Psychiatric Pharmacology & the Role of Supplements in Pediatric Patients

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Introduction

- No conflicts of interest to disclose
- Generic names will be used whenever possible, but the brand name drug may be referenced if appropriate. Inclusion of a brand name drug in this presentation does NOT represent endorsement

Preface

- Treatments, not diagnosis
  - Based on proper diagnostic assessment & ongoing evaluation and adjustments
- Therapy or Psychotherapy
- Focus on evidence & safety ≥ practicality
  - Practicality: ease of use, adherence, cost and insurance barriers

Outline

- Depression/Anxiety
  - Latest guidelines and landmark clinical trials
  - Considerations for pediatric vs adult patients
  - Prescribing trends among child psychiatrists and PCPs
  - (Clinically relevant) drug-drug interactions
  - How to safely titrate and cross-taper between agents
  - Avoiding and overcoming common insurance barriers
- ADD/ADHD
  - Review of guidelines and general recommendations
  - Stimulant shortages
  - Newest formulations

Outline (continued)

- Role of supplements in pediatric psychiatry
  - Importance of diet
  - Risks of “natural” remedies
  - Integrative medicine and evidence-based recommendations
    - Vitamin D
    - Fish Oil
    - St. John’s Wort
    - Medical Marijuana
    - Iron
    - SAM-e
    - NAC
    - Melatonin
- Conclusion
- Q&A
- Case Presentation

Depression/Anxiety – Pediatric Considerations

- Medication is only recommended as adjunct to psychotherapy
- STAR*D trials
- Black Box Warning
- Bipolar Disorder
- Adherence is likely the biggest barrier to treatment
- Start low…go slowly

Antidepressants & Anxiolytics

Fluoxetine

Sertraline

Escitalopram

Venlafaxine

Duloxetine*

Bupropion

Citalopram

Paroxetine

Fluvoxamine

*Honorable mentions: Hydroxyzine, Trazodone, Mirtazapine

Antidepressants & Anxiolytics

Fluoxetine

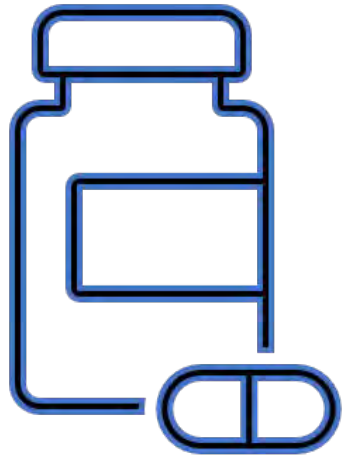
Sertraline

Escitalopram

- Most evidence in pediatric patients (except citalopram)
- Easy to titrate, taper, and cross taper
- Liquid formulations available, can also cut/crush
- Flexibility with dosing and schedule
  - Give any time of day
- 1st line for Pediatric GAD
- Weight neutral

Antidepressants & Anxiolytics

Fluoxetine



- CAPSULES not TABLETS
- 10-20mg starting dose – up to 60mg
- Long half-life
- Drug interactions
- FDA approved for Pediatric Depression (8yo+)
- Most evidence for treatment, preferred initial choice in guidelines

Antidepressants & Anxiolytics

Sertraline

- 25-50mg starting dose – up to 200mg daily
- Take with food
- Liquid formulation needs to be further diluted
- Small tablets, scored

Antidepressants & Anxiolytics

Escitalopram

- S stereoisomer of citalopram
  - Half the dose of citalopram
- 5-10mg starting dose – up to 20mg
- Much less toxic in OD
- Less titrating to get to final dose
- FDA approved for Pediatric Depression (12y+)

Antidepressants & Anxiolytics

- Also recommended first-line for Pediatric GAD
- 20-30mg starting dose – up to 120mg
- Much less toxic in OD
- Only FDA approved agent for Pediatric GAD (7y+)

Duloxetine*

Venlafaxine

- Little evidence in peds
- Serotonergic until 150mg, then becomes an SNRI
- Weight neutral or weight loss
- Starting dose 37.5-75mg up to 300mg
- Poor choice for nonadherent patients
    - Withdrawal symptoms - ALWAYS use extended-release capsules

