Piecing Together the Pharmacotherapy Puzzle for Children with Autism Spectrum Disorder

Jennifer A. Donaldson, Pharm.D., BCPPS
Riley Hospital for Children at Indiana University Health
Indianapolis, Indiana
Disclosure

• Faculty have nothing to disclose.
Objectives

• Design a medication regimen and monitoring plan for a pediatric patient with autism presenting with irritability.

• Make recommendations for the use and monitoring of stimulant drug therapy in a pediatric patient with attention-deficit hyperactivity disorder and inattention.

• Make recommendations for the use and monitoring of selective serotonin reuptake inhibitor therapy for depressive symptoms or repetitive behaviors in a pediatric patient with autism.
Introduction

• The prevalence of autism spectrum disorder (ASD) is approximately 1 in every 68 children

• Pharmacotherapy for comorbid conditions often involves psychotropic medications

• An estimated 27 – 64 % of patients with ASD are on at least one psychotropic medication
  – And 4.5 – 15 % of patients may be on polypharmacy (three or more medications)


Introduction

• The amount of evidence-based data is increasing

• But psychotropic medications may be used off-label, in younger patients with limited data, and in combinations that may have unwarranted adverse effects (AEs)


Case 1

- EM is a 6 year-old boy presenting to child psychiatry clinic for evaluation of impulsive and aggressive behaviors. Father desired an evaluation for autism.

- EM was born 38 weeks gestation due to placental abruption. Due to periventricular leukomalacia, he has cerebral palsy with spastic diplegia and epilepsy with focal seizures.
Case 1

• His communication skills have never been on par with his peers, but the family is able to identify what he needs. The differences between EM and his peers became more evident once he started school.
Case 1

• EM’s aggressive behaviors (biting, kicking) occur when he has to stop an activity he likes.
• He ‘acts out’ when his ‘ritual behaviors’ are interrupted.
• When in group play with other children, he will not wait his turn and has difficulty focusing on an activity and staying seated.
Case 1

• The behavior outbursts are worsening and are occurring without an identifiable reason (to the father) and EM no longer can self-calm.
• The outbursts typically lasted five minutes, now they may last up to 20 minutes, even with interventions from the family.
Case 1

• EM’s recent lab work shows complete blood count, chemistry panel, and liver enzymes all within normal limits. Current weight is 27.5 kg. Medications include:
  – Levetiracetam 500 mg, orally, twice a day
  – OnabotulinumtoxinA, intramuscular, every 3 months
  – Baclofen 10 mg, orally, three times a day
Case 1—Question 1

• The physician and father agree to initiate a second-generation antipsychotic to help with the worsening aggressive behaviors. What other baseline laboratory tests should be obtained prior to starting the antipsychotic?
Time for a Poll
How to vote via the web or text messaging

From any browser

From a text message
How to vote via text message

How's my presentation so far?

- Respond at PollEv.com/ashp
- Text a **KEYWORD** to 22333

<table>
<thead>
<tr>
<th>Comment</th>
<th>Votes</th>
</tr>
</thead>
<tbody>
<tr>
<td>It's amazing.</td>
<td>152964</td>
</tr>
<tr>
<td>It's incredibly amazing!</td>
<td>152965</td>
</tr>
<tr>
<td>It's aw-right.</td>
<td>152968</td>
</tr>
</tbody>
</table>

From a text message
How to vote via the web

How's my presentation so far?

- Respond at PollEv.com/ashp
- Text a KEYWORD to 22333

<table>
<thead>
<tr>
<th>Rating</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>It's amazing.</td>
<td>152964</td>
</tr>
<tr>
<td>It's incredibly amazing!</td>
<td>152965</td>
</tr>
<tr>
<td>It's aw-right.</td>
<td>152968</td>
</tr>
</tbody>
</table>

From any browser
Case 1—Question 1

- Prolactin level
- Lipid panel
- Thyroid studies
- Prothrombin time/INR
Your poll will show here

1. Install the app from pollev.com/app
2. Make sure you are in Slide Show mode

Still not working? Get help at pollev.com/app/help
or
Open poll in your web browser
Case 1—Question 1

