

Pediatric Drug Therapy 2020

Medical Considerations When Using Psychotropic Medications in Children and Adolescents

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Objectives for Learning Outcomes:

1. Promote safe use of psychotropic medications in children & adolescents.
2. Review recommended baseline medical screening prior to initiation of psychotropic medications.
3. Understand recommendations for medical monitoring to mitigate risks associated with psychotropic medications.

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Medical Considerations When Using Psychotropic Medications in Children & Adolescents

Speaker Disclosure

- I have no actual or potential conflict of interest in relation to this presentation.
- Will be discussing off label uses of medications

Objectives:

- Promote safe use of psychotropic medications in children & adolescents
- Review recommended baseline medical screening prior to initiation of psychotropic medications
- Understand recommendations for medical monitoring to mitigate risks associated with psychotropic medications

Background

- Children are commonly affected by psychiatric disorders
- The vast majority of children with mental health problems do not receive appropriate services
- High quality assessment and practices for prescribing result in better outcomes for children and adolescents

Classes of Psychotropic Medications

- Stimulants and Non-Stimulants (ADHD)
- Antipsychotics
- Mood Stabilizers
- Antidepressants
- Anxiolytics and sleep medications



ADHD Pharmacotherapy



ADHD Pharmacotherapy

- **Primary symptom targets:** concentration, attention span, distractibility, hyperactivity, impulsiveness
- **Stimulant Medications**
 - methylphenidates
 - amphetamines
- **Non stimulant Medications**
 - atomoxetine (Strattera)
 - alpha agonist (guanfacine, clonidine)
 - bupropion (Wellbutrin)

Methylphenidate – based stimulants

- FDA indications: ADHD – ages 6 & up
- Ritalin (IR, SR, LA)
- Methylin
- Methylin ER
- Metadate ER
- Concerta
- QuillChew ER
- Quillivant XR
- Metadate CD
- Aptensio XR
- Daytrana
- Cotempla XR- ODT
- Jornay PM
- Focalin - Dexmethylphenidate

Amphetamine based stimulants

- FDA Indications:
 - ADHD ages 3 & up (Adderall, Evekeo)
 - ADHD ages 6-17 (many other formulations including Vyvanse)
 - Narcolepsy ages 6 & up
 - Exogenous obesity (Evekeo ages 12 & up)
- Adderall (IR, XR)
- Adzenys (ER, XR-ODT)
- Dexedrine
- Desoxyn
- Dyanavel
- Evekeo (XR, ODT)
- Mydayis
- Procentra
- Zenzedi
- Vyvanse – Lisdexamphetamine



Specifics of ADHD Medications

Drug	Peak (hours)	Duration (hours)	FDA-Approved
Amphetamine			
Adderall	3	6-9	3-12
Adderall XR	7	6-10	6-17, adults
Dexedrine	3	4-6	3-16
Dexedrine Spansules	4	6-10	3-16
Vyvanse	3.5	10-12	6-12, adults
Methylphenidate			
Ritalin, Methylin	1-2	4-5	6-12
Focalin	1-2	4-5	6-17
Ritalin SR, Methylin SR	5	8	6-15
Concerta	6-8	12	6-17
Focalin XR	Biphasic: 1-2 and 6-7	12-16	6-17, adults
Daytrana	7-10	12	6-12
Ritalin LA	7-10	>5	6-12
Metadate-CD	Biphasic: 1-2 and 4-5	6-8	6-15
Non-stimulants			
Strattera, Atentin	1-2	20	6-18, adults
Tenex	1-4	24	Children and adults
Intuniv*	~ 12	>24	Children and adults
Wellbutrin, Zytan	10-17	14-24	18-83
Provigil	2-4	15-30	adults

Stahl, S. M. (2013). Stahl's essential psychopharmacology: Neurobiologic basis and practical applications (4th ed.). Cambridge University Press.

Potential Contraindications

- Structural cardiac abnormalities/CV disease, tachyarrhythmias, severe hypertension
- History or current functional psychosis
- Anorexia nervosa
- Severe anxiety or agitation
- Hyperthyroidism, narrow-angle glaucoma

Stahl, S. M., & In Grady, M. M. (2019). Stahl's essential psychopharmacology: Prescriber's guide children and adolescents.

