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Antidepressant and Anti-Anxiety medication use in children and adolescents

What we will cover today

- FDA Status
- Informed consent
- Medications
- Non-medication treatments
- Ways to engage the prescriber
- Interactive discussion/questions using ‘Chat’ function

What does FDA approval mean

- The FDA has decided the benefits outweigh the potential risks
  - FDA= Food and Drug Administration
- No drug is entirely risk-free
- Research and testing must show that the benefits of the drug for a particular condition outweigh the risks to patients of using the item.

Antidepressants

- Labeled as antidepressants but
  - Used for depression and anxiety
- Several classes in this category of antidepressant based on neurotransmitter affected
  - SSRI's (selective serotonin reuptake inhibitors)
  - TCA's (tricyclic antidepressants)
  - SNRI's (selective norepinephrine reuptake inhibitors)
  - MAOI's (monoamine oxidase reuptake inhibitors)

FDA Approved Medications

- Antidepressants
  - Approved for OCD
    - Clomipramine- 10 years or older
    - Fluvoxamine- 8 to 18 years
    - Sertraline- 6 to 17 years
    - Fluoxetine- 7 to 18 years or
  - Approved for Depression
    - Fluoxetine—8 to 18 years
    - Escitalopram—12 years and older
  - Approved for Non-OCD anxiety
    - Duloxetine-7 to 17 years for GAD

‘Off-Label’ Medications

- We prescribe medications that are ‘off-label’
- This means they are not FDA approved
- The importance is to describe that the use is ‘off-label’ when obtaining informed consent to treat with medications
  - ‘Off-label’ does not mean bad
  - In Child Psychiatry many medication treatments are off label

Antidepressants used in children

SSRIs:

- Citalopram, Escitalopram,
- Fluoxetine, Fluvoxamine,
- Paroxetine, Sertraline

TCAs:

- Amitriptyline,
- Clomipramine, Doxepin,
- Desipramine, Imipramine,
- Nortriptyline

SNRIs:

- Duloxetine, Venlafaxine,
- Desvenlafaxine,
- Levomilnacipran

MAO-I:

- Phenelzine,
- Tranylcypromine, Selegiline

Other:

- Bupropion, Mirtazapine
- Nefazodone, Trazodone
- Vilazodone, Vortioxetine

Antidepressants approved for use by the FDA

SSRIs:

- Escitalopram, Fluoxetine,
- Fluvoxamine, Sertraline

TCAs:

- Clomipramine,
- Imipramine

SNRIs:

- Duloxetine

MAO-I:

- None

Other:

- None

Anti-anxiety medications used in children

Atypical anti-anxiety med:

- Buspirone

Antihistamine:

- Hydroxyzine

Benzodiazepines:

- Lorazepam, Clonazepam
- Alprazolam, Diazepam

Anti-anxiety approved for use by the FDA

Anxiolytic:

- None

Antihistamine:

- Hydroxyzine

Benzodiazepines:

- Lorazepam (age 12 years and up)
  - Approved for anxiety and insomnia
- Diazepam (age 6 months and older
  - Approved for seizures and skeletal muscle spasms

Elements of Informed Consent

- Informed Consent
  - The information needed about treatment that needs to be communicated to the guardian in order to get consent to treat
- Elements of Informed consent
  - Purpose of proposed treatment (expected outcome)
  - Risk and benefit of treatment
  - Alternatives for treatment
    - Including non-medication options
  - Risks and benefit of alternatives
  - Risk and benefit of not receiving treatment
  - FDA status of medication options
  - Possible side effects (aka: adverse drug reactions or ADR's)

Case Example

- 8 y/o AAF who has had increased days of sadness. Foster mom feels she has been sad since Spring Break and it is Memorial Day. She cries a lot, sleeps as soon as she comes home from school until dinner time and goes back to sleep after dinner, has to be forced to eat most of the time, feels she is a bad kid, and does not want to be around people anymore. She does not want to go outside to play. There has been no change in her daily life, no known increase or change in stressors. She has been in this foster home for 1 ½ years.
- Diagnosis: Major Depression

Case Example

- 16 y/o WF who can't stop worrying. She seems to spend several hours each day worrying and has for the past 8 months. She has headaches on a regular basis, stomachaches when things are on her mind and can't fall asleep at night due to the constant thoughts. She is not able to function on her school work and has had a drop in her grades on the most recent quarter report. She used to make A's but now has primarily C's.

