Improving Standards for Prescribing Psychotropic Medications in People with Intellectual and Developmental Disabilities

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Disclosure
- Drs. Noel and Hovermale report no relevant relationship to commercial interests producing health care goods and services
- Due to the limitations in availability of approved drug products for patients with intellectual and developmental disorders, this presentation will contain discussion of off-label use of drugs.

Learning Objectives
1. The Participant will acquire a systemized strategy for evaluating the PWIDD in order to more effectively categorize target behaviors.
2. The Participant will understand a proposed method of tracking the response of target symptoms to psychotropic medications.
3. The Participant will better understand the possible starting medication choices for target behaviors.

Prevalence
- 1997-2008 National Health Interview Surveys analyzing children aged 3-17 (n = 119,367)
  - Any developmental disability – 13.7%
  - Autism – 0.47%
  - Intellectual Disability – 0.71%
  - Cerebral Palsy – 0.39%
- Increase prevalence noted in lower income families, lower maternal education, and Medicaid recipients


Prevalence of Psychiatric Problems
- Overall: estimated between 32 – 40%
- Autistic Spectrum Disorder
  - Mild ID: 5-10%
  - Moderate-Severe ID: up to 30%
- ADHD
  - ID: 8.7-16%
  - General Population: ~5%
- Major Depression
  - 1.5-2 times higher in ID than in general population
- Schizophrenia and Bipolar Disorder
  - Up to twice the prevalence in ID than in general population
- High rates of anxiety issues in ID reported as well

Boyle CA et al, Pediatrics 2011;127:1034-42

Challenging Behaviors
- Behaviors not necessarily associated with Axis I Disorder
  - Aggression (2-28%)
  - Self-injury (10-31%)
  - Property destruction (7-30%)
- Inappropriate social or sexual behavior
- Self-stimulation
- Prevalence is 3-5 times greater in the ID population
- Up to 40% of individuals with ID may receive psychotropics for these issues


Psychopathology in ID

- Cortical and subcortical damage may confer increased vulnerability
- Reduced cognitive capacity may decrease ability to cope with stress
- Lack of good psychological care lessens preventative care
- Caution against diagnostic overshadowing and “over-pathologizing”
  - Pathology is attributed to ID or is inappropriately assumed to be part of an illness

Etiology

- Postnatal
  - Childhood meningitis or encephalitis
  - Head injury
  - Environmental toxins – lead, mercury,
- Poverty and Cultural Deprivation
- No etiology identifiable in up to 30% of cases

DM-ID

  - A diagnostic manual designed to facilitate making accurate DSM-IV diagnoses
  - Developed by the National Association for the Dually Diagnosed (NADD) in association with the American Psychiatric Association (APA)

Adjustment Disorder

- DSM-IV-TR Criteria Adaptation of Criteria for Individuals with Mild to Moderate ID
  - Adaptation of Criteria for Individuals with Severe to Profound ID

1. The development of emotional or behavioral symptoms in response to an identifiable stressor(s) occurring within 3 months of the onset of the stressor(s).
   - No Adaptation
   - Note: Stressors in the lives of persons with Mild to Moderate ID can include any need for an increase in autonomous functioning (move to a new home or away from family, loss or change of status of important caregiver, promotion to educational, vocational or residential placement beyond one’s level of comfort, onset of illness).  

2. Anxiety and depression may manifest in persons with Mild/Moderate ID as they would in persons without ID, but also as clinging, apparent loss of skills, withdrawal, or irritability.
   - Distress in excess of the individual’s known baseline of distress responses.
   - Impairment compared to baseline functioning

Axis I Disorders in DM-ID

- Major Depressive Disorder – DM-ID adds ‘irritable mood’ as core symptom (in addition to depressed mood and loss of interest)
- Bipolar Disorder – DM-ID allows for fewer symptoms of mania to be present in a Manic Episode for individuals with limited expressive language skills
- Schizophrenia – DM-ID discourages use of schizophrenia subtypes (e.g. Paranoid, Disorganized, etc.) for people with severe to profound MR

**Diagnostic Patterns**

- More frequently diagnosable in ID
  - Autistic Spectrum Disorders
  - Impulse Control Disorders
  - Bipolar Disorders
  - Psychotic Disorders