- Little evidence in peds
- Often used as adjunct
- Bupropion XL (24 hour formulation) 150mg-300mg daily
- IR 75mg (TID), SR (12 hour formulation) 100mg, 150mg, 200mg
- Give in the morning
- Toxic in OD

Bupropion

- Least preferred options

Citalopram

Paroxetine

Fluvoxamine

- Toxic in OD
  - Seizures
  - QTC prolongation
- Tested in pediatrics
- Rarely prescribed over escitalopram

Citalopram

- No pediatric indications
- Hazardous to Handle
  - Cannot crush, split tablets
- Weight gain
- Drug interactions
- Withdrawals
- Poorly tolerated

Paroxetine

- Indicated for OCD
- Drug interactions – CYP1A2 inhibitor
- Short half-life, may need BID dosing

Fluvoxamine

Hydroxyzine

- Often 10, 25, or 50mg PRN at the beginning of treatment for anxiety or sleep
- May receive alert for QTc prolongation

Trazodone

- Adjunct for sleep
- 25-50mg QHS PRN
  - may increase up to 150mg

Mirtazapine

- 7.5mg more potent than 15mg for sleep
- May help with weight gain
- 7.5mg or 15mg used as adjunct for sleep, higher doses for depression

How to titrate and cross-taper

- To avoid insurance issues, prescribe the target dose and have patient **split tablet** for first 7-10 days
  - E.g. escitalopram 10mg: take ½ tablet by mouth once daily, then increase to a full tablet after one week
  - Exception: fluoxetine may take 2 prescriptions if insurance doesn't allow for more than one capsule/strength/day

How to titrate and cross-taper

- Do NOT put refills on a titration
  - Causes insurance issues and delays
- Cross taper between agents within a week or less
  - Fluoxetine self-tapers
- Plan for drug destruction in the event of discontinuation
- Determine an “adequate drug trial” appropriate for your patient

ADD/ADHD Medications

- Overall, medications haven’t changed
  - Formulations have multiplied
  - Generic availability has eased ability to access
  - Increased flexibility in dose timing
- Stimulant shortages may pose a barrier to use
  - Potential to work around this with different formulations
- One new medication in 2021 (not in guidelines yet)

Methylphenidate & Derivatives

Amphetamine & Derivatives

OR

Atomoxetine

Viloxazone

+/-

Guanfacine ER

Clonidine ER

Methylphenidate

- Immediate release
  - Tablets, can all be cut/crushed, added to food
  - Ritalin ®, Methylin ®
- Extended release –
  - Capsules can be poured out onto food, ER tablets cannot
- Liquid and chewable formulations

Methylphenidate Extended Release

- Monophasic: Methylphenidate ER tablets
  - Onset at 90 minutes, duration 3-8 hours
  - Generic
- Biphasic (IR:ER): Metadate CD ® (30:70), Ritalin LA ® (50:50) & Aptensio XR ® (40:60) capsules
  - Generic – Metadate CD ® & Ritalin LA ® (some forms)
- Triphasic: Concerta ® tablets & Adhansia XR ® capsules
  - Mimics BID-TID dosing (i.e. Concerta ® 18mg dose is the same as 5mg BID-TID; Adhansia XR ® 100mg similar to 20mg BID-TID)
  - Generic - Concerta ®
- Dexmethylphenidate: Focalin ® tablets & Focalin XR ® capsules

Methylphenidate Extended Release

- Quilivant XR ® liquid
  - Brand only – need to reconstitute an entire bottle
- Quilichew ® chewable tablet
  - Generic available
- Daytrana ® Patch
  - Brand only
  - Not widely available or covered – 2 hours until onset, wear up to 9 hours total
- Jornay PM ® capsule
  - Brand only
  - 5% of drug released in first 10 hours

