BHIPP BRIEFS:

PRACTICAL MEDICATION MANAGEMENT OF PEDIATRIC ANXIETY IN PRIMARY CARE

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OBJECTIVES

Review–for the non-psychiatrist pediatric clinician–of:

1. Pharmacological treatment options for pediatric anxiety disorders (non-OCD and non-PTSD, excluding pregnancy)
2. Possible side effects.

This webinar is meant only as an educational tool and not as a substitute for the primary care provider's clinical judgment. The use of many off-label medications will be presented. The recommendations presented do not indicate an exclusive course of treatment nor represent a standard of medical care.

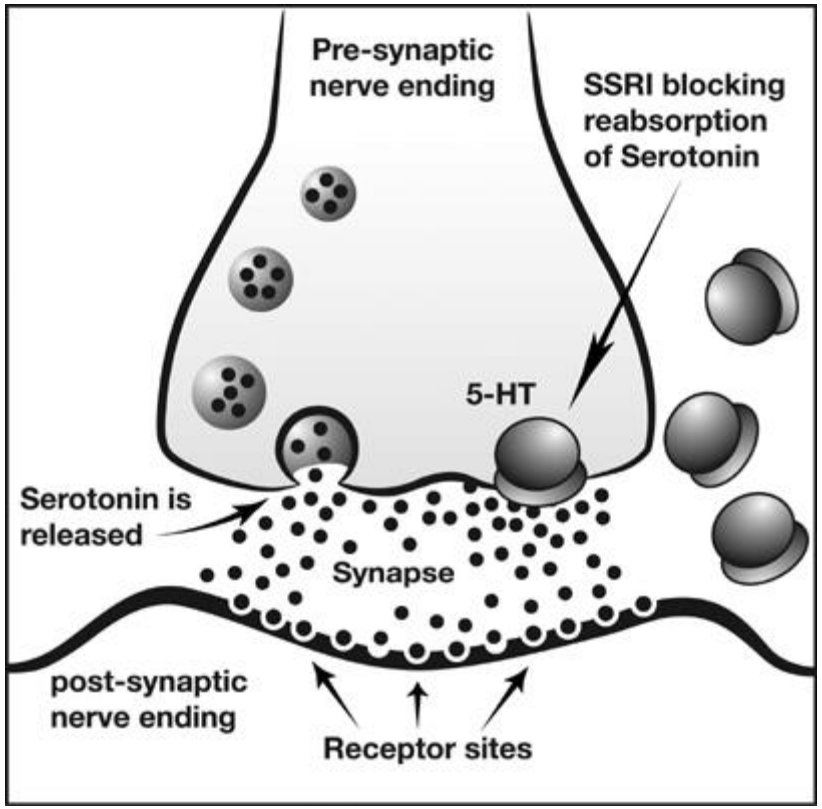
Anxiety disorders refers to non-OCD and non-PTSD anxiety disorders in this webinar. Efforts have been made to set forth medication dosages and choices. Variations may be appropriate. It is the health care professional's responsibility to check the medication's package insert of each drug for changes in doses or indications and for added precautions.

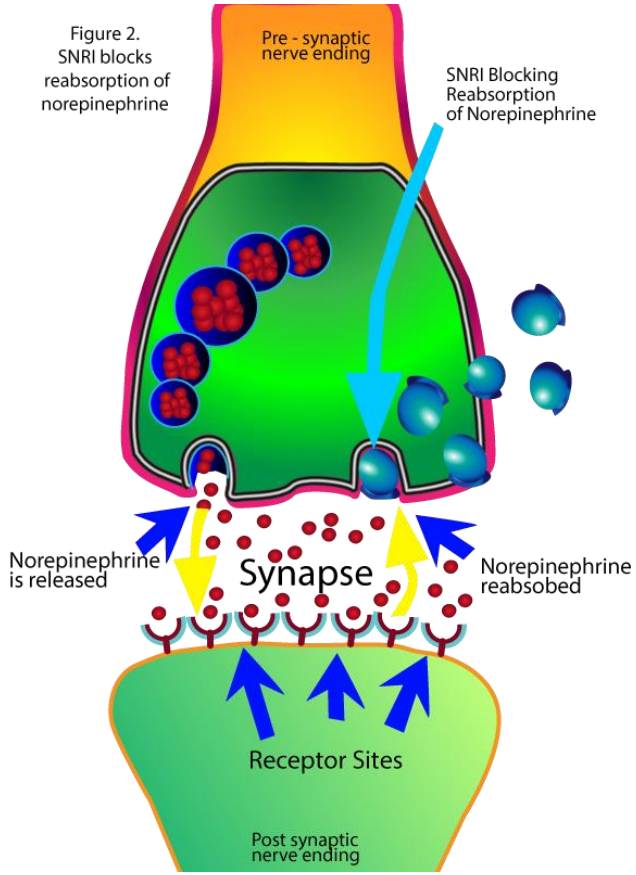
Please call our BHIPP telephone consultation line (**855-MD-BHIPP**) for specific- treatment related questions.

