Medications for Behavioral Health Concerns in ASD

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No conflicts of interest

ASD
• Autism Spectrum Disorder
OBJECTIVES

• Identify three behavioral health concerns in ASD

• Identify three common families of medication that may be supportive for behavioral health concerns in ASD

• Identify three evidence based medications for co-occurring behavioral concerns for an individual with ASD

Key Challenges for a Child or Adolescent

• Social engagement/loneliness and isolation (24%)
• General behavioral issues (19%)
• Speech/language/communication (19%)
• Psychological co-morbidities/anxiety (14%)
• Engagement in enriching activities (13%)

Key Challenges for Family

• Getting the help and services needed (18%)
• Financial issues (16%)
• General behavioral issues (15%)
• Family stress (15%)
• Transition to more independent living/issues of adulthood (15%)
Common Symptoms Not Unique to Autism

- Attentional impairment
- Hyperactivity
- Aggression
- Decreased pain sensitivity
- Sensory differences
- Sleep disturbance

Most Common Behavioral Symptoms

- Hyperactivity and Impulsiveness
- Repetitive behavior (stereotyped motor mannerisms and inflexible adherence to non-functional routines)
- Irritability and aggression, temper outbursts and self-injury
- Anxiety and Depression
- Insomnia

Evidence Based Psychopharmacology targeting specific symptoms

- Anxiety and obsessions and rigidity: SSRIs (fluoxetine, sertraline) helpful
- Hyperactivity, attention and concentration issues can be helped with ADHD meds
- Aggression or irritability helped with risperidone and aripiprazole
- Insomnia helped with melatonin
More than half of all children with ASD struggle with sleep disorders.
Insomnia most common.
Frequent night awakenings 3 or more times a night and prolonged awakenings.
Can exhaust entire family and impact child’s ability to learn.
Can cause hyperactivity, inattiveness and aggression.

Sleep Difficulties
May be caused by medical issues such as
Obstructive sleep apnea
symptoms of loud snoring, gasping, overweight
Gastrointestinal reflux (GERD)
Enuresis (Bedwetting)

Sleep Strategies
Establish regular bedtime routine
Visual schedule of routine
Start routine 30 minutes before bed
Avoid stimulating activities or bright lights
Avoid caffeine and sugar in evenings
Sleep Difficulties

- If sleep routine and strategies not successful
- And
- If no underlying medical issues found
- Talk with a physician about sleep medications

Melatonin for insomnia

- Melatonin supplements have shown effectiveness in improving sleep in some children.
- Melatonin is a neuro-hormone produced in the pineal gland and responsible for circadian rhythm
- Lower nighttime melatonin or melatonin metabolite concentrations found in ASD compared to controls.

Melatonin

- 20 clinical trials have reported improvements including longer sleep duration, less nighttime awakenings, and quicker sleep onset
- 6 studies associated with better daytime behavior
- 4 studies reported improvements when other meds had failed.
Melatonin
- 24 children ages 3-9 years
- 1-6 mg helped with sleep onset within a weeks time
- Benefits lasted 14 weeks (length of study)
- No significant side effects
- Improved daytime behavior

Melatonin Extended Release

Anxiety
- Research suggests that 30% with ASD also have an anxiety disorder
- Included:
  - Social phobia
  - Separation Anxiety
  - Obsessive Compulsive Disorder
  - Generalized Anxiety
Adolescents with ASD may be particularly prone to anxiety. Rates of anxiety among younger children with ASD may be the same as peers. CBT is particularly helpful and with behavioral interventions over 6-16 weeks most children experience significant improvement in anxiety as well as social communication improvement and other daily living issues.

Medication

Outside of PDDs, SSRIs are used to treat depression, anxiety, and obsessive compulsive disorder. Within PDDs, SSRIs are studied for potential to ameliorate repetitive and problem behaviors (irritability/agitation) and to try to ameliorate comorbid symptoms of anxiety and depression.
Recently identified as the most common class of medications prescribed for children with PDD (Oswald and Sonenklar, 2007; Mandel et al., 2008).

- Non-addictive

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Sertraline (Zoloft)
First placebo-controlled trial by Hollander et al. (2005) showed a small effect compared to placebo (CYBOCS-PDD) in decreasing repetitive behavior.

Showed that there was increased tolerability with low doses and slow titration.

Doses of 9.9 + or – 4.35 mg/day (btw 5 and 15 mg/day).

Most common adverse side effects were increases in irritability, insomnia, hyperactivity and lethargy.

No long term negative effects noted.
Symptoms of Anxiety and Depression both may co-exist with ASD

Individuals with ASD and Depression are at similar risk for suicide as others

Medication recommendations are same for individuals with ASD and Depression
SSRIs are recommended first-line medication
Lower initial dosages may cause less side effects
Research team at the Kennedy Krieger Institute found that almost one third of children with ASDs also showed clinically significant symptoms of ADHD.

