Children's Hospital of Wisconsin
MEDICAL COLLEGE OF WISCONSIN
Children's Specialty Group

Child & Adolescent Psychiatry and Behavioral Medicine Center

Basic Principles in the Pharmacologic Management of ADHD

Overview

- Therapy may be indicated in ADHD to address organizational skills deficits or oppositional behavior. Nonetheless, medication is a first line treatment for ADHD. It is appropriate to start with either of the two stimulant classes (methylphenidate or amphetamine) or with atomoxetine. Stimulants have been shown to be effective more often than atomoxetine. The decision regarding which medication to start and when to start will need to be made as part of an informed consent discussion with the patient and parent/guardian.
- A routine physical exam, including blood pressure, pulse, height and weight, should be performed prior to initiating stimulants. Vital signs should then be checked at each visit for potential tachycardia or hypertension. Obtaining a lead level should be considered for exposed children, but is not part of routine assessment.
- If the child doesn't respond to the first stimulant tried (at maximum dosage) or has prohibitive side effects, try using another stimulant type or another medication class.
- "Rebound" in symptoms of ADHD is common in the late afternoon as the stimulant wears off, even with the sustained-release formulations. An immediate release dose may be given late in the afternoon to help avoid this phenomenon. Watch for sleep disturbances when the stimulants are given later in the day.
- The American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameters for ADHD (http://www.aacap.org/galleries/PracticeParameters/JAACAP_ADHD_2007.pdf) note the following contraindications to the use of stimulants: glaucoma, symptomatic cardiovascular disease, hyperthyroidism, hypertension, active psychosis, and concomitant use of an MAO-I (monoamine oxidase inhibitor). Caution should be exercised when there is a history of substance abuse in the home. In this case Atomoxetine or Vyvanse might be considered. Baseline EKG's are not recommended for otherwise healthy individuals (see N.B. "2)" below).
- The Food and Drug Administration has added other contraindications including motor tics, severe anxiety, and a family history or diagnosis of Tourette's Disorder, although these are relative contraindications and these conditions may not be worsened by stimulants. In the presence of seizure disorder, it is best to initiate stimulant treatment following adequate seizure control with anticonvulsants.
- Consider referring to a child psychiatrist if two adequate trials of stimulants or Strattera have failed.

Treatment

METHYLPHENIDATE

- For immediate release methylphenidate (e.g., Ritalin, etc.), begin with 2.5 mg (<6 y.o.) or 5 mg (>6 y.o.) twice daily (about 4 hours apart). Reassess for effectiveness and side effects (in person or by phone, as appropriate) every 1-2 weeks. If symptoms remain, continue to increase methylphenidate by 2.5-5 mg twice daily every 1-2 weeks until symptoms have resolved and impairment has been diminished. Maximum recommended dose is 1.5 mg/kg/d, up to 60 mg/day. Usually a longer duration of action is preferable; therefore it is common to add a third dose after school to help with homework and social activities. Alternately, start with or change to a sustained release formulation (Concerta, Metadate CD, Metadate ER, Methylin ER, or Ritalin LA). Ritalin LA and Metadate CD can be sprinkled. Focalin is the d-enantiomer of methylphenidate and requires half the dose up to a recommended maximum of 20mg/day. Focalin XR can be sprinkled.

- The Daytrana patch is a formulation for methylphenidate. The starting dose is generally 1/3 to ½ of the oral methylphenidate dose (maximum dose 30mg/patch/day). Allow 15 hours before the next application. The patch should be applied to the hip at least two hours before the desired effect. Be sure to alternate hips with each new application and avoid the waistline. The patch can be worn up to 9 hours. Once removed it will continue to have effects for about three hours. Keep in mind that it needs to be worn at least 4 hours to get the additional three hours of efficacy after removal. The benefit to this preparation is the flexibility of the wear time. Watch for the possible side effect of allergic contact dermatitis. This should be suspected if erythema accompanied by edema, papules and/or vesicles appear and spread beyond the patch site. Irritant contact dermatitis, primarily seen as erythema, tends to dissipate quickly and is generally not a concern.

