

Managing the Behavior Problems of Children With Fragile X Syndrome by Using Medication Ave M. Lachiewicz, MD, Duke University Medical Center

Abstract: The majority of boys and many girls with fragile X syndrome are reported to have behavior problems that can be helped by the use of medication. Some of these behavior problems include attention-deficit/hyperactivity disorder, sleep problems, anxiety, and aggression. Some medications are commonly used, and some are reserved for children with severe behavior problems.

This workshop will focus on the commonly used medications including the stimulants (such as Ritalin), the α_2 -adrenergic agonists (such as clonidine), and the selective serotonin reuptake inhibitors (such as Prozac). The indications for these medications will be provided. Dose ranges and side effects will be covered. We will discuss how and why these medications are often used together. Case illustrations will be provided.

Other less commonly used medications will also be discussed such as melatonin and the atypical antipsychotic medications if time permits. Time will be allotted for questions and answers.

Basic concepts

Often children with fragile X present with several behavior problems.

Medication management requires many considerations.

1. figuring which problem to treat first – hyperactivity?, anxiety?
2. choosing the right medication or medications
3. being willing to experiment with several medications if the first one isn't right
4. using medications that are safe and FDA approved
5. using medications that have few side effects or the side effects that are the most tolerable
6. using medications that have few long term side effects
7. using medications that the family approves of
8. using combinations to reduce the risk of side effects since lower doses of drugs can be used.

Psychopharmacology refers to the science and prescription of psychiatric medications. Drugs used for the treatment of psychiatric conditions are called *psychotropic drugs*. They are divided into seven *classes* but many drugs serve many functions.

1. **Stimulants.** Prescribed for ADHD or hyperactivity. Ritalin, Dexedrine, Adderall. Amantadine is related to the stimulants and is also used for hyperactivity in developmentally disabled individuals.
2. **Antidepressants.** These include the SSRIs (Prozac, Zoloft, Luvox, Lexapro); other novel antidepressants like Wellbutrin, and the tricyclic antidepressants.
3. **Antipsychotics.** These include the newer atypical antipsychotic drugs: Abilify, Risperdal, Zyprexa and the older neuroleptics, like Haldol and Mellaril.
4. **Anxiolytics** drugs for anxiety, like Valium, Klonopin, Ativan, Xanax and BuSpar.
5. **Mood Stabilizers** include Lithium, used to treat manic-depression, and drugs that were originally introduced as antiepileptic drugs, Tegretol and Lamictal.

6. **Odd Drugs.** These are medications used originally for various medical conditions, but which are sometimes useful for their behavioral or emotional effects. They include the beta blockers, like Inderal and the anti-hypertensives, Clonidine and Tenex.
7. **Vitamins and Nutraceuticals** which sometimes may be helpful: melatonin, St John's Wort, folic acid, Vitamins C, E and B₆.

Specific reasons to use medication: Several medications can be used for each problem.

1. Attention-deficit /hyperactivity disorder. stimulants, clonidine, Tenex, Wellbutrin, amantadine
2. Anxiety, Panic. antidepressants, BuSpar, benzodiazepines, clonidine, Tenex.
3. Bedwetting: imipramine or DDAVP
4. Sleep disorders: clonidine, Trazodone, Ambien, imipramine, Chloral Hydrate, melatonin
5. Self-injury: atypical antipsychotics, SSRIs
6. Aggression: clonidine, Tenex, atypical antipsychotics, Propranolol, Depakote, SSRIs, stimulants, amantadine.
7. Obsessive-compulsive symptoms: SSRIs, BuSpar, atypical antipsychotics.
8. Depression: antidepressants, sedatives for sleep.
9. Mood disorders. antidepressants, Lithium, Tegretol, Depakote
10. More complex problems, like the psychotic disorders and manic depression usually require antipsychotic and mood-stabilizing drugs, often in combination.

A medication can also be used for several different problems

The various psychotropic drugs are often effective for more than one condition. For example, a drug that is classified as an "antidepressant" doesn't mean that its usefulness is limited to depression. The antidepressants are some of the most effective drugs for anxiety.

The antipsychotics are good for psychotic disorders and also severe hyperactivity, tics, self-injury, and compulsive disorders.

Anti-epileptic drugs like Tegretol and Depakote are among the most effective treatments for psychiatric disorders and for behavior problems like aggression.

Combinations of drugs often work well for individuals with Fragile X.

Stimulants with clonidine or Tenex

Stimulants with a SSRI

An antidepressant with BuSpar.

Complications/Combinations to avoid - drugs from the same drug family or drugs that have exactly the same purpose. We might use a drug for hyperactivity and a different medication for sleep but we don't typically use two medications for sleep.

Typical success rates for various drugs. The main reasons why we do not use a drug is because it doesn't work for a given individual or because it has side effects that are difficult to tolerate. For example, mild appetite suppression may be okay if the child is

overweight but not if the child is very thin. Many drugs work approximately 50% of the time. This makes medication management very challenging.

