

# MEDICATIONS USED IN THE TREATMENT OF DISRUPTIVE BEHAVIOR IN CHILDREN WITH FASD - A GUIDE

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## ABSTRACT

The majority of children with FASD suffer from disruptive behaviors and most of them need medications to modify these behaviors. The objective of this review is to familiarize professionals caring for children with FASD with stimulants and other drugs for ADHD, and the second generation antipsychotic risperidone - for aggressive and defiant behaviors.

The majority of children with Fetal Alcohol Spectrum Disorder (FASD) suffer from disruptive behaviors, most commonly in the form of attention deficit hyperactivity disorder (ADHD), Oppositional Defiant Disorder (ODD) or Conduct Disorder (CD). Most of them need medications to modify these behaviors and allow them to participate in school and in social activities.

The objective of this review is to familiarize professionals caring for children with FASD with medications more commonly used - stimulants and other drugs for ADHD, and the second generation antipsychotic risperidone - for aggressive and defiant behaviors.

## A. Treating ADHD

Attention deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder in children and adolescents with FASD and may deeply affect their academic achievement and social interactions.<sup>1</sup> Psychostimulant drugs, such as methylphenidate (Ritalin<sup>®</sup>, Concerta<sup>®</sup>), amphetamine and dextroamphetamine combination (Adderall<sup>®</sup>), and lisdexamphetamine (Vyvanse<sup>®</sup>), are recommended as first-line treatment for these symptoms in primary ADHD, as well as in FASD.<sup>2,3</sup> A selective norepinephrin reuptake inhibitor, atomoxetine and two selective

alpha-2-adrenergic agonists (extended release clonidine and extended release guanfacine) have slightly weaker beneficial effects in children with ADHD. These two extended release medications achieved FDA approval to be used as an adjunctive treatment with stimulant medications. All these medications are approved for use in school-aged children and dextroamphetamine is the only medication approved by FDA for use in children younger than 6 years of age.<sup>1</sup>

The most common adverse effects of stimulants are appetite loss, abdominal pain, headaches and sleep problems. Decreased growth velocity is another concern. Children younger than 6 years of age may experience increased mood lability. Although there were some concerns regarding cardiac adverse events, it has been shown that sudden cardiac death in children on stimulant medication is very rare.<sup>4</sup> However, great caution is advised when considering stimulant and non-stimulant medications for children with ADHD with a personal or family history or other known risk factors for cardiovascular disease such as WPW syndrome, long QT syndrome, hypertrophic cardiomyopathy and sudden death in the family.<sup>5</sup>

Stimulant medications affect most children with ADHD positively causing improvement in the symptoms in 80% of them. Children perform better in school, have better relationships with peers and family members,

have increased attention during sports and other activities and are less distractible and impulsive.<sup>3</sup> However, data suggest that children with FASD respond less optimally in terms of inattention, with a good response in hyperactivity and impulsivity.<sup>6</sup>

According to the ADHD treatment guidelines published by the American Academy of Pediatrics, before commencing drugs for adolescents with newly diagnosed ADHD, clinicians should rule out substance abuse. If substance abuse is identified, ADHD medications with no abuse potential such as atomoxetine, extended-release guanfacine, extended-release clonidine or stimulant medications with less abuse potential, such as lisdexamphetamine, transdermal methylphenidate or osmotic-release oral system (OROS) methylphenidate should be preferred.<sup>1,7</sup>

## 1. METHYLPHENIDATE (Concerta<sup>®</sup>, Ritalin<sup>®</sup>, Biphentin<sup>®</sup>)

**Indications:** ADHD and narcolepsy

**Mechanism of Action:** Although the exact mechanism of action in humans is not completely understood, the stimulatory effects of methylphenidate is thought to be produced by blocking the reuptake of norepinephrine and dopamine into the presynaptic neurons and increasing the release of these neurotransmitters into the extraneuronal space in prefrontal cortex.<sup>7</sup> Methylphenidate is a central nervous system stimulant.

