A Rational Approach to Psychopharmacology

Disclosure Statement

- Full-time employed physician with MaineGeneral Medical Center in Waterville and Augusta
- No conflicts of interest to disclose

Goals

Promote safe and effective use of medications known to be beneficial

Reduce use of ineffective and inappropriate medications and medication combinations

Objectives

- General principles of treatment planning and use of psychopharmacology in practice
- Treatment strategies for common comorbidities
- Guidelines for use of atypical antipsychotic agents in youth
- Guidelines for pharmacotherapy for treatment of mood disorders in youth

Factors Promoting Pharmacological Use in Children

- Increasing evidence for biological basis of some disorders
- Increasing evidence of efficacy for some medications in childhood disorders
- Increasing advocacy and awareness of mental health disorders in children
- Reductions in funding and reimbursement for mental health care
- Marketing efforts of pharmaceutical companies to consumers

Efficacy and Safety Data for Specific Medications for use in Youth

- ADHD, Tic Disorders
- GAD, OCD, Specific Phobias, Social Phobia
- Major Depressive Disorder
- Aggression, Impulse Dyscontrol
- Irritability associated with Autistic Spectrum Disorders

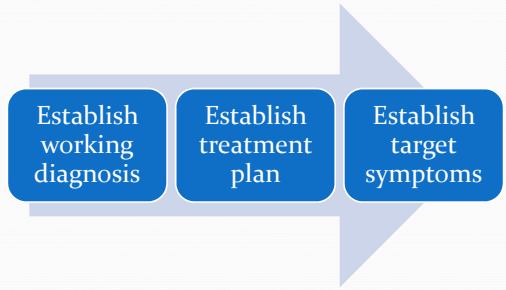
Evaluation: Medical, Psychosocial, Psychiatric

Medical: birth history (exposures), illnesses, surgeries, allergies, current medications, past medication trials, lab data

Psychosocial: ACES, school, family, safety of the environment for prescribing medication

Psychiatric: family mental health history, presenting problems, target symptoms, mental status exam, clinical symptoms, substance use

Pathway to Rational Psychopharmacology in Children

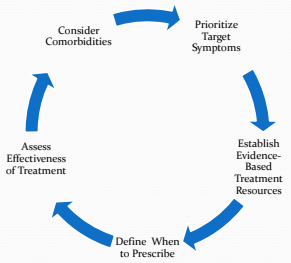


Create an Integrated Team for Assessment and Treatment

Treatment Modalities Based on Evidence

Biopsychosocial Treatment Plan		
Medication prescription and monitoring; developmental therapies	Psychotherapy: individual, parent guidance; resources for parent mental health	Family supports , transportation, extracurriculars, attention to safety of home environment

Plan Strategy Based on Evidence



Case #1

- 10 y.o. boy with ADHD, Combined Type referred to primary care provider for medication upon suggestion of the school psychologist.
- Medical history is unremarkable. Child is small in stature; height and weight are proportionate. No cardiac history; no family history of fatal arrhythmias. On exam, you notice bouts of eye-blinking; family is not concerned (dad has "habits," too)
- No past medication trials. Mother reports occasional use of Melatonin (1 mg.) with good effect.

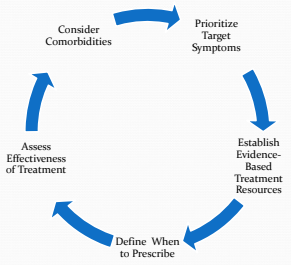
Case #1

- Father recognizes that he likely had ADHD, never treated; had trouble finishing high school.
- Family is intact. Both parents employed. Extended family supportive. Teachers concerned and supportive.
- No trauma history. Family supports extracurricular activities. Child was not chosen for baseball team this year because of his distractibility.

Case #1

- No current substance abuse in the family. Father is active in recovery. He was charged with OUI before child was born; attended AA and established recovery.
- Child has no history of mental health treatment. Behavior is generally manageable at home. At school, he is often distracted, and distracts others, especially in unstructured activities. No aggression. Attentional dysregulation is affecting academic achievement.

Plan Strategy Based on Evidence



Treatment Guidelines and Resources

American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameters

- www.aacap.org

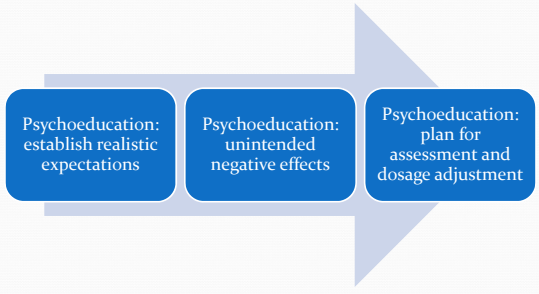
Texas Medication Algorithm Project

- http://www.dshs.state.tx.us/mhprograms/TMAPover.shtm

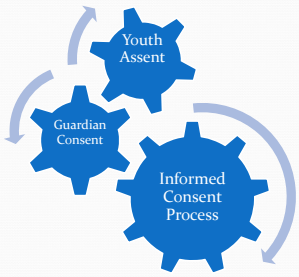
Basic Guideline for Prescribing Psychopharmacology in Youth