Cardiac Risk with Stimulants

- Screen for CV risk in initial assessment
- Rule out history of syncope, family sudden cardiac death, cardiac abnormalities, CP on exertion. Complete physical exam and ROS.
- Cardiology referral with positive risks prior to initiation of stimulant.
- ECG not necessary if no evidence of cardiac risk factors present.
- Pulse and BP at baseline and every 6 months



Piscka, Steven; Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. Journal of the American Academy of Child & Adolescent Psychiatry, Volume 46, Issue 7, 894 - 921

Stimulants, Appetite & Growth

- Monitor weight & height at least every 6 months
- Monitor appetite- consider pre vs post treatment eating habits
- For appetite suppression consider giving meds after meal (such as breakfast), consider shorter acting formulations
- Encourage late PM eating, and high calorie snacks
- Consider med holidays or a different stimulant
- Endocrine referral if below critical thresholds (growth chart, BMI)



Pliszka, Steven. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. Journal of the American Academy of Child & Adolescent Psychiatry, Volume 46, Issue 7, 894 - 921.

Substance Use/Misuse

- Stimulant abuse more likely in patients who do NOT have ADHD.
- Effective treatment for ADHD makes children less likely to abuse substances compared to those with untreated ADHD
- More likely in ADHD patients with pre-existing history of substance use disorder
- Misuse more likely with IR formulations – consider XR, Vyvanse, or non-stimulant medications

Non Stimulant ADHD Pharmacotherapy

- Alpha Agonists:
 - **Clonidine** (Clonidine IR, Kapvay)
 - FDA indications: ADHD ages 6-17
 - Off label uses: motor tics, ODD, anxiety disorders/PTSD
 - **Guanfacine** (Intuniv, Tenex)
 - FDA indications: ADHD ages 6-17
 - Off label uses: ODD, conduct disorder, PDD, motor tics
- Baseline: BP (orthostatic) & HR
- Ongoing monitoring: periodic orthostatic BP & HR (and with dose changes). Advise families to report any cardiac symptoms (dizziness, fainting, or unexplained change in HR)

Pliszka, Steven. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. Journal of the American Academy of Child & Adolescent Psychiatry, Volume 46, Issue 7, 894 - 921.

Non Stimulant ADHD Pharmacotherapy

- Atomoxetine (Strattera)
 - FDA Indications: ADHD ages 6 & up
 - Selective NE Reuptake Inhibitor
 - 2nd line treatment for ADHD (could be 1st line with active substance use or comorbid anxiety)
 - BP & HR at baseline, ongoing (increases & periodically), Ht, Wt
 - CV screen (can increase HR & BP)
 - Rare liver injury, rare increase in suicidal thinking
- Bupropion (Wellbutrin):
 - No FDA indication for children.
 - Off label uses include Depression, ADHD
 - Noradrenergic antidepressant
 - BP at baseline, and during tx periodically, Ht/weight
 - May lower seizure threshold – contraindicated if current seizure disorder

Pliszka, Steven. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. Journal of the American Academy of Child & Adolescent Psychiatry, Volume 46, Issue 7, 894 - 921.

Antipsychotic Medications



Antipsychotic Medications

- Despite categorization into classes- classes are heterogeneous, and vary in pharmacology, AE profiles, & costs
- High potency FGAs more associated with EPS & TD
- SGAs more associated with metabolic SE's
 - Metabolic SE burden appears higher in children & adolescents as compared to adults
 - SGAs remain preferred first line likely due to decreased likelihood of TD/EPS
- All classes have demonstrated efficacy in treating + symptoms of psychosis
- Many off label uses in children & adolescents
- Children & adolescents more sensitive to effects- including metabolic and neurologic effects

Bazzill/Buller, K.Z. & Ebb, D., Wiant, A. S. & Procyshyn, R.M. (Eds.). (2014). Clinical handbook of psychotropic drugs for children and adolescents. Hogrefe & Huber Publishers.