AMPHETAMINE

- For mixed salts of amphetamine (Adderall), start at 2.5 mg (3-6 y.o.) or 5 mg (>6 y.o.) in the morning. Reassess every 1-2 weeks for effectiveness and side effects. Increase the dose in 2.5-5 mg intervals every 1-2 weeks until symptoms resolve, or to a maximum recommended dose of 1mg/kg or up to 40 mg/day. Increasing the dose of Adderall prolongs its duration of action. In addition, a second dose (4-6 hours after initial dose) or switching to Adderall XR (which can be sprinkled) can achieve a longer duration of action.
- For dextroamphetamine (Dexedrine), start with 2.5 mg daily (3-6 y.o.) and 5 mg daily to twice daily (> 6 y.o.), given 4-5 hours apart. Reassess every 1-2 weeks for effectiveness and side effects. Increase the dose in 2.5-5 mg intervals until symptoms resolve. The maximum recommended dose is 1 mg/kg/day, up to 40mg daily. If a longer duration of action is needed, a third dose (half of the amount of the earlier doses) can be given. Alternately, change to Dexedrine Spansules.
- Vyvanse is a prodrug of dextroamphetamine and is an option if diversion is a concern. It is a therapeutically inactive molecule until after ingestion. Vyvanse is converted to l-lysine and active d-amphetamine. It is still a scheduled medication and therefore one cannot write refills on the prescription. For pediatric patients starting treatment or switching from another medication the recommended dose is 30 mg once daily in the morning. At weekly intervals the dose may be titrated in 20 mg increments to a maximum recommended dose of 70 mg per day.

OTHER

- Atomoxetine (Strattera) may be used as either first or second choice in the treatment of ADHD. Strattera would be a good choice to use first line in children with a history of stimulant or substance abuse, where there is a high potential for diversion, when control of symptoms in the evening is crucial, when anxiety or depression is co-morbid, or when requested by the patient/parents. Start at 0.5 mg/kg/d or lower, titrating up in increments every 2 weeks (while assessing for effectiveness and side effects) to a maximum recommended dose of 1.4 mg/kg/d. The FDA black box warning regarding suicidal ideation with antidepressants is also applicable to Strattera as noted (N.B."3)") below.

- Bupropion (Wellbutrin) is useful in co-morbid ADHD and depression when depression is primary. Start with 37.5 – 50 mg bid of immediate release or 100mg qAM of SR titrating up by 50mg per month as tolerated. Maximum is 6mg/kg/day up to 300mg/day (SR) or 300mg/day (XL or regular). Use with seizure disorder or eating disorders is contraindicated. The FDA black box warning regarding suicidal ideation with antidepressants is applicable as noted below.

- Long acting α_2-agonists (Intuniv and Kapvay) have recently gained FDA-approval for use in ADHD. All forms of α_2-agonists (clonidine, guanfacine) can be helpful in treating hyperactive/impulsive symptoms or (after initiation of stimulants) to treat tics, aggression, or sleep difficulties. α_2-agonists are contraindicated if there is a history in the patient or first degree relatives of sudden death, repeated fainting episodes, or arrhythmia. The AACAP does not recommend a baseline EKG in otherwise healthy individuals. They must be tapered slowly when discontinuing due to the risk of rebound hypertension.
    - Clonidine (Catapres): Start with 0.05mg (1/2 tablet) bid (only qhs if treating sleep difficulties) and watch carefully for sleepiness or hypotension. Titrate slowly as needed to a maximum of the lesser of 0.01mg/kg/day or 0.4mg/day (or single dose maximum of 0.2mg).
    - Kapvay: Dosing should be initiated with one 0.1 mg tablet at bedtime, and the daily dosage should be adjusted in increments of 0.1 mg/day at weekly intervals until the desired response is achieved. Doses should be taken twice a day, with either an equal or higher split dosage being given at bedtime.
    - Guanfacine (Tenex): Start with 0.5mg at night and titrate by 0.5mg in bid dosing to a maximum of the lesser of 0.1mg/kg or 4 mg.
    - Intuniv: Dose once daily. Tablets should not be crushed, chewed or broken before swallowing. Do not administer with high-fat meals, because of increased exposure. Do not substitute for immediate-release guanfacine, because of differing pharmacokinetics. If switching from immediate-release guanfacine, discontinue that treatment and begin at a dose of 1 mg once daily and adjust in increments of no more than 1mg/week. Maintain the dose within the range of 1 mg to 4 mg per day, depending on clinical response and tolerability. When discontinuing, taper the dose in decrements of no more than 1 mg every 3 to7 days.

NB:

1) Clonidine or Melatonin may be helpful in treating sleep difficulties related to stimulant use.

2) The FDA issued a black box warning regarding the risk of sudden death on stimulants. The rate of sudden death in children on stimulants does not exceed the rate in the general population. There is no evidence to suggest the need for pre-treatment cardiac evaluation (such as EKG) in otherwise healthy individuals. Cardiac evaluation should be undertaken for children with a history of cardiac disease and those with symptoms suggestive of significant cardiac disease or if there is a family history of cardiac disease including but not limited to sudden cardiac death before the age of 50 years old, cardiomyopathy, arrhythmias or tachycardia.

   This recommendation is based on the most recent AACAP Practice Parameter which states:
   "This would include a history of severe palpitations, fainting, exercise intolerance not accounted for by obesity, or strong family history of sudden death. Postoperative tetralogy of Fallot, coronary artery abnormalities, and subaortic stenosis are known cardiac problems that require special considerations in using stimulants. Chest pain, arrhythmias, hypertension, or syncope may be signs of hypertrophic cardiomyopathy, which has been associated with sudden unexpected deaths in children and adolescents. Before a stimulant trial, such patients should be referred for consultation with a cardiologist for possible electrocardiography and/or echocardiography. If stimulants are initiated, then the patient should also be studied by the cardiologists during the course of treatment."