A. Prolactin level
B. Lipid panel
C. Thyroid studies
D. Prothrombin time/INR
Case 1

• The decision is made to initiate risperidone at 0.5 mg PO at bedtime. Of note, the lipid panel did show an elevated LDL of 113 mg/dL and his current weight of 27.5 kg, which is ~95th percentile on the growth chart.
Risperidone for autistic behaviors

- Primary outcome at 8 weeks was assessed by:
  - Irritability subscale of the Aberrant Behavior Checklist (ABC) assessed by family/caregivers
  - Clinical Global Impressions—Improvement (CGI-I) assessed by clinician

<table>
<thead>
<tr>
<th>Weight</th>
<th>Initial dose</th>
<th>Possible maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25 kg</td>
<td>0.25 mg QHS</td>
<td>1 mg QAM/1.5 mg QHS</td>
</tr>
<tr>
<td>25 – 45 kg</td>
<td>0.5 mg QHS</td>
<td>1 mg QAM/1.5 mg QHS</td>
</tr>
<tr>
<td>&gt; 45 kg</td>
<td>0.5 mg QHS</td>
<td>1.5 mg QAM/2 mg QHS</td>
</tr>
</tbody>
</table>

## Risperidone for autistic behaviors

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Risperidone</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>52</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td><strong>Initial ABC score</strong></td>
<td>25.5±6.6</td>
<td>26.2±7.9</td>
<td></td>
</tr>
<tr>
<td><strong>8-week ABC score</strong></td>
<td>21.9±9.5</td>
<td>11.3±7.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Improvement in CGI-I</strong></td>
<td>12%</td>
<td>69%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- Children ages 5 – 17 years
- ABC assessment at least 18 at baseline

Risperidone for autistic behaviors


### Adverse effects

- **Weight gain (kg)**: 0.8 (Placebo) vs. 2.7 (Risperidone) (P<0.001)
- **Drowsiness (N)**: 6 (Placebo) vs. 24 (Risperidone) (P<0.001)
- **Fatigue (N)**: 14 (Placebo) vs. 29 (Risperidone) (P=0.003)

Cochrane review 2016: Aripiprazole for ASD

• Significant results for improvement of symptoms associated with ASD
  – ABC—Irritability and CGI—I scales
  – Hyperactivity and stereotypy
  – No improvement in social withdrawal or obsessive compulsive outcomes

• Potential for adverse effects: Sedation, drooling, weight gain, and tremor

## Potential AEs from antipsychotic agents

<table>
<thead>
<tr>
<th></th>
<th>Wgt gain</th>
<th>Diabetes</th>
<th>↑Lips</th>
<th>↑Prolactin</th>
<th>Tardive Dyskinesia</th>
<th>Extra-pyramidal symptoms</th>
<th>↑QTc interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole*</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>↓↓</td>
<td>**</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>0/+</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>**</td>
<td></td>
<td>0/+</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>**</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>**</td>
<td>0/+</td>
<td>+</td>
</tr>
<tr>
<td>Risperidone*</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>0/+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>+</td>
<td>0/+</td>
<td>0/+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

*Approved by the FDA for the treatment of irritability associated with autistic disorder

**Limited or no long-term data in children/adolescents

Potential effect: 0/+ minimal, +mild, ++moderate, +++severe

Case 1

• At a 9 month follow-up visit, father reports some improvement in behaviors, especially after increasing the risperidone dose to 1 mg at bedtime.

• EM has gained weight since initiation of risperidone with no major changes in physical activity or diet. He currently weighs 29.3 kg.
Case 1

• The physician wishes to change risperidone to aripiprazole in an attempt to minimize the continued weight gain. EM is transitioned to a dose of 5 mg daily.