Antipsychotic Medications:

- First Generation or Typical Antipsychotics (Haloperidol, chlorpromazine).
- Second Generation or Atypical Antipsychotics (Risperidone, lurasidone, olanzapine, quetiapine, clozapine, etc.)
- Third Generation Antipsychotics (Aripiprazole)

Metabolic Monitoring

- **Conservative approach:** Weight & BMI at baseline, once monthly for first 3 months, then every 3 months.
 - Best for patients with obesity or rapid weight gain with use of medication, or family history of diabetes.
- **At a minimum:** Weight & BMI at baseline, Q 6 months weight checks
- **Labs at Baseline:** fasting blood glucose or HbA1c; at 3 months, then yearly if not gaining weight. If gaining weight, Q 4 months.
- Obtain electrolytes, renal function tests, liver function tests, thyroid function tests, and CBC at baseline and as clinically indicated.
 - Pts with low WBC or hx of drug induced leukopenia/neutropenia should have CBC monitored monthly in first few months.

American Academy of Child and Adolescent Psychiatry. AACAP practice parameter for the use of atypical antipsychotic medications in children and adolescents. 2011. Retrieved from <https://www.aacap.org/resources/practice-parameters/2011-practice-parameter-for-the-use-of-atypical-antipsychotic-medications-in-children-and-adolescents>

Metabolic Monitoring

Table 1 – Metabolic monitoring parameters based on American Diabetes Association/ American Psychiatric Association consensus guidelines*

	Baseline	Week 4	Week 8	Week 12	Every 3 months thereafter	Annually
Medical history [†]	X		X	X	X	X
Weight (BMI)	X	X	X	X	X	X
Waist circumference	X					X
Blood pressure	X			X		X
Fasting glucose/hemoglobin A _{1c}	X			X		X
Fasting lipids	X			X		X

* Personal and family history of obesity, diabetes, hypertension, and cardiovascular disease.

Retrieved May 6th, 2020.

Cardiac Monitoring

- All antipsychotic medications have the potential to prolong the QTc interval.
 - Abnormally long QTc is a risk factor for life-threatening arrhythmias.
- Ranking of risk for QTc prolongation: Ziprasidone > quetiapine = risperidone = olanzapine = haloperidol > clozapine > aripiprazole
- Obtain baseline ECG and serum K⁺ and Mag. Use antipsychotics with caution in electrolyte disturbances, or with prolonged baseline QTc.

Bezdubnyk-Bulter, K. Z. & Elbe, D., Virani, A. S. & Procyshyn, R. M. (Eds.). (2014). Clinical handbook of psychotropic drugs for children and adolescents. Hogrefe & Huber Publishers.

ABNORMAL INVOLUNTARY MOVEMENT SCALE (AIMS)

Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration
National Institute of Mental Health

NAME: _____
DATE: _____
Prescribing Practitioner: _____

CODE: 0=None
1=Minimal, may be extreme normal
2=Mod
3=Marked
4=Severe

INSTRUCTIONS: Complete Examination procedure (attachment 4) before making ratings.

MOVEMENT RATINGS: Rate highest severity observed. Rate movements that occur upon activation are less than those observed spontaneously. Record movement as well as code number that applies.

		DATE	DATE	DATE	DATE
Facial and Oral Movements	1. Muscles of Facial Expression e.g. movements of forehead, eyebrows, perioral area, etc.; squinting, blinking, smiling, grimacing.	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	2. Lips and Perioral Area e.g. puckering, smiling, smacking.	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
Extremity Movements	3. Jaw e.g. biting, clenching, chewing, mouth opening.	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	4. Tongue e.g. sticking out; movements in mouth; out of mouth; NCT stability to sustain movement. Clinging to oral or dental work.	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	5. Upper arms, wrists, hands, fingers Involuntary, chorea, movements (i.e. rapid, jerky, purposeless, irregular, spontaneous) abnormal movements (i.e. slow, irregular, complex, repetitive); SO NOT INCLUDE TREMOR (i.e. rhythmic, regular, rhythmic).	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
Trunk Movements	6. Lower legs, shins, ankles, feet e.g. slow, slow movement; foot tapping; heel dragging; foot tapping; normal and abnormal.	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	7. Neck, shoulders, hips e.g. rocking, twisting, swaying; head-gritting.	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
Global judgments	8. Severity of abnormal movements overall	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	9. Inappreciation due to abnormal movements	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
Dental Status	10. Patient's awareness of abnormal movements (Rate only patient's report) No awareness 0 Aware, no distress 1 Aware, mild distress 2 Aware, moderate distress 3 Aware, severe distress 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4	0 1 2 3 4
	11. Current problems with teeth and/or dentures?	No Yes	No Yes	No Yes	No Yes
	12. Any dentures usually worn?	No Yes	No Yes	No Yes	No Yes
	13. Edentulous?	No Yes	No Yes	No Yes	No Yes
Dental Status	14. Do movements disappear in sleep?	No Yes	No Yes	No Yes	No Yes
		No Yes	No Yes	No Yes	No Yes

- Perform AIMS at baseline and Q6 months due to risk of Tardive Dyskinesia.
- Warn of risk for Dystonia.