- Less frequently diagnosable in ID
  - Personality Disorders
  - Anxiety Disorders

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**Limitations of Evidence-based Drug Treatment in ID**

- Lack of rigorous published clinical trials
- Research consent issues in adults
- Heterogeneity of clinical presentations; uncertainty of diagnosis
- Publication bias

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**Autistic Disorder**

**Epidemiology**
- Autistic spectrum disorders present in 1/88 children
- 4-5 times more males than females are affected

**Etiology**
- Genetics – risk of recurrence in families with one affected child is 3-8%
- Prenatal factors – e.g. intrauterine rubella
- Brain abnormalities – hydrocephalus
- Postnatal factors – infantile spasms, herpes simplex, encephalitis, neoplasm, untreated phenylketonuria
- Controversial link to MMR vaccination

MMWR 2012;61(SS03):1-19

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**Autistic Disorder**

**Goals of therapy**
- Reduce disruptive behaviors
- Promote learning – e.g. appropriate nonverbal communication
- Attempt to engage individual into recreational, social, and/or occupational activity

**Nonpharmacologic**
- Education to improve behavior and communication disorders
- Occupational and physical therapy
- Counseling and training for parents

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**Autistic Disorder**

**75% have MR**

**Psychiatric/Behavioral**
- Hyperactivity
- Impulsivity
- Aggression
- Self-Injury

**Medical**
- Seizure disorder
- May be associated with a genetic syndrome (e.g. Fragile X)
Autistic Disorder – Drug Treatment
- Second Generation Antipsychotics
  - Risperidone and aripiprazole are FDA approved for treatment of "irritable" behavior
  - Treats ritualistic behaviors, aggression, self-injury
- Stimulants
  - For inattention and hyperactivity
- Anticonvulsants
  - For mood lability, aggression
- SSRI
  - Obsessions, perseveration
- Traditional antipsychotics, naltrexone, beta-blockers may have a role for certain challenging behaviors
- Secretin – neuropeptide hormone involved in digestion
  - Noted to exhibit short-term improvement in symptoms in children in a few anecdotal reports

Down Syndrome
- Occurs in 1 per 650-1000 live births
- Chromosomal abnormality – Trisomy 21
- Risk factors
  - Maternal age: 1:2500 in women < 30 yrs, 1:80 in women over 40 yrs
- Behavioral Phenotype
  - Usually good tempered individuals
  - Language delay
  - Early onset Alzheimer’s disease
  - Autistic features, hyperactivity and aggression are rare

Down Syndrome – Medical Issues
- Hearing impairment
- Congenital heart defects
- GI defects
- Otitis media
- Orthopedic problems
- Thyroid disease
- Congenital cataracts
- Transient myeloproliferative disorder, leukemia
- Seizures
- Dental problems

Down Syndrome – Treatment
- Dementias
  - Cognitive enhancement – data limited to small studies and case series
  - Acetylcholinesterase inhibitors (e.g. donepezil 5-10 mg/d)
  - Affective and behavioral manifestations – limited data for SSRI’s
- Heart defects
  - Surgical correction of septal defects
  - Antibacterial prophylaxis for valvular problems
- Thyroid – hormonal replacement indicated for clinically evident hypothyroidism
- Leukemias – very responsive to chemotherapy

Fragile X Syndrome
- Prevalence – most common form of inherited mental retardation
  - 1 in 4,000 males
  - 1 in 6,000-8,000 females
  - Up to 1:1000 females may be asymptomatic carriers
- Chromosomal abnormality – trinucleotide (CGG) repeat expansion on the X chromosome

Fragile X Syndrome – Features
- Physical
  - Long face, large ears
  - Short stature
  - Arched palate
  - Hyperextensible finger joints
- Medical
  - Mitral valve prolapse
  - Seizures
  - Recurrent infections
  - Scoliosis
- Behavioral/Neurodevelopmental – symptoms more prominent in males
  - Mtd to severe mental retardation
  - Hyperactivity, distractibility – 70% have ADHD
  - Decreased social interaction – 15% have Autism
  - Stereotypies
  - Self-injurious behavior
  - Anxiety – e.g. social phobia, selective mutism
Fragile X Syndrome