### Dosage Forms

Oral tablet, as hydrochloride:

Ritalin<sup>®</sup>: 5 mg, 10 mg, 20 mg (scored)

Oral tablet, Extended Release, as hydrochloride:

Concerta<sup>®</sup>: 18 mg, 27 mg, 36 mg, 54 mg

Ritalin SR<sup>®</sup>: 20 mg

Oral capsule, Controlled Release, as hydrochloride:

Biphentin: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 80 mg

Ritalin LA<sup>®</sup>: 10 mg, 20 mg, 30 mg, 40 mg

Transdermal Patch:

Daytrana<sup>®</sup>: 10 mg/9 hr, 15 mg/9 hr, 20 mg/9 hr, 30 mg/9 hr<sup>8</sup>

### Doses

Treatment of ADHD:

Immediate release products (e.g., Ritalin<sup>®</sup>):

Limited data are available in children with ADHD between 3-5 years, with moderate to severe dysfunction. American Academy of Pediatrics (AAP) considers methylphenidate as a first-line agent in this patient population.<sup>1</sup> The initial dose should be 1.25 mg twice daily and the dose may be increased at weekly intervals. Usual reported daily dose is 3.75-30 mg/day divided into two or three daily doses.<sup>8-10</sup>

In children  $\geq 6$  years and adolescents: The initial dose should be 0.3 mg/kg/dose or 2.5-5 mg/dose given before breakfast and lunch and it can be increased by 0.1 mg/kg/dose or by 5-10 mg/day at weekly intervals. Usual dose is 0.3-1 mg/kg/day or 20-30 mg/day in 2-3 divided doses. Maximum daily dose of Ritalin<sup>®</sup> is dependent upon patient's weight and is 2 mg/kg/day or if patient's weight  $\leq 50$  kg: 60 mg/day; in patients  $>50$  kg: 100 mg/day.<sup>8,11,12</sup>

Extended release, sustained release and long acting products

Ritalin-SR<sup>®</sup>: In children  $\geq 6$  years and adolescents: Sustained release and extended release tablets (duration of action  $\sim 8$  hours) may be given in place of immediate release tablets after dose adjustment. Ritalin SR<sup>®</sup> may be administered once or twice daily.<sup>1,8</sup> Maximum daily dose is dependent upon patient weight:  $\leq 50$  kg: 60 mg/day;  $>50$  kg: 100 mg/day.<sup>8,11,12</sup>

Concerta<sup>®</sup>: In children  $\geq 6$  years and adolescents:

In methylphenidate-naïve patients: Initial dose is 18 mg once daily.

In children on immediate release methylphenidate:

\*Changing from methylphenidate immediate release 5 mg 2-3 times daily: Concerta<sup>®</sup> 18 mg once daily

\*Changing from methylphenidate immediate release 10 mg 2-3 times daily: Concerta<sup>®</sup> 36 mg once daily

\*Changing from methylphenidate immediate release 15 mg 2-3 times daily: Concerta<sup>®</sup> 54 mg once daily

\*Changing from methylphenidate immediate release 20 mg 2-3 times daily: Concerta® 72 mg once daily

Maximal daily dose of Concerta®:

\*In children 6-12 years: 54 mg/day; for patients >50 kg, higher maximum daily doses may be considered (108 mg/day)

\*In adolescents:

≤50 kg: 72 mg/day; not to exceed ~2 mg/kg/day

>50 kg: 108 mg/day<sup>8,10,11</sup>

Topical: Transdermal patch (Daytrana®) In children and adolescents 6-17 years the initial dose should be 10 mg (12.5 cm<sup>2</sup>) patch once daily. It should be applied to hip 2 hours before effect is needed and should be removed 9 hours after application. The patch may be removed before 9 hours if a shorter duration of action is required. Although plasma concentrations start to decline when the patch is removed, drug absorption may continue for several hours after its removal. The dose should be adjusted according to clinical response and tolerability. If needed the dose may be increased but no more frequently than once a week. Patients switching from another formulation of methylphenidate to the transdermal patch should be started with 10 mg regardless of their previous dose and their dose should be adjusted due to the differences in bioavailability of the transdermal formulation.<sup>8,13</sup>

### Administration

Last daily dose should be administered several hours before going to bed to avoid insomnia.

#### Immediate release formulations:

\*Ritalin® tablet: It should be taken on an empty stomach ~30-45 minutes before meals. .

#### Extended/sustained release formulations:

\*Ritalin SR® tablet: It should be taken 30-45 minutes before the meal. It should be swallowed as a whole. Tablets should not be crushed, chewed, or broken.