Atypical or Second Generation Antipsychotic Medications (SGA)

Risperidone (Risperdal)

- FDA Indications: Schizophrenia (13-17yo), acute mania or mixed episodes (10-17 yo), "irritability" associated with Autism Spectrum Disorder.
- Off label indications: bipolar depression, behavioral disturbances in children and adolescents, disorders associated with impulse control.
- Before starting risperidone: BMI, family history of metabolic syndromes, blood pressure, fasting glucose/lipid panel.
- Only order prolactin level if screening questions indicate possible hyperprolactinemia.

Stahl, S. M., & In Grady, M. M. (2019). *Stahl's essential psychopharmacology: Prescriber's guide children and adolescents.*

Lurasidone (Latuda)

- Indications: Schizophrenia (ages 13 & up), Bipolar depression (ages 10 & up)
- Off label uses: acute mania/mixed mania, other psychotic disorders, bipolar maintenance, treatment resistant depression, behavioral disturbances in children & adolescents, disorders associated with problems with impulse control, Unipolar and bipolar depression with mixed features.
- Advantages: Perhaps less metabolic effects, not documented to cause QTc prolongation
- Disadvantages: need to take with food, can cause nausea/vomiting (especially at higher doses)

Stahl, S. M., & In Grady, M. M. (2019). *Stahl's essential psychopharmacology: Prescriber's guide children and adolescents.*

Quetiapine (Seroquel)

- FDA Indications: Schizophrenia (13 & up), Acute Mania (10 & up)
- Off label uses: behavioral disturbances in children & adolescents, disorders associated with problems with impulse control.
- Baseline: Weight, BMI, glucose, A1C, lipid panel
- **Somnolence common, more associated with weight gain and other metabolic effects**
- Less common- motor side effects, prolactin elevation

Beauchamp-Buller, K. Z. & Elin, D. Veen, A. S. & Procyshyn, R. M. (Eds.). (2014). *Clinical handbook of psychotropic drugs for children and adolescents.* Hogrefe & Huber Publishers.

Olanzapine (Zyprexa)

- FDA Indications: Schizophrenia (13 & up), Manic or mixed episode of bipolar I disorder.
- Off label uses: behavioral disturbances in children & adolescents, disorders associated with problems with impulse control.
- Baseline: Weight, BMI, glucose, A1C, lipid panel
- Associated with **greatest risk of weight gain, increased cholesterol**
- "more efficacy but also more side effects"

Stahl, S. M., & In Grady, M. M. (2019). *Stahl's essential psychopharmacology: Prescriber's guide children and adolescents.*

Clozapine (Clozaril)

- FDA Indications: None for children or adolescents
- Off label uses: psychosis, treatment resistant bipolar disorder, violent aggressive patients with psychosis not responsive to other treatments. **NOT A FIRST LINE TREATMENT**
- Baseline: LFTs, ECG, CV assessment, CBC with differential, weight, BMI, lipid panel, HgbA1C, Vital signs, troponin, CKMB, C-RP
- Because of the risk of severe neutropenia, clozapine is available only through a restricted program under a Risk Evaluation Mitigation Strategy (REMS) called the Clozapine REMS Program.
 - Baseline ANC must be at least 1500/mm³ for the general population
 - ANC must be at least 1000/mm³ for patients with Benign Ethnic Neutropenia.
 - Must adhere to REMs monitoring protocols for ANC
- Orthostatic hypotension, bradycardia, syncope, tachycardia have all occurred with treatment.
- Myocarditis (early in treatment) and cardiomyopathy (late in treatment) have occurred with treatment.