- ADHD Symptoms –
  - Stimulants improved inattention, impulsivity, and hyperactivity in a crossover trial (n=15)
- Hyperarousal and explosive aggression
  - Anecdotal evidence for improvement with clonidine and guanfacine
  - Some success noted with SSRI in select patients
- No data available on mood disorders or psychotic disorders – trials of standard treatments are generally warranted
- Seizure disorders – standard anticonvulsant therapy

Psychiatric Illness in ID

- Environmental Factors
  - Lack of attention
  - Boredom
  - Task avoidance
  - Preferred staff member
  - Desire for specific item (food/cigarettes)
  - Discomfort (e.g. temperature too hot/too cold)
  - Physical/medical problems

Assessment Techniques

- Functional Analysis
  - Used to determine if behavior is due to an environmental issue
  - Involves the manipulation of probable environmental variables to elicit the problem behavior in a controlled setting
- Direct behavioral observation
- Rating scales/checklists
- Patient and caregiver interview
- Self-assessments

General Approach to Drug Treatment

- Treatment should be based on underlying cause(s) of behavior
  - Medical conditions (if applicable)
  - Less restrictive interventions should be employed first in non-emergent situations
  - Change environment
  - Teach functional alternatives (e.g. appropriate ways to communicate desires)
  - Identify potential drug-responsive target symptoms if drugs are being considered

Depression

- Target Symptoms
  - Crying
  - Weight loss
  - Sleep disturbance
  - Self-injurious behavior
  - Aggression, agitation
  - Loss of interest in usual activities
  - Decrease in skills in activities of daily living

Treatment

- Same antidepressants and dosages as for those used in the general population
- Therapy should be individualized
- Serotonin reuptake inhibitors and newer antidepressants are preferred
- Avoid antidepressants which can lower the seizure threshold
  - TCA
  - Bupropion
Bipolar Disorder

- **Target Symptoms (Manic, Mixed Episode)**
  - Sleep disturbance
  - Hyperactivity
  - Sexual acting out, public masturbation
  - Aggression
  - Self-injurious behavior
  - Distractibility in occupational settings
  - Grandiosity, flight of ideas (may be difficult to detect)
  - Cyclic patterns of behavior

- **Treatment**
  - Same mood stabilizers and dosages as for those used in the general population
  - Anticonvulsants (VPA and CBZ) – may provide dual benefits for seizures and mood disorder
  - Lithium – note that risk of hypothyroidism is elevated in certain developmental syndromes
  - Newer anticonvulsants – limited literature support for their use in people with MR

Psychotic Disorders

- Other psychiatric disorders may be confused with schizophrenia – e.g. PDD
- Bizarre behaviors may be stereotypical rather than symptoms of psychosis
- Factors that may aid diagnosis
  - Disorganized speech and behavior representing a change from baseline
  - Deterioration of self care skills
  - Family history
  - History of response to antipsychotic medication
- Treatment – similar for people with MR as with the general population

Anxiety Disorders

- All anxiety disorders can occur in people with developmental disabilities
- Treatment
  - Treatment approaches are the same as for people in the general population
  - Cognitive-behavioral therapy may be a challenge or impossible in some individuals due to limitations in communication and cognitive skills
  - Judicial use of benzodiazepines is recommended

Self-Injurious Behavior (SIB)

- Self-inflicted repetitive behavior that causes external trauma
- Seen in about 7-9% of people with DD
- Common behaviors
  - Head banging
  - Sore or skin picking
  - Lesch-Nyhan syndrome
  - Cornelia de Lange syndrome
  - Prader-Willi syndrome
- Assessment
  - Functional analysis or assessment
  - Medical and/or dental work up
- Treatment
  - For environmental cause – institute appropriate environmental changes
  - Select drug to address underlying psychopathology
  - Naltrexone – mixed results
    - 1-2 mg/kg/day
    - Response should be seen within a week
  - Monitor LFT’s
  - Serotonin-dopamine antagonists
    - Clozapine – reported to decrease self-injury in refractory cases
  - Dopamine antagonists
    - Low doses of fluphenazine or haloperidol
  - SSRIs, Anticonvulsants, Beta-blockers
**Aggression**
- Often a symptom of an underlying environmental, physical or psychiatric problem
- Directed against
  - Other people
  - Property
  - Self
- May also include verbal threats