• While seizure control has been stable with levetiracetam (about 1 seizure a week that is self limited), the neurologist wishes to change antiepileptic therapy to determine if that may help with behavior improvements.
Case 1—Question 2

• Which antiepileptic would be an optimal choice to substitute the levetiracetam for treatment of EM’s focal seizures?
Case 1—Question 2

A. Carbamazepine
B. Phenobarbital
C. Valproic acid
D. Topiramate
Your poll will show here

1. Install the app from pollev.com/app
2. Make sure you are in Slide Show mode

Still not working? Get help at pollev.com/app/help
or
Open poll in your web browser
Case 1—Question 2

A. Carbamazepine
B. Phenobarbital
C. Valproic acid
D. Topiramate
### Pharmacokinetic Considerations

<table>
<thead>
<tr>
<th>Drug</th>
<th>CYP3A4</th>
<th>CYP2D6</th>
<th>CYP1A2</th>
<th>UGT</th>
<th>Aldehyde Oxidase</th>
<th>T ½ (hr)</th>
<th>Protein Binding (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>★</td>
<td>★</td>
<td></td>
<td></td>
<td></td>
<td>75</td>
<td>99</td>
</tr>
<tr>
<td>Olanzapine</td>
<td></td>
<td>★</td>
<td>★</td>
<td></td>
<td></td>
<td>33</td>
<td>93</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>★</td>
<td>★</td>
<td></td>
<td></td>
<td></td>
<td>24</td>
<td>74</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>★</td>
<td></td>
<td>★</td>
<td></td>
<td></td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td>Risperidone</td>
<td>★</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
<td>89</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>★</td>
<td></td>
<td>★</td>
<td></td>
<td></td>
<td>4-10</td>
<td>99</td>
</tr>
</tbody>
</table>

- ★ Extensive metabolism pathway
- ★ Partial or minor metabolism pathway

Case 2

• LA is a 7-year-old boy diagnosed with autism at age 2 ½ years when he was not on par with peers with language and communication skills.

• LA’s past medical history reveals nothing significant with birth history.

• Behavior changes started happening at age 4
  – Exaggerated reactions to being put in time out
  – Hitting his head with body rocking
  – Screaming
Case 2

• Behaviors started to escalate at age 5 when tantrums on the school playground were resulting in LA running off into the street. At that point, he was initiated on aripiprazole.

• Current medications (all oral): aripiprazole 5 mg daily, trazodone 25 mg at bedtime (sleep), loratadine 5 mg daily (allergy symptoms), senna 8.8 mg daily (constipation), gabapentin 100 mg at bedtime (leg pain)
Case 2

• Aripiprazole has helped with the tantrums and minimizing self-injurious behaviors.
• Now LA has difficulty focusing at school and he is easily distracted from tasks and will speak loudly out of turn in the classroom.
• Despite redirection and more 1:1 class/assistant time, LA is not able to focus on class work
Case 2

• LA’s weight is 21.7 kg (~ 25th percentile) and height is 122 cm (~35th percentile)

• Lab work done about 3 months prior showed normal CBC and slightly hyponatremic (133 mmol/L)
Case 2—Question 3

• The family and physician agree medication is needed for LA’s attention deficit-hyperactivity disorder. What would be the most appropriate initial medication for LA?
Case 2—Question 3

- Methylphenidate
- Amphetamine salts
- Atomoxetine
- Guanfacine
Your poll will show here

1. Install the app from pollev.com/app
2. Make sure you are in Slide Show mode

Still not working? Get help at pollev.com/app/help
or
Open poll in your web browser
Case 2—Question 3

- A Methylphenidate
- B Amphetamine salts
- C Atomoxetine
- D Guanfacine
Treatment recommendations

• While there are some data specifically evaluating treatment of ADHD in patients with ASD, recommendations are based on:
  – Existing data in treating patients with both conditions
  – Treating non-ASD patients with ADHD
  – Clinical experience

Methylphenidate in PDD with hyperactivity

• Enrolled patient with autistic disorder, Asperger disorder, or pervasive developmental disorder (PDD) not otherwise specified with interfering symptoms of hyperactivity and/or impulsiveness

• Comparing placebo with three different dosage levels of methylphenidate utilizing a double-blind, crossover phase study design

Methylphenidate in PDD with hyperactivity

<table>
<thead>
<tr>
<th>Weight group</th>
<th>Low dose</th>
<th>Medium dose</th>
<th>High dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 - &lt; 24 kg n=29</td>
<td>2.5, 2.5, 2.5</td>
<td>5, 5, 2.5</td>
<td>10, 10, 5</td>
</tr>
<tr>
<td>24 – 34 kg n=20</td>
<td>5, 5, 2.5</td>
<td>10, 10, 5</td>
<td>15, 15, 10</td>
</tr>
<tr>
<td>&gt;34 kg n=17</td>
<td>5, 5, 2.5</td>
<td>10, 10, 5</td>
<td>20, 20, 10</td>
</tr>
</tbody>
</table>