\*Concerta® tablet: May be given before or after the food, but must be taken with water, milk, or juice. The dose should be given once daily in the morning and the tablets should not be crushed, chewed, or divided.

#### Topical formulations:

\*Transdermal patch (Daytrana®): It should be applied immediately after opening pouch and its protective liner should be removed. The patch should not be used if pouch seal is broken. The patches that are cut or damaged should not be used. It should be applied to clean, dry, healthy skin on the hip and not to oily, damaged, or irritated skin. It should not be applied to the waistline as well. The patch should be applied to alternate hip at the same time each day, 2 hours before effect is needed and should be removed 9 hours after application.<sup>8</sup>

### Adverse Effects

Central nervous system: Headache, poor sleep, irritability, emotional lability, vocal tics.

Gastrointestinal: Decreased appetite, nausea, abdominal pain.

Growth velocity: Children treated with methylphenidate had 1 cm/year decrease in height over 3 years of continuous treatment and weight deficit of 3 kg for the first year and 1.2 kg for the second year of treatment.<sup>14</sup>

Miscellaneous: Fever, eye pain

## 2. AMPHETAMINE & DEXTROAMPHETAMINE (Mixed amphetamine salts) (Adderall®)

**Indications:** ADHD and narcolepsy

**Mechanism of Action:** Amphetamine & dextroamphetamine works by increasing the activity of the neurotransmitters norepinephrine and dopamine in the brain. They block presynaptic dopamine and norepinephrine reuptake. Amphetamine & dextroamphetamine combination is a central nervous system stimulant.<sup>11</sup>

### Dosage Forms

#### Oral tablets

Adderall®: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 30 mg

Adderall XR®: 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg, 20 mg, 30 mg

## Doses

### Treatment of ADHD

#### Immediate release tablets (Adderall®):

In children 3-5 years: It should be started as 2.5 mg daily given every morning and the daily dose should be increased by 2.5 mg at weekly intervals until optimal response is obtained.

Maximal daily dose is 40 mg/day given in 1-2 divided doses per day. Current guidelines do not recommend amphetamine & dextroamphetamine use in children  $\leq 5$  years due to insufficient evidence.<sup>1,8</sup>

In children  $\geq 6$  years and adolescents: The initial dose is 5 mg once or twice daily and the daily dose should be increased 5 mg at weekly intervals until optimal response is obtained. Usual maximum daily dose is 40 mg/day given in 1-2 divided doses per day. In patients  $>50$  kg a maximum daily dose of 60 mg/day in divided doses has been used.<sup>8,11,12</sup>

Extended release capsules (Adderall XR®): The patients taking divided doses of immediate release tablets may be switched to extended release capsule using the same total daily dose (taken once daily) and the dose should be titrated at weekly intervals to achieve optimal response.<sup>8,11,12</sup>

In children 6-12 years: The initial dose should be 5-10 mg daily given every morning and the daily dose should be increased by 5 mg or 10 mg at weekly intervals until optimal response is obtained. Usual maximum daily dose is 30 mg/day. In patients  $>50$  kg a maximum daily dose of 60 mg/day has been used.<sup>8,11,12</sup>

In adolescents 13-17 years: The initial dose should be 10 mg daily given every morning and it may be increased to 20 mg daily after 1 week if symptoms are not controlled. Usual maximum daily dose is 20 mg/day. In patients  $>50$  kg a maximum daily dose of 60 mg/day has been used.<sup>8,11,12</sup>

## Administration

Immediate release tablet: Last daily dose should be administered at least 6 hours before going to bed to avoid insomnia.

Extended release capsule: Afternoon doses should be avoided to prevent insomnia. The capsule should be swallowed as a whole and should not be chewed or divided. It may be taken with or without food. The capsule may be opened and the

contents may be mixed with applesauce and it should be taken immediately.<sup>8</sup>

## Adverse Effects

Because of the appetite suppression may occur; weight should be monitored during therapy, particularly in children. Amphetamine & dextroamphetamine is not recommended for children younger than 3 years.