Amphetamine-based drugs

- Mixed Amphetamine Salts
  - Adderall ® IR tablets, Adderall XR ® capsules
- Mixed salts of a single-entity amphetamine
  - Mydayis ® ER capsules
- Amphetamine sulfate
  - Evekeo ® tablets, Evekeo ODT ®, Dynavel XR ® suspension, Adzenys ER ® suspension, Adzenys XR-ODT ®
- Lisdexamfetamine
  - Vyvanse ® capsules
- Dextroamphetamine
  - Dexedrine ® tablets and ER capsules, Dexedrine Spansule ®, Zenzedi ® tablets, ProCentra ® liquid

Mixed Amphetamine Salts (Adderall ® IR and XR)

- Most prescribed agents from this group
- All generic
- Predictable kinetics
- Easy to dose, titrate
- Can pour capsules into food, crush tablets
- Abuse and diversion potential

Lisdexamfetamine (Vyvanse ®)

- Brand name only – manufacturer coupon on website
- Unique mechanism of action means it has LOW abuse potential
  - Absorbed through GI tract into blood
  - Enzyme in blood cleaves Lysine and releases dextroamphetamine throughout the day
  - May pour capsule into food

Dextroamphetamine

- Many generic forms available
- Dextro isomer only
- May be better tolerated in some patients
- Same abuse and diversion potential as Adderall* formulations

*Adderall is the brand name recognized by those looking to abuse stimulants and can refer to several different amphetamine-derived substances

Atomoxetine (Strattera ®)

- Generic, cost is quickly decreasing
- Alternative to stimulants, especially if concerns for abuse
- Delayed onset of action
- CANNOT open capsule – ocular irritation
  - Small capsules anyway
- Sometimes better tolerated than stimulants
- Dosing – 0.5mg/kg/day to 1.2mg/kg/day if <70kg, otherwise start at 40mg
  - 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg

Viloxazine (Qelbree ®)

- Brand name only – manufacturer coupon on website
- Newest ADHD agent
- Similar place in therapy as atomoxetine
- May sprinkle capsule into applesauce

Clonidine (Kapvay ®)

- Generic available
- Duration of action ~12 hours
- Dosed twice daily
- 0.1mg-0.4mg daily dose

Guanfacine – Intuniv ®

- Generic available
- Duration of action ~18-24 hours
- Dosed once daily
- 1mg-4mg daily dose

