

Medication Management of Children with ASD

Veena Tripathi Ahuja, MD Child, Adolescent, and Adult Psychiatry Balanced Innovative Care, LLC

There are no disclosures for this presentation.

Today's Discussion

- What can we do?
- Why is it difficult to find the right medication?
- Treating the Symptoms
- Questions?

What is Neurodivergence?

Per Cleveland Clinic (06/22):

"Neurodivergent is a nonmedical term that describes people
whose brain develops or works differently for some reason.
This means the person has different strengths and struggles
from people whose brains develop or work more typically.
While some people who are neurodivergent have medical
conditions, it also happens to people where a medical condition
or diagnosis hasn't been identified."

Terms:

- neurodivergent neuroatypical
- neurotypical
- autistic person versus person with ASD
- differently abled versus disabled

How does this help us? How does this hurt us?

What can we do? - Strategies

- Strategies for Coping with Autism
 - Look for support groups and credible sources of health information
 - Dietary changes like gluten-and dairy-free guidelines
 - Behavioral treatments, like occupational therapy and relational development intervention
 - Medication
 - When in doubt, consult a doctor

Source: https://www.verywellhealth.com/autism-coping-4686275

What can we do? - Therapies

- Per Linden et al (2022):
 - Reviewed 71 randomized controlled trials
 - Cognitive behavioral therapy
 - may decrease depression and anxiety scores in autistic children and adults
- Mindfulness therapy
 - may decrease anxiety and depression scores in autistic adults with previous mental health conditions
- Behavioral interventions
 - may help to treat depression in autistic children
- Radically Open Dialectical Behavioral Therapy (RO-DBT)

Treatment

- There is no cure!
- Goals
 - Minimize core features
 - Maximize functional independence
 - Alleviate family distress
- How?
 - Facilitate learning
 - Promote socialization
 - Reduce maladaptive behaviors
 - Educate and support families

Focus on symptoms that are

- causing distress for patient
- causing distress for family
- making it hard for the patient to be in public and explore the community

Why is it difficult to find the right medication?

- There is no FDA approved medication to treat ASD
 - Risperidone (Risperdal) and aripiprazole (Abilify) are FDA approved to treat irritability in patients with ASD
- There are a lot of comorbid conditions
 - depression
 - anxiety
 - ADHD
- Patients with ASD tend to be more sensitive to medication changes
- Patients with ASD may need multiple medications to target all comorbid conditions
- Patients with communication issues may not be able to explain improvement in symptoms or side effects
 - Can be helpful to rely on more objective info (behavioral charts provided by therapists)
- Many children with ASD struggle to take medication
 - Look for different forms (liquid, crush tablets, etc.)

We know the Neurotypical Symptoms...

Anxiety

- scared
- crying often
- worried

Mood Lability

- poor frustration tolerance
- mood swings
- erratic behavior

Inattention

- difficulty with focus
- getting easily distracted

Hyperactivity/Impulsivity

- restless and cannot sit still
- doing things without thinking

Identify the *Neuroatypical* Symptoms

Anxiety or Rigidity

- Could appear scared or worried
- getting stuck or repetitive questions
- poor sleep before big events
- irritable when pushed or when they are not in control

Inattention

- difficulty with focus
- getting easily distracted
- unable to engage
- frustrated when they have to end hyperfocus or leave preferred interest
- irritable when pushed to focus or after missing details

Irritability or Mood Lability

- poor frustration tolerance
- heightened or on edge
- quick to anger and unable to regulate
- irritable throughout the day with small to no triggers

Hyperactivity and/or Impulsivity

- restless and cannot sit still
- doing things without thinking
- can be held in by some when anxious (such as during the school day)
- outbursts when they have to end hyperfocus or leave preferred interest
- irritable when pushed to remain still or with small triggers

Treat the Symptoms Systematically

Anxiety or Rigidity

- antidepressants like SSRIs (Zoloft (sertraline) or Lexapro (escitalopram))
- alternate options (gabapentin, hydroxyzine)
- propranolol for daytime anxiety
- prazosin for nightmares
- increase only once every 2-3 weeks

Irritability or Mood Lability

- atypical antipsychotics ((Risperdal (risperidone) or Abilify (aripiprazole))
- could try mood stabilizers (Depakote (valproic acid) or Lamictal (lamotrigine))
- Always watch out for weight gain
- Some meds can be used as needed
- Some of these symptoms may improve when other symptoms improve