Augmenting the use of medication - what has been the most useful

Calming techniques

Visual aids such as schedules may be organizing

Predictable routines with structure

Behavior management programs

Many of our patients with fragile X have been helped by being in a school setting for autistic children.

Counseling and psychotherapy

OT - enhances fine motor skills and adaptive functioning.

SI therapy - gives better sense of body in space. Helps children adapt to sensory experiences (loud malls, movies, restaurants) that may be normal for others but are difficult for them.

Speech and Language Therapy—enhances communication ability and ability to express ones' needs.

Multiple vitamins—probably a good idea for poor eaters or children who have been on multiple medications.

Interesting hobbies and recreational opportunities - Activities can involve music, sports, Special Olympics, etc. This is an area where the life can be fairly normal.

Major Issues and Pitfalls in Medication Management

The environment should be as good as it can be for the drug to work best. A child, who is in a very chaotic classroom, is not going to get better by simply taking Ritalin.

Behavior checklists filled out by the parents and teachers can be very helpful to assess the behaviors of the individual and the response to medication.

Low doses may give some relief of symptoms. High doses may give relief but cause too many side effects. A low dose of a medication may be more helpful than nothing.

Stimulants may work better in school age children than in very young children.

Sometimes two or three drugs in low dose or in combination may be more helpful than a high dose of single drug. For example, an extremely hyperactive child with aggressive outbursts and a sleep disorder might do better with a stimulant and an alpha-2 agonist than a high dose of a stimulant.

Antipsychotics may cause tardive dyskinesias. Some cause excessive weight gain.

Clonidine can cause drowsiness and sleep problems in the middle of the night.

SSRIs can cause sexual dysfunction.

While some medications like stimulants are widely used by primary care providers, other drugs like antipsychotics are used far less frequently by primary care providers.

Individuals, who need these less frequently used medications, may better be served by specialists.

Some medications require bloodwork. Most of these medications do not.

Table 1. Commonly used drugs to manage problems in individuals with fragile X. Dosages vary somewhat from guide to guide, and individual people have varying responses to medications. Our general experience is that individuals with fragile X do not usually require high doses of medication. 1 kg = 2.2 lbs.

Stimulants - used to treat ADHD. Inattention is best treated with stimulants. Hyperactivity often responds to other meds as well.

| Drug | Forms | Pediatric Doses | Adult Doses | Side Effects/Considerations |
|---|-------------------------|---|---|---|
| methylphenidate short-acting Ritalin | 5, 10, 20 mg | .7-1.0 mg/kg/day 2-3 times/day start with 5 mg twice a day and increase the dose up to 60 mg | up to 60 mg/day divided 2-3 times/day | irritability, trouble sleeping weight loss, headaches stomachaches, tics sad or muted affect, rebound give before meals; last dose before 6 pm if medication keeps patient awake |
| Methylin | 2.5, 5, 10, 20 mg | same | same | same |
| methylphenidate liquid Methylin Oral Solution | 5 mg/5 mL 10 mg/5 mL | start with 5 mg 2x/day give 2-3 times daily | same | same |
| methylphenidate chewable tablets Methylin Chewable Tablets | 2.5, 5, 10 mg | same | same | same |

| Drug | Forms | Pediatric Doses | Adult Doses | Side Effects/Considerations |
|---|-------------------------------------|---|---------------------|---|
| methylphenidate intermediate acting Metadate ER | 10, 20 mg | start with 10 mg | up to 60 mg per day | same lasts about 8 hrs. |
| Ritalin SR | 20 mg | start with 20mg | up to 60 mg per day | rarely used |
| methylphenidate long-acting Concerta | 18, 27, 36, 54 mg 1 time per day | .7-1.0 mg/kg/day begin with 18 mg | up to 72-108 mg/day | same as above side effects should be milder must be able |
| Ritalin LA | 10, 20, 30, 40 mg | same | up to 60 mg/day | spansule - can sprinkle |
| Metadate CD | 10, 20, 30, 40, 50, 60 mg | same | up to 60 mg per day | spansule - can sprinkle to swallow |
| Methylin ER | 10, 20 mg | start with 10 mg | same | pill form |
| methylphenidate patch Daytrana | 10, 15, 20, 30 mg | begin with 10 mg advance gradually and as needed to 30 mg use two hrs before effect is needed | up to 30 mg | need about ½ as much as the other medications effects of patch will last 2 hrs after the patch has been removed removed; patch should be placed on hip on alternating days adhesive should be wiped off |