- Doses given 8 AM, 12 PM, and 4 PM
- Optimal dose defined as dose at which ABC hyperactivity subscale score was the lowest
- Initially enrolled 66 patients to the crossover phase

ABC hyperactivity subscale score
(Parent assessment)

Placebo (n=60)
Low dose (n=62)
Med dose (n=63)
High dose (n=47)
Optimal dose (n=64)

P=0.03
P<0.001
P=0.003
P<0.001

ABC hyperactivity subscale score (Teacher assessment)

- Placebo (n=46)
- Low dose (n=45)
- Med dose (n=52)
- High dose (n=33)
- Optimal dose (n=58)

P-values:
- Placebo vs Low dose: P=0.03
- Placebo vs Med dose: P=0.008
- Placebo vs High dose: P=0.002
- Placebo vs Optimal dose: P<0.001

Case 2—Question 4

• What co-existing condition may be worsened for LA after starting methylphenidate for ADHD?
Case 2—Question 4

- A Constipation
- B Difficulty with sleep
- C Hyponatremia
- D Leg pain
Your poll will show here

1. Install the app from pollev.com/app
2. Make sure you are in Slide Show mode

Still not working? Get help at pollev.com/app/help
or
Open poll in your web browser
Case 2—Question 4

A. Constipation
B. Difficulty with sleep
C. Hyponatremia
D. Leg pain
Percent patients reporting AEs

Thirteen patients (18%) withdrew due to intolerable adverse effects

* = statistically significant compared to placebo

Methylphenidate in PDD with hyperactivity

- Response to methylphenidate not as robust compared to non-ASD patients
  - Response rate 49% compared to 70 – 80%
- Noted that non-ASD patients tolerated higher doses with lower drop out rate due to adverse effects
  - Study high dose ~0.625 mg/kg/dose versus 0.8 mg/kg/dose
  - Study dropout rate of 18% versus 1.4%

Medication utilization for ADHD with ASD

- Methylphenidate (first line)
- Amphetamine salt (second line)
- Atomoxetine -OR-
- Guanfacine
- Atypical antipsychotic

Medication use for ADHD symptoms

• Methylphenidate
  – Best evidence with pediatric patient population
  – Screen for cardiac abnormalities
  – Monitor appetite and sleep patterns
  – Several dosage forms with varying duration of action

• Amphetamine salts
  – If no significant benefit from methylphenidate or intolerable adverse effects from methylphenidate

Medication use for ADHD symptoms

• Atomoxetine
  – Increased data to support use, better results in higher functioning ASD patients
  – Gastrointestinal symptoms (nausea, decreased appetite) common
  – Increases in irritability and moodiness

Medication use for ADHD symptoms

- Guanfacine/Clonidine
  - Primarily used for hyperactivity and impulsivity, but may be beneficial with aggressive behaviors
  - May cause sedation (but may be beneficial for those patients with sleep issues)
  - Monitor blood pressure
  - Limited use for inattentiveness

Medication use for ADHD symptoms

- Risperidone/Aripiprazole
  - In trials for treatment of irritability and agitation, did show an improvement of ADHD symptoms
  - ASD patients more sensitive to adverse effects
    - Weight gain, metabolic syndrome
  - Reserved for patients with concomitant agitation, aggression, irritability or if the impulsivity actions are a safety concern

Case 3

- AJ is a 10-year-old child with a history of epilepsy, autism, asthma, developmental delay, cerebral palsy and chromosomal 1p36 deletion. Developmentally, he functions at about a 3-year-old level.
- About 8 weeks ago, he needed a dental surgery to remove three teeth and have five teeth crowned.
Case 3—medications