**Assessment**
- Functional analysis or assessment
- Medical workup
- Screen for akathisia and other side effects of drugs

**Aggression – Treatment**
- Treat the underlying cause
- Acute aggression treated as in the general population (e.g. lorazepam, haloperidol)
- Assess for side effects of medications (e.g. disinhibition from benzodiazepines)
- Serotonin-dopamine antagonists
  - Clozapine – may be useful in treating brain damaged individuals with aggression
  - Risperidone – effective in published reports
- Propranolol
  - Up to 1400 mg reported in open trials to decrease aggression
  - Response may have been due to treatment of akathisia

**Antipsychotic Considerations**
- Tardive dyskinesia
  - Monitor on a regular basis – every 6-12 months
  - Risk factors similar to those in general population. Also lower IQ may increase risk
  - Must attempt to differentiate abnormal movements related to tardive dyskinesia, neurologic disease or stereotypes
  - Rating scales – AIMS, DISCUS
- Seizure threshold – antipsychotic medications may lower seizure threshold
  - Clozapine
  - Loxapine
  - Chlorpromazine

**Antipsychotic Considerations**
- Metabolic effects – people with ID may be especially prone to weight gain and related complications
  - Can be worsened with polypharmacy
  - Use of lower metabolic risk drugs can reduce risks

**Drug-Specific Considerations**
- Benzodiazepines – long term use for behavioral problems is avoided due to side effects
  - Disinhibition
  - Cognitive effects
  - Withdrawal
  - Motor impairments

**Drug-Specific Considerations**
- Anticonvulsants
  - Monotherapy is always preferred
  - Phenobarbital is most frequently implicated in cognitive difficulties and behavioral disturbances
- Antidepressants
  - May promote clinical worsening in bipolar diathesis
  - Caution with P450-mediated drug interactions and lowering of seizure threshold
Self-Assessment Question

2. Which of the following adverse effects of topiramate potentially presents a unique challenge in the intellectually disabled population?
   a. Weight loss
   b. Cognitive impairment
   c. Angle closure glaucoma
   d. Metabolic acidosis

Prescribing Standards

- Established by CMS and state regulations
  - Full diagnostic and functional assessments to establish diagnosis and/or environmental and behavioral antecedents
  - Written informed consent from competent patients or designated guardian
  - Objective and specific goals to measure medication efficacy
  - Written integrated behavioral/medication plans

Data Sources

- Reliable direct-care informants
- Daily notes
- Sleep data
- Weights
- Individual subjective report

Treatment Trials

- Alternating treatment design
  - Each medication is initiated, gradually titrated, and assessed
  - Discontinue or cross-titrate to new medication in event that first drug fails
  - Polypharmacy can be appropriate if each medication is titrated and evaluated independently

Behavioral Intervention

- Demonstrated to improve behaviors in a wide range of clinical presentations in ID
  - Functional Assessment – a critical first step
    - Defines nature of problem behavior
    - Identifies frequency and duration
    - Identifies antecedents and consequences
    - Establishes reinforcers to be rescheduled or removed
  - Goal – replace problem behaviors with more appropriate behaviors
**Multimodal Therapy**

- **Autistic disorder**
  - Medications – reduction of irritable and ritualistic behaviors
  - Nonpharmacologic – socialization and functional communication training

- **Psychotic disorders**
  - Medications – reduce aggression, suspiciousness, hallucinations
  - Nonpharmacologic – skill remediation, socialization

**Self-Assessment Question**

3. Which of the following is most useful for determining the environmental cause(s) of problem behavior?
   - Functional analysis
   - Medications
   - Restraints
   - Noncontingent reinforcement

**Multimodal Therapy**

- **Major Depression**
  - Medications – mood and vegetative symptoms
  - Nonpharmacologic – coping skills, psychotherapy

- **Impulse Control and other behavioral disorders**
  - Medications – impulsive aggression, agitation
  - Nonpharmacologic – token economies/response cost