Medication Management in FASD

Presenter: Dr. David Shih, MD, FRCP
Date: November 25, 2009

Learning Objectives

- Learn the steps before using medications
- Learn the basics of medication choices for treating insomnia, aggression, Anxiety Disorders, ADHD, and Mood Disorders in FASD
- Understand what medications can do and cannot do

Before Using Psychiatric Medications
Before Using Psychiatric Medications

Psychological Interventions

- Review and enhance life-style changes
- Behavioral modification
- Psychotherapy to work through emotions and past trauma (e.g. Play Therapy or Talk Therapy)
- Group therapy or family therapy
- Psychotherapy to work on attachment for younger children
- Specific treatment of certain conditions e.g. treat concurrent substance abuse (AADAC)

Social Interventions

- Environmental modification (e.g. visual cues)
- Consider a case conference with school or other providers
- Encourage parents to talk to friends and pharmacists, to consult parent groups, and to check internet resources for information on medications
Medical check to make sure the problems are not due to a physical problem.
Medical Tests

Recent medical examination
And
Basic blood tests
➢ To rule out other medical problems
  • Anemia
  • Hypothyroid

Medical Tests

Basic blood tests (continued)
➢ As baseline if anticipating the use of certain medications
  • CBC
  • TSH
  • Prolactin
  • Fasting blood sugar
  • Lipid profile

How Psychiatric Medications Work

➢ Increase amount of neurotransmitters
  • Serotonin
  • Dopamine
  • Noradrenaline

in the synapse
  • SSRIs
  • Stimulants
How Psychiatric Medications Work

- Improve the function of Inhibition circuits in the brain
  - Clonidine

- Block the effects of neurotransmitters on certain brain cells
  - Risperidone

Psychiatric Medications

- Improves the connections and regulation of existing brain cells and circuitry
- They do not teach the brain how to work better
- They do not create new circuits

  - Only environmental teaching and learning creates new brain circuits

Making Sure You Have the Right Diagnosis

- Full psychiatric history and mental status examination
  
  And
  
  - Formulation (biological-psychological-social understanding of the child or teen)
  
  - DSM IV Multi-Axial Diagnosis
Disclosure to Parents

- Inform parents of the **level of evidence** in the use of medications
- Often medications are used in an “off-label” manner in treating disorders in children and teens
- Provide medication information sheets
- Disclose any side-effect that may be fatal no matter how rare

What Alcohol Does to the Fetal Brain
Alcohol As Neurotoxin on the Developing Brain

Alcohol damages
- The inside of brain cells
- The positioning of cells during brain growth
- The brain circuits
- The Serotonin and Dopamine brain circuits
- Alcohol kills brain cells

Medications Used in Persons with FASD

Because of the damage to the brain cells and circuits
- Medications may not work the way we expect
- Lower doses may help
- Higher doses may be needed
- There may be more side-effects than expected

Points to Remember

- Many organs in the body can be damaged
- Make sure the child has been fully examined by a Pediatrician
- FASD is not just a pediatric condition – it is a medical condition that impacts the individual across the lifespan
FASD and Accompanying Conditions

Accompanying Conditions

- Insomnia
- Aggression
- MOOD DISORDERS
  - Major Depressive Disorder
  - Bipolar Disorder
- ANXIETY DISORDERS
  - Generalized Anxiety Disorder
  - Obsessive-Compulsive Disorder
- Attention Deficit Hyperactivity Disorder (ADHD)
Presentation Framework for Each Condition

- What are the medication choices?
- What is the evidence for this medication?
- What are the common and serious side-effects of the medications?
- Assessing response and when to stop?

Levels of Evidence for Medications

1. Randomized double blind placebo-controlled trial “RDBPC” (best evidence)

2. Open studies (where the people know what medications they are taking)

3. Case reports

Medications Used for Insomnia
Medications Used for Insomnia

Sleep Hygiene

- No television/computer/videogames in the bedroom
- Avoid caffeine four (4) hours before bedtime
- A light snack before bedtime is alright
- Hour before bedtime should be a quiet time
- Use the bed only for sleeping
- Sleeping is better in a cool room

Medications That Have Been Used for Sleep Problems in Children and Teens

**OVER the COUNTER**
- Antihistamines
  - Benadryl
- Melatonin

**PRESCRIPTION**
- Chlорal Hydrate
- Clonidine
- Trazadone
- Zopiclone
- Neuroleptics
  - Neuleptil
  - Risperidone
  - Seroquel
Medications Used for Sleep in Children

- There are no medications for sleep approved by Health Canada for use in children
- There are no adequate studies in children of medications for sleep