- Albuterol 2.5 mg neb q4hr prn (asthma)
- Budesonide 0.5 mg neb twice a day (asthma)
- Cetirizine 10 mg G-tube daily (allergies)
- Cyproheptadine 2 mg G-tube twice a day (appetite)
- Lactobacillus 1 cap G-tube daily (regularity)
- Risperidone 2 mg G-tube twice a day (irritability)
- Clonidine 0.2 mg G-tube at bedtime (for sleep)
- Guanfacine 1 mg G-tube daily (irritability/focus)
- Levetiracetam 400 mg G-tube twice a day (epilepsy)
- Omeprazole 15 mg G-tube daily (reflux)
Case 3

• Since the dental procedure, AJ has started with a repetitive behavior of biting his hands. The family has tried to redirect him to other activities and follow up examination from the dental team shows the mouth healing well from the surgery. The family is concerned that the bite marks on the hand will lead to an infection and are seeking treatment for the repetitive behaviors.
Case 3

• Current weight is 20.4 kg (< 3rd percentile) and laboratory values obtained 3 months ago were within normal limits.

• The physician prescribes fluoxetine 5 mg G-tube daily for 7 days, then increase to 10 mg G-tube daily thereafter.
Case 3

• After 10 days on fluoxetine, AJ seems more irritable and is constantly moving about. He no longer will sit for any amount of time and the family can’t seem to calm him down when he gets “worked up”

• The hand biting has not gotten any better and now he is flapping his hands throughout the day
Case 3—Question 5

• What is the most likely cause of AJ’s acute akathisia?
Case 3—Question 5

A. CYP3A4 inhibition of clonidine metabolism by fluoxetine

B. Enhanced effect of fluoxetine with cyproheptadine

C. CYP2D6 inhibition of risperidone metabolism by fluoxetine

D. Enhanced paradoxical effect of cetirizine with fluoxetine
Your poll will show here

1. Install the app from pollev.com/app
2. Make sure you are in Slide Show mode

Still not working? Get help at pollev.com/app/help
or
Open poll in your web browser
Case 3—Question 5

A. CYP3A4 inhibition of clonidine metabolism by fluoxetine

B. Enhanced effect of fluoxetine with cyproheptadine

C. CYP2D6 inhibition of risperidone metabolism by fluoxetine

D. Enhanced paradoxical effect of cetirizine with fluoxetine
Case 3—Question 6

• After removal of the offending agent that induced the akathisia, which would be the best agent to use at home for short term management of akathisia symptoms in AJ?
Case 3—Question 6

A. Mirtazapine
B. Propranolol
C. Trihexyphenidyl
D. Diphenhydramine
Your poll will show here

1. Install the app from pollev.com/app
2. Make sure you are in Slide Show mode

Still not working? Get help at pollev.com/app/help
or
Open poll in your web browser
Case 3—Question 6

A Mirtazapine
B Propranolol
C Trihexyphenidyl
D Diphenhydramine
# Potential SSRI Interactions

<table>
<thead>
<tr>
<th>Drug and inhibitory effects on cytochrome P450 enzymes</th>
<th>CYP2D6</th>
<th>CYP2C9</th>
<th>CYP2C19</th>
<th>CYP3A4</th>
<th>CYP1A2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+/++</td>
<td>+</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>+</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>+/++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Level of inhibition: +++ potent, ++ moderate, + weak

Also consider additive effects of the safety profile (e.g., insomnia, EPS)

Potential utilization of SSRIs for pediatric patients

<table>
<thead>
<tr>
<th>FDA labeled pediatric indications for SSRIs</th>
<th>Citalopram</th>
<th>Escitalopram</th>
<th>Fluoxetine</th>
<th>Fluvoxamine</th>
<th>Sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depressive disorder</td>
<td>*</td>
<td>12 – 17 yr</td>
<td>8 – 17 yr</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Obsessive compulsive disorder</td>
<td></td>
<td>7 – 17 yr</td>
<td>8 – 17 yr</td>
<td>6 – 17 yr</td>
<td></td>
</tr>
<tr>
<td>Depressive disorder with bipolar I disorder</td>
<td></td>
<td></td>
<td>10 – 17 yr</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Not approved by FDA for pediatrics, but recommended by treatment algorithm