Third Generation Antipsychotic Medication (TGA)

Aripiprazole (Abilify)

- Partial agonist of D2
- **Indications:**
 - Schizophrenia (ages 13 & up)
 - acute mania/mixed mania (ages 10 & up),
 - Autism related irritability (ages 6-17yo)
 - Tourette Syndrome (ages 6-18yo)
- Off label use: bipolar depression, other psychotic disorders, behavioral disturbances in children & adolescents, disorders associated with problems with impulse control, post traumatic stress disorder, obsessive compulsive disorder (adjunct to SSRIs).
- Akathisia
- Baseline: Weight, BMI, glucose, A1C, lipid panel

Typical or First Generation Antipsychotic Medications (FGA)

Haloperidol (Haldol)

- FDA Approved for:
 - Tics with Tourette syndrome
 - Second line treatment for severe behavioral problems in children of combative, explosive, & hyper-excitability, second line short term treatment of hyperactive children (Oral only, ages not specified)
- Off label use: bipolar disorder, delirium
- Baseline: BMI, lipid panel, liver enzymes, abnormal involuntary movements, EKG to assess QTc.
- Less associated with weight gain & metabolic affects
- More associated with neurologic AE's (dystonia, EPS, TD, NMS), even at low doses.

Chlorpromazine (Thorazine)

- FDA Indications:
 - Severe behavioral problems associated with oppositional defiant disorder or other disruptive behavior disorders
 - ADHD in pediatric patients who show excessive motor activity with accompanying conduct disorders (oral, IM for acute, severe agitation in hospitalized patients)
- Off label uses: agitation or delirium in hospitalized patients without underlying psychiatric illness, bipolar disorder
- Baseline: BMI, lipid panel, liver enzymes, abnormal involuntary movements, EKG to assess QTc.
- More sedating.

Stahl, S. M., & In Grady, M. M. (2019). Stahl's essential psychopharmacology: Prescriber's guide children and adolescents.

Neuroleptic Malignant Syndrome (NMS)

- Life threatening neurologic emergency – associated with use of antipsychotic medications. 0.02-3% incidence with antipsychotic use.
- More associated with FGAs, however potential to happen with any antipsychotic medications (and antiemetic drugs such as metoclopramide, promethazine)
- Usually develops within first 2 weeks of therapy, not dose dependent- though higher doses are a risk factor.
- **Tetrad of symptoms:**
 - Mental status changes- initial symptom
 - Muscular rigidity- generalized and extreme
 - Hyperthermia
 - Autonomic instability- typically tachycardia (labile or high BP, diaphoresis, tachypnea can also occur)
- **Treatment:**
 - Stop causative agent
 - Supportive care
 - Close inpatient monitoring/treatment

Wikipedia, E.P.M. (2019). Neuroleptic Malignant Syndrome. UpToDate. https://www.uptodate.com/contents/neuroleptic-malignant-syndrome?search=neuroleptic%20malignant%20syndrome&source=search_result&content_id=1003&usage_type=detailview&rank=1. Retrieved May 19, 2020.

Mood Stabilizers (anticonvulsants)

- Lithium
- Valproic Acid/Depakote
- Carbamazepine



Lithium



- No FDA indications for children/adolescents
- the original mood stabilizer – introduced in 1960's
- Narrow therapeutic index- toxicity can occur close to therapeutic level
- Dehydration can cause acute toxicity
- **Baseline:** ECG, kidney function tests, thyroid function tests, CBC, BMI.
- Obtain Li trough after 5 days – therapeutic level 0.6-1.2 (higher end for acute mania)
- Monitor Li levels weekly until desired therapeutic concentration, then Q3 months.
- Monitor TSH, Kidney function Q6 months (salt, renal excretion)
- Monitor BMI/weight- lithium associated with weight gain.

(2020) Lithium. Drug information. Retrieved from <https://www.upToDate.com/contents/lithium-drug-information?search=results&selectedTopic=1468&age=type=general&tab=drug-general&display=rank=1>

Valproic Acid (Depakote)

- FDA indications: treatment of complex partial seizures
- Off label uses: treatment of bipolar disorder, psychosis, schizophrenia
- Baseline: CBC, Liver function tests, weight, BMI
- Repeat CBC, LFTs at 3months, then Q6months
- Frequent weight gain, sedating, rare hepatotoxicity, thrombocytopenia, teratogenic- pregnancy screen prior to initiation
- Monitor serum VPA levels - after dose changes, concerns for compliance, & Q6 -12 months

Beauchamp-Builer, K. Z. & Elbe, D., Vranik, A. S. & Procyshyn, R. M. (Eds.). (2014). Clinical handbook of psychotropic drugs for children and adolescents. Hogrefe & Huber Publishers.