- Establish working diagnosis and consider pharmacology accordingly
- Establish target symptoms and realistic expectations for pharmacological effect
- Start low and go slow with dosing
- Establish assessment resources
- Choose medication based on clinical evidence, *NOT* on hypotheses about neurotransmitter effects or SPECT results

Safe and Effective Use of Psychopharmacology in Youth



Informed Consent Process



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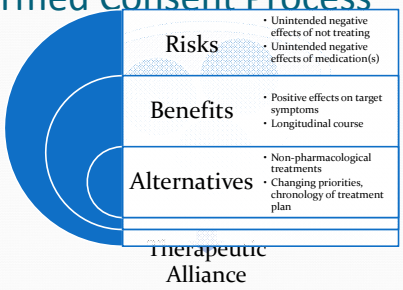


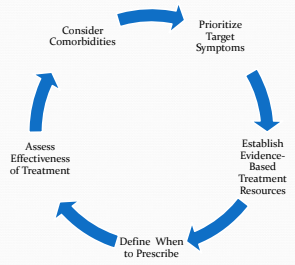
Discontinuation of Medications

- Gather history regarding medication choice and effects
- Establish "safety net" team of providers and observers
- Psychoeducation: what to expect, unintended negative effects
- Taper *SLOWLY*; observe *frequently*

Treatment of Common Comorbidities

ADHD	Tics	OCD
• Psychostimulants • Alpha Agonists • Buproprion, atomoxetine	• Alpha Agonists • Antipsychotics	• Cognitive Behavioral Therapy • SSRI's

Plan Strategy Based on Evidence



Polypharmacy vs. Rational Co-pharmacy

Polypharmacy

- *Polypharmacy* refers to the process of adding on multiple medications, often within the same class, usually with no added benefit, and cumulative risk of additive negative effects or unintended interactions

Rational Co-pharmacy

- *Rational co-pharmacy* refers to medication combinations to treat comorbid disorders, or combinations of medications that offer unique treatment advantages for a single disorder

Polypharmacy vs. Rational Co-pharmacy

Polypharmacy

- Prescription of two antipsychotic medications, two SSRI antidepressant medications, or two long-acting psychostimulant medications, simultaneously

Rational Co-Pharmacy

- Prescription of long-acting psychostimulant with short-acting formulation to optimize dosing; or combination of psychostimulant and alpha agonist to treat comorbid ADHD and tics; or combination of stimulant and SSRI to treat ADHD and OCD

Guidelines for Rational Co-Pharmacy

- ✓ Clearly identify target symptoms for each medication prescribed
- ✓ Consider pharmacokinetic and pharmacodynamic interactions
- ✓ Consider non-pharmacologic treatment modalities to enhance outcomes
- ✓ Combinations may allow for lower doses of each respective agent

Guidelines for Rational Co-Pharmacy

- ✓ Use combination pharmacotherapy only as long as clinically indicated and useful
- ✓ Introduction of a medication with a more favorable side effect profile may allow for discontinuation of less favorable agent (for example, alpha agonist may replace need for antipsychotic)
- ✓ *ALWAYS* start low and go slow

Atypical Antipsychotic Medications

Indications and Guidelines for Safe Monitoring

History and Overview

- "Atypical" refers to significantly lower propensity to cause Extra Pyramidal Symptoms as compared with older "typical" antipsychotic medications
- Agents differ with respect to degree of D2 and other receptor binding
- Unintended negative effects ("side effects") are related to effects on receptors (dopaminergic, serotonergic, noradrenergic, etc.)
- Though developed to treat psychosis in adults, most common pediatric use is for aggression

FDA Approved Uses for AAGs in Youth

- Irritability associated with Autistic Disorder
  - Risperdal: ages 5-16
  - Aripiprazole: ages 6-17
- Schizophrenia
  - Risperdal, aripiprazole, olanzapine, quetiapine: ages 13-17
- Mixed/Manic Episodes of Bipolar I Disorder
  - Risperdal, aripiprazole, olanzapine, quetiapine: ages 10-17

Risperidone (Risperdal)

- Best methodologically stringent evidence for use in children and adolescents
- Randomized, multisite, double-blind trial of Risperidone compared to placebo for youth (ages 5-17) with autism completed and published in NEJM August 2002
- Risperidone was effective and well tolerated for target symptoms of tantrums, aggression, self-injurious behavior in youth with Autistic Disorder

Risperidone (Risperdal)

- Risperidone group was associated with unintended negative effects of weight gain, fatigue, drowsiness, dizziness, drooling
- Other clinical indications:
  - Impulsive/reactive aggression
  - Tics
  - Severe mood reactivity
  - Refractory OCD

AAG Use in Youth (limited studies)

Quetiapine	Ziprasidone	Aripiprazole
• Psychosis in bipolar mania, schizophrenia • Aggression, tics	• Tourette's Syndrome • Bipolar mania	• Irritability in Autistic Disorder • Mania • Aggression

