Practical Aspects of Medication Treatment in Autism

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Disclosures of Potential Conflicts

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<tr>
<th>Source</th>
<th>Consultant</th>
<th>Advisory Board</th>
<th>Stock or Equity</th>
<th>Board or Gray Interests</th>
<th>Research Support</th>
<th>Research for this presentation or meeting</th>
<th>Expenses related to this presentation or meeting</th>
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<tbody>
<tr>
<td>Kentucky Autism Training Center</td>
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<td>Fragile X Research Foundation</td>
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Target Symptoms for Medication

- Motor hyperactivity and inattention
- Interfering ritualistic behavior
- Aggression, self-injury, property destruction
- Mood disturbances: depression, bipolar
- Others: sleep disturbances, pica, inappropriate sexual behavior

Motor Hyperactivity and Inattention

- Psychostimulants: methylphenidate, dextroamphetamine
- Alpha-2 agonists: guanfacine, clonidine, Intuniv
- Non-stimulants: atomoxetine, bupropion, tricyclic antidepressants

Psychostimulants

- Work quickly
- Side effects: reduced appetite, insomnia, tics
- May cause behavioral worsening
- May need to be given multiple times per day
- Need new prescription each month
**Alpha-2 Agonists**

- Need to monitor blood pressure and heart rate
- Can be sedating
- Generally don’t make symptoms worse
- 2/3 need to be given 2-3 times per day
- Intuniv now FDA-approved for ADHD in children

**Non-Stimulants**

- Atomoxetine: effective in ADHD; preliminary studies in developmental disabilities. May take longer to work than stimulants. Generally won’t make tics worse. May help with comorbid mood and/or anxiety.

**Non-Stimulants (Cont’d)**

- Bupropion: has been shown to be effective for ADHD. Not well-studied in developmental disabilities. Can lower the seizure threshold and should NOT be given to a patient with a history of seizures or active seizure disorder. Can make tics worse.

**Non-Stimulants (Cont’d)**

- Tricyclic antidepressants: not well-studied in developmental disabilities. Associated with side effects including: dry mouth, blurry vision, constipation. Can lower the seizure threshold. Can affect cardiac rhythm.

**Ritualistic Behavior**

- Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Fluoxetine
  - Fluvoxamine
  - Sertraline
  - Paroxetine
  - Citalopram
**SSRIs**

- Data indicate SSRIs may be more effective in post-pubertal vs. pre-pubertal individuals with developmental disabilities
- Side effects: insomnia, sedation, stomach upset, sexual dysfunction, weight gain
- Can generally be given once a day
- Concern about increasing suicidal thinking/behavior

**Aggression/Self-Injury/Property Destruction**

- Typical antipsychotics
- Atypical antipsychotics
- Mood stabilizers
- Alpha-2 agonists
- Naltrexone

**Aggression (Cont’d)**

- Typical Antipsychotics
  - Haloperidol
  - Thioridazine
  - Chlorpromazine
- Side effects: acute extrapyramidal symptoms (EPS), tardive dyskinesia (TD), sedation, weight gain, drooling

**Aggression (Cont’d)**

- Atypical Antipsychotics
  - Clozapine
  - Risperidone
  - Olanzapine
  - Quetiapine
  - Ziprasidone
  - Aripiprazole
  - Paliperidone

**Clozapine**

- Common side effects include weight gain, sedation, drooling
- Can lower the seizure threshold
- Agranulocytosis and need for careful blood monitoring