Inattention

- prefer to start with methylphenidate (Ritalin/Concerta/Metadate CD) or dexmethylphenidates (Focalin)
- some do better with amphetamines (Adderall or Vyvanse)
- nonstimulant options Strattera (atomoxetine) - take more time to work but can help with anxiety
- Start low and go slow
- Better to start with immediate release if younger or sensitive to medications

Hyperactivity and/or Impulsivity

- Stimulants and mood stabilizers can help!
- alpha agonists (Intuniv/Tenex (guanfacine) or Kapay (clonidine))
- may improve with better sleep
- may improved with decreased anxiety

By Medication Class

Antidepressants

SSRIs

- Zoloft (sertraline)
- Lexapro (escitalopram)
- Celexa (citalopram)
- Prozac (fluoxetine)
- Luvox (fluvoxamine)
- look out for activation, headaches, stomach upset

SNRIs

- Wellbutrin (bupropion)
- Effexor (venlafaxine)
- Cymbalta (duloxetine)

Methylphenidate

- Ritalin/Concerta/Metadate CD
- dexmethylphenidates (Focalin)

Amphetamines

- Adderall short or long acting
- Vyvanse lasts the longest
- Start low and go slow
- Better to start with immediate release if younger or sensitive to medications

Nonstimulant options

 Strattera (atomoxetine) - take more time to work but can help with anxiety

Atypical antipsychotics

- Risperdal (risperidone)
- Abilify (aripiprazole))
- Always watch out for weight gain
- Some meds can be used as needed

Mood stabilizers

- Depakote (valproic acid)
- Lamictal (lamotrigine))
- Always watch out for weight gain

Alpha agonists

- Intuniv/Tenex (guanfacine)
- Kapay (clonidine)
- Some meds can be used as needed
- short or long acting
- Look out for dry mouth, constipation, sleepiness
- Sedation can improve after 2 weeks

Pre-submitted questions

What other therapies can be done in conjunction with medication for ADHD?

- behavioral therapy
- parent training
- working with an executive functioning coach
- coping skills and relaxation techniques
- EXERCISE!

Most effective forms of medication to manage aggression AND sleep sustainability.

- Intuniv/Tenex (guanfacine)
- Remeron (mirtazapine) helps with sleep, appetite, nausea
- trazodone
- hydroxyzine
- Treating anxiety can help
- look for sleep apnea!

What Meds are available for kids with anxiety besides SSRIs?

- If SSRIs are not helpful SNRIs (Wellbutrin (bupropion), Effexor (venlafaxine), Cymbalta (duloxetine) could be tried
- blood pressure medications calm the sympathetic NS (propranolol, guanfacine)

What kind of help is recommended for a child with anxiety and ASD, in particular if the child is feeling low about not fitting in with others or is being bullied?

- Focus on their interests → join a club they would actually enjoy
- Work on standing up to bullies, knowing their friends, and asking for help

Research Studies

Symptom	Drug Class	Most Commonly Used Drugs(a)
Repetitive and stereotypic behavior	Selective serotonin reuptake inhibitors	Fluoxetine, escitalopram
	Atypical antipsychotics	Risperidone
	Mood stabilizers	Valproate
Hyperactivity/inattention	Psychostimulants	Methylphenidate
	Nonstimulants	Atomoxetine
Irritability	Atypical antipsychotics	Aripiprazole(b), risperidone(b)
Aggression	Antipsychotics	Risperidone
	Selective serotonin reuptake inhibitors	Fluoxetine
	α2-Agonists	Clonidine, guanfacine
	Psychostimulants	Methylphenidate
	Mood stabilizers	Valproate

⁽a) Medications with the strongest support for each drug category. (b) Approved by US Food and Drug Administration to treat irritability in autistic patients.

Treatment - Medications

- Risperidone and aripiprazole FDA approved for irritability in patients with ASD
- Fluoxetine and fluvoxamine for repetitive, maladaptive behaviors
- Stimulants for hyperactivity, impulsivity, and inattention (more studies show methylphenidate than amphetamines, go slow)
- Alpha agonists for hyperactivity, irritability, and outbursts
- Atomoxetine for ADHD-like symptoms?
- Naltrexone may impose SIB, hyperactivity, social withdrawal, agitation, irritability

Placebo Response

Siafis et al., 2020: Analyzed 86 RCTs with 2360 participants on placebo (87% children)

- Most trials were small for duration of 8-12 weeks
- Placebo response in social communication, repetitive behaviors, and in scales measuring overall core symptoms were similar
 - 19% responded with "at least much improved with placebo"
- Larger placebo response with
 - Caregiver ratings
 - Lower risk of bias
 - Flexible dosing
 - Larger sample sizes and number of sites
 - Less recent publication year
 - Baseline levels of irritability
 - Use of a threshold of core symptoms at inclusion