3) Selective Serotonin Reuptake Inhibitors (SSRI), Bupropion, and Atomoxetine (in cases of comorbid ADHD) are important medications in the treatment of pediatric depression and can be used safely. They do, however, require close supervision in the initial stages of treatment and at subsequent dosage alterations. The current recommendation by both the FDA and the American Academy of Child and Adolescent Psychiatry is that the patient *ideally* be monitored weekly for the first month (phone contact is okay), bi-weekly for the next month, and monthly thereafter. The FDA placed a "black box" warning on all antidepressants in October 2004 due to evidence of increased suicidal thinking in children and adolescents prescribed these medications. This was based on review of FDA clinical trials involving 4300 youth who received any of the currently available antidepressants. Analysis of the studies revealed a 4% risk of suicidal thinking for children on medication compared with 2% of those taking a placebo. A subsequent meta-analysis funded by the NIMH found a 3% risk of suicidal thinking for children on medication for depression compared with 2% of those taking placebo. ***No completed suicides occurred in any of these studies*.** For more information, please refer to www.parentsmedguide.org.

Revised 5/27/11

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ADHD Medication Information

Active ingredient	Medication Brand Name	Dosing	Duration of effect
Mixed salts of amphetamine	Adderall* tablets (scored): 5, 7.5, 10, 12.5, 15, 20, 30 mg	Start with 2.5 (3 - 5yo) - 5 mg 1-2 times per day and increase by 5 mg every 1-2 weeks until good control is achieved. MAX dose: lower of 1mg/kg/day or 40 mg/day	4-8 hours depending on dose
	Adderall XR capsule (can be sprinkled): 5, 10, 15, 20, 25, 30 mg	Start 5-10 mg in AM and increase by 5-10 mg every 1-2 weeks until good control is achieved. Conversion: total daily dose of Adderall = am dose of Adderall XR. MAX dose: lower of 1mg/kg/day or 40 mg/day	8-12 hours
Dextroamphetamine	Dexedrine* tablet: 5, 10 mg	Start with 5 mg 1-2 times per day and increase by 5 mg each week until good control is achieved. MAX dose: lower of 1mg/kg/day or 40 mg/day	Tablet: 4-5 hours
	Dexedrine Spansules* (can be sprinkled): 5, 10, 15 mg	Start at 5 mg in am and increase by 5 mg every 1-2 weeks until good control is achieved. MAX dose: lower of 1mg/kg/day or 45 mg/day	4-8 hours
	Vyvanse (can be dissolved in water): 20, 30, 40, 50, 60, 70mg	Start at 30mg in am and increase by 20mg every week until good control is achieved. MAX dose: 70mg/day (Bound to lysine to decrease abuse potential)	8-12 hours
Methylphenidate	Concerta capsule (noncrushable): 18, 27, 36, 54 mg	Capsule cannot be split, so best to titrate with regular methlyphenidate and then switch to Concerta. Start at 18 mg in the a.m. and increase every 1-2 weeks until good control is achieved. Conversions: Ritalin 5 mg tid = Concerta 18 mg, Ritalin 10 mg tid = Concerta 36 mg, Ritalin 15 mg tid = Concerta 54 mg. MAX dose: lower of 1.5mg/kg/day or 54 mg/day (child), 72 mg/day (adolescent)	8-12 hours
	Focalin tablets (scored): 2.5, 5, 10 mg	Start with 2.5 mg 1-2 times per day and increase by 2.5 mg every 1-2 weeks until good control achieved. May need 3rd reduced dose in PM. Conversion: half of total Ritalin daily dose = total Focalin daily dose. MAX dose: lower of 0.8mg/kg/day or 20 mg/day	3-4 hours
	Focalin XR (can be sprinkled): 5, 10, 15, 20, 30, 40 mg extended release	Start 5 mg in the am and increase dose by 5 mg every 1-2 weeks. Conversions: total daily dose of Focalin = dose of Focalin XR in AM.; half of total Ritalin dose = Focalin XR dose in am. MAX dose: lower of 0.8mg/kg/day or 20 mg/day	8-12 hours
	Metadate ER tablets: 10, 20 mg extended release	Start at 10 mg in the am and increase by 10mg every 1-2 weeks until good control is achieved. May need second Metadate ER dose or Ritalin dose in PM. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	4-8 hours
	Metadate CD capsule (may be sprinkled): 10, 20, 30 mg extended release	Start at 20 mg in the am and increase by 10-20 mg every 1-2 weeks until good control is achieved. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	8-12 hours
	Methylin tablets (scored): 5, 10, 20; chewable 2.5, 5, 10; 5 mg/5 ml, 10 mg/5 ml solution	Start with 5 mg twice daily and increase by 5 mg every 1-2 weeks until good control is achieved. May need 3rd reduced dose in PM. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	3-4 hours
	Methylin ER tablet: 10, 20 mg extended release	Start at 10 mg in the am and increase by 10 mg every 1-2 weeks until good control is achieved. May need a dose of Ritalin in PM. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	4-8 hours
	Ritalin* tablets (scored): 5, 10, 20 mg	Start with 5 mg twice daily and increase by 5 mg every 1-2 weeks until good control is achieved. May need 3rd reduced dose in PM. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	3-4 hours
	Ritalin* SR tablet: 20 mg	Start at 20 mg in the am and increase by 20 mg every 1-2 weeks until good control is achieved. May need second dose of SR or Ritalin in PM. Conversions: total daily dose of Ritalin = AM dose of Ritalin SR. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	4-8 hours
	Ritalin LA capsule (can be sprinkled): 10, 20, 30, 40 mg	Capsule cannot be split, so best to titrate with regular methlyphenidate and then switch to Ritalin LA. Conversions: total daily dose of Ritalin = AM dose of Ritalin LA. MAX dose: lower of 1.5mg/kg/day or 60 mg/day	8-12 hours
	Daytrana patch (worn on hip for 9 hours) 10mg,15mg, 20mg, 30mg	Apply the patch to a clean, dry area of the hip (avoid waistline) 2 hours before an effect is needed. Increase by 5-10mg every 1-2 weeks until good control achieved. MAX dose: 30mg/day. DO NOT apply heat onto patch or apply to inflamed skin. Change to po for rash.	9-12 hours

