Medication treatment for people with Autism Spectrum Disorder

Autism Society of Wisconsin
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Disclosures
In accordance with the ACCME policy on relevant financial disclosure, I have nothing to disclose

I WILL be discussing both FDA approved and non-FDA approved uses of medications for children, adolescents and adults

Case 1
Paul is 5—he is in ½ day kindergarten at his local school after 2 years in an Early Childhood Program
He has intensive in-home therapy for ~30 hrs/wk for his ASD
His teacher is concerned about his inability to focus and his hyperactivity

Case 2
Anne is 5—she has ASD and ‘language disorder’ (prior she would ‘fit’ PDD-NOS)
She is in ½ day kindergarten after 2 yrs. in an Early Childhood Program and has ~30 hrs/wk of in-home therapy
She also has ‘private’ speech therapy (2x/wk)
She resists all intervention and is aggressive to teacher, therapists, parents, sibs & self

Case 3
Suzanne is 15, she has ‘high functioning autism’ per mom
In her small parochial grade school, her ‘stims’ were seen by staff/peers as “just Sue!”
Now in a large public HS, she is being ostracized and bullied, has become anxious and is tearfully refusing to go to school

Case 4
“Buddy” is 26, he self identifies as ‘autistic’
He works 3 days/wk at a sheltered setting where there are frequently changing co-workers. They all have different needs/skills
He is often ‘inappropriate’ (e.g. sexual) in his social approaches, to females, some of whom fear him
Autism Spectrum Disorder

**Core** features of Autism Spectrum D/o are:
- social communication and interaction deficits
- restricted, repetitive patterns of behavior, interests or activities

**ASD vs. “ASDs”**

The ‘variations’ in expression of ASD are dependent on the
- **severity** of impairments in core features
- the degree of **intellectual** impairment
- the degree of **language** impairment
- associated **medical/genetic** diagnoses

**DSM5 ‘Severity’ levels**

Three levels of severity are defined:
1 – requiring **support**
2 - requiring **substantial support**
3 - requiring **very substantial support**

**DSM5 ‘Severity’ levels**

**Level 1** – requiring **support**

‘**Inflexibility**’ causes interference with functioning
‘**problems planning**’ hampers independence
‘**odd**’ social interaction attempts
‘**fails**’ in social conversations

**DSM5 ‘Severity’ levels**

**Level 2** - requiring **substantial support**

‘**distress**’ with attempts to change focus or interactions
‘**inflexibility**’ obvious
‘**markedly odd**’ nonverbal communication
social interactions limited to ‘**special interests**’

**DSM5 ‘Severity’ levels**

**Level 3** - requiring **very substantial** support

‘**great distress**’ with attempts to change focus/interactions
‘**very limited**’ initiation of social interaction
‘**few words**’ of intelligible speech
‘**minimal response**’ to social bids
Treatment of ASDs

“treatable” symptoms have been identified in both core areas

Re: social interaction
- non-verbal interactions (e.g., eye gaze, facial expression, gesture)
- peer interactions
- social/emotional reciprocity

Re: social communication:
- delays in language development
- stereotyped/repetitive/idiosyncratic speech/language
- inability to sustain conversations

“treatable” core symptoms

Re: some behavior issues
- encompassing interests
- inflexible routines/rituals
- preoccupation with “part objects”
- lack of make-believe and shared play

Treatment of the ASDs

All are judged treatable via:
- intensive ABA training
- social skill training (PEERS)
- individual psychotherapy with an emphasis on ‘modeling’ & ‘role play’

Autistic Spectrum Disorders

There are NO medication/pharmacotherapy approaches which have been reliably found effective for ‘core’ features

Therefore: medication use in people with an ASD is directed towards
- ‘comorbid’ disorders
- ‘target’ symptoms
**DSM5 & ‘Comorbid’ disorders**

Most DSM5 disorders no longer have the DSM-IV “ASD” exclusion criteria.

The exceptions are:
- separation anxiety d/o,
- selective mutism
- Obsessive Compulsive Disorder

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**‘Comorbid’ disorders**

In DSM5

‘Unspecified’ disorders are an active category of diagnoses often used in combination with an ASD diagnosis.

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**‘Comorbid’ disorders**

However,
- good language skills
- ability to self reflect
- ability to communicate reliably about internal percepts/affects

Are still needed to clarify most diagnoses.