Methylphenidate & Derivatives

Amphetamine & Derivatives

OR

Atomoxetine

Viloxazone

+/-

Guanfacine ER

Clonidine ER

Supplements

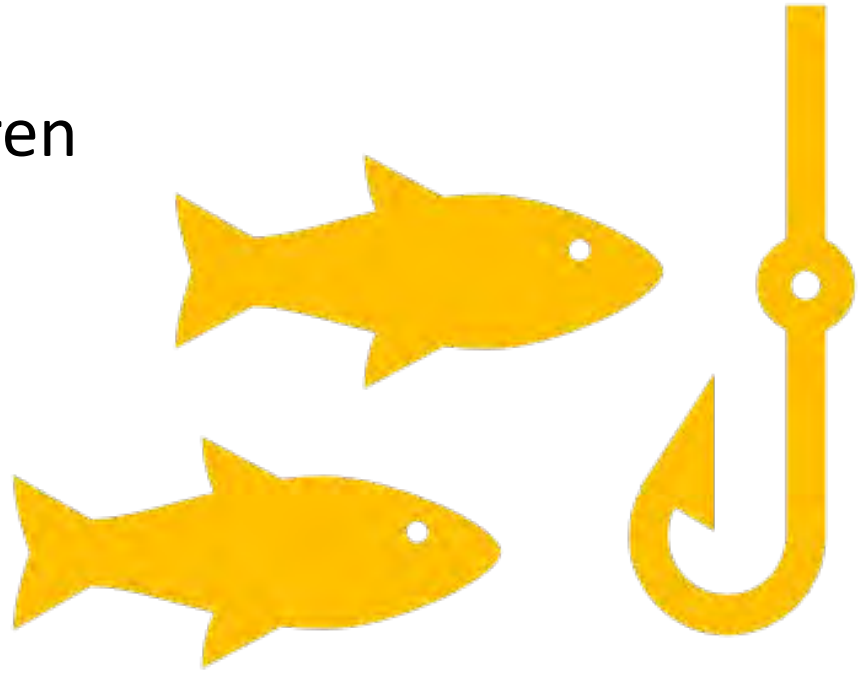
- Diet
- Safety/Risks
- Potency

Vitamin D

- Often difficult to treat in overweight and obese patients – stores in fat
- Low levels correlated with depression, little evidence to suggest that it is a causative agent
- Typically treated to levels above 30ng/ml
- Labeling change from Int Units to mcg
  - 1000 IU = 25mcg
- Daily vs weekly supplementation

Fish Oil

- May have CV benefits, but no known efficacy in psychiatric illness in adults or children
- Potential adjunct for ADHD in children
- 1000-2000mg daily



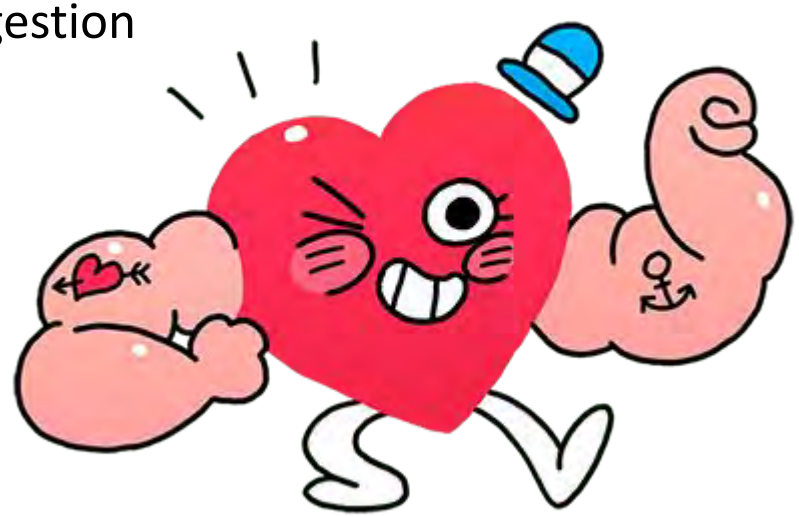
St John’s Wort

- Evidence is modest for depression
- In the guidelines for mild depression for adults
  - Mild depression isn’t treated with medication in pediatrics
- Major drug-drug interactions, including oral contraceptives
- Dosing is 300mg TID

