Psychopharmacologic and Alternative Medicine Interventions for Autism Spectrum Disorders

Symptoms of Aggression and Self Injury

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Irritability is one of the most frequent behavioral issues that bring children into Primary Care and Mental Health Care Practices for evaluation and treatment.

Objectives

- Identify questions to help determine possible triggers of acute aggressive behaviors.

- Identify what behavioral treatments/interventions and medications to consider for co-occurring behavioral challenges in Autism Spectrum Disorders.

Objectives

- Describe the balance between the benefits and adverse events for medications commonly used in individuals with ASD and aggressive behaviors.

- Develop clinical justification for when to consider medications in an individual with Autism Spectrum Disorder and co-0ccurring symptoms.

Irritability and Aggression

- Aggression directed at others, severe tantrums, quickly changing moods, and self injurious behavior.

Your experience

- What percentage of patients with ASD present because of irritability and aggression?

- 5%
- 25%
- 50%
- 75%

Occurrence Estimates

- UP to 20 % of children with ASD have symptoms of irritability and aggression including aggression, severe tantrums, self injurious behaviors and quickly changing moods.

- Robb, Adelaide S. Developmental Disabilities Research Reviews 2010

Acute or Non- Acute Behavior?

Acute Behavioral Change

- Often can find a trigger
- but child may not be able to make the connection

Acute Behavioral Change

- **Medical**

  - Pain
  - Infection
  - Seizure
  - Pharmacology

- **Environmental**

  - New teacher, therapist, bus driver, child in classroom….
  - Family stressors

Medical

Increased Risk for Health Concerns

- 1.8 X asthma
- 1.6 X eczema or skin allergies
- 1.8 X food allergies
- 2.2 X chronic severe headaches
- 3.5 X chronic diarrhea or colitis

Gastrointestinal Disorders

- GI Disorders affect up to 85 % of children with ASD

- Chronic constipation
- Chronic diarrhea
- Encopresis
- Gastro-esophageal reflux (GERD)

Identifying GI pain

- Pain or discomfort caused by GI issues can prompt behavioral changes that can be difficult to interpret and can be as severe as outbursts of aggression or self injury.

Markers of Abdominal Pain

- <u>Vocal behaviors</u>

  Frequent clearing of throat, swallowing

  sobbing

  delayed echolalia that includes reference to pain or stomach

Markers of GI Pain

- <u>Motor Behaviors</u>
- Facial grimacing or gritting teeth
- Constant eating/drinking/swallowing
  (“grazing behavior”)
  Mouthing behaviors: chewing on clothes
  Spitting up food
  Application of pressure to abdomen
  Finger tapping to throat or belly
  Unusual posturing in jaw, neck or back
  Aggression: onset of or increase in

Seizure Disorders

- Occurs in as many as 39 % of children
- Usually start either in early childhood or during adolescence, but may occur at any time
- More common in children who also have cognitive challenges .
- Some researchers have suggested it is more common when child has shown regression or loss of skills.

Recognizing seizure symptoms

- Unexplained staring spells
- Stiffening of muscles
- Involuntary jerking of limbs
- Facial twitching
- Unexplained confusion
- Severe headaches
- less specific:
- sleepiness or sleep disturbance
- marked or unexplained irritability
- regression

Pharmacology causing irritability

- Important to ask about supplements as well as other medications

Jaxson

- 10 years old and accompanied by both parents
- Diagnosed with Autism at 2 .7 years, language and social regression began at 2 years
- Chief complaint “ meltdowns where he goes ballistic”

Jaxson

- No chronic medical issues reported
- No behaviors suggestive of seizures
- No gastrointestinal changes
- No dental concerns
- No recent injuries
- Behaviors seemed to occur most when demands not met or when
- demands placed on him.

Jaxson

- Family history

  Uncle with subclinical OCD

  medication naïve

History of separation difficulties

Panic like symptoms in new situations

History of agitation with a previous methylphenidate trial

“meltdowns”

- Biting self on wrists
- Biting others
- Screaming and throwing objects and breaking things
- Gouging at his eyes

History of “meltdowns”

- Chronic history of repetitive and perseverative behaviors with low frustration tolerance and occasional behavioral dys-control
- Around 8 years perseverative requests and demands that parents respond physically and verbally in certain ways increased
- If demands not met , he would pinch mother who was primary care giver . Mother with multiple bruises on her arms.