ADHD Medication Information

Atomoxetine	Strattera capsule: 10, 18, 25, 40, 60 mg	Start 10mg in the a.m.; titrate up every 2 weeks until good control is achieved. qD or bid. MAX dose: 1.4 mg/kg/day, up to 80mg/day.Useful for comorbid anxiety or depression and ADHD.***FDA Black Box warning re suicidal ideation is applicable.***	24 hours
Bupropion	Wellbutrin SR: 100, 150	Not for young children. Start at 100mg 1/2 tab qAM for 4 - 6 days (not scored), then 1 tab qAM. Titrate up by 50mg/day each month until desired effect. MAX dose: lower of 6mg/kg or 400mg/day. Useful for comorbid depression and ADHD. Contraindicated with history of seizures or eating disorder.***FDA Black Box warning regarding suicidal ideation is applicable.***	24 hours
Alpha 2 agonist	Clonidine 0.1, 0.2 mg Kapvay 0.1mg, 0.2mg	Clonidine: Start 0.05mg qhs to address sleep difficulties, 0.05 bid for tics, impulsivity or aggression and increase by 0.05mg/dose every 4 weeks until good control is achieved. Watch carefully for sleepiness or hypotension. Titrate slowly as needed to a maximum of the lesser of 0.01mg/kg/day or 0.4mg/day (or single dose maximum of 0.2mg). Kapvay: start one 0.1 mg tablet at bedtime, and the daily dosage should be adjusted in increments of 0.1 mg/day at weekly intervals until the desired response is achieved. Doses should be taken twice a day, with either an equal or higher split dosage being given at bedtime. ***α2-agonists are contraindicated if there is a history in the patient or first degree relatives of sudden death, repeated fainting episodes, or arrhythmia. AACAP does not recommend a baseline EKG in otherwise healthy individuals. They must be tapered slowly when discontinuing due to the risk of rebound hypertension.***	Clonidine 6-10 hours; Kapvay 12-18 hours
	Guanfacine 1, 2 mg Intuniv 1, 2, 3, 4mg	Guanfacine: Start with 0.5mg at night and titrate by 0.5mg in bid dosing to a maximum of the lesser of 0.1mg/kg or 4 mg. Intuniv: Start with 1 mg once daily and adjust in increments of no more than 1mg/week. Maintain the dose within the range of 1 mg to 4 mg per day, depending on clinical response and tolerability.***α2-agonists are contraindicated if there is a history in the patient or first degree relatives of sudden death, repeated fainting episodes, or arrhythmia. AACAP does not recommend a baseline EKG in otherwise healthy individuals. They must be tapered slowly when discontinuing due to the risk of rebound hypertension.***	Guanfacine 10-18 hours; Intuniv 24 hours

*indicates generic available

Common side effects of stimulants: decreased appetite, symptom rebound, sleep disturbance, nausea, headache (transient), stomachache, tearfulness

Possible strategies to address side effects:

Decreased appetite: dose after meals, frequent snacks, drug holidays, liquid supplements (e.g. Boost, Ensure)