_Autism: The International Journal and Practice_ (June 2013, issue)

Psycho-stimulants demonstrate some benefits for children with ASDs, but less efficacious and with more adverse effects compared with children with ADHD.

Alpha-2 agonists (clonidine and guanfacine) and atomoxetine are also effective.

**Psycho-stimulants**
- Methylphenidate (Ritalin)
- Dexedrine
- Dextro-amphetamine (Adderall)
Methylphenidate (RUPP 2005)

- 72 children (5 to 14 years of age)
- Dose strengths were described as low, medium, high (0.15mg/kg, 0.25mg/kg, and 0.5mg/kg)
- Week long test dose period followed by 4 week double blind randomized with active med or placebo.
- Teacher and parent ratings used in algorithm to find best dose for each child.

Methylphenidate

- At doses ranging from 12.5 to 25 mg per day methylphenidate appears to be effective for 50-60% of children with a PDD accompanied by hyperactivity
- Likely to be well tolerated by school age children with PDD
- An effort to produce greater improvement with higher doses is likely to result in adverse effects

Methylphenidate and Preschoolers

- Ages 3-5 years with developmental disorders, most with ASDs
- Randomized, placebo-controlled, crossover study
- Dosages from 5 to 20 mg day
- showed a 50% response rate to MPH
- 3% showed adverse effects
These centrally acting antihypertensive agents have more recently been reported as alternative or adjunctive treatments for:

- ADHD
- Tourette disorder
- behavior disorders with severe agitation, self-injury, or aggression

Oral and/or transdermal clonidine is moderately efficacious in treating hyperactivity and irritability (double-blind placebo control in ages 5 to 13 years).

Also helpful for sleep initiation and maintenance, specifically for reducing sleep initiation latency and night awakening.

• most common side effect is sedation
  other side effects include:
  - hypotension
  - other cardiovascular effects
  - headache and dizziness
  - stomach ache, nausea, vomiting
  - available in a skin patch
Guanfacine (Tenex)

- 8 week open label companion trial with RUPP methylphenidate
- Parents rated as 40% improved and teachers 25% improved (ABC hyperactivity subscale)
- Also rated as showing medium improvement on parent rated irritability subscale (tantrums, aggression, and self injury)
- Attentional gains as well (using SNAP-IV)

Guanfacine

- Dose limiting effects include drowsiness, irritability, enuresis, mid sleep awakening.
- In many cases can manage by dose manipulation.
- Guanfacine seems to be tolerated better than clonidine in several small studies in this population (Jaselskis et al. 1992)

Autism and Irritability and Meltdowns

- Moderate to severe irritability is known to occur in 30% of children with ASDs
Autism and Disruptive Behavior Disorder

Antipsychotics are the most efficacious medications for the treatment of irritability in ASDs (2012 Dialogues in Neuroscience)

Atypical antipsychotics have a decreased risk of extrapyramidal symptoms

Risperidone and Aripiprazole are the only medications FDA approved for irritability in Autism Spectrum Disorders

RUPP Autism Network investigators reasoned that if risperidone could reduce serious behavioral problems in children with autism, it could help the child be more available for other interventions. Reasoned that risperidone might also have secondary benefits in social domain.
70 per cent of children with Autism accompanied by serious maladaptive behavior are likely to show benefit with an expected magnitude of improvement about 50% compared to base line.

Weight gain appears to be greater compared to aripiprazole.

Metabolic syndrome: Increased lipid levels and hyperglycemia.

Associated with increase in serum prolactin.

Gains are stable over time.

Relapse is likely if medication is withdrawn at 6 months.
Aripiprazole (Abilify)

- 2009 Study found Aripiprazole at dosages of 5mg, 10mg, and 15 mg efficacious in decreasing tantrums, aggression, and self-injurious behavior at eight weeks in children with ASD (218 children ages 6-17 years)
- Adverse events were sedation, one episode of pre-syncope and one episode of aggression
- Mean weight gain was 1.3 kg, p<.05 versus placebo

Behavioral Health Concerns

- Insomnia
- Anxiety
- ADHD
- Depression
- Irritability and Aggression

Medication Classes

- Melatonin - Insomnia
- SSRIs - Anxiety and Depression
- Psycho-stimulants and Alpha-Adrenergic Agonists - Attention, Hyperactivity
- Anti-psychotics - Irritability
References


References

- Dialogues in Clinical Neuroscience 2012 September 14(3) 263-279 Pharmacologic treatments for the behavioral symptoms associated with autism spectrum disorders across the lifespan