AAG Safety Concerns

- Weight gain, hyperlipidemia, diabetes
- Prolonged QTc, orthostatic hypotension, tachycardia
- Agranulocytosis and neutropenia; hepatic dysfunction
- Hyperprolactinemia
- EPS, tardive dyskinesia, withdrawal dyskinesias, neuroleptic malignant syndrome

AAG Monitoring in Youth

History

- Family history of diabetes, hyperlipidemia, seizures, cardiac abnormalities
- Personal or family history of AAG use

Monitoring parameters

- Vital signs, BMI, glucose, lipids, hepatic functioning, CBC
- Abnormal Involuntary Movement Scale (AIMS), waist circumference

ADA Screening Guidelines for Patients on AAG's

Baseline

- Weight, BMI, waist circumference, blood pressure
- Personal & family history
- Fasting glucose, lipid profile

Quarterly

- BMI (also at 4 & 8 wks. after initiation), BP
- Fasting glucose, lipid profile

Annually

- Waist circumference, BP, fasting glucose
- Update personal & family history
- AIMS q 6 months

AAG Prescribing for Youth

- *ALWAYS* start low, go slow
- Aim to achieve the lowest effective dose
- Strive to limit the duration of administration by engaging other resources or considering alternative pharmacotherapy
- *Do the benefits outweigh the risks?*

Antidepressant Pharmacotherapy in Youth

- SSRI's best studied and tolerated; sound evidence for treatment of depression in youth with fluoxetine
- No evidence in RCT's for effectiveness of venlafaxine, mirtazapine
- Small open-label studies suggest effectiveness of buproprion in adolescent MDD with and without comorbid ADHD.
- RCT's and meta-analysis do not support effectiveness of TCA's in child and adolescent depression
- High placebo response rates (30-60%) in youth

Unintended Negative Effects of SSRI's in Youth

- Relatively common: GI disturbance, insomnia, vivid dreams, headaches, diaphoresis, akathisia, changes in appetite, sexual dysfunction
- 3-8% of children experience increased impulsivity, agitation, irritability, silliness, behavioral activation

Antidepressant Pharmacotherapy and Suicidality in youth

Summary:

- ✓ Spontaneously reported suicidal ideation is more common in youth treated with anti-depressant medications
- ✓ There is a positive relationship between antidepressant (SSRI) use and decrease in the adolescent suicide rate
- ✓ Meta-analyses indicate nearly 11 times more depressed patients respond favorably than may spontaneously report suicidality

Antidepressant Pharmacotherapy and Suicidality in Youth

Summary:

- ✓ Risk to benefit ratio for SSRI use in pediatric depression supports pharmacotherapy with careful monitoring
- ✓ Psychoeducation with parent and youth about this issue: plan for communication and assess viability of the plan
- ✓ Communicate regularly with therapist about suicide assessment, level of risk, crisis plan

Pharmacotherapy for Mood Disorders in Youth

- ➢ *Start low, go slow*
- ➢ Initial goal should be remission of symptoms at 12 weeks
- ➢ FDA Monitoring guidelines: every week for the first 4 weeks; biweekly thereafter
- ➢ Continue treatment for 12 months once response is achieved. Monitor carefully during period of slow taper to avoid relapse

Pharmacotherapy of Mood Disorders in Youth

- Lithium is the only agent with FDA approval for treatment of Bipolar Disorder in youth age 12 and older (based on adult literature)
- Pharmacotherapy of Biplolar I Disorder is extrapolated from adult data
- Careful diagnosis is essential; pharmacotherapy is more safe and benefits more likely to outweigh risks in older adolescents

FDA Approved Pharmacotherapy for Bipolar Disorder in Adults

- Lithium approved for youth 12 and older for acute mania and maintenance therapy
- Aripiprazole, valproate, olanzapine, risperidone, quetiapine, ziprasidone approved for acute mania in adults
- Lamotrigine and olanzapine approved for maintenance therapy in adults
- Olanzapine + fluoxetine approved for bipolar depression in adults

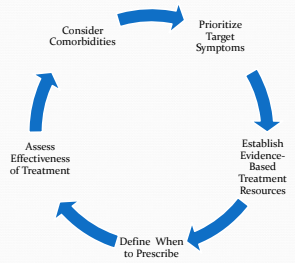
Case #2

- 10 yr. old boy with history of early childhood trauma, presents with episodes of explosive aggression. Family history is significant for completed suicide, schizophrenia, bipolar disorder, PTSD.
- Mental status exam reveals perseverative thought processes, feelings of hopelessness, intermittent suicidal ideation with no plan or intent, high psychomotor activity level, impulsivity, intermittent bouts of eye-blinking tics

Case #2, cont.

- Review of psychological testing reveals significant cognitive strengths and weaknesses. Full-scale IQ is within borderline range of intellectual abilities. Child is below grade level academically; on behavior plan at school
- Child is now in a stable foster family, who is in the process of pursuing adoption

Plan Strategy Based on Evidence



Rational Co-Pharmacy, Case #2

Fluoxetine	• Depression, suicidal ideation • Perseverative thought processes
Guanfacine	• Impulsivity, hyperactivity • Involuntary movements
Risperidone	• Aggression/agitation • Irritability/mood reactivity

Sources

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