

Autism Spectrum Disorders and Comorbid Behavioral Health Symptoms

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Psychopharmacologic and Alternative
Medicine Interventions in
Autism Spectrum Disorders
Anxiety , Depression, Insomnia and ADHD

Objectives

- Identify two interventions for insomnia in ASD
- Identify three interventions that are supportive in co-morbid Anxiety or Depression
- For children with ADHD and ASD, identify two effective classes of medications , their dosing strategies and potential side effects

Prevalence of ASDs

- 1 in 88 children
- 1 in 54 boys

Autism Spectrum Disorder and Insomnia

Sleep Dysfunction

- 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, inattentiveness and aggression.

Sleep Dysfunction

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

Sleep Strategies

- Autism Intervention Research on Physical Health
Sleep Toolkit

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 Dysfunction

- If sleep routine and strategies not successful

And

- If no underlying medical issues found
- Talk with physician about sleep medications

Melatonin for sleep

- 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

- Dosing strategy
- For 3-4 year olds start with 1 mg and can increase to 3 mg nightly
- For school age children use between 3 and 6 mg nightly

Melatonin

- Melatonin for Sleep in Children with Autism: A controlled trial examining dose, tolerability and Outcomes. Journal of Autism and Developmental Disorders. August 2012, Volume 42, Issue 8, pp 1729-1739
- 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

Clonidine

- Helpful for sleep initiation and maintenance , specifically for reducing sleep initiation latency and night awakening.
- Dosing strategy
- Begin with 0.05 mg at bedtime and increase to 0.1 mg if needed
- There is a transdermal patch as well TTS-1 but skin irritation is common

Autism Spectrum Disorders and Anxiety

Anxiety

- Research suggests that 30% with ASD also have an anxiety disorder
- Included:
- Social phobia
- Separation Anxiety
- Obsessive Compulsive Disorder
- Generalized Anxiety

Anxiety

- Adolescents with ASD may be particularly prone
- Rates of anxiety among younger children with ASD may be same as peers

Anxiety Treatment

- CBT or Cognitive Behavioral Therapy
- CBT 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.

Selective Serotonin Reuptake Inhibitors

- 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

SSRIs

- Recently identified as the most common class of medications prescribed for children with PDD (Oswald and Sonenklar 2007; Mandel et al. 2008)

SSRIs

- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)
- Paroxetine (Paxil)
- Sertraline (Zoloft)

Fluoxetine

- 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

Fluoxetine

- Doses of 9.9 ± 4.35 mg/day
(btw 5 and 15 mg/day)

Adverse Effects of Fluoxetine

- Most common adverse side effects were increases in irritability, insomnia, hyperactivity and lethargy
- No long term negative effects noted

ASD and ADHD



Attention Deficit Hyperactivity Disorder

- 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)

Hyperactivity and inattention

- Psychostimulants 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.

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 4week 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
- ½ showed adverse effects

Alpha-Adrenergic Agonists

- **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**
 - **adjunctive treatment of schizophrenia and mania**

Clonidine

- 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.

Clonidine (Catapres)

- **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**

Clonidine dosing strategy

- Begin with 0.05 mg at bedtime and can advance to 0.1 mg at bedtime
- If no excessive daytime sedation and still concerns of hyperactivity can add 0.05 to 0.1 mg two to three times a day

Guanfacine

- 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)

Guanfacine dosing strategy

- Can begin with $\frac{1}{2}$ to 1 mg nightly (unless causes sleep disturbance)
- Then titrate to effect by $\frac{1}{2}$ mg weekly up to total of 3 mg /day
- An ER preparation that is also effective up to 4 mg/day

Atomoxetine

- Moderately efficacious in treatment of hyperactivity and possibly attention in children with ASDs.
- Double blind, PC study in 16 children aged 5 to 15 years revealed a 56% response to hyperactivity.
- Dosages ranged from 1.2-1.4 mg/kg/day

Atomoxetine

Safety data

- diastolic BP and heart rate increase in a statistically but not clinically significant manner
- 20% with decreased appetite - weight decreased in first 9-12 weeks of treatment, then begins to catch up and parallel growth curve
- no significant lab or EKG changes
- no exacerbation of tics or anxiety
- insomnia not a significant side effect
- *** need to watch for abnormal liver function
- *** black box warning – may increase suicidal thoughts

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

Complementary and Alternative Medicine



Casein and Gluten Free

1/3 of children have been treated with diet

Many parents report improvement

Casein and Gluten free Diets

Plausible that many children may have lactose intolerance or milk allergy . Sleep, stool quality, and mood may be improved by having less discomfort.

- Consider removing either casein or gluten
- Consider that if more healthy foods are substituted , may also cause some benefit

Casein and Gluten free Diets

initial theory of increased opiate peptides was not substantiated

More research needed

Probiotics

- Recommend probiotic yogurt
- If intent on giving supplements , check label for amount of viable organisms in supplement(should be in billions)
- If don't see clear improvement in few weeks, stop using –If no clear benefit ,don't risk potentially negative side effects

Omega -3 Fatty Acids

- Fatty acids are essential for brain development and function
- Several small studies have suggested supplements may reduce autism related symptoms such as repetitive behavior and hyperactivity
- Pilot study in 2011 found with 1.3 grams per day found improvement in hyperactivity

Omega -3 Fatty Acids

- Still trying to find optimal dose and optimal ratio of two main components
- EPA/DHA
- Further study is needed before experts can make reliable recommendations