Medical Marijuana

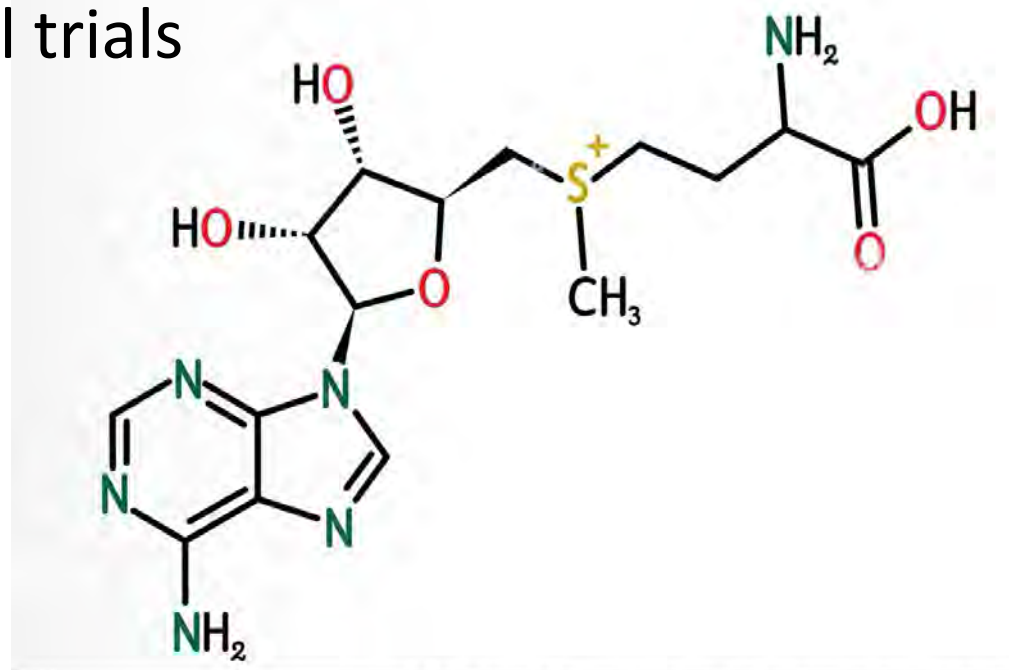
Iron

- May prefer to treat to a higher serum ferritin level due to low iron stores in children with ADHD
- Formulations that may improve adherence
  - Multivitamins with iron – 9-27mg elemental Fe per daily serving
    - Gummies do NOT contain iron
  - Vitron – C ®
    - Carbonyl iron with vitamin C to increase absorption and ease digestion
  - Slow Fe ®
  - Ferrous Gluconate
    - Only 45mg elemental iron
  - Adjunct Miralax ® to combat constipation



SAM-e

- Methyl donor in DA and 5HT synthesis
- Lower concentrations in CSF of those with severe depression
- PO 800-1600mg/day or IM 400mg/day
- No evidence of efficacy in several clinical trials

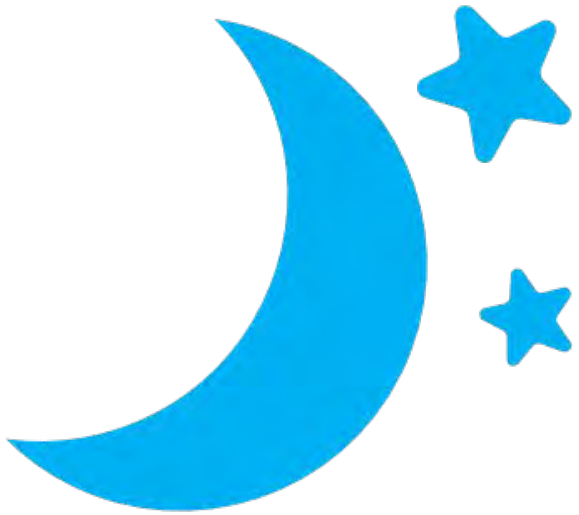


NAC (N-Acetylcysteine)

- Dosed 600-1200mg BID
  - Sulfur smell
- Some evidence in SUD
- Prescribing trend to use for self-harm, but no strong evidence available

Melatonin

- Some evidence
  - 1-3mg recommended
- Very safe, even in OD
- Several formulations available, including ER (Natrol ® brand)



Conclusion

- Guidelines and recommendations have largely stayed the same
- Formulations and practice trends have changed

Questions?