## 3. LISDEXAMPHETAMINE (Vyvanse®)

### Indication: ADHD

**Mechanism of Action:** Lisdexamfetamine dimesylate is a prodrug that is converted to the active component dextroamphetamine. It contains an additional lysine molecule. Lisdexamphetamine increases dopamine and norepinephrine neurotransmission in the brain and improves brain development and nerve growth. Lisdexamfetamine is a central nervous system stimulant.<sup>8,11</sup>

### Dosage Forms

Capsule, Oral, as dimesylate

Vyvanse®: 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg

### Doses

#### In children $\geq 6$ years and adolescents:

The initial dose should be 30 mg once daily in the morning; and daily dose may be increased 10 mg or 20 mg/day at weekly intervals until optimal response is obtained. Maximum daily dose is 70 mg/day.<sup>8</sup>

### Administration

It should be administered in the morning with or without food and it should not be given in the afternoon to prevent insomnia. The capsule should be taken as a whole and should not be chewed. The capsule may be opened and the entire contents may be dissolved in glass of water and should be taken immediately.<sup>8</sup>

### Adverse Effects

Appetite suppression may occur; particularly in children. Use of stimulants has been associated with weight loss and slowing of growth rate. So,

weight and growth rate should be monitored during treatment. Treatment interruption may be necessary in patients who are not increasing in height or gaining weight as expected.<sup>1,8</sup>

#### 4. ATOMOXETINE (Strattera®)

**Indications:** ADHD

**Mechanism of Action:** Atomoxetine is a selective norepinephrine reuptake inhibitor.<sup>11</sup>

##### **Dosage Forms**

Strattera® capsule: 10 mg, 18 mg, 25 mg, 40 mg, 60 mg

##### **Doses**

In children >6 years and adolescents, weighing ≤70 kg: The initial dose should be 0.5 mg/kg/day and should be increased after a minimum of 3 days to ~1.2 mg/kg/day. It may be given once daily in the morning or as 2 divided doses in the morning and late afternoon/early evening. Maximum daily dose is 1.4 mg/kg/day or 100 mg/day, whichever is less. Doses more than 1.2 mg/kg/day have not been shown to provide additional benefit.

Dosage adjustment should be done with concurrent use of strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine) or in patients known to be CYP2D6 poor metabolizers. In those patients the initial dose should be 0.5 mg/kg/day for 4 weeks and it should be increased to a maximum dose of 1.2 mg/kg/day only if clinically needed.

In children >6 years and adolescents, weighing >70 kg: The initial dose should be 40 mg daily and increased after a minimum of 3 days to ~80 mg daily. It may be given once daily in the morning or divided into 2 doses and administered in morning and late afternoon/early evening. Dosage adjustment should be done with concurrent use of strong CYP2D6 inhibitors (e.g., paroxetine, fluoxetine, quinidine) or in patients known to be CYP2D6 poor metabolizers. In those patients initial dose should be 40 mg daily for 4 weeks and the dose should be increased to a maximum dose of 80 mg/day.<sup>8</sup>

##### **Administration**

The capsules may be administered before or after food. The capsule should not be crushed, chewed, or opened and should be taken as whole with water or other liquids. Atomoxetine is an ocular irritant and eye should be washed with water immediately if capsule is opened accidentally and contents come into contact with eye and medical advice should be seek.<sup>8</sup>

##### **Adverse Effects**

Decreased appetite, abdominal pain, vomiting, nausea, diarrhea, tachycardia, headache, fatigue, somnolence, hallucinations and psychotic symptoms.

##### **Warnings**

There is an US boxed warning for atomoxetine because it has been associated with an increased risk of suicidal thinking in children and adolescents with ADHD. The patient should be closely monitored for clinical worsening, suicidality, or unusual changes in behavior; especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. The family or caregiver should be instructed to closely observe the patient and communicate condition with healthcare provider.

Use of atomoxetine should be avoided in patients with known serious structural cardiac abnormalities, cardiomyopathy and serious heart rhythm abnormalities.

