Antipsychotic Medication to Address Challenging Behavior of People with Intellectual Disability: Assessment with the MEDS

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Many group-home residents with mental retardation are receiving psychotropic medications that may be doing far more harm than good.
Major Issues

• Research on the efficacy of antipsychotics for this use in ID is minimal with little benefit

• Medication side effects and adverse events are significant with inadequate monitoring

• Limited informed consent to the risks & benefits for people with ID
Antipsychotic Medication USA

• 2008 Domino & Swartz USA
  • (1997) 0.72% to (2005) 1.17%

• 2012 Pillarella et al. USA bipolar dx
  1998 (18% visits) – 2009 (49% visits)
  decreasing use of mood stabilizers
Psychopharmacology

Antipsychotic epidemiology studies

- Tsiouris et al. 2013 NY State 45%
- de Kuijper 2010 Netherlands 32%
- Holden & Gitlesen 2004 Norway 31.6%
- Lott et al. 2004 California 32%
- Spreat 2000 et al Oklahoma 20.8%
- Robertson et al 2000 UK 56/27/17%
- Branford, 1994 UK 44/13%
- Jacobson 1988 NY 39.9/24.8/10.1%
- Intagliata & Rinck, 1985 Missouri 45/29%
Efficacy of atypical antipsychotic behaviour children & adolescents ID / borderline ID: review  Unwin Deb 2011

- 442 citations ➔ 40 title ➔ 18 abstract ➔ 6 RCTs full text (4 & 2 extension)
- risperidone significantly effective
- adverse events somnolence/weight gain
- concurrent behavior treatment typically not curtailed, metabolic syndrome not fully measured
Tyrer et al. Lancet 2008
RCT blinded ID/CD/Antipsychotics

- Multi-center international study
- Multiple measures: CGI, ABC, MOAS, quality of life, carer uplift & burden, side-effects
- Excluded those with psychosis
Tyrer et al. Lancet 2008

- Multicentre: Wales, England, Australia
- 180 patients
- 94 excluded various reasons (e.g., inability to swallow a pill)
- 86 randomized to 12-week trial:
  - 29 risperidone
  - 28 haloperidol
  - 29 placebo
Median scores on the Modified Overt Aggression Scale for 12 weeks

Tyrer et al. 2008 Lancet
Placebo Effect

- We get “better” because we are seeing a caring health practitioner----
- Recent research suggests physiological effects
- Staff-family report he/she is a little better, or worse… but no real test of efficacy
• **Side effects** are problems that occur when treatment goes beyond the desired effect, or problems that occur in addition to the desired therapeutic effect.

• An **adverse drug reaction** is “an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen or withdrawal of the product” (Edwards & Aronson, 2000).
Side Effects (Adverse Events) Monitoring

• Performed by physician
• Conversation with patient
  o (self-report)
• Examination
• Studies & laboratory tests
Benzodiazepines

- lorazepam
- diazepam
- clonazepam
- **Side Effects:** motoric problems, fatigue, less focus, dependence, disinhibition, irritability, reflux, dizziness (low blood pressure)
Side Effects Benzodiazepines

**Observable**
- irritability
- disinhibition
- walking, chewing
- balance

**Self-Report**
- fatigue
- less focus
- reflux-nausea
- dizziness
Side Effects-Adverse Events
conventional antipsychotics-1st generation

- Anticholinergic (dry mouth, ocular changes, constipation)
- Extrapyramidal (dystonia, akathisia, TD)
- Sedation, feeling no energy
- Cardiovascular (arrhythmias, blood pressure)
- Metabolic (weight gain, glucose, hyperlipidemia)
- Altered hormones (hyperprolactinemia, FSH, LH)
- Lowered seizure threshold
Side Effects-Adverse Events
atypical antipsychotics-2nd generation

• Improved motor side effects but not all atypicals, with long-term health consequences
  o Significant weight gain
  o Increased hyperglycemia and type 2 diabetes
  o Altered lipid profiles
  o Cardiac effects (orthostatic hypotension, tachycardia and QTc prolongation)
  o Over time, motor side-effects, e.g., TD
<table>
<thead>
<tr>
<th>Observable</th>
<th>Self-Report or Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>appetite ↑</td>
<td>fatigue</td>
</tr>
<tr>
<td>weight gain↑</td>
<td>cardiac effects</td>
</tr>
<tr>
<td>movement disorders</td>
<td>diabetes</td>
</tr>
<tr>
<td>constipation</td>
<td>lipids</td>
</tr>
<tr>
<td></td>
<td>headache</td>
</tr>
<tr>
<td></td>
<td>dry mouth</td>
</tr>
<tr>
<td></td>
<td>hormones</td>
</tr>
</tbody>
</table>
Proxy Decision Making

- Parents, guardian, care staff seeking help
- **Risk-Benefit discussion** about treatment made my proxy
- Limited ability to self-report side effects/adverse events
- Limited assessment if medicine is helping or causing more distress
Antipsychotic Monitoring Standards
2\textsuperscript{nd} generation

- Used NICE and Deb (2006)
- 1. Indication for antipsychotic treatment clearly documented
- 2. Continuing need reviewed at least once a year
- 3. Side effects reviewed yearly for EPS and metabolic syndrome: BP, obesity, glycemic control, plasma lipid profile
Psychopharmacology  UK Leicester
Atypical antipsychotics audit  Tin et al 2008

• 3400 people with ID
• 983 saw ID psychiatry services in 2000
• 185 (18.9%) SGA
  o 45 FGA
  o 36 anticholinergic
  o 50 antidepressant
  o 15 mood stabilizer
  o 54 antiepileptic
  o 46 anxiolytics
Psychopharmacology  UK Leicester  
Atypical antipsychotics baseline audit  Tin et al 2008

- Mental illness use  30.3%
- Challenging behavior  57.4%
- No side effects reported  69.7%
- EPS and weight gain most reported
- Majority had no screening for metabolic syndrome
- residences (67%)(2x more likely) vs. community (33%)
- males (58%) females (42%)
Antipsychotic prescribing in UK psychiatry ID services  Paton et al. 2011

• 145 teams, 39 MH Trusts, 2,319 pts
• Used NICE and Deb (2006) for audit
• 1. Indication for antipsychotic treatment clearly documented
• 2. Continuing need reviewed at least once a year
• 3. Side effects reviewed yearly for EPS and metabolic syndrome: BP, obesity, glycemic control, plasma lipid profile
Antipsychotic prescribing in UK psychiatry ID services  Paton et al. 2011

- Indication clearly documented and reviewed 85%
- 40% psychotic disorder-multiple reasons
- EPS 40%
- Metabolic syndrome
  - 40% no evidence of BP, weight, blood glucose, lipids
Discontinuing Medicines

• The longer on a medicine, the more difficult due to adaptation
• Antipsychotics have effects that cause difficulties, e.g. motor problems, tardive dyskinesia, in withdrawal
• Multiple medicine regimens complicate all problems in discontinuation
• Usually, d/c is very slow, one drug at a time
Discontinuation Study de Kuijper, 2013 JIDR

- 99 pts randomly assigned:
  - 14 or 28 weeks discontinuation protocol
  - 12.5% dose reduction q 2 or 4 weeks – baseline
  - ABC & Visual Analogue Scale
- 43 achieved complete discontinuation: All improved on ABC even if not