Fluoxetine for repetitive behaviors in autism patients

- Patient age 5 – 17 years meeting criteria for ASD
- Assessed using the Children’s Yale-Brown Obsessive-Compulsion Scale, compulsions subscale (CY-BOCS)
- Initial fixed dose of fluoxetine 2.5 mg/day (then titrated up on a mg/kg dose)
  - Week 2 → 0.3 mg/kg/day
  - Week 3 → 0.5 mg/kg/day
  - Week 4-8 → 0.8 mg/kg/day maximum

Mean CY-BOCS scores

Combined mean scores from the two randomization conditions

Fluoxetine had a greater effect based on linear trend (p=0.015)

Fluoxetine for repetitive behaviors in autism patients

• Secondary analysis showed no statistically significant differences between groups using the Clinical Global Improvement Scale Adapted to Global Autism (CGI-AD)

• Noted in Cochrane analysis that when comparing data within a phase, there were no statistical differences

Reported adverse events

Values reported as percentage
No statistical significant difference between groups

Cochrane review (2013): SSRIs for ASD

• There were five studies with children and four studies with adults that met review criteria
• Due to different medications, small sample sizes (different patient ages), and various outcome measures, a meta-analysis was not possible
• Evaluated effect on core ASD features, non-core features and potential for adverse effects

Cochrane review (2013): SSRIs for ASD

- Did not find significant data to support the use of SSRIs for core features (including repetitive behaviors) for children or adults
- SSRIs may be of benefit for adults patients in treating non-core symptoms (aggression, obsessive-compulsive disorder, anxiety)

Cochrane review (2013): SSRIs for ASD

- Some patients did warrant a dose reduction of the SSRI due to adverse effects, and one patient had a prolonged seizure
- Conclusion: Decisions about the use of SSRIs for established clinical indications that may occur with autism, such as OCD, depression (in children and adults), or anxiety (adults), should be made on a case-by-case basis

Treatment for depression

• If medication therapy warranted for a patient with ASD, utilize the current treatment algorithms for non-ASD patients
  – In conjunction with cognitive behavioral therapy

Antidepressant efficacy and tolerability meta-analysis (2016)

• Limited efficacy in pediatric patients
  – Evaluated 34 trials with a combined 5260 patients utilizing 14 different antidepressants
  – Only fluoxetine showed significant efficacy versus placebo
  – Tricyclic antidepressants showed less efficacy compared to other agents and were not as well tolerated

SSRIs adverse effect considerations

• Potential increase in suicidality (boxed warning)
  – Highest risk in pediatric and young adult patients up to 24 years of age

• Potential adverse effect of ‘behavioral activation’
  – Recurrence or worsening of agitation or irritability

U. S. Food and Drug Administration. Anti-depressant Drug Use in Pediatric Populations.
Considerations in initiating an SSRI

• Initiate at a low dose and titrate up slowly
• Continue to monitor for general adverse effects
  – Gastrointestinal symptoms
  – Sleep disruption
  – Changes in appetite
• Counsel on potential severe adverse effects
  – Behavior activation
  – Serotonin syndrome

Conclusions

• Atypical antipsychotic agents are utilized for the irritability and aggression associated with ASD
  – Dose escalation
  – Baseline/follow-up laboratory monitoring
  – Drug/drug interactions
Conclusions

• Stimulant medications are the first-line therapy for ASD patients with ADHD symptoms
  – Proper dose initiation/escalation
  – Consider dosage forms for optimal efficacy and to minimize adverse effects
  – Consider other agents depending on clinical condition
Conclusions

• The utilization of SSRIs should be limited to specific indications and considered on a case-by-case basis
  – Diagnosis of depression or obsessive compulsive disorder
  – Consider drug/drug interactions and additive adverse effects
  – Monitor for increased risk of suicidality
Key Takeaways

• Key Takeaway #1
  – Medication management of non-core ASD symptoms is evolving with psychotropic medications and may involve polypharmacy

• Key Takeaway #2
  – Pharmacists can play a significant role in ensuring proper medication initiation, monitoring for drug/drug interactions, and counseling on potential adverse effects

• Key Takeaway #3
  – Updated clinical data can be found through American Academy of Pediatrics and the Autism Speaks Autism Treatment Network websites
Questions?