Although atomoxetine has been associated with less growth suppression compared with stimulants, growth should be monitored during treatment. Height and weight gain may be reduced during the first 9 to 12 months of treatment, but should recover by 3 years of therapy.<sup>8,11</sup>

#### 5. GUANFACINE (Extended release) (Intuniv XR®)

**Indications:** ADHD, hypertension

**Mechanism of Action:** Guanfacine is a selective- $\alpha$ -2-adrenergic agonist.<sup>11</sup>

##### **Dosage Forms**

Extended release 24 hour tablet:

Intuniv XR®: 1 mg, 2 mg, 3 mg, 4 mg

### Doses

In children and adolescents 6-17 years:

The initial dose of extended release product should be 1 mg once daily given at the same time of day and the dose may be increased by no more than 1 mg/week increments. Usual maintenance dose is 1-4 mg/day and the maximum daily dose is 4 mg/day.<sup>8</sup>

Dosing adjustment should be done for concomitant use of CYP3A4 inhibitors/inducers. Strong CYP3A4 inhibitors: When initiating guanfacine while taking a strong 3A4 inhibitor, the maximum dose of 2 mg/day should not be exceeded. When continuing guanfacine if strong CYP3A4 inhibitor added to treatment, guanfacine dose should be decreased by 50%. If the strong CYP3A4 inhibitor is discontinued, the guanfacine dose should be doubled (maximum daily dose: 4 mg/day).

Strong CYP3A4 inducers: When initiating guanfacine while taking a strong CYP3A4 inducer, the dose may be titrated up to 8 mg/day. If continuing guanfacine and adding a strong CYP3A4 inducer, the dose of guanfacine should be gradually increased over 1-2 weeks to double the original dose, as tolerated. If the strong CYP3A4 inducer is discontinued, guanfacine dose should be decreased by 50% over 1-2 weeks (maximum daily dose: 4 mg/day).

If patient misses two or more consecutive doses, titration of the dose should be repeated. During discontinuation, the dose should be tapered by no more than 1 mg every 3-7 days. In children with renal impairment, no dosage adjustments are necessary. In patients with moderate hepatic impairment 50% of the normal dose and in the patients with severe hepatic impairment 25% of the normal dose should be given.<sup>8</sup>

### Administration

The capsule should be taken at the same time each day (either morning or evening) and the tablet should be swallowed as whole with water, milk, or other liquid. It should not be crushed, broken, or chewed and it should not be taken with high-fat meal.

### Adverse Effects

Headache, somnolence, fatigue, upper abdominal pain, and dry mouth.<sup>11</sup>

## 6. CLONIDINE (Extended release) (Kapvay™)

**Indications:** ADHD, hypertension, analgesia, neuropathic pain, tic disorders and Tourette's syndrome, clonidine tolerance test (test of growth hormone release from the pituitary).<sup>8</sup>

**Mechanism of Action:** Clonidine is a selective alpha-2-adrenergic agonist.<sup>11</sup>

### Dosage forms

Extended release 12 hour tablet as hydrochloride: Kapvay™: 0.1 mg

### Doses

In children ≥6 years and adolescents:

The initial dose should be 0.1 mg at bedtime; and it should be increased in 0.1 mg/day increments every 7 days until desired response. The doses should be given twice daily (either split equally or with the higher split dosage given at bedtime). The maximum dose is 0.4 mg/day. Maintenance treatment for >5 weeks has not been evaluated. In patients with renal impairment the manufacturer recommends dosage adjustment, however it has not been studied yet.<sup>8</sup>

### Administration

Clonidine may be given before or after the meals. Extended release tablets (Kapvay™) should be swallowed as a whole. It should not be crushed or chewed and it should not be split. It should be tapered in decrements of ≤0.1 mg in every 3-7 days.<sup>8</sup>

### Adverse Effects

Bradycardia, somnolence and dry mouth<sup>11</sup>

## B. Treatment of Aggression and Defiant Behavior: RISPERIDONE (Risperdal®)

Very large numbers of children with FASD are treated with neuroleptics, with risperidone being the most prevalent; yet the published experience in these children is very limited. For the purpose

of this report, we have reviewed a one year experience in Motherisk FASD diagnostic clinic at Tel Aviv University (see Table 1). A total of 10 children, aged 5-16 year, diagnosed with FASD received risperidone. All of them had ADHD and ODD with very severe behavioral issues at home and in school. The children (7 boys and 3 girls) received risperidone in doses ranging from 0.2 mg among the youngest and up to 1.5mg, and all received stimulants for their ADHD. A good response to aggressive behavior and impulsivity was reported in 8 cases, partial response in one case, and lack of response in one. Three children experienced serious dose-dependent adverse effects that settled at lower doses.

**Indications:** Autism, bipolar mania, schizophrenia, disruptive behavior disorders (e.g., conduct disorder, oppositional defiant disorder), pervasive developmental disorders (e.g., disruptive behaviors, aggression, irritability), Tourette's syndrome, tics.