Symptom rebound: try sustained release stimulant, add small dose of short-acting in late afternoon

Sleep disturbance: bedtime routine, reduce afternoon dose, move dosing regimen to earlier time, eliminate caffeine, use medication as a last resort

Irritability or tearfulness (less common): decrease dose, try another medication, consider comorbid conditions

Exacerbation of tics (rare): observe, reduce dose, try another medication

Psychosis/euphoria/mania/severe depression (rare): stop stimulant, refer to mental health specialist

N.B. The FDA issued a black box warning regarding the risk of sudden death on stimulants. The rate of sudden death in children on stimulants does not exceed the rate in the general population. There is no evidence to suggest the need for pre-treatment cardiac evaluation (such as EKG) in otherwise healthy individuals. Cardiac evaluation should be undertaken for children with a history of cardiac disease and those with symptoms suggestive of significant cardiac disease or if there is a family history of cardiac disease including but not limited to sudden cardiac death before the age of 50 years old, cardiomyopathy, arrhythmias or tachycardia. This would include a history of severe palpitations, fainting, exercise intolerance not accounted for by obesity, or strong family history of sudden death. Postoperative tetralogy of Fallot, coronary artery abnormalities, and subaortic stenosis are known cardiac problems that require special considerations in using stimulants. Chest pain, arrhythmias, hypertension, or syncope may be signs of hypertrophic cardiomyopathy, which has been associated with sudden unexpected deaths in children and adolescents. Before a stimulant trial, such patients should be referred for consultation with a cardiologist for possible electrocardiography and/or echocardiography. If stimulants are initiated, then the patient should also be studied by the cardiologist during the course of treatment.

(Revised 05/27/11)

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Basic Principles in the Pharmacologic Management of Pediatric Anxiety Disorders

Overview

- The basic anxiety maintenance cycle in all the anxiety disorders involves exposure to an anxiety trigger, anxiety rising to high levels, and some kind of escape behavior that produces immediate relief of anxiety. The relief is so rewarding that the escape behavior becomes habitual.
- In general, Cognitive-Behavioral Therapy (CBT) should be initiated first line for mild to moderate anxiety disorders, with medications used in conjunction with CBT for more severe or refractory cases of anxiety disorder.
- Most medications are not approved specifically by the FDA for the treatment of anxiety disorders in children and adolescents. However, certain medications have been shown to be helpful in pediatric populations. For example, some of the SSRIs (Selective Serotonin Reuptake Inhibitors) have been approved for school-aged children: fluvoxamine (8+ years), fluoxetine (7+ years), and sertraline (6+ years).
- SSRIs are important medications in the treatment of pediatric anxiety and can be used safely. They do, however, require close supervision in the initial stages of treatment and at subsequent dosage alterations. The current recommendation by both the FDA and the American Academy of Child and Adolescent Psychiatry is that the patient *ideally* be monitored weekly for the first month (phone contact is okay), bi-weekly for the next month, and monthly thereafter.
- The FDA placed a "black box" warning on all SSRIs in October 2004 due to evidence of increased suicidal thinking in children and adolescents prescribed these medications. This was based on review of FDA clinical trials involving 4300 youth who received any of the currently available antidepressants. Analysis of the studies revealed a 4% risk of suicidal thinking for children on medication compared with 2% of those taking a placebo. A subsequent meta-analysis funded by the NIMH found a 1% risk of suicidal thinking for children on medication for non-OCD anxiety disorders compared with 0.2% of those taking placebo. ***No suicides occurred in any of these studies.*** For more information, please refer to www.parentsmedguide.org.

Treatment

- The Selective Serotonin Reuptake Inhibitor (SSRI) class of medications is considered first line pharmacotherapy for pediatric anxiety disorders. SSRI medications in children and in adolescents include fluoxetine (Prozac), sertraline (Zoloft), citalopram (Celexa), escitalopram (Lexapro) and fluvoxamine (Luvox). **Paroxetine (Paxil) and venlafaxine (Effexor) are not recommended for use in children due to increased concerns about suicidality and adverse cardiovascular effects.**
- These medications are generally thought to be equivalent in efficacy for the treatment of anxiety. Dosing strategies for SSRI medications outlined below are general guidelines for use in children and adolescents.
- If the first choice of SSRI is not tolerated or is ineffective, a trial of a different SSRI can be used. An ineffective SSRI trial is defined as no or minimal reduction of symptoms despite adequate dosage for a period of two months, or inability to tolerate SSRI due to side effects. Antidepressants should not be discontinued abruptly, but rather titrated down slowly. Decreasing the dose by 25% each week is a reasonable tapering strategy.