Side-Effects of Medications Used for Sleep

Antihistamines
- Anticholinergic side-effects such as constipation
- May cause paradoxical excitation
- Overdose causes hallucinations and convulsions

Chloral hydrate
- Discontinuation after long term use might cause withdrawal delirium and seizures

Clonidine
- Sudden stoppage can cause rebound hypertension
**Side-Effects of Medications Used for Sleep**

**Melatonin**
- Largely unknown
- Abdominal cramps with large doses
- Fatigue
- Headache
- Dizziness
- Irritability

**Update or Unique Characteristics of Medications Used for Sleep**
- It is really not ideal to use medications for sleep for children unless there is **parental exhaustion**
- Relief for a side-effect from another medication which is required (e.g. insomnia caused by stimulant)
- Often **unknown environmental factors or family factors** are influencing the sleep of children and we may never know what they are

**Additional Medications for Sleep in Adults**

**Sedative antidepressants**
- Trazadone
- Amitriptyline
- Mirtazapine/Remeron

**Anticholergic side-effects**
- Dry mouth
- Constipation
- Urination difficulty
- Side-effects
- Can be fatal in overdose
**Additional Medications for Sleep in Adults**

**Benzodiazepines**
- Diazepam
- Valium
- Oxazepam
- Temazepam

**Side-effects**
- Can cause habituation (need more and more)

**Medications Used to Reduce Aggression**
Theory of What Medications Do in Treating Aggression

- The medication reduces impulsivity
- The medications lengthen the fuse, thereby giving the person more time to make a choice
- The person still makes the choice and can be aggressive
- “Chemical restraint”

Choices and Evidence for Medications Used to Control Aggression

NEUROLEPTICS

- **Risperidone**
  - Has the best evidence from many large RDBPC trials showing it reduces aggressiveness in children over placebo
- **Olanzapine (Zyprexa)** and **Quetiapine (Seroquel)**
  - Have no RDBPC trials for aggression
- **Chlorpromazine**
  - Oldest medication

Side-Effects of Neuroleptics

- **Extrapyramidal** side-effects (muscle stiffness)
- Significant **metabolic** side-effects
  - Excessive weight gain
  - Alterations in glucose metabolism
  - Increase lipids
- Long term use of Neuroleptics increase the emergence of **Tardive Dyskinesia**
Choices and Evidence for Medications Used to Control Aggression

**MOOD STABILIZERS**
- **Divalproex (Epival)**
  - One RDBPC trial of explosive youth found 80% response versus 25% on placebo
- **Carbamazepine (Tegretol)**
  - Some case reports
- **Lithium**
  - Two RDBPC trials of hospitalized children with conduct disorder lithium better than placebo

**PSYCHOSTIMULANTS**
- **Methylphenidate and Dextroamphetamine**
  - Nine studies show some decreased aggression response in children with both Attention Deficit Hyperactivity Disorder and Conduct Disorder

**Update on Medications Used for Aggression**
- **Rapid-onset preparations of Risperidone (Risperidal M tabs) and Olanzepine (Zyprexa Zydis)** used sublingually can provide quick pharmacological control (without using injections) if the person cooperates with taking the medication
- Regular medication management visits, fasting blood work, height and weight (BMI), and case conferences are essential
**Purpose of Medications in Anxiety Disorders**

- Reset the “panic alarm” so that it goes off less easily
- Turns down the volume of the anxiety signal by reducing the physiological responses
- Reduces the intensity of the cognitive worrying
High anxiety is like walking down a river with the water level high, making it harder to walk forwards.

The medication lowers the level of water in the river, making it easier to walk forwards.

Dr Shih's "Walking Down The River Metaphor"

---

**Choices and Evidence for Medications Used for Anxiety Disorders in Children**

For **Generalized Anxiety Disorder**
- Positive RDBPC trial evidence
  - Sertraline (Zoloft)
  - Fluoxetine (Prozac)
  - Fluvoxamine (Luvox)
- No evidence for Venlafaxine (Effexor)

---

**Anxiety Disorders in Children**

Do not use Benzodiazepine for anxiety disorders in children because of habituation and risk of disinhibition.
Choices and Evidence for Medications Used in Obsessive Compulsive Disorder (OCD) in Children and Teens

USA FDA labeling approval for
- Sertraline (Zoloft)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)

In several studies
- Cognitive Behavioural Therapy (CBT) is as good as Medication for OCD

Unique Characteristics of Medications Used for Anxiety Disorders and OCD

- Start lower and slower in anxiety kids to reduce adverse effects
- Lower doses may be helpful
- Need higher doses for OCD
- Look at functional outcomes and not just reduction of anxiety or symptoms

Medications for Attention Deficit Hyperactivity Disorder
Medications for Attention Deficit Hyperactivity Disorder