- At 8 years he responded positively to sertraline 12.5 mg-25 mg. Mother reported fewer and less severe meltdowns, able to sit through a movie, more “ lovable”.

- Once he got a dose of 50 mg sertraline and became agitated. Continued at 25 mg for several days but could not get back to previous gains, and so discontinued meds.

- Meltdowns became more frequent almost hourly
- Perseveration on taking off body parts of toys transferred to asking parents to take off his finger, arms, and eyes.

Like a Deer in the headlights

Many possible targets for treatment

- Medical comorbidity (start here)
- Core symptoms of ASD (behavioral treatment)
- Communication (behavioral and speech therapy)
- Psychosocial stress (structure and family treatment)
- Psychiatric comorbidity (psychopharmacology)

General Principles

Form a partnership with the parent and child

Do no harm

-avoid hospitalization if safe

- avoid chronic response to an acute problem

- manage benefit : risk ratio

Target a clear symptom

Start low, go slow

Jaxson

- Behaviors lessened with fluoxetine 5 mg per day
- Less perseverative, more compliant with requests, less SIB, seemed to process spoken language more easily

- Then came back “almost as bad as before” and increased eye gouging and trying to pull out eye during meltdowns.

- Decision to increase fluoxetine to 10 mg, but while waiting for effect, added risperidone 0.25 mg BID

Autism, Irritability, and Aggression

- 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

Most Commonly Used Medications

- Antipsychotics (risperidone, haloperidol)
- Selective serotonin reuptake inhibitors
  (SSRIs) fluoxetine, citalopram)
- Stimulants (methylphenidate)

(Aman et al. 003;Oswald and Sonenklar2007;Mandel et al. 2008)

Risperidone

- 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.

Risperidone Results

- 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

Risperidone

- Weight gain appears to be directly related to increased appetite
- Metabolic syndrome: Increased lipid levels and hyperglycemia
- Associated with increase in serum prolactin

Risperidone Results

- Gains are stable over time (12 months in study)
- 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

Other Meds for Irritability

- Clonidine > placebo
- Guanfacine 23 % responders
- Fluvoxamine 50% improved
- Lithium improved
- Divalproex 71 % improved
- Lamotragine 62 % improved
- Amantadine 47%,37% responders
- Memantine 61%,NSD

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

- Dosages ranged from 0.1 to 0.2 mg /day
- Adverse effects included drowsiness, sedation, and decreased activity

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, irritabilty, 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)

Disclosure

- Off label use of medication
- Risperdal and Aripiprazole are the only medications with FDA approval for Irritability in Autism
- They are most efficacious per studies, but also carry highest side effect risks of metabolic syndrome and much lower risk of tardive dyskinesia

Pathway for medication for irritability and Aggression in ASD

- 1) Guanfacine/clonidine (may fail if severe aggression)
- 2) Atypical antipsychotic
- risperidone, aripiprazole
- 3) typical antipsychotic
- haloperidol
- 4)N-acetylcysteine (PharmaNAC)
- 5) Propranolol –perhaps
- 6)Divalproex/Lithium/Oxcarbazepine-most helpful when epilepsy +ASD
- 7)Benzodiazepines(Be cautious with disinhibition)
- Veenstra-vanderWeele, MD Review of Evidence and Practice Pathways for Medication Treatment in ASD

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When should I use an antipsychotic?

- 1) Is someone getting hurt or likely to get hurt?
- -aggression
- -self injury
- -extreme impulsivity (elopement , street and car behavior)
- 2) Is a child likely to lose access to educational or therapy setting without medication intervention?
- 3) Has everything else failed ?

Summary

- Antipsychotic medications help with co-morbid irritability/agitation in ASD and are most efficacious
- Antipsychotic medications carry heaviest side effect profile
- Psychopharmacology targets symptoms rather than disorders
- Ultimate goal for most difficult to treat symptoms is combined medical and behavioral treatment
- Partnership with parents is most important , and it is important to develop plan for taper off of effective medications if side effects outweigh long-term benefits

References

- Veenstra-VanderWeele, Jeremy MD Review of Evidence and Practice Pathways for Medication Treatment in ASD for Outpatient Providers 2015 AACAP

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

Questions