Carbamazepine

- No FDA indications for children/adolescents in psychiatry; No RCT evidence for children
- Baseline- CBC with platelets (risk for aplasia's), LFT, electrolytes, creatinine – then Q 3-6 months
- Serum level monitoring – two levels to establish therapeutic dose 4 weeks apart (5 days after change in dose), or as clinically indicated.
- SJS rash & toxic epidermal necrolysis – Patients of Asian ancestry and with + HLA-B*1502 are at increased risk for serious skin reactions.

Beauchamp-Builer, K. Z. & Elbe, D., Vranik, A. S. & Procyshyn, R. M. (Eds.). (2014). Clinical handbook of psychotropic drugs for children and adolescents. Hogrefe & Huber Publishers.

Antidepressant Medications



Selective Serotonin Reuptake Inhibitors

- Fluoxetine:
 - FDA Indications: Major depressive disorder (ages 8 & up), Obsessive compulsive disorder (ages 7 & up), bipolar depression [combo with olanzapine (Symbyax)] ages 10 & up.
 - Considered 1st line
 - Advantages: long half life (no SE from missing dose)
 - Disadvantages: insomnia/agitation, headaches
- Escitalopram:
 - FDA Indication: Major Depressive Disorder (ages 12 & older)
 - Considered 2nd line
 - Advantages: may be better tolerated, few drug interactions
 - Disadvantages: newer, less robust evidence for depression tx
- Sertraline:
 - FDA Indication: Obsessive Compulsive Disorder (ages 6 & older)
 - Considered 2nd line
 - Advantages: wide dose range, activating for kids with fatigue/low energy
 - Disadvantages: GI problems/diarrhea, insomnia/agitation

Hirsch, M. and Blinbaum, R. (2020). Up to date.

Selective Serotonin Reuptake Inhibitors

- Citalopram (Celexa): No FDA indication for children/teens.
 - Off label: depression & anxiety disorders
 - Advantages: May be better tolerated by some, fewer drug interactions than other SSRI's (except escitalopram).
 - Disadvantages: Doses > 40mg not recommended due to risk of QTc prolongation.
 - Avoid use in patients with CV risks due to QTc prolongation risk
- Paroxetine: No FDA indication for children/teens.
 - Off label: depression & anxiety disorders
 - 3 placebo controlled trials in pediatric patients with depression lacking evidence to support indication.
 - Disadvantages: Short half life, more likely to result in withdrawal effects with missed doses or discontinuation. Anticholinergic effects (drowsiness, weight gain, orthostatic hypotension)

Hirsch, M. and Blinbaum, R. (2020). Up to date.

Alternative Antidepressant Medications

- Selective Norepinephrine Reuptake Inhibitors:
 - Check BP, weight & height at baseline, regularly during treatment
- Venlafaxine (Effexor):
 - No FDA indication for children/teens.
 - Off label: MDD, GAD, separation & social anxiety disorders
 - Disadvantages: SE profile (nausea, hypertension)
- Duloxetine (Cymbalta):
 - FDA Indication for GAD ages 8 & up, off label use for MDD, diabetic peripheral neuropathic pain, fibromyalgia and chronic musculoskeletal pain.
 - Disadvantages: frequent nausea, can increase agitation
- Alternative Antidepressant Medication:
 - Mirtazepine (Remeron): No FDA indications for children/teens (no RCT evidence)
 - Sedating, appetite stimulation

Serotonin Syndrome (toxicity)

- Potentially life threatening condition- increased serotonergic activity in CNS
- Inadvertent drug interactions, intentional ingestions, medication use
 - Importance of detailed history of Rx, OTCs, illicit drugs, and dietary supplements.
- Physical Exam: Triad- 1. mental status changes, 2. autonomic hyperactivity, and 3. neuromuscular abnormalities.
 - Mental status changes
 - Agitation, delirium, restlessness, disorientation, exaggerated startle.
 - Autonomic hyperactivity
 - Tachycardia, hyperthermia, hypertension, diaphoresis, vomiting/diarrhea.
 - Neuromuscular abnormalities
 - Hyperreflexia, clonus, tremor, muscle rigidity, myoclonus, bilateral Babinski sign.
 - Hyperreflexia, clonus and muscle rigidity more pronounced on lower extremities.