Two Guidelines for Using Medications in ADHD
Canadian Attention Deficit Hyperactivity Disorder Resource Alliance (CADDRA)
www.caddra.ca

Texas Department of State Health Services algorithm for ADHD
www.dshs.state.tx/mhprograms/adhdpage.shtm

Factors in Choosing a Medication for ADHD
- Duration of action
  - 4 hours
  - 6 hours
  - 12 hours
  - 24 hours
- Types of side-effects
  - Stimulant
  - Versus non-stimulant
- Flexibility
- Tablets or Capsules or Sprinkle
- Cost
**Approach to Medications for ADHD**

- First choice is a Stimulant medication
  - Ritalin
  - Dexedrine
- Second choice is a Non-stimulant medication
  - Ritalin, Dexedrine, Strattera, and Desipramine all have very good positive RDBPC trials

---

**First Choice Is a Stimulant Medication**

**METHYLPHENIDATE (RITALIN)**

- Regular fast acting tablets (4 hours)
- 6 hours Ritalin 20 mg SR tablet
- 12 hours Concerta or Biphentin (sprinkle)

---

**First Choice Is a Stimulant Medication**

**DEXTROAMPHETAMINE (DEXEDRINE)**

- Regular fast acting tablet (4 hours)
- 6 hours Dexedrine Spansule
- 12 hours Adderall XR capsule (sprinkle)
**Side-Effects of Psychostimulants for ADHD**

- May slow growth but ultimate height is not affected
- High doses associated with compulsive behaviours in vulnerable individuals with movement disorders
- Very high doses especially Dexedrine can cause damage to CNS and Cardiovascular system such as hypertension
- Main side-effects are insomnia, decreased appetite, and tics

**Discussion on CADDRA Guidelines**

The CADDRA guidelines recommend starting first line with the new long acting preparations

- Adderrall XR
- Biphentin
- Concerta
- Strattera

My concerns are that these are expensive medications that the family may not be able to afford, and if there is a disturbing side-effect during the day, it will last for 12 hours.

**Second Non-Stimulant Choices for ADHD**

- **ATOMOXETINE (STRATTERA)**
  - Begins working after 10 days
  - 24 hours duration/ take every day
- **BUPROPION (WELLBUTRIN)**
- **DESIPRAMINE or IMIPRAMINE**
- **CLONIDINE**
Side-Effects of Non-Stimulants Used for ADHD

Strattera’s most common side-effects are:
- Decreased appetite
- Vomiting
- Somnolence
- Irritability
- Two cases of liver failure reported worldwide

Side-Effects of Non-Stimulants Used for ADHD

Desipramine/Imipramine can cause:
- A tachycardia
- In some cases a dangerous heart block
- Slow metabolizers can have toxic serum concentrations

Unique Characteristics of Medications Used for ADHD

The effectiveness of medications used for ADHD is measured by:
- Using rating scales (e.g., Conner’s, SNAP)
- Or asking for feedback from the teacher
Medication for ADHD is like a bicycle.

Child says he has to push the pedals to make the bicycle move.

The metaphor bicycle helps the child to get the work done faster in the time allocated.

Therefore the improved school marks are credited to the motivation of the child and not to the medication.

Dr. Shih’s “Bicycle Metaphor” for ADHD Medications

Unique Characteristics of Medications Used for ADHD

- Medications may produce unpredictable and paradoxical effect in preschool children
- Medications are not as effective in adults

Medications for Mood Disorders
Medications for Mood Disorders

Mood Disorders

- Major Depressive Disorder
- Dysthymia
- Bipolar Disorder

Research Evidence in Treating Depression

The Treatment for Adolescent with Depression Study (2006) showed Combined Fluoxetine and CBT appears superior to either medication or CBT alone, had a faster response, and improved functioning and quality of life.
**Medications in Major Depression in Children and Adolescents**

**Selective Serotonin Reuptake Inhibitors (SSRI)**
- Prozac
- Zoloft
- Paxil
- Luvox
- Celexa

**Norepinephrine Dopamine Reuptake Inhibitor (NDRI)**
- Wellbutrin

**Selective Serotonin Norepinephrine Reuptake Inhibitor (SNRI)**
- Effexor

**Selective Serotonin Reuptake Inhibitors (SSRI)**

- **Fluoxetine (Prozac)**
- Sertraline (Zoloft)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Citalopram (Celexa)
- Escitalopram (Lexapro)

**Only Fluoxetine has RDBPC trial evidence in children and teens**
Unique Characteristics of Medications Used in Major Depression

SSRI’s inhibit the P450 liver enzyme and slow down the breakdown of many other medications (watch for drug interactions)

