

Pharmacological Management of Behavioral Symptoms in Autism Spectrum Disorders

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Disclosure of Potential Conflicts

None

Off-Label Use Of Medication

In this presentation, all discussion of use of medication refers to “**off-label**” use other than risperidone and aripiprazole for irritability in children and adolescents with autistic disorder

Target Symptoms for Medication

- Motor hyperactivity and inattention
- Interfering ritualistic behavior
- Aggression, self-injury, severe tantrums
- Mood disturbances: depression, bipolar
- Anxiety
- 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
 - Escitalopram

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/Severe Tantrums/ Self-Injury

- 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

Olanzapine

- Only small controlled studies in developmental disabilities
- Common side effects: weight gain (at times significant), has been associated with glucose and lipid dysregulation, sedation

Quetiapine

- No controlled studies in developmental disabilities
- Common side effects: weight gain (may be less prominent than with clozapine and olanzapine), sedation, orthostatic hypotension if dose increased too quickly

Ziprasidone

- No controlled studies in developmental disabilities
- Common side effects: sedation (transient), occasional insomnia or behavioral activation. Not associated with significant weight gain
- Should not be given to patients with cardiac problems
- Must be taken with food

Aripiprazole

- FDA-approved for “irritability” in children and adolescents with autism.
- Common side effects: EPS and nausea/vomiting if given at too high a starting dose. Occasionally transient sedation or activation.
- Most weight-neutral other than ziprasidone
- No prolactin elevation

Paliperidone

- Major active metabolite of risperidone
- Potentially fewer drug-drug interactions
- Once daily dosing
- Potentially less weight gain and prolactin elevation

Aggression (Cont'd)

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

Valproic Acid

- A 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

Lamotrigine

- Controlled study in autism found no drug vs. placebo difference
- Must increase the dose very slowly
- Steven's – Johnson rash

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
- Tricyclic antidepressants

Mood - Bipolar

- Valproic acid
- Lithium
- Carbamazepine
- Gabapentin
- Topiramate
- Lamotrigine (Steven's Johnson Syndrome)

Anxiety

- Mirtazapine (weight gain, sedation)
- Buspirone
- SSRIs (low dose)

Sleep Disturbance - Insomnia

- Melatonin
- Clonidine
- Trazodone (priapism)
- Mirtazapine
- Tricyclic Antidepressants (Doxepin, Amitriptyline)
- Chloral Hydrate
- Benzodiazepines (Paradoxical rxt'n)
- Diphenhydramine (Paradoxical rxt'n)

Pica

- SSRIs
- Behavioral strategies

Inappropriate Sexual Behavior

- SSRIs
- Hormonal strategies
- Behavioral strategies

QUESTIONS?

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- Susan Connors, MD
- Gillian Erhabor, Ph.D
- Nora Friedman, MD
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<http://www.massgeneral.org/children/services/treatmentprograms>

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