WHEN ARE MEDICATIONS PRESCRIBED FOR PEDIATRIC ANXIETY DISORDERS?

- *Sufficient symptoms* to support a syndrome/disorder?
- Symptoms present for a *sufficient period of time*?
- Significant *impairment/distress* affecting school, family, social, emotional function?
- Significant *differences from normal* (activity, worry, sadness)?
- Have other *interventions been unsuccessful*?

HOW DO SSRI'S & SNRI'S WORK?





SSRI = Selective Serotonin(5-HT) Reuptake Inhibitor

SNRI = Serotonin-Norepinephrine (NE) Reuptake Inhibitor

SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI): USE IN PEDIATRIC ANXIETY DISORDERS

- **Child/Adolescent Anxiety Multimodal Study (CAMS)**
  - Cognitive Behavioral Therapy (CBT) vs placebo vs sertraline only (n=488)

  Improvement at 12 weeks:
  - CBT 60%
  - SERT 55%
  - PBO 24%
  - **Combination CBT and sertraline (81%)> all**

SSRI'S

Generic	Brand Name
Fluoxetine (MDD 8+; OCD)	Prozac
Escitalopram (MDD 12+)	Lexapro
Sertraline (OCD)	Zoloft
Fluvoxamine	Rarely used for non-OCD
Citalopram	QTc prolongation
Paroxetine	Nonlinear kinetics

SSRIS: SIMILARITIES & DIFFERENCES

Similarities

- mechanism of action
- efficacy
- once-a-day dosing

Differences

- duration of effect
- CYP450 isoenzyme effects (hepatic metabolism)

SSRIs FOR ANXIETY

SSRI	Indication(s)	FDA Approval/ Approved Age	Level of Evidence	Generic
Fluoxetine	**ANX** OCD	**No** Yes; ≥ 7	B A	Yes
Sertraline	**ANX** OCD	**No** Yes; ≥ 6	B A	Yes
Fluvoxamine	**ANX** OCD	**No** Yes; ≥ 8	B A	Yes

TYPICAL DAILY DOSES (MG)/DAY

Medication	Start (mg/day) total daily dose	Maximum (mg/day dose)(NOTE: typical total dose is lower)	Increments (mg/day) (as per clinical indications and tolerability over time)
Sertraline	6-12 yrs : 12.5 or 25 13-17 yrs: 25	200 200	12.5 or 25-50 50
Fluoxetine	5 or 10 mg	60	5 or 10

SNRI'S

Generic	Brand Name
Venlafaxine	Effexor
Duloxetine*	**Cymbalta***
	***FDA approved GAD 7-17 years**

DULOXETINE (CYMBALTA)

- Characteristics
  - SNRI (like venlafaxine)
  - *New FDA indication in youth for generalized anxiety – ONLY FDA approved Rx*
- Side effects
  - Same as SSRIs plus somnolence, increased HR and BP
  - RARE: liver damage, skin reactions, bleeding, visual problems
- Monitoring
  - Same as SSRIs plus BP, P

TYPICAL DAILY DOSES (MG)/DAY

Medication	Start (mg/day)	Maximum (mg/day)	Increments Over time as per recommendations
Duloxetine	15 or 30	60	15 or 30 (mg/day)