**Mechanism of Action:** It is a serotonin-dopamine antagonist possessing anti-serotonergic, anti-adrenergic and anti-histaminergic properties.<sup>8,15</sup> Risperidone is a second generation antipsychotic.

#### **Dosage Forms**

Liquid: 1 mg/mL

Tablet: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg

#### **Doses**

Treatment of aggression and defiant behavior:

The available data are limited.

In children  $\geq 4$  years and adolescents: The initial dose should be 0.01 mg/kg/dose once daily for 2 days, then 0.02 mg/kg/dose once daily. The dose may be increased on weekly basis to 0.06 mg/kg/dose once daily. Optimal doses are 0.75 to 1.8 mg/day and usual maximum daily dose is 2 mg/day. Improvement in target symptoms is expected typically within 1 to 4 weeks.<sup>8,15,16</sup> Half of the daily dose can be given twice daily if breakthrough symptoms occur in the afternoon or evening.

#### **Administration**

Risperidone may be given before or after the meals. Oral solution can be administered directly from the

provided pipette or may be mixed with water, coffee, orange juice, or low-fat milk, but is not compatible with cola or tea.

In children or adolescents experiencing somnolence, half the daily dose may be administered twice daily or the once-daily dose may be administered at bedtime.<sup>8</sup>

#### **Adverse Effects**

Central nervous system: Dystonia, fatigue, parkinsonian-like syndrome, sedation (somnolence)

Endocrine & metabolic: Increased thirst (more common in children), weight gain

Gastrointestinal: Abdominal pain, increased appetite, nausea, vomiting, dry mouth, constipation

Cardiovascular: Prolonged Q-T interval on ECG, syncope, bradycardia

Genitourinary: Urinary incontinence

Respiratory: Nasopharyngitis, cough, rhinorrhea

Miscellaneous: Fever<sup>8</sup>

#### **COMMENTS**

Often, parents and caretakers are reluctant to treat children with FASD pharmacologically, citing adverse effects and fears of long term damage. However, many children with FASD cannot cope with the challenges of school due to their disruptive behavior, characterized by symptoms of ADHD and aggressive behavior. Not allowing these children the benefits of available medications will negatively affect their ability to participate in school. It is therefore critical to manage them carefully with medications, while monitoring the balance between the improvement of their symptoms with any adverse effects that may happen. This process necessitates the participation of a physician familiar with the child and his/her response, as well as parent's literacy of the effects and the adverse effects of the medications.

Successful therapy with these medications entails careful dose-finding and combination of medications for both symptoms of ADHD and aggression. It is important to carefully record the response of the child in order to decide on dose or schedule changes.

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**TABLE 1** Response to Risperidone among Children with FASD

Patient	Sex	Age (yr)	Diagnoses	Risperdal dose	Other drugs	Response to Risperdal	Adverse effects
1	F	16	ADHD, ODD, CD	1mgx1/d	Ritalin SR®	Favorable	None
2	M	6.5	ADHD, ODD	1mgx1/d	Concerta®	Favorable	None
3	M	11	ADHD, ODD	1mgx1/d	Concerta®, Aderall®, Ritalin®	Favorable	None
4	M	10	ADHD, ODD	0.5mgx1/d	Concerta®	No response	Creatinine elevation
5	M	16.5	ADHD, ODD, CD	1.5mgx1/d	Concerta®	Favorable	None
6	M	13.4	ADHD, ODD	1.5mgx1/d, decreased to 1mg	Stratera®	Favorable	Depression, suicide ideation (settled with decreased dose to 1mg)
7	M	5	ADHD, ODD	0.2mgx1/d, 0.3mgx1/d, 0.25mgx1/d	Ritalin®	Favorable	Very silent and depressed on 0.3mg; OK on 0.25mg
8	M	5	ADHD, ODD	0.1mg, 0.3mg	Ritalin®	Favorable	Needed dose escalation to have effect
9	F	9.5	ODD, ADHD	0.5mg	Concerta®, Lamictal®, Zyprexin®	Favorable	None
10	F	7.5	ADHD, ODD	0.5mg, 1.5mg	Ritalin®, Concerta®		Baseline anxiety, Ritalin increased anger



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