Atypical Antipsychotics

Risperidone – FDA approved for treatment of irritability

- May be helpful for irritability, repetitive behavior, aggression, anxiety, depression
- Neuroprotective effect with only mild sedative effect
- Weight gain, gynecomastia

Aripiprazole – FDA approved for treatment of irritability

Weight gain

Clozapine

 Improved hyperactivity and aggression in children with ASD but limited use due to risk

Neurotransmitter Reuptake Inhibitors

Fluoxetine

- Decreased rituals, stereotyped/repetitive behaviors
- May cause disinhibition, activation, agitation, hyperactivity

Fluvoxamine

- Well tolerated in adults with ASD
- Has been shown to improve compulsive/repetitive behaviors and aggression

Other SSRIs (sertraline, paroxetine, escitalopram)

Similar benefits/side effects

Venlafaxine

 Improvements in restricted behaviors, decreased interests, social deficits, hyperactivity, and communication in 2 studies

Anticonvulsants

Lamotrigine

No clear benefit

Valproic acid

- Some improvements in receptive language, affective instability, aggression (Jobski et al., 2017)
- Works as in inhibitor for histone deacetylase
- Can cause some issues if exposed in utero

Tricyclic Antidepressants

Nortriptyline

- Can be used for nocturnal enuresis
- Improved hyperactivity/aggression in children (1966, 1971)

Clomipramine

- One study found 58% of patients had improved anger and compulsive behaviors (Gordon et al., 1993)
- Another study found significant side effects sedation, worsened aggression, irritability, hyperactivity (Sanchez et al., 1996)

Desipramine

Imipramine

Not well tolerated in some studies

Thank you for your time!

References

Antshel, K. M., & Russo, N. (2019). Autism spectrum disorders and ADHD: Overlapping phenomenology, diagnostic issues, and treatment considerations. *Current psychiatry reports*, *21*(5), 1-11.

Charalampopoulou, M., Choi, E. J., Korczak, D. J., Cost, K. T., Crosbie, J., Birken, C. S., ... & Anagnostou, E. (2022). Mental health profiles of autistic children and youth during the COVID-19 pandemic. *Paediatrics & Child Health*, 27(Supplement_1), S59-S65.

Dellapiazza, F., Michelon, C., Picot, M. C., & Baghdadli, A. (2022). Early risk factors for anxiety disorders in children with autism spectrum disorders: results from the ELENA Cohort. *Scientific Reports*, *12*(1), 1-8.

Horowitz, L. M., Thurm, A., Farmer, C., Mazefsky, C., Lanzillo, E., Bridge, J. A., ... & Siegel, M. (2018). Talking about death or suicide: Prevalence and clinical correlates in youth with autism spectrum disorder in the psychiatric inpatient setting. *Journal of Autism and Developmental Disorders*, 48(11), 3702-3710.

Hudson, C. C., Hall, L., & Harkness, K. L. (2019). Prevalence of depressive disorders in individuals with autism spectrum disorder: A meta-analysis. *Journal of Abnormal Child Psychology*, *47*(1), 165-175.

Johanning-Gray, K., Vandana, P., Wynn, J., & Hamel-Lambert, J. (2022). Preventing Suicide in Youth with Intellectual and Neurodevelopmental Disorders: Lessons Learned and Policy Recommendations. In *Youth Suicide Prevention and Intervention* (pp. 125-132). Springer, Cham.

Linden, A., Best, L., Elise, F., Roberts, D., Branagan, A., Tay, Y. B. E., ... & Gurusamy, K. (2022). Benefits and harms of interventions to improve anxiety, depression, and other mental health outcomes for autistic people: A systematic review and network meta-analysis of randomised controlled trials. *Autism*, 13623613221117931.

Mayes, S. D., Calhoun, S. L., Murray, M. J., & Zahid, J. (2011). Variables associated with anxiety and depression in children with autism. *Journal of Developmental and Physical Disabilities*, 23(4), 325-337.

Pezzimenti, F., Han, G. T., Vasa, R. A., & Gotham, K. (2019). Depression in youth with autism spectrum disorder. *Child and Adolescent Psychiatric Clinics*, 28(3), 397-409.

White, S. W., Oswald, D., Ollendick, T., & Scahill, L. (2009). Anxiety in children and adolescents with autism spectrum disorders. *Clinical psychology review*, 29(3), 216-229.