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**‘Comorbid’ disorders**

Using DSM5...a child (like Paul)

a 5y/o in intensive therapy for his ASD with teacher’s concern about
‘inability to focus’
‘hyperactivity’

Can be diagnosed with:

**Paul**

1. Attention Deficit Disorder (314.01)
   and
2. Autism Spectrum Disorder (299.00) with language and intellectual impairment requiring level 3 support

**Anne** (5y/o - ASD, resists all intervention and aggressive to all, including self) may fit diagnoses of:

1. Autism Spectrum Disorder with language impairment (299.00) - level 3 support
2. Unspecified impulse control disorder(?) (she does not ‘fit’ age criteria for Intermittent Explosive disorder)
‘Comorbid’ disorders

Suzanne — (teen with ASD related ‘stims’ with anxiety and school refusal) could be diagnosed with

1. Unspecified Anxiety Disorder (300.00)
2. Autism Spectrum Disorder (299.00)
   without intellectual or language impairment, minimal support required

A young adult (like “Buddy” – ASD, with his inappropriate/sexualized social behavior) might be diagnosed with

1. Impulse control disorder with sexual impulses (312.89)
2. Autism Spectrum Disorder (299.00)
   with mild intellectual and language impairment, requiring support

‘comorbid’ diagnoses

Research studies for the use of medication rarely use ‘unspecified’ diagnoses as targets for treatment

This is especially true when requesting indications and approval from the FDA for marketing

‘Approved’ medications

Medications are “approved” by the FDA for a specific purpose after studies targeted for a specific diagnosis or disorder

e.g. Lipitor® for hyperlipidemia
     Zoloft® for depression in adults & anxiety in teens

However –

After a medication has been approved for any single indication

all prescribers can use any medication for any reason

‘Approved’ medications

Non ‘approved’ uses are called OFF LABEL
Pharmacotherapy for ASD’s

The only FDA approved pharmacotherapy for symptoms of any ASD are risperidone (Risperdal®) & aripiprazole (Abilify®) for ‘irritability associated with autism’

‘Irritability associated with autism’

This is a ‘target symptom’

Neither a core symptom of the ASD diagnosis nor a comorbid disorder

‘Target symptoms’

Using target symptoms for care recognizes that - a diagnosis is not necessary for care and - accepts that problems exist on a continuum

‘Target symptoms’

The concept has been proven to be both: ‘measurable’ (in RUPP studies) and ‘acceptable’ (to parents)

‘Target symptoms’

In ASD medication treatment studies, the most commonly used outcome measure is the Aberrant Behavior Checklist (ABC)

The ‘irritability’ scale of the ABC was the primary target for the RUPP risperidone study (NEJM 2002)
‘Approved’ medications

‘Irritability’ as a target includes:
- aggression
- deliberate self-injury (SIB)
- temper tantrums
in children and adolescents

FDA approved treatments

Paul could be treated with any of the medications approved for ADD
Suzanne could be treated with any of the medications approved for Anxiety d/o
Anne would likely be treated for her aggression/‘irritability’ with risperidone or aripiprazole as approved indications

Dosing of Risperdal®

• Study #1: n=101, ages 5-16yrs
  – 0.25-3.5 mg/day (2X/d after initiation)
  – ‘average’ dose 1.9mg/day (0.06 mg/kg/d)
  – 63 pts followed 4-6 months
• Study #2: n=55, ages 5-12
  – 0.01-0.06 mg/kg/day (daily or 2X/d)
  – ‘average’ dose 1.4mg/day (0.05 mg/kg/d)

Pharmacotherapy for ASD

SUMMARY: the vast majority of medication use for people with ASD is
- for co-morbid diagnoses
- for target symptoms
  &
- off label

‘Target symptoms’

Typical target symptoms are:

PRESCHOOLERS: sleep
hyperactivity
inattention
aggression
SCHOOL AGE: all of the above + ‘stims’

TEENS: all of the above +
  “anxiety”
  “depression”
  “too sexual”
ADULTS: all of the above!
‘Target symptoms’

**PITFALL**

Target symptom treatment almost always leads to **POLYPHARMACY**

**POLYPHARMACY**

The use of multiple medications
- for a single problem
- or
- for multiple problems
- or
- to treat ‘negative effects’
  of primary medication(s)