- Diagnosis: Generalized Anxiety Disorder

Case Example

- 13 y/o WM who is late to school at least 3 days per week. His foster parents have started having him lay out his clothes and pack his backpack every night in order to prevent this. It still is not helping. He can't leave the house until everything is done. He has to shower several times because if his body touches something he feels he is dirty and repeats showering. He has to make sure that he washes and re-washes his hands and never feels clean enough. He feels if he does not do these things something terrible will happen to him or his foster parents. He has always been focused on being clean but this has increased in the last 6 months. He gets up at 4:00 AM in order to be ready but spends at least 2 ½ hours in the morning washing and re-washing. He continues this behavior at school
- Diagnosis: Obsessive Compulsive Disorder

How a prescriber determines what medication to use

- History of response
- Family history to medication response
- Receptor profile of medication
- Drug interactions
- Dosing and dosage forms
- Monitoring/adherence issues
- Concurrent medical history
- Cost
- Treatment refractory
- Pregnancy and Lactation
- Patient preference
- Side Effects
- Efficacy

Black Box Warning

- WARNING:SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compare to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders . Short-term studies did not show an increase in the risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber.

SSRI medication class-side effects

- Gastrointestinal upset
- Headache
- Anxiety
- Insomnia
- Sexual dysfunction
- Withdrawal syndrome
- Serotonin syndrome

SSRI withdrawal syndrome

- Also called Discontinuation Syndrome
- Can happen with any SSRI
- More common in those with short half life (example: Paroxetine)
- Symptoms include
  - Dizziness
  - Numbness, electric-shock sensations
  - Extreme fatigue called lethargy
  - Headache
  - Tremor
  - Sweating
  - Anorexia (loss of appetite)
  - Nausea, vomiting, diarrhea

Serotonin Syndrome

- Occurs when medications cause high levels of the chemical (serotonin) to accumulate in your body
  - Not just caused by SSRI's
- Can occur when you increase dose or add a new drug
- Can be life threatening when **severe** and signs include:
  - High fever
  - Seizures
  - Irregular heartbeat
  - unconsciousness

Serotonin Syndrome

- Signs and symptoms of serotonin syndrome
  - Agitation or restlessness
  - Confusion
  - Increased heart rate and high blood pressure
  - Enlarged (dilated) pupils
  - Low muscle coordination or twitching muscles
  - Muscle rigidity
  - Diarrhea
  - Shivering
  - Goose bumps

More about Serotonin Syndrome (so you don't forget it)

- Serotonin syndrome is a rare, potentially life-threatening, adverse drug reaction associated with increased serotonergic activity in the central nervous system
- The Clinical Triad of Symptoms:
  - Mental Status Changes--**confusion**
  - Autonomic Hyperactivity--**increased heart rate and high blood pressure**
  - Neuromuscular Abnormalities—**muscle rigidity, twitching, low muscle tone**
- Rapid onset
- Most individuals have symptom onset within 6 hours of initiation or dose increase

SNRI medication class-side effects

- Nausea
- Constipation
- Headache
- Insomnia
- Sexual dysfunction
- Initiation and withdrawal syndrome
- Potential for blood pressure increases (venlafaxine)

TCA Medication Class-side effects

- Significant risk for drug interactions
- Block Histamine – sedation and weight gain
- Block Alpha 1 – orthostasis / tachycardia
- Block Acetylcholine – constipation, urinary retention, dry mouth, dry eyes, confusion
- Elevated liver enzymes
- Sexual dysfunction
- Withdrawal syndrome
- Risk of death with overdose

TCA's

- Not used much any more due to side effects (cardiac toxicity)
- Lethal in overdose

Monoamine Oxidase Inhibitors (MAOI)

- Usually prescribed when other antidepressants fail
- Newer drugs often more effective and have fewer side effects
- Serious side effects especially when combined with certain foods
  - Avoid foods with high levels of tyramine, dopamine and tryptophan
    - Some include: Aged cheeses, yogurt, cured meats, fermented sausages (pepperoni, salami, bologna), anchovies, sauerkraut
  - Can get list of foods to avoid from pharmacy where meds are filled
- Significant risk for drug interactions
  - OTC meds, vitamins, dietary supplements, herbal remedies

MAOI Medication Class-side effects

- Most common side effects
  - Dry mouth
  - Nausea
  - Dizziness
  - Constipation
  - Drowsiness
  - Headache
  - Insomnia

Bupropion side effects

- Dry mouth
- Constipation
- Headache
- Dizziness
- Nausea or vomiting
- Nervousness
- Heavy sweating
- Lowers the seizure threshold if eating disorder or seizure disorder co-exists

Mirtazapine side effects

- Drowsiness
- Dizziness
- Strange dreams
- Vision changes
- Dry mouth
- Constipation
- Increased appetite
- Weight gain

Trazodone side effects

- Drowsiness or sleepiness
- Dry mouth
- Blurry vision
- Nausea or vomiting
- Mild headache
- Dizziness or dizziness when standing up suddenly
- RARE BUT SERIOUS—PRIAPISM—sustained painful erection requiring medical attention