| Drug | Forms | Pediatric Doses | Adult Doses | Side Effects/Considerations |
|--|------------------------------------|---|----------------------|--|
| Dexmethylphenidate short-acting Focalin | 2.5, 5, 10 mg | .3-.5 mg/kg/day begin with 2.5 mg once or twice a day and advance | 10 mg twice a day | with oil such as baby oil may cause fewer stomach problems morning and afternoon dose |
| dexmethylphenidate long-acting Focalin XR | 5, 10, 15, 20, 25 mg 30, 35, 40 | .3-.5 mg/kg/day | 30 mg | can sprinkle; lasts 8-12 hrs |
| combined dexedrine salts short acting Adderall | 5, 7.5, 10, 12.5 15, 20, 30 mg | .6-.7 mg/kg/day begin with 2.5 -5 mg once and then twice per day | 40-60 mg/day | same |
| long acting Adderall XR | 5,10,15, 20, 25, 30 mg | same as above one time per day | 40- 60 mg | same |
| lisdexamfetamine Vyvanse | 20, 30, 40, 50, 60 70 mg | begin with 30 mg advance as needed | 100 mg | can sprinkle lasts through the afternoon |

| Drug | Forms | Pediatric Doses | Adult Doses | Side Effects/Considerations |
|---|----------------------------------|---|--------------------|--|
| dextroamphetamine short-acting Dexadrine | 5 mg tablets | .6-.7 mg/kg/day begin with 5 mg in the morning and afternoon | 40 mg/day | same |
| dextroamphetamine long-acting Dexadrine spansules | 5,10,15 mg | .6-.7 mg/kg/day begin with 5-10 | 40 mg/day | same |
| Selective norepinephrine reuptake inhibitor | | | | |
| atomoxetine Strattera | 10, 18, 25, 40 60, 80, 100 mg | 1.2-1.4 mg/kg start with .5mg/kg | 100 mg | preferred dosing in evening at the beginning, can give 1 to 2 times qd |
| Alpha-2-adrenergic agonists - used to treat hyperactivity, tics, aggression and sleep problems | | | | |
| clonidine | | | | |
| Catapres | .1, .2, .3 mg tablet | ¼ - 1 tablet 3-4 times per day | .4 mg/day | blood pressure changes drowsiness nightmares |
| Catapres Patch | .1, .2, .3 mg | one patch q 5 – 7 days | .3 mg | drowsiness |

| Drug | Forms | Pediatric Doses | Adult Doses | Side Effects/Considerations |
|---|-------------------|---|--------------------|------------------------------------|
| guanfacine Tenex | 1, 2 mg tablet | up to 3 mg divided twice per day | 3 mg/day | drowsiness |
| guanfacine extended-release Intuniv | 1, 2, 3, 4 | up to 4 mg | 4mg/day | drowsiness |
| clonidine extended release Kapvay | 0.1, 0.2 mg | begin with 0.1 mg At bedtime. Advance As needed up to 0.2 mg twice per day | up to 0.4 mg | drowsiness |

SSRIs (serotonin specific reuptake inhibitors) - used to treat depression, obsessive-compulsive disorder, may also work as a mood stabilizer

| | | | | |
|----------------------|--|---|--------------------|---|
| fluoxetine Prozac | 20 mg/5ml liquid 10, 20 mg tablets 20, 40 mg capsule 90 mg weekly | 5-10 mg q day begin with 4-5 mg q d | 80 mg/24 hr max | anxiety, insomnia weight gain, nausea, vomiting headache drowsiness |
| fluvoxamine Luvox | 25, 50, 100 mg | begin with 25-50 | 100-300 mg | dizziness |

| Drug | Forms | Pediatric Doses | Adult Doses | Side Effects/Considerations |
|-------------------------|--|---------------------------------|------------------------------|---|
| | tablets | mg at bedtime | divided bid | constipation dry mouth |
| sertraline Zoloft | 25, 50, 100 mg tablets 20 mg/1mL | 12.5-25 mg/day then increase | 200 mg/day max | nausea, diarrhea tremor, sweating, fatigue sweating, insomnia |
| escitalopram Lexapro | 5, 10, 20 mg tablets 5mg/5mL | begin with 5 mg | 10-20 mg one time per day | nausea, insomnia sexual dysfunction |

**Antipsychotics - may assist with severe psychotic behaviors, severe hyperactivity, aggressive outbursts
May be useful in an emergency situation. Antipsychotics are sometimes used for tics or bipolar disorder.**

| | | | | |
|---|---|-----------------------------------|--|--|
| risperidone Risperdal | 1, 2 mg tablets 1 mg/mL liquid | begin with ½ mg advance slowly | 6 mg max divided twice a day | weight gain, sedation, orthostatic hypotension low risk for tardive dyskinesia |
| aripiprazole Abilify | 2, 5, 10, 15, 20, 30 1 mg/mL liquid | begin with 2 mg | start with 5 to 10 mg. Advance to 30 mg. | headache nausea dyspepsia |
| For difficulty with sleep melatonin | 3 mg tabs mouth spray | begin with 3 mg | 1-3 tabs no more than 3 times per day user adjusts as | |

2 sprays = 3 mg

needed

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