- Common side effects from SSRI medications include increased energy, restlessness, behavioral disinhibition, stomach upset and appetite change. The SSRI medications are metabolized in part via the cytochrome P450 system, and should be administered with caution when used with other medications metabolized through this pathway.
- Buspirone, a serotonin 1A agonist is used as a second line agent for Generalized Anxiety Disorder. Propranolol, a non-selective, centrally and peripherally acting beta-blocker, or Atenolol, a peripherally acting beta-blocker, are used as second line agents for Specific Phobia and performance anxiety.
- Benzodiazepines can be used to treat anxiety during the latent period of antidepressant usage (about the first 4 weeks). However, they should only be used in extreme circumstances as they are prone to cause disinhibition and to impair learning in children and youth.
- A general rule of thumb with these medications is to start low and go slow.
- A relatively symptom free period of 8 to 12 months is considered appropriate treatment duration. At that point, a taper should be considered.
- If the patient fails both CBT and pharmacotherapy trials with utilizing two pharmacologic strategies (e.g., two different SSRI trials for Generalized Anxiety Disorder), consider referral to psychiatry.

Pharmacologic Treatment of Specific Anxiety Disorders

Disorder	First Line	Second Line
Separation Anxiety Disorder	SSRI	Another SSRI
Generalized Anxiety Disorder (GAD)	SSRI (Fluvoxamine has demonstrated efficacy in pediatric GAD)	Another SSRI, then Buspirone
Panic Disorder with or without Agoraphobia	SSRI	Another SSRI
Social Phobia	SSRI	Another SSRI, Propranolol or Atenolol
Specific Phobia	SSRI	Another SSRI, Propranolol or Atenolol
Posttraumatic Stress Disorder (PTSD) Acute Stress Disorder	SSRI	Another SSRI
Obsessive Compulsive Disorder (OCD)	SSRI (Sertraline in ages 6-17, Fluoxetine in ages 7 – 17, and Fluvoxamine in ages 8-17 are FDA approved for treatment of pediatric OCD)	

Note: Clonidine or trazadone can be used for sleep difficulties related to PTSD.

(Revised 05/27/11)

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Anti-anxiety Medication Information

Name	Starting Dosage	Maximum Dosage	Possible Side Effects/Cautions
SSRI class: Fluoxetine (Prozac)	Begin at 5 - 10 mg per day and increase by 5- 10 mg at 4 weeks and every month thereafter until clinical response. qD.	Max dose 60 mg/day (10 – 40mg in most diagnoses; 30 – 60mg in OCD).	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome, Stevens-Johnson syndrome, or Toxic Epidermal Necrolysis
Sertraline (Zoloft)	Begin at 12.5 mg for children or 25 mg for adolescents per day and increase by 12.5 mg or 25 mg for either the child or adolescent respectively each month until clinical response. qD or bid.	Max dose 150 mg/day for children and 200 mg per day for adolescents.	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome.
Citalopram (Celexa)	Begin at 5 - 10 mg per day and titrate up by 5 -10 mg each month until clinical response. qD or bid.	Max dose 40 mg/day.	Same as above.
Fluvoxamine	Begin at 25 mg at night and increase by 25 mg each month thereafter until clinical response. Divide the dose if > 50 mg per day. qD or bid.	Max dose 200 mg/day.	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome, Stevens-Johnson syndrome and Toxic Epidermal Necrolysis.
(Lexapro)	Begin at 5 mg per day and titrate up by 5 mg each month until clinical response.	Max dose 20 mg/day.	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome. Can cause QTc prolongation in overdose. Consider baseline EKG.
Buspirone (Buspar)	Begin at 5 mg bid or tid and titrate by 5mg per dose every 2 to 4 weeks until clinical response.	Max dose 60 mg per day.	Common side effects include nausea, diarrhea and headache. Buspirone should not be discontinued abruptly. Decreasing the dose by 25% per week is a reasonable discontinuation strategy.
Propranolol (Inderal)	Begin dose at 0.5-1 mg/kg/day and use 30 minutes prior to performance and/or confrontation with specific phobia. Can be used every 6 to 12 hours.	Max dose 8 mg/kg per day.	Common side effects include fatigue, hypotension, bradycardia and possible bronchospasm. Propranolol is **contraindicated** in asthmatics and relatively contraindicated in diabetics.
Atenolol (Tenormin)	Begin 0.8 – 1 mg/kg/day. Use 30 – 60 minutes prior to performance and/or confrontation with specific phobia. Daily as needed.	Max dose 2mg/kg/day	Common side effects include fatigue, hypotension, bradycardia and possible bronchospasm. Atenolol is **contraindicated** in asthmatics and relatively contraindicated in diabetics.
Clonidine (Catapres)	Begin dose at 0.05 mg at bedtime or bid and titrate up every 2 weeks for continued sleep disturbance.	Max dose 0.2 mg per day.	Common side effects include sedation, dry mouth, constipation and rarely, hypotension. Clonidine should not be discontinued abruptly due to the potential for rebound hypertension. Clonidine should be tapered gradually. Decreasing the dose by 25% per week is a reasonable discontinuation strategy.
Benzodiazepines (see note below): Lorazepam (Ativan - short acting)	Begin dose at 0.25 mg bid and titrate up every week for continued symptoms.	Max dose 3.0 mg per day (1mg tid)	Common side effects include drowsiness, confusion and ataxia. Benzodiazepines should not be used for more than 3-4 weeks in children and adolescents. With prolonged use benzodiazepines carry the risk of dependence. Benzodiazepines should not be discontinued abruptly, but rather, tapered gradually to limit rebound anxiety, potential for seizures, and withdrawal symptoms.
Clonazepam (Klonopin - long acting)	Begin dose at 0.25 mg qd or bid and titrate up weekly for continued symptoms.	Max dose 2.0 mg per day in divided doses.	Same as above.