Buspirone side effects

- Dizziness
- Nausea
- Headaches
- Nervousness
- Lightheadedness
- Constipation
- Blurred vision
- Feeling tired
- Sleep problems (insomnia or strange dreams)

Hydroxyzine side effects

- Fatigue
- Nausea
- Dizziness
- Dry nose, mouth, or throat

- RARE—cardiac abnormality (prolonged Q-T interval on EKG)

Benzodiazepine medication class-side effects

- **Rarely used in children and adolescents due to addiction potential**
- **Possible paradoxical effect**
  - Instead of calming effect may cause increased agitation
- **Withdrawal when it is stopped abruptly**
  - May lead to seizures

Benzodiazepine medication class-side effects

- Amnesia
- Depression
- Confusion
- Drowsiness
- Impaired coordination
- Dizziness

Labs/medical monitoring

- SSRI's—no monitoring required except with serotonin syndrome
- SNRI's
  - Venlafaxine XR—blood pressure checked periodically after starting or increasing the dose
  - Duloxetine—may increase ALT (a liver enzyme) in 1% patients, check after starting med
- TCA's
  - patient with pre-existing cardiac disease order before starting and when dose therapeutic.
  - Some value in getting nortriptyline levels (range 5-150 ng/mL correlate with best results)
- MAOI's
  - Phenelzine reported to cause liver failure; so recommend monitoring liver function tests (LFT's) after starting

Labs/medical monitoring

- Bupropion—no monitoring required
- Mirtazapine-no monitoring required
- Trazodone—no monitoring required
- Buspirone—no monitoring required
- Hydroxyzine--no monitoring required except in overdose
- Benzodiazepines

Non-medication treatments

- There are evidence based therapies for anxiety and depression
  - Both depression and anxiety respond to Cognitive Behavior Therapy (CBT)
  - Trauma Focused CBT (TF-CBT) specifically targeted to those who have experienced trauma
  - Eye Movement Desensitization Reprocessing (EMDR) for those who have experienced trauma
  - Child Parent Psychotherapy (CPP) for children under 5 who have experienced trauma. Dyadic therapy with caregiver

Non-medication treatments

- Lifestyle activities
  - Exercise
  - Increased activity in areas of interest
  - Social interactions
  - Stable/consistent sleeping and appetite

How to engage your provider/physician

- In the past the relationship between physicians and patients was paternalistic
- **Currently** the expectation is that the provider works with the patient
  - We expect questions, dialogue, and your input into the process of evaluation and decision making
- It may not be a physician--you may have a nurse practitioner, physician assistant, or resident in training that you are working with

How to engage your provider/physician (Providing information on past treatment)

- It is tremendously helpful for the provider/physician to be informed of prior treatments
- Providing documentation of past hospitalizations, outpatient treatment, medications, any medical history is critical
- This is sometimes challenging for children in custody but anything you can do to facilitate quick access to treatment history is critical

How to engage your provider/physician (be empowered to question)

- **A key component of informed consent includes**: the information needed about treatment that needs to be communicated to the guardian in order to get consent to treat
- If you are not receiving the information needed to give consent **ask for it**
- If you don't understand what is being told to you **ask questions until you do understand**

How to engage your provider/physician (ongoing feedback to them is important)

- The black box warning states: Families and caregivers should be advised of the need for close observation and communication with the prescriber

- It is **critical for ongoing treatment to have the input of those who spend time with the child.**
  - This can be the caseworker, foster parent, teacher, etc.

How to engage your provider/physician (obtain the information you need)

- Educate yourself on the treatment provided
- Be familiar with possible side effects
  - If you don't know them then ask about them
  - Be aware of possible side effects the child is experiencing so you can communicate them
- Be aware of monitoring necessary for medications used

How to engage your provider/physician

- **Questions you have re: how to engage your provider/physician**

Medication Information Resources

- American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameters
  - https://www.aacap.org/AACAP/Resources_for_Primary_Care/Practice_Parameters_and_Resource_Centers/Practice_Parameters.aspx
- National Alliance on Mental Illness (NAMI) Treatment Resources, Mental Health Medications
  - http://www.nami.org/Learn-More/Treatment/Mental-Health-Medications
- Psychotropic Medication Utilization Parameters for Children and Youth in Foster Care (5th Version)
  - https://www.dfps.state.tx.us/Child_Protection/Medical_Services/documents/reports/2016-03_Psychotropic_Medication_Utilization_Parameters_for_Foster_Children.pdf
  - Tables begin on page 8

Possible Resources

- Treatment for Adolescents with Depression Study **(TADS)**
  - Clinical summary of findings
  - Safety result (discussion of suicidality)
  - Long-term effectiveness
- Treatment of Resistant Depression in Adolescents **(TORDIA)**
  - What to do after failure of an SSRI

Questions