Psychopharmacology of Autism Spectrum Disorder

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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.
Pervasive Developmental Disorders DSM-IV

- Autistic Disorder
- Asperger’s Disorder
- Rett’s Disorder
- Childhood Disintegrative Disorder
- Pervasive Developmental Disorder Not Otherwise Specified

- DSM-5 Autism Spectrum Disorder
Evaluation

• Diagnosis
• Physical Examination
• Neuropsychological Testing
• Genetic Testing
• Electroencephalogram (EEG) and/or Brain Imaging (CAT scan or MRI scan)
Treatment Options

- Behavior therapy
- Speech and Language therapy
- Occupational therapy
- Physical therapy
- Social skills therapy
- Special educational services (academic vs. life skills track)
- Treatment of comorbid medical problems, including seizures
- Vocational training
- Pharmacotherapy
Treatment Options (cont’d)

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  (academic vs. life skills track)
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Target Symptoms for Medication

- Motor hyperactivity and inattention
- Interfering ritualistic behavior
- Aggression, self-injury, severe tantrums
- Mood disorders: depression, bipolar
- Anxiety disorders
- 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
- May cause constipation
- 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; effective for ASD in children. 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 intellectual disability 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 (akathisia)
• No prolactin elevation
Paliperidone

- Major active metabolite of risperidone
- Potentially fewer drug-drug interactions
- Once daily dosing
- Potentially less weight gain and prolactin elevation than risperidone
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
  - Occasionally effective on a clinical basis
  - No significant side effects
  - Need to monitor liver function
Mood - Depression

- Bupropion
- Venlafaxine (elevated blood pressure)
- Duloxetine
- SSRIs
- Mirtazapine (weight gain, sedation)
- Tricyclic antidepressants
Mood - Bipolar

- Valproic acid
- Lithium
- Carbamazepine
- Gabapentin
- Topiramate
- Lamotrigine (Steven’s Johnson Syndrome)
Sleep Disturbance - Insomnia

- Melatonin
- Clonidine
- Trazodone (priapism)
- Mirtazapine
- Tricyclic Antidepressant (Doxepine, Amitriptyline)
- Chloral Hydrate
- Benzodiazepines (Paradoxical rxt’m)
- Dephenhydramine (Paradoxical rxt’n)
Anxiety

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

- SSRIs
- Behavioral strategies
Inappropriate Sexual Behavior

- SSRIs
- Hormonal strategies
- Behavioral strategies
QUESTIONS?
Lurie Center for Autism

- Christopher J. McDougle, MD
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