**Risperidone**

- Well-studied in autism (FDA approval) and mental retardation associated with behavioral dyscontrol
- Common side effects: weight gain, sedation (transient), drooling, elevated prolactin
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<tr>
<th><strong>Olanzapine</strong></th>
<th><strong>Quetiapine</strong></th>
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<td>• Only small controlled studies in developmental disabilities</td>
<td>• No controlled studies in developmental disabilities</td>
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<tr>
<td>• Common side effects: weight gain (at times significant), has been associated with glucose and lipid dysregulation, sedation</td>
<td>• Common side effects: weight gain (may be less prominent than with clozapine and olanzapine), sedation, orthostatic hypotension if dose increased too quickly</td>
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<tr>
<th><strong>Ziprasidone</strong></th>
<th><strong>Aripiprazole</strong></th>
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<td>• No controlled studies in developmental disabilities</td>
<td>• FDA-approved for “irritability” in children and adolescents with autism.</td>
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<td>• Common side effects: sedation (transient), occasional insomnia or behavioral activation. Not associated with significant weight gain</td>
<td>• Common side effects: EPS and nausea/vomiting if given at too high a starting dose. Occasionally transient sedation or activation.</td>
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<td>• Should not be given to patients with cardiac problems</td>
<td>• Most weight-neutral other than ziprasidone</td>
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<td>• Must be taken with food</td>
<td>• No prolactin elevation</td>
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<th><strong>Paliperidone</strong></th>
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<td>• Major active metabolite of risperidone</td>
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<td>• Potentially fewer drug-drug interactions</td>
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<tr>
<td>• Once daily dosing</td>
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<td>• Potentially less weight gain and prolactin elevation</td>
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Aggression (Cont’d)

- Mood Stabilizers
  - Valproic acid
  - Lithium
  - Carbamazepine
  - Gabapentin
  - Topiramate

Valproic Acid

- The only controlled study in autism found no drug vs. placebo difference
- Common side effects: sedation, weight gain
- Need to monitor blood level for therapeutic range and to follow liver function tests
- May be useful in patients with seizures and aggression

Lithium

- No controlled studies in developmental disabilities
- Common side effects: tremor, polydipsia, polyuria, weight gain
- Need to monitor blood for therapeutic range and to follow kidney and thyroid function

Carbamazepine

- No controlled studies in developmental disabilities
- Common side effects: dizziness
- Need to monitor blood level for therapeutic range and to follow blood count and sodium level

Gabapentin

- No controlled studies in developmental disabilities
- Common side effects: some sedation, some weight gain
- No need to monitor blood levels
- Not particularly effective on a clinical basis

Topiramate

- No controlled studies in developmental disabilities
- Common side effects: sedation, cognitive dulling. Not associated with weight gain
- No need to monitor blood levels
Aggression (Cont’d)

• Alpha-2 Agonists
  – Guanfacine: not particularly effective for aggression
  – Clonidine: can be effective for aggression. Need to balance sedation vs. clinical benefit
• Need to monitor blood pressure and heart rate

Aggression (Cont’d)

• Naltrexone
• Not effective on a clinical basis
• No significant side effects
• Need to monitor liver function

Mood - Depression

– SSRIs
– Bupropion
– Venlafaxine (elevated blood pressure)
– Mirtazapine (weight gain, sedation)
– Duloxetine (recently released)
– Tricyclic antidepressants

Mood - Bipolar

• Valproic acid
• Lithium
• Carbamazepine
• Gabapentin
• Topiramate
• Lamotrigine (Steven’s Johnson Syndrome)

Sleep Disturbance - Insomnia

• Diphenhydramine (paradoxical rxt’n)
• Clonidine
• Trazodone (priapism)
• Chlortal hydrate
• Benzodiazepines (paradoxical rxt’n)
• Melatonin
• Mirtazapine
Pica

- SSRIs
- Behavioral strategies

Inappropriate Sexual Behavior

- SSRIs
- Hormonal strategies
- Behavioral strategies

Questions Parents Should Ask Physicians

- Do you have experience using medication to treat symptoms associated with autism?
- If so, how many patients with autism do you currently treat in your practice?
- If not, can you recommend someone in the community you have confidence in for this purpose?

- Will a medication “cure” my child?

- How will you know if a medication is working?

- How long will my child need to be on medication?

- How often would you want to see my child if she/he is on medication?

Questions Physicians Should Ask Parents
- Does your child have symptoms of irritability (aggression, self-injury, severe tantrums), hyperactivity, inattention, interfering rituals, sleep disturbance, anxiety, or depression?

- If so, attempt to determine frequency, duration and intensity of symptoms.

- Does your child have a seizure disorder?

- Ask about prior medication treatment, including drug, dose, duration and response.

- List the top 3 things you would like to see improve.
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QUESTIONS?