SSRI’s or Venlafaxine (Effexor) if taken alone in overdose has very low risk of being fatal

Unique Characteristics of Medications Used in Major Depression

Fluoxetine (Prozac)

➢ Has long half life, which is useful if there are concerns about compliance

Bupropion (Wellbutrin)

➢ Has strict dosage guidelines because doses above 300 mg daily can increase risk of seizures

Precautions for Using SSRIs

➢ Recent concern about emergence of suicidal ideation with use of antidepressants especially SSRIs
➢ Serotonin syndrome (diarrhea)
➢ Withdrawal syndrome (flu-like)
➢ First trimester use of SSRIs and risks of birth defects
SSRIs and Suicide

- Every year, 19% of teenagers in the general population think of suicide and 9% make an actual attempt
- Antidepressant 2 - 9% had suicidal ideation, and Placebo 0 - 7%

Careful Monitoring of SSRI Treatment

- Measure the symptoms of depression using rating scales
- Check for suicidality
- Provide details on side-effects and expected time-lines on improvement

Medication Management SSRI Treatment

- Give small test dose of medication, and if OK, start with very low dose, and if possible see within 3-4 days of starting treatment
- Increase dose slowly every 3-4 days to therapeutic dose and wait 6-8 weeks with weekly visits or telephone check-ins
Bipolar Disorder

- Remember the diagnosis of Bipolar Disorder in children is controversial and difficult.
- Classic Bipolar Disorder is not an outcome of manic symptoms that occur in childhood.
- No medications have been approved by the FDA for pediatric Bipolar Disorder.
- Only Lithium was grandfathered in with approval for treating teens over age 13 years old.

Medications Used in Bipolar Disorder in Children and Adolescents

There are no RDBPC trials done in children and teens, and evidence is derived from adult studies.

- Valproate/ Divalproex
- Carbamazepine
- Lamotrigine

Medications Used in Bipolar Disorder in Children and Adolescents

- Lithium
  - Only medication approved by FDA for treating acute mania and maintenance in children.

- Clonazepam
  - No evidence.
Double-Blind Placebo-Controlled Trials on Medications for Bipolar Disorder

<table>
<thead>
<tr>
<th>DRUG</th>
<th>Age 18 and Over</th>
<th>Age under 18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Beneficial</td>
<td>2 studies pending</td>
</tr>
<tr>
<td>Valproex</td>
<td>Beneficial</td>
<td>FDA study No benefit</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Beneficial</td>
<td>Beneficial</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Beneficial</td>
<td>Data being analyzed</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Beneficial</td>
<td>Being studied</td>
</tr>
<tr>
<td>Topiramate</td>
<td>No benefit</td>
<td>No benefit</td>
</tr>
</tbody>
</table>

Side-Effects of Medications Used in Bipolar Disorder

- Anti-convulsants
  - Can have serious adverse effects on the blood production system in the bone marrow
  - May cause fatal conditions with reductions in white blood cells, red blood cells, and platelets
- Lithium
  - Can cause hypothyroidism and kidney changes with long term use

Unique Characteristics of Medications Used in Bipolar Disorder

- Avoid using Valproate in girls and women because of risk of polycyclic ovaries
- Response to medication is not proof of diagnosis
- Periodic blood tests are mandatory
Conclusion

Practical Points About Medications

➢ Talk to your pharmacist
➢ Special packaging
  • Stripes
  • Bubble packs
➢ Safe storage
  • Locked up

➢ Compliance
  • Supervise taking of medication
➢ Compounding
  • Tablets
  • Capsules
  • Liquids
  • Sprinkle
  • Special formulation
**STATIC:** Alcohol damaged the **hardware** and wiring circuits (every person with FASD is different). Medications try to patch or boost some of the hardware.

**DYNAMIC:** Environmental stimulation, strategies and teaching are the **software** that programs the brain, and can change some of the circuits.

Dr Shih’s “Computer Metaphor” for FASD

---

**Take Home Messages**
- Medical check to make sure the problem is not due to a physical problem
- Try environmental and social changes first
- Medications may not work the way we expect in a person with FASD because of the different ways the alcohol damages the brain

---

**Take Home Messages**
- Start low and go slow
- Medications patch hardware not software problems
- Medications provide a more solid biological platform for thinking and decision making
Thank You for Your Attention and Questions Please

Reference

- Contact Information
- Source Material

Contact Information

Dr. David Shih
CASA Child, Adolescent, and Family Mental Health
780-438-0011
For Information on Upcoming Sessions in the Series: www.fasd-cmc.alberta.ca

Please Take the Time to Fill Out the On-Line Evaluation

Thank You!