- Meta-analysis by Dobson et al (2019) found likelihood of treatment response = greater for SSRI vs SNRI (odds ratio 1.9 [95% confidence interval 1.1-3.5])

VENLAFAXINE (EFFEXOR)

- Characteristics
  - SNRI
  - “behaves” like SSRI at lower doses
  - used for depression and/or anxiety
- Side Effects
  - similar to SSRIs plus decreased appetite, pain, somnolence
  - ***hypertension and tachycardia***
  - ***Significant discontinuation syndrome symptoms***
- Monitoring
  - same as other SSRIs plus BP and P

MEDICATION: GENERAL PRINCIPLES

- **START LOW, GO SLOW…….**
- Effectiveness varies and response not usually 100%
  - Effect size 0.7 for anxiety (stimulants 0.8-1.0 for ADHD)
- 4-8 weeks to reach therapeutic dose and maximal benefit
- Compliance?
- Informed consent with guardian/parent and youth …

MEDICATION: ADVERSE EFFECTS

- ***COMMON: GI pain, nausea, diarrhea, headache***
- Activation
- Apathy
- Bleeding/nosebleeds
- Discontinuation syndrome
- Hypomania/mania
- Synergy with alcohol
- Serotonin syndrome
- Sexual (decreased libido, orgasm)
- Suicidality

Anxious kids are more aware of their bodies and thus more sensitive to…

SEROTONIN SYNDROME

- GI symptoms – Nausea, vomiting, **diarrhea**
- Fever, sweating
- Autonomic symptoms (pulse, blood pressure)
- Change in mental status
- Risk increase when more than one serotonergic medication.

ACTIVATION

- Who is at increased risk?
- What are the symptoms to monitor for?
- When are youth most at risk? Titration contribution ?
- What can we do?

ANTIDEPRESSANTS AND SUICIDALITY

- Mechanism possibly related to activation?
- **Black box warning**: 4% incidence in kids vs 2% on placebo
- Later study (Bridge et al 2007) found smaller **0.7%** difference (95% CI 0.1-1.3%)→-→ (roughly **1 in 133 treated patients**)
- Subsequent studies noted decrease in SSRI prescriptions in adolescents and concurrent increase in suicide attempts: Benefit > Risk
- Discuss with each patient/family and monitor

Conclusion → Rare
Monitoring = Safety

DISCONTINUATION SYNDROME

- Flu-like symptoms
- GI symptoms – nausea, vomiting, diarrhea
- Dizziness, vertigo
- Tingling/numbness, electric-shock-like sensations
- Sleep disruption
- Anxiety, irritability, agitation, low mood

- Slow & gradual taper if possible

QUESTION

A 9-year-old girl presents with her mother who complains that the child tantrums when prevented from sleeping near her. The girl worries about mom, school, and money daily for the last year and has had stomachaches and headaches, with a generalized anxiety diagnosis. She has been in therapy for at least 6 months and her symptoms are still very disabling. She has no significant past medical history or meds. **You decide to start a medication to target her anxiety disorder-related symptoms; which of the following medications would be your first choice:**

- A. Sertraline 12.5 mg daily
- B. Quetiapine 12.5 mg daily
- C. Methylphenidate 5.0 mg daily
- D. Paroxetine 5.0 mg daily

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A 9-year-old girl presents with her mother, who complains that the child tantrums when prevented from sleeping near her. The girl worries about mom, school, and money daily for the last year and has had stomachaches and headaches, with a generalized anxiety diagnosis. She has been in therapy for at least 6 months and her symptoms are still very disabling. She has no significant past medical history or meds. **After informed consent with the guardian, you decide to start a medication to target anxiety disorder-related symptoms; which of the following medications would be the best first choice:**

- ***A. Sertraline 12.5 mg daily***
- B. Quetiapine 12.5 mg daily
- C. Methylphenidate 5.0 mg daily
- D. Paroxetine 5.0 mg daily

SUMMARY

- Treatment can greatly improve level of functioning and quality of life
- Many effective pharmacological treatments for anxiety can be initiated in the PCP's office
- SSRIs are 1st line medication for anxiety – used in combo with CBT
- SNRI Duloxetine is the only FDA approved choice for GAD
- Monitor closely for side effects

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