Be Happy Child and Adolescent Mental Health ECHO:

Medication Management for Depression in Children and Adolescents in Primary Care

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Learning objectives

1. Increase familiarity with standardized assessments for depression in children and adolescents.
2. Increase comfort in use of pharmacologic treatments for depression.

AAP: Guidelines for Adolescent Depression in Primary Care (2018)

- GLAD- PC I: Practice Preparation, Identification, Assessment, and Initial Management
- GLAD –PC II: Treatment and Ongoing Management
- GLAD PC Toolkit: DSM 5 Criteria, Screening tools (in multiple languages), Monitoring guidelines, Flowcharts, Family Handouts

AACAP: 2020 Clinical Practice Guidelines for the Assessment and Treatment of Anxiety Disorders in Children and Adolescents – ages 6-18

12yo F presents for annual well child check.

Mom reports she doesn't seem to be enjoying things or engaging with the family as much. Grades have decreased this year. When asked, pt says she's just "bored with life." Denies trauma. No previous mental health treatment. Family has had difficulty finding a therapist. Mom has depression and has improved with Zoloft.

Depression: Assessment/Screens (all free)

GLAD-PC (12 and older) recommends annual screens in primary care + any concerns

12 and older: PHQ9A

- validated as diagnostic screener and tracking changes over time

- suicide question at the end

<12: Pediatric symptom checklist (4 – 16), APA cross cutting symptom checklists (6-17)

Mood and feelings questionnaire (8-16)

Columbia Suicide Rating Scale

Yellow Mild – close monitoring, increased level of care

Orange Mod – close monitoring, increased level of care (IOP, PHP)

Red Sev – ED assessment

Ask questions that are in bold and underlined.	Past month	
Ask Questions 1 and 2	**YES**	**NO**
1) ***Have you wished you were dead or wished you could go to sleep and not wake up?***		
2) ***Have you had any actual thoughts of killing yourself?***		
If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6.		
3) ***Have you been thinking about how you might do this?*** e.g. "*I thought about taking an overdose but I never made a specific plan as to when where or how I would actually do it....and I would never go through with it.*"		
4) ***Have you had these thoughts and had some intention of acting on them?*** as opposed to "*I have the thoughts but I definitely will not do anything about them.*"		
5) ***Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?***		
6) ***Have you ever done anything, started to do anything, or prepared to do anything to end your life?*** Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc.	**Lifetime**	
	Past 3 Months	
If YES, ask: ***Was this within the past 3 months?***		

PHQ9A: Moderate Depression

Call Be Happy!

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Be Happy Rec: provided Cognitive Behavioral Therapy (CBT) resources, recommend starting an SSRI

Depression and Anxiety Treatment Approach

Mild: active monitoring + CBT.

Moderate/Severe: CBT +

1. **SSRI** 4-6 weeks *at optimal dose*
2. **Other SSRI** 4-6 weeks *at optimal dose*
3. **SNRI – (duloxetine, venlafaxine)**

Need to give our patients the best chance to use the most evidence-based, effective, safest medications!!! = SSRIs

Treatment for Adolescent Depression Study (TADS)

- 12 weeks, n = 439, ages 12-17.
- Prozac: start 10 mg, increase by 10 mg weekly (end ave: 30mg)
- Response rates:
  - Prozac: 60%
  - Prozac + CBT: 71%
  - CBT: 43%
  - Placebo: 35%
- Additional conclusions:
  - Combo had 3x greater probability of sustained response
  - Suicidal ideation improved in all groups, though improved in CBT groups more (CBT protective against SI)

Treatment of Resistant Depression in Adolescents

- n = 334, ages 12 – 18, MDD did not respond to 2 months optimal SSRI dose
- Response:
  - Different SSRI (fluoxetine, citalopram, paroxetine): 41%
  - Different SSRI + CBT: 56%
  - Venlafaxine (Effexor): 40%
  - Venlafaxine + CBT: 55%
- Conclusions:
  - Combo helps more regardless of med
  - Not a significant response difference between SSRI and venlafaxine
  - different SSRI: more rapid improvement in depressive symptoms and SI
  - Venlafaxine had more side effects compared to other SSRI, including SI – though mitigated by CBT

