Challenging Behavior and Psychotropic Medication: Evidence-based Practices

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How do we avoid the inappropriate use or overuse of medication?
The Use of Psychotropic Medication with individuals with autism and ID

- Estimated that between 20% to 45% of people with autism and ID are taking psychotropic medication
- 14% – 30% are taking them to control challenging behavior
- 27% taking multiple medications
- Up to 36% of people with ID in residential settings are prescribed meds in absence of psychiatric diagnosis
Medication Interventions

Nearly all psychotropic medications have been evaluated with people with ASD

Yet only two have been specifically approved by the FDA for individuals with ASD (none for individuals with ID)

Most common problem behaviors for which meds are prescribed: aggression, self-injury, repetitive behavior, hyperactivity, mood, anxiety and sleep problems
Medications - Stimulants

- ADHD/ADD symptoms reported in more than half of children with ASD
  - Often attribute symptoms of ADD to the individual’s diagnosis of autism rather than as a separate condition even though none of the behaviors associated with ADD are core symptoms of ASD
Medications - Stimulants

- Target behaviors: inattention, hyperactivity
- Side effects: decreased appetite, insomnia, tics, increased irritability, paradoxical increase in hyperactivity, restlessness, slowed growth
- Strattera - not a stimulant so doesn’t have same side effects; recent warnings of suicide risk
- Data to date show that while may decrease hyperactivity and inattention, doesn’t treat any of the core symptoms of autism
Medications – Antipsychotics/neuroleptics

- Typical versus atypical
- Most commonly used medication and most studied with individuals with ASD
- Target behaviors: aggression, irritability, disruption, self-injury, repetitive behavior
- Risperdal and Abilify only ones approved for ASD
- Side effects: increased sleep/lethargy, increased appetite, hyperprolactinemia, tardive dyskinesia (typical antipsychotics only)
Medications - Antidepressants

- Older antidepressants: tricyclics and MAO inhibitors not used due to severe side effects and lack of effectiveness
- Currently use selective serotonin reuptake inhibitors (SSRIs) in treatment of anxiety, repetitive behavior, OCD in autism
Medications - Antidepressants

- Several good clinical trials indicating their effectiveness in addressing repetitive and OCD symptoms in individuals with autism (Prozac, Zoloft, Paxil)
- Fluvoxamine (Luvox) and sertraline (Zoloft) also may be effective in treatment of behavior problems and mood
Additional Medications Used

- Guanfacine (Tenex or Intuniv) approved for blood pressure, but used for anxiety and mood stability
- Seizure medications (e.g., Depakote, Neurontin) used for mood stabilization
- Clonidine and Melatonin used for sleep
Do people with intellectual disabilities respond to medications in the same way as others?

- Some evidence that
  - More sensitive to behavioral effects
  - More sensitive to side effects

- But when deciding how to prescribe, have to use:
  - guidelines developed for people (adults) without a disability (so being used “off label”)
  - or clinical judgment
Issues regarding Clinical Practice

Clinicians often go by experience rather than data; trial and error approach

Hard to determine effects to child due to language problems, thus rely on parent/staff report only

Usually no data collected

Lack of collaboration between doctor and other people supporting individual

Treat side effects with additional meds
One way to improve the science: Randomized Clinical Trials (RCT)

- Initially used in the field of medicine to evaluate the effects of an intervention
- Now be used across a variety of fields to evaluate the effects of behavioral, educational, and medical interventions
Randomized Clinical Trials – Best Practices

- Double blind
- Placebo controlled
- Use multiple, standardized doses
- Evaluation of dependent variable using well-validated instruments
- Random assignment of participants

Sprague and Werry, 1971
Additional Important Criteria

- Keep all other interventions constant
- Watch for placebo or honeymoon effects (either for caregiver or person with ID)
- Use direct observation measures
- Obtain measure of social validity and consumer satisfaction
- Ideal is to evaluate separate and combined effects of medication and behavioral interventions

Napolitano et al., 1999
Clinical Trials in a Nut Shell

- Approved Protocol
- Investigator selection
- Approval Process
- Statistical Analysis
- Data Entered and reviewed
- Patient recruitment and participation
- Presentation and publication of report
- Data filed and registration obtained
Clinical Trials in a Nut Shell

Write grant or find $ support; find a medical setting; identify who might volunteer for study

Find a physician who is willing to work with you and has some free time; find graduate students or research assistants

Find a physician who is willing to work with you and has some free time; find graduate students or research assistants

Approval Process
Spend 8 months getting IRB approval

Patient recruitment and participation

Write another grant to keep your research alive!

Statistical Analysis

Data Entered and reviewed

Write another grant to keep your research alive!

Presentation and publication of report

Piece of cake, ha!
The Role of the Behavior Analyst or Psychologist during Clinical Trials

Indirect measures of behavior (rating scales)
Operational definitions of behavior of interest
Collect direct observation data
  - across settings
  - across behaviors
Functional analysis
Use of Functional Analysis during Medication Evaluations

- Schaal & Hackenberg (1994) first suggested use of FA during medication treatment
- Very little clinical trial research
- Northup et al. (1997, 1999)
  - MPH with kids with ADHD
  - Medication serves as an establishing operation => modifying the efficacy of reinforcement
- Garcia & Smith (1999)
  - naltrexone tx in two adults with SIB
Functional Analysis during Risperidone Treatment

Purpose of the study was to conduct a functional analysis concurrent with a double-blind, placebo-controlled trial of the atypical antipsychotic risperidone