Boyer, E. (2020). Serotonin Syndrome (serotonin toxicity). UpToDate. <https://www.uptodate.com/contents/serotonin-syndrome-serotonin-toxicity>

Serotonin Syndrome (toxicity)

- Hunter Toxicity Criteria Decision Rules
 - Must have 1. taken a serotonergic agent 2. meet one of the following:
 - Spontaneous clonus
 - Inducible clonus + agitation or diaphoresis
 - Ocular clonus + agitation or diaphoresis
 - Tremor + hyperreflexia
 - Hypertonia + temperature above 38 deg C + ocular/inducible clonus
- Management:
 - Stop serotonergic medicines
 - Supportive care to normalize VS
 - Sedation with benzodiazepines
 - Administer serotonin antagonists
- Prevention: avoid polypharmacy when possible!

Boyer, E. (2020). Serotonin Syndrome (serotonin toxicity). UpToDate. <https://www.uptodate.com/contents/serotonin-syndrome-serotonin-toxicity>

Anxiolytic & Sleep Medications



Anxiolytic Medications

- Selective Serotonin Reuptake Inhibitors
 - Fluoxetine & Sertraline 1st line medications for child anxiety disorders
 - OCD: fluoxetine (7 & up), sertraline (6 & up), and fluvoxamine (8 & up)
 - SSRI trial → adequate does for adequate length of time
 - If failed one SSRI, trial a second SSRI
 - Once stable, continue SSRI for 6 months (with OCD continue for at least one year).

Kodish I, Rockhill C, Ryan S, Varley C. Pharmacotherapy for anxiety disorders in children and adolescents. *Pediatr Clin North Am.* 2011;58(1):55-72.

Anxiolytic Medications

- Duloxetine (Cymbalta)- FDA indication: GAD ages 7 & up
 - Check BP, weight & height at baseline, regularly during treatment
- Buspirone (BuSpar): partial agonist of serotonin receptors. No RCT evidence in children.
 - Monitor for serotonin syndrome, especially if in combo with serotonergic agents (SSRI's, SNRI's)
- Benzodiazepines: evidence does not support the use with children
 - May provide short term relief for severe symptoms.
 - Risk of tolerance, paradoxical reactions, effects on memory/learning, and risk of seizure with abrupt discontinuation.
 - "Band-Aid"- prevents learning adaptive skills to gain mastery of anxiety
- Tricyclic Antidepressants:
 - Clomipramine: FDA indication for OCD 10 & up
 - Disadvantages: anticholinergic SE's, cardiac monitoring, risk of fatality with OD
 - Monitor ECG, Wt/BMI, lipids, electrolytes (especially if on diuretics), plasma drug levels if possible

Kodish I, Rockhill C, Ryan S, Varley C. Pharmacotherapy for anxiety disorders in children and adolescents. *Pediatr Clin North Am.* 2011;58(1):55-72.

Hypnotic/Sleep Medications

- Sleep hygiene
- CBT-I (CBT for insomnia)
- Use of Medications for sleep- generally short term
 - Rule out OSA, restless legs, other potential medical causes prior to initiating medication treatment
- Melatonin
 - Best for sleep onset insomnia and circadian phase delay.
 - Not regulated by the FDA
 - Take one hour prior to bedtime, then dim lights

Liver Tox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012. Trazodone. [Updated 2020 Feb 26]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK548567/>.

Hypnotic/Sleep Medications

- Hydroxyzine:
 - FDA approved in pediatrics as an antiemetic, antipruritic. No FDA indication for anxiety in children/teens
 - First generation antihistamine
 - Not a lot of supporting data, typically short term/occasional use
 - Monitor for drowsiness, xerostomia, risk for QTc prolongation in those with additional risk factors. Largely well tolerated.
- Trazodone: No FDA indication for children/teens
 - Serotonin reuptake inhibitor/antagonist; at low doses, significantly blocks histamine (H1) and alpha adrenergic receptors (more serotonergic at higher doses)
 - Baseline LFT, periodically during treatment
 - Monitor for serotonin syndrome, suicidality
 - Monitor BP/HR- may cause hypotension or orthostasis
 - Priapism: use with caution in patients with predisposed risk (sickle cell anemia, multiple myeloma, leukemia)

Any Questions???