Note:

1. **Paxil (paroxetine) and Effexor (venlafaxine) are not recommended for use in children due to concern about suicidality and adverse cardiovascular effects.**
2. **Benzodiazepines can be used to treat anxiety during the latent period of antidepressant usage (about the first 4 weeks). However, they should only be used in extreme circumstances as they are prone to cause disinhibition in children and youth.**

(Revised 05/27/11)

Approved by: Robert P. Chayer, MD
Office phone: (414) 266-2932

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Child & Adolescent Psychiatry and Behavioral Medicine Center

Basic Principles in the Pharmacologic Management of Pediatric Depression

Overview

- In general, Cognitive-Behavioral Therapy (CBT) should be initiated first line for mild to moderate depression, with medications used in conjunction with CBT for more severe or refractory cases of depression.
- Selective Serotonin Reuptake Inhibitors (SSRI) are important medications in the treatment of pediatric depression and can be used safely. They do, however, require close supervision in the initial stages of treatment and at subsequent dosage alterations. The current recommendation by both the FDA and the American Academy of Child and Adolescent Psychiatry is that the patient *ideally* be monitored weekly for the first month (phone contact is okay), bi-weekly for the next month, and monthly thereafter.
- The FDA placed a "black box" warning on all antidepressants in October 2004 due to evidence of increased suicidal thinking in children and adolescents prescribed these medications. This was based on review of FDA clinical trials involving 4300 youth who received any of the currently available antidepressants. Analysis of the studies revealed a 4% risk of suicidal thinking for children on medication compared with 2% of those taking a placebo. A subsequent meta-analysis funded by the NIMH found a 3% risk of suicidal thinking for children on medication for depression compared with 2% of those taking placebo. ***No suicides occurred in any of these studies*****.** For more information, please refer to www.parentsmedguide.org.
- All SSRI-class medications have been shown to be roughly equivalent in terms of symptom improvement, though they differ on side effect profile and metabolism.
- Common side effects from SSRI medications include increased energy, restlessness, behavioral disinhibition, stomach upset and appetite change. Starting at a low dose and increasing in small increments every 4 weeks until the desired effect is achieved is key to success with the SSRI's. The SSRI medications are metabolized in part via the cytochrome P450 system, and should be administered with caution when used with other medications metabolized through this pathway.
- Avoid abrupt cessation of medication unless absolutely necessary. Withdrawal symptoms can occur with any of the anti-depressants; however, they are least likely to occur with fluoxetine due to its long half-life. Gradual weaning is recommended unless using fluoxetine.
- The average duration of Major Depressive Disorder is 7-9 months with as many as 50% of youth experiencing a relapse. In general, treatment should continue for at least 6-12 months following remission of symptoms.

Treatment

- **Fluoxetine (Prozac):** Highly consider starting this first. Start with a LOW dose—in very young children 5mg/day (1/2 tab or liquid); adolescents 10mg/day. Increase initially after 4 weeks, then every 2-4 weeks until improvement in clinical symptoms is noticed. Maximum dose for depression is 60mg/day.
- **Sertraline (Zoloft):** A reasonable alternative to fluoxetine. Start with 12.5mg/day for young or anxious children; 25mg/day in adolescents. Increase by 12.5 to 25mg/day initially after 4 weeks, then every 2-4 weeks until clinical improvement is noticed. Maximum dose is 150mg in children; 200mg/day in adolescents.