Med	Half life (hrs)	Dosing	Liquid	Increments (q2-4 weeks)	Common AEs
Prozac (Fluoxetine) ***1st line GLAD-PC** **- FDA approved for adolescent depression**	**48-96**	10 mg – 60 mg	20mg/5mL	10 – 20 mg (10→20→**40 →60)** **TAD ave dose: 30**	Headaches GI upset insomnia agitation anxiety
Zoloft (Sertraline)	22-36	25 mg – 200mg	20 mg/1mL	25 – 50 mg (25→ 50 → 100→**150 →200)** **CAM ave dose: 145**	Headaches GI upset activation
Celexa (Citalopram) -lower risk for interactions	23-45	10 mg – 40 mg	10mg/5mL	10 - 20 mg (10 →20 →**40**)	Headaches GI upset Insomnia **Avoid in long QT**
Lexapro (Escitalopram) **2nd Line GLAD-PC** - **FDA approved for adolescent depression** - Lower risk for interactions	27	5 mg – 20 mg	5 mg/5mL	5 - 10 mg (5 →10 →**20**)	Headaches GI upset insomnia

What to talk about when starting an SSRI

1. **Work Best with CBT!**
2. **Anticipated time to effect**
   - 2 weeks: Statistically (not clinically) significant improvement
   - 6 weeks: Clinically significant improvement
   - 12 weeks: maximal improvement
3. **Anticipated Dose** (optimal)
4. **Anticipated Duration** (12 months of good effect)
5. **Side Effects/Serotonin Discontinuation Syndrome/Somatic symptoms of Depression**
6. **Black Box Warning**

Need to give our patients the best chance to benefit from SSRIs!

Side effects? – take a careful adherence history

Common

- Dry mouth
- Constipation
- Sweating
- Nausea
- Diarrhea
- Sexual dysfunction
- Sleep disturbance
- Irritability/Agitation (activation)
- Headache
- Appetite changes

Serotonin Discontinuation Syndrome

- Dizziness
- Nausea
- Diarrhea
- Lethargy/malaise
- Insomnia
- Anxiety/Irritability
- Headache

Purple: common in depression and anxiety

Blue: overlap side effect and discontinuation syndrome

Side effects

- Meta analyses of SSRI and SNRI side effects have **generally failed to detect treatment-related differences** in frequency of headaches and GI side effects
  - Occur at a high rate in patients with anxiety and depression

- Treatment emergent side effect that trended towards statistical significance: **activation**: mild irritability, mild disinhibition, increased restlessness, insomnia
  - more common in children (10.7%) than adolescents (2.1%)

Addressing Side Effects

Need to give the best chance to use SSRIs!

1. If mild (GI upset, irritability) – wait up to 1 week
2. Irritability – lower dose
3. Sleep issues – change dose timing
4. Sexual side effects (erectile dysfunction, delayed ejaculation, anorgasmia): trial alternative, buspar add on
5. Severe/persistent >1 week: lower dose/discontinue

SSRIs: Black Box warning

Suicidal **Ideation** in **Adolescents (up to 24)** with **Depression** *(spontaneous report)*

-No single study showed statistically significant increase in SI
-No suicides occurred in any of the trials
-Pooled meta-analysis risk difference compared to placebo: 0.7%
-**NNH: 143 NNT: 3**
-Almost all adolescents who die by suicide who were prescribed SSRIs do not test positive for SSRIs in postmortem toxicology
-Pharmaco-epidemiologic evidence: inverse relationship between SSRI rxs and suicides

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Switching SSRIs (CALL BE HAPPY!)

Indications to switch:

1. When maximum dose is reached and maintained for 4-6 weeks without response in target symptoms = fail

2. Major, persistent side effects (not a failed SSRI trial)

Cross taper:

- Same dose intervals every 2-4 weeks

Maintaining/Discontinuing SSRIs

Continue medication for **12 months** following cessation of symptoms. (fewer relapses)

Follow up when stabilized:

- monthly initially and no longer than q3 months to check efficacy of medication
- Obtain screens each visit

Discontinue:

- Slowly (4-6 months or longer)
- With consideration of stressors (spring is a good time)

Pharmacogenetic testing? - Not Yet

AAP News Jul 2020: Pharmacogenetic testing for psychotropic medications of limited value in children
https://www.aappublications.org/news/2020/07/01/focus-pharmacogenetic070120

AACAP Policy Statement:
https://www.aacap.org/AACAP/Policy_Statements/2020/Clinical-Use-Pharmacogenetic-Tests-Prescribing-Psychotropic-Medications-for-Children-Adolescents.aspx

The American Academy of Child and Adolescent Psychiatry recommends:

- **Clinicians avoid using pharmacogenetic testing to select psychotropic medications in children and adolescents.**
- **Future high-quality prospective studies to assess the clinical significance of pharmacodynamic and combinatorial pharmacogenomic testing in children and adolescents.**

Only a small fraction of the available commercial products have undergone randomized controlled trials in adults only and those studies are limited by:

- Potential conflicts of interest
- Small sample sizes
- Short duration of follow-up
- Lack of blinding
- Lack of appropriate control groups

- numerous factors affect medication response unaccounted for by genetic variation

- provides little meaningful information when two or more medications are used concurrently.