Goal: to determine how environmental variables are modified by medication
Double-blind Placebo Controlled study of Risperidone

Crossover design so each participant got
- placebo,
- a low dose (1 mg/day for children or 2 mg/day for adults)
- a high dose (0.05 mg/kg/day)
Results of Clinical Trial

52 participants enrolled
40 completed

- 27 (67.5%) “Responders” to the medication (as measured by improvement on the Aberrant Behavior Checklist Irritability Subscale and Clinical Global Impressions scale)

Zarcone et al. (2001); Hellings et al. (2006).
<table>
<thead>
<tr>
<th>Phase</th>
<th>Low Dose (n=39)</th>
<th>High Dose (n=36)</th>
<th>Placebo 2 (n=31)</th>
<th>Maintenance (n=31)</th>
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<tr>
<td><strong>Rating Scales</strong></td>
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**Mean Percentage Change from Placebo**

- Low Dose: -50.0%
- High Dose: -30.0%
- Placebo 2: -20.0%
- Maintenance: 20.0%
21 participants enrolled
  ◦ 4 dropped out
    • 3 dropped med trial, 1 dropped FA only
  ◦ 17 completed
  ◦ 12 (71%) were responders to the medication

Crosland et al (2003); Zarcone et al. (2004)
Demographics - Functional Analysis
Participants (N = 17)

Gender:
- male - 11
- female - 6

Age:
- children - 8
- adults - 9

Level of functioning:
- mild - 3
- moderate - 3
- severe - 4
- profound - 7

Diagnosis: autism/PDD - 13
Functional Analysis Sessions

- Sessions conducted at home/school/work
- Once per week throughout med trial
- Multielement experimental design

Conditions:
- Demand
- Tangible
- Play/leisure (control)
Findings – 4 Patterns

1) No challenging behavior observed (N=4)

2) No improvements with the medication (N=3)

3) Undifferentiated functional analysis with a general suppression of behavior (N=5)
4th Pattern

4) Differential effect of risperidone on escape behavior (N=4)

- Two participants had escape behavior only
- Two participants had behavior maintained by escape + positive reinforcement

=> risperidone only affected the escape behavior
Findings, continued

Example participant - Reggie

- 6-year-old diagnosed with autism, fragile X syndrome, and profound ID

Primary target behaviors: aggression, disruption, and elopement
Sessions

Destructive Behavior (RPM)

Baseline

PBO

1.0 mg

1.5 mg

BL

Attention

Demand

Play

Tangible

Reggie
Destructive Behavior (Resp/min)

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<th>Medication Conditions</th>
<th>Tangible</th>
<th>Demand</th>
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Conclusion of Study

Risperidone was effective in reducing problem behavior in 67% of participants

Based on results of FA –

- a general suppressive effect on behavior or
- selectively affect escape or avoidance behavior

These data may help us to identify those individuals who may be the best responders to certain types of medication
Clinical Trials and ASD

- Clinicaltrials.gov search
- 100 clinical trials of drug interventions
  - Aripiprazole (Abilify) and D-Cycloserine (antibiotic for tuberculosis tx) for aggression and self-injury and social and communication skills
  - Oral N-Acetylcysteine (NAC) for the treatment of the core symptoms of autism include severe deficits in social relatedness and communication, and repetitive behavior
  - two doses (high and low) of risperdal (Risperidone) on irritability in adolescents with autism
Clinical Trials with Children and Adolescents with ASD

66 clinical trials of *behavioral* interventions:
- Cognitive Behavior Therapy and anxiety,
- gluten and casein free diet on behavior,
- relationship training for children with ASD and their peers
Adolescents and Clinical Trials

- Most of pediatric research is being done with children ages 5-12 years
- Only 5% of over 9,000 clinical trials included adolescents
- Why isn’t more research being done with adolescents?
  - Hormonal and developmental influences => results in unpredictable pharmacokinetic differences
  - Uncertain legal and ethical status
  - Compliance/adherence issues
  - Psychosocial complications and peer influences
  - One exception: treatment of depression
Going beyond the Typical Clinical Trial

Randomized clinical trial:
  Intervention versus “placebo” or no intervention

Practical Clinical Trial:
  Intervention versus “standard of care”

Comparative Effectiveness Research:
  Intervention 1 versus intervention 2 (e.g., behavioral vs medical intervention)
Comparing Discrete Trial Teaching with Interpersonal Developmental Approach

- A comparison across three sites (UCLA, UR, and Kennedy Krieger Institute)
- Looking at language acquisition and play skills in 150 preschoolers with autism
- Randomly assigned to either DTT or developmental, play-based therapy
Evidence-based Practices in Evaluating Medication Effects

- Randomized Clinical Trials are ideal, but
  - Expensive
  - Time consuming
  - Unavailable to average practitioner

- What key elements can we use and still be able to draw conclusions regarding efficacy of the medication?
Guidelines for Conducting Community-based Medication Evaluations

- Collaborate with medical team to collect data from a variety of sources
  - Biological information (e.g., sleep, diet)
  - Behavioral rating scales
  - Direct observation data
    - Problem behavior
    - Adaptive behavior
    - Side effects
Guidelines for Conducting Medication Evaluations in Community Settings

- Keep data collector blind
- Implement interventions systematically and one and a time
- Develop a collaborative relationship with medical team
Overall Conclusions

- Data-based decision making regarding the efficacy of medication effects
- Use it as an opportunity to bring together biomedical and behavioral expertise
- There are going to be more and more funding opportunities for comparative effectiveness research
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