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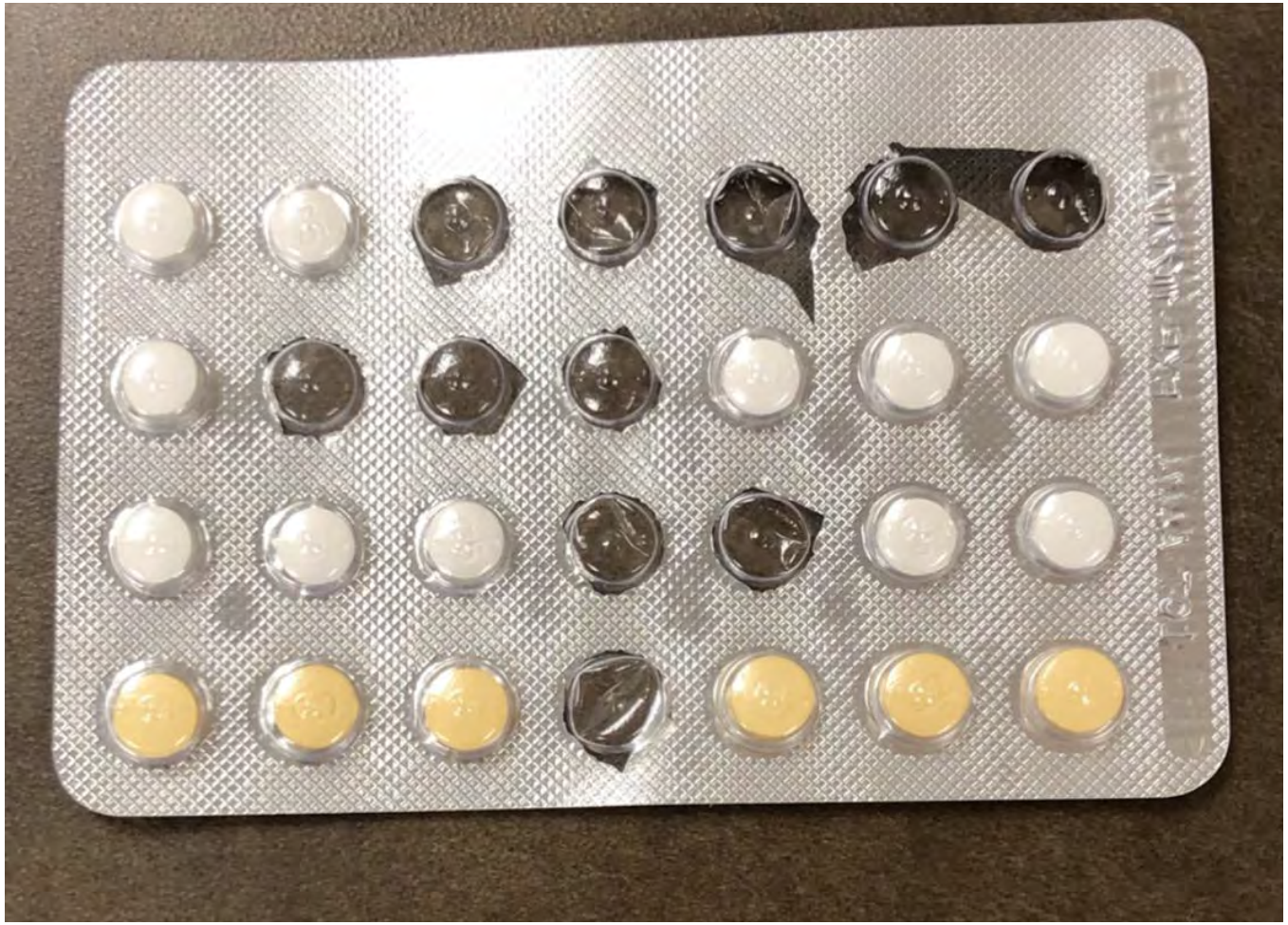
Case Presentation

- AM is a 13yo female diagnosed 2 months ago with depression, moderate, without psychotic features
- Diagnosed with ADHD at 7yo, takes Adderall XR ® 30mg once daily
- On oral contraceptive to regulate irregular periods
- Started with therapy twice weekly, still has bothersome symptoms such as decreased appetite, difficulty sleeping
- Vitamin D levels WNL, thyroid levels normal
- Soccer practice 3x weekly, 30-60 minutes of vigorous exercise
- Yoga for relaxation on weekends
- Counseled on sleep hygiene, recommendations helpful per pt and parents

Case Presentation

- What medication do you start, and how do you titrate it?
- How soon do you increase the dose?
- What if parents wanted a more “natural” approach?

Birth Control Package



One month later…

- Started on fluoxetine 10mg capsules (7 day prescription), then increased to 20mg capsules (30 day supply)
- Finished 10mg capsules, has about half her bottle of 20mg capsules left
- Sleep is somewhat improved but still laying in bed for a couple hours 3-4 nights per week
- Next steps….?

Thank you!

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