difficulty in following directions, disorganization, and forgetfulness. She does not have any symptoms of depression, psychosis, or developmental problems.

- ③ What is the most likely diagnosis?
- ③ What are the recommended treatments for this disorder?

## Atomoxetine

- Selective norepinephrine reuptake inhibitor
- Indicated by FDA for the treatment of ADHD in children (down to age 6), adolescents, adults
- Not typically used for other psychiatric conditions
- Atomoxetine has been studied as a potential treatment for depression, but was found to be ineffective

# Advantages of Atomoxetine compared with Stimulants

- 24 hour coverage
- No potential for drug abuse
- Less likely to be used for weight loss in an individual with an eating disorder
- Little or no long term effect on growth in children followed up to 5 years (Spencer et al., 2007;Donnelly et al., 2009)
- <sup>®</sup>Possibly lower risk of exacerbating tics
- Less concern about sudden cardiac death (although 3 cases were reported from 2003 to 2005 (FDA, 2006)

## Disadvantages of Atomoxetine compared with Stimulants

- Smaller effect size (especially in adults)
- Longer titration period
- Need to wait weeks to months for improvement
- Drug interactions with 2D6 inhibitors (Fluoxetine, Paroxetine) increase Atomoxetine levels
- Concern about suicidality
- It's still fairly new, so we have less experience with it

## Monitoring

- HR and BP
- Height and Weight
- Baseline LFTs are not necessary, but LFT should be done at the first symptom or sign of liver dysfunction
- Adverse effects
- Suicidal ideation

## Adverse effects

- Appetite suppression , weight loss
- Nausea, vomiting, dyspepsia
- Somnolence, fatigue, lethargy
- **€**<sup>™</sup>Insomnia
- **●**<sup>™</sup>Constipation

- ●<sup>™</sup> Dry mouth
- Urinary hesitation or retention
- **●**<sup>™</sup>Dysmenorrhea
- Sexual dysfunction
- Small increase in HR and BP

Pharmacotherapy for ADHD with little evidence

• **&** Combined treatment

Despite little evidence to support it, the combination of a Stimulant and Atomoxetine is generally safe and may be tried before Bupropion, TCAs, Clonidine, or Modafinil

## Stimulants

• Methylphenidate A.Ritalin, Ritalin SR **B**.Concerta C.Biphentin **2**Amphetamines A.D-Amphetamine \*Dexedrine, Dexedrine spansule Mixed salts Amphetamine (D-Amphetamine В. and I-Amphetamine salts in ratio of 3:1) \*Adderall XR

## Indications

	FDA
Ritalin and Ritalin SR	Youth ≥6 yrs, adults
Concerta	Youth 6-17 yrs, adults 18-65 yrs
Biphentin	Not available
Dexedrine and Dexedrine spansule	Youth 3-16 yrs
Adderall XR	Youth ≥6 yrs, adults

## Onset and duration of action of stimulants

	Onset of action (minutes)	Duration of action (hours)
Ritalin	30	3-4
Ritalin SR	45-90	8
Concerta	30	12
Biphentin	30	10-12
Dexedrine tablet	30	3-6
Dexedrine spansule	45-90	10-12
Adderall XR	30	12

## Side Effects of Methylphenidate

- • Decreased appetite
- **•** Insomnia
- • Stomachaches
- • Headaches
- ●<sup>™</sup>Prone to crying
- • Tics
- • Dizziness
- **●**<sup>™</sup>Drowsiness

- ●<sup><sup>™</sup> Nail biting</sup>
- **•** Talks less
- ●<sup>※</sup>Anxiousness
- • Disinterested in others
- • Euphoria
- • Irritable
- ●<sup>™</sup>Nightmares
- **●**<sup>™</sup>Sadness
- **●**<sup>™</sup>Staring

Texas Children's Medication Algorithm Project (CMAP)

## ADHD

- ③ Stimulant (MPH or AMP)
- ③ Alternative stimulant
- ③ Atomoxetine
- © Bupropion or Tricyclic Antidepressant
- ③ Alternative not used in stage 4
- <sup>©</sup> Alpha agonist

## ADHD and Aggression

- Treat ADHD, determine whether aggression resolves
- Add Behavioral intervention to Stimulant
- Add Atypical Antipsychotic to Stimulant
- Add Lithium or Divalproex Sodium to Stimulant
- ⊖ Add Agent not used in stage 4

## ADHD and Depression

- ⊗ Use stimulant to treat ADHD first, then add an SSRI if depressive symptoms do not remit with successful treatment of ADHD (1998-2004 Algorithm)
- ⊗Treat whichever disorder is most severe first, then add treatment for the second disorder if monotherapy does not result in remission of both disorders. (2005)

## ADHD and Anxiety

☺ Use Atomoxetine to treat both ADHD and Anxiety, or first treat ADHD with Stimulant, then add an SSRI for treatment of Anxiety

## ADHD and Tic Disorders

- ⊖ Stimulant monotherapy
- ☺ Stimulant required for ADHD , but if Tics continue to impair add Alpha agonists
- Add an Atypical Antipsychotic
- Add Pimozide or Haloperidol only after failure of several atypical antipsychotics

## Troubleshooting



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## "He won't stop twitching"

- On average, stimulants do not bring out or exacerbate tics (Roessner et al.,2006; TSSG,2002), although some individuals may experience this
- ⊗Remember that tics are very common (up to 25% of children), are usually transient, and typically have their onset around age 5or 6
- ⊗Remember that tics wax and wane on their own, so tic exacerbation may not be related to the stimulant

- ☺ Weigh benefit of improved ADHD symptoms of tic exacerbation
- Consider lowering the dose, switching to a different formulation of the same stimulant or a different stimulant, or adding Clonidine

## "She's got stomachaches"

Give stimulant on a full stomach
 Remember that absorption and bioavailability may increase when stimulants are taken with food

## "He won't eat "

- <sup>©</sup> Assess eating habits
- ③ Assess for other possible causes of anorexia
- ② Encourage big breakfasts (before or with first dose), later dinners, and big bed time snacks
- © Encourage high calorie foods that kids like (e.g. pizza, ice cream, milkshakes)
- © Consider consultation with a dietitian
- © Consider shorter acting formulation of the same stimulant, or a different stimulant
- Substantial Consider Adding a medication to increase appetite, e.g. Cyproheptadine, mirtazapine

## "She won't fall asleep"

- ☺ Assess and optimize sleep hygiene
- ⇒ Assess for other possible causes of sleep disturbance
- Short acting formulation: decrease or eliminate last dose, or give it a little earlier
- ⇒ Long acting formulation: give it earlier in the morning
- Consider shorter acting formulation of the same stimulant, or a different stimulant
- Last resort: consider adding asleep medication, e.g. Melatonine, Clonidine, Diphenhydramine, Trazodone, or Mirtazapine

## "The medication isn't doing anything"

- ⊗What are the parents expectations for improvement?
- ⊗Distinguish between core ADHD symptoms and other behavioral, emotional, or learning problems
- ② Parent/teacher rating scales at different doses of the medication
- ⊗ Have parent give the child the stimulant before your next appointment
- $\otimes$  If the child is tolerating the stimulant well, consider increasing the dose
- $\otimes$  Reevaluate the diagnosis

### "He's a zombie"

- Assess for other causes of social withdrawal (e.g. depression)
- Consider lowering the dose, trying a different formulation of the same stimulant, or switching to a different stimulant

## Questions



♣ In contrast with stimulants, Atomoxetine is characterized by all of the following Except: A.24 hr coverage of symptoms B.No potential for abuse C.Little or no long term effect on growth D.Higher risk of exacerbating tics E.Less likely to cause insomnia

♣You prescribe Atomoxetine to a 12 year old boy. Over the following weeks and months, you monitor for the following: A.Suicidal ideation **B.**Psychotic symptoms C.Liver dysfunction D.A and C E.All of the above

- ★You start a 30kg child on Atomoxetine 15 mg daily (0.5 mg/kg). After 2 weeks, you increase the dose to 24 mg daily (0.8 mg/kg) and 2 weeks later you prescribe the target dose of 36 mg (1.2 mg/kg). Six weeks later, the child still has not achieved an adequate response. You recall that the maximum safe and studied dose is:
- A.1.4 mg/kg B.1.6mg/kg C.1.8mg/kg D.2.0mg/kg E.2.2mg/kg

- The mother of a child with exercise induced asthma (treated with Ventolin)asks about possible drug interactions with Atomoxetine. Which of the following statements is false?
- A.There is no interaction with stimulants
- B.Interaction with Ventolin could lead to decrease in heart rate and blood pressure
- C.Interaction with MAOI could lead to serotonin syndrome
- D.Interaction with Paroxetine (2D6 inhibitor) could lead to increased Atomoxetine levels