**WHY?**

**THE MOVING SIDEWALK ANALOGY**

**POLYPHARMACY**

**Study #1**

- 2853 children, 27% taking psychotropics
  - 15% - 1 medication
  - 7.4% - 2 medications
  - 4.5% - ≥3 medications
  - ≥3 for ages 3-5 y/o - 11%
  - 6-11 - 46%
  - 12-17 - 66%

Coury et al (2012)

**POLYPHARMACY**

**Study #2** – 33,565 ‘children’ age 0-20 (2001-09, sleep meds not included)

- 64% - 1 medication
- 35% - ‘multiclass polypharmacy’
  - 38% antidepressant + ADHD med
  - 28% neuroleptic + ADHD med
  - 20% antidepressant + neuroleptic
  - 18% all three classes

Spencer (2013)
**Target symptoms**

Study # 2

15% of children with no comorbid psychiatric disorder were taking a psychotropic

Psychotropic medication use was most related to sleep and gastrointestinal problems

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**Target symptoms**

University of Indiana study of polypharmacy for aggression/SIB/tantrums (e.g. irritability)

135 people with ASD (ages 2-54) 52% with DSM-IV ‘Autistic disorder’

93 (63% of total) had A/S/T treated with approved AND/or ‘off label’ medications

53 (57% of treated) were judged ‘drug refractory’ (more likely >12y/o and cognitively impaired)

Adler (2015)

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**‘Drug refractory’ problems**

Drug refractory aggression, self-injurious behavior, or severe tantrums in people with ASD are

“Continuing problems despite previous trials of risperidone and aripiprazole or three drugs targeting the symptom cluster, including risperidone or aripiprazole.”

Adler (2015)

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**What happened to “Buddy”?**

“Buddy” – young man with ASD & social behavior is inappropriate/’sexualized’

**NO**

medication treatment is appropriate (nor legal) for his problem he needs a careful behavioral plan to sustain his work placement

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**Approaching “targets”**

- Sleep
- Hyperactivity
- Inattention
- Aggression
- ‘Stims’
- Anxiety
- Self Injurious Behavior

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**Three recent articles**

1 – Atomoxetine for children with ASD and ADHD; summary helps, not as much as stimulants but less negative effects

Hadden et al 2015

2 – Guanfacine XR for ADHD in children with ASD; summary safe and effective

Scahill et al 2015

3 – Melatonin XR for insomnia with ASD; summary small improvements

Gingras et al 2017
Approaching “targets”

For medication treatment

Parent (school, therapist, caretaker, etc) report driven medication trials are the most common strategy

Medication trials

A ‘trial’ must be of sufficient
- time
- dose/level
As determined by the medication
- pharmacodynamic properties
- pharmacokinetic properties

Trials must attend to:
- positive (desired) effects
  &
- negative (undesired, nuisance, ‘side’) effects
ALL medications have BOTH

Negative effects

Despite TV’s legal advertisements weight gain is the major negative effect of both approved and commonly used off label medications for ‘irritability’/aggression

Medication ‘trials’

A difficult concept for those who feel these are ‘experiments’ and wish to have ‘certainty’ about care plans

Reality check – this is the way all illness is cared for (e.g. ↑BP, diabetes)

Pharmacotherapy in ASD

Pharmacotherapy can include the use of:

Approved
Unapproved, but studied
Novel
medication(s) for target symptoms
Questions?

Pharmacotherapy in ASD

Three tasks:

YOU – develop a list of medications

WE – classify the medications

I – give you my thoughts about the medication – a mix of my review of the literature and clinical experience

Pharmacotherapy in ASD’s

Let’s learn what you’ve done

Pharmacotherapy in ASD’s

YOU... use your paper

1) list the drug(s)
2) reasons for use
3) helped?
4) problems?

Then take a brief break!

References I like

Wilens & Hammerness (2016) Straight talk about psychiatric medications for kids, 4th ed, Guilford, ~$18

Resources

‘Autism Speaks’ website - autismspeaks.org
under tool kits find the ATN/AIR-P

Autism and Medication: Safe and Careful Use
American Academy of Child and Adolescent Psychiatry website – aacap.org

Autism Spectrum Disorder: Parents’ Medication Guide

Recent articles


summary: ‘approved’ meds fail frequently


summary: nice review of all medication classes, children “more susceptible to adverse effects”

Recent articles


summary: little research in this age, risperidone +/-


Recent articles


summary: all medications cause weight gain

Two useful articles