- **Citalopram (Celexa)**: Citalopram has fewer drug-drug interactions than Prozac and Zoloft. It currently does not have an FDA indication for use in children/adolescents. Start with 5 mg/day. Titrate as with other SSRI medications. Maximum dose is 40 mg/day.
- **Escitalopram (Lexapro):** This medication is the S-enantiomer of citalopram and has, possibly, a more favorable side-effect profile. This medication is especially good if a child is medically ill and drug-drug interactions are a concern. It is FDA approved for depression in adolescents. Start with 5mg/ day. Titrate as with the other SSRI medications. Maximum dose is 20mg/day.
- **Buproprion (Wellbutrin SR or XL):** Buproprion is a good choice with co-morbid ADHD or nicotine or marijuana abuse. It does not currently have an FDA indication for use in children/adolescents. Bupropion is contraindicated in children and adolescents with eating disorders or seizure disorder. Start with 100mg qAM of SR formulation ½ tab for the first 4 – 6 days, then 1 tab qAM and increase as needed by 50mg initially after 4 weeks, then every 2 – 4 weeks until achieving the desired effect. Begin bid dosing at 200mg/day. One can switch to the XL formulation for once a day dosing. Dose limits: lower of 6mg/kg/day or Regular – 150mg/dose, 300mg/day; SR – 200mg/dose, 300mg/day; XL – 300mg/dose and per day.
- **Mirtazapine (Remeron):** Especially good for anxious youth who are having difficulty eating/sleeping. Start with 7.5mg to 15mg QHS and increase as needed. Maximum dose is 30mg/day. Monitor closely for weight gain.
- **Venlafaxine (Effexor) and Paroxetine (Paxil):** In general these medications are not recommended for children or adolescents doe to increased concerns about suicidal ideation and withdrawal symptoms.

(Revised 05/27/11)

Children's Hospital of Wisconsin
Medical College of Wisconsin
Children's Specialty Group

Antidepressant Medication Information

Antidepressant	Tablet/Capsule Strength, Other Formulations	Starting Dosage for Children/Adolescents	Usual Effective Dose/Max dose	Possible Side Effects/ Cautions
First Line: Fluoxetine (Prozac) FDA approved for depression in adolescents	10 & 20mg tabs; 10, 20, 40 mg caps 20mg/5ml solution	5 mg/day for children 10 mg/day for adolescents	20-40 mg/day for depression/anxiety * OCD may require higher doses. Max dose 60mg/day.	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome, Stevens-Johnson syndrome, or Toxic Epidermal Necrolysis
Second Line: Sertraline (Zoloft)	25, 50, 100 mg tabs 20mg/ml solution	12.5 mg/day for children 25 mg/day for adolescents	25-50 mg/day for depression/anxiety *OCD may require higher doses. Max dose 150mg/day in children, 200mg/day for adolescents.	Same as above.
Escitalopram (Lexapro) FDA approved for depression in adolescents	10, 20 mg tabs 5 mg/ml solution	5 mg/day	10-20 mg/day *OCD may require higher doses. Max dose 20mg/day.	Same as above. Can cause QTc prolongation in overdose. Consider baseline EKG.
Citalopram (Celexa)	10, 20, 40 mg tabs 10 mg/5 ml solution	5-10 mg/day	10-40 mg/day. Max dose 40mg/day.	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome.
Third Line: Bupropion SR (Wellbutrin SR)	100 mg, 150, 200 mg (start BID dosing at 200mg/day)	100 mg qAM	100-300 mg/day; Max dose lower of 6mg/kg/day or 200mg/dose, 300mg/day.	Contraindicated in seizure disorder and eating disorder. Monitor for emergence of suicidal thinking, mania. May rarely cause Stevens-Johnson syndrome, or Toxic Epidermal Necrolysis
Bupropion XL (Wellbutrin XL)	300mg tabs in generic; 150, 300 mg tabs in brand.	150 mg qAM	150-300 mg/day; Max dose lower of 6mg/kg/day or 300mg/dose and per day.	Same as above.
Fourth Line: Mirtazepine (Remeron)	15, 30, 45 mg 15, 30, 45 mg soluble tabs	7.5 mg qhs	15-30 mg for children 15-45 mg for adolescents Max dose 30mg in children, 45mg in adolescents	Can cause weight gain and sedation. Monitor for emergence of suicidal thinking, mania. May rarely cause agranulocytosis, Torsades des pointes. Consider baseline EKG.
Fifth Line: Fluvoxamine	25, 50, 100 mg tabs	For children with OCD, 25 mg qhs. May increase by 25 mg after 4 weeks, then every 2 – 4 weeks. Total daily doses above 50 mg should be divided into 2 doses.	100-300 mg. Max dose 300mg/day	Increased energy, restlessness, behavioral disinhibition, stomach upset, and appetite change. Interactions with other p450 2D6 medications. Monitor for emergence of suicidal thinking, mania. May rarely cause serotonin syndrome, Stevens-Johnson syndrome and Toxic Epidermal Necrolysis.

NOTE: Avoid paroxetine (Paxil/Paxil CR™)and venlafaxine (Effexor/Effexor XR™), or MAOIs in children/adolescents. All antidepressant medications carry the black-box warning of an associated increased risk of suicidality in children/adolescents.

(Revised 05/27/11)

Approved by: Robert P. Chayer, MD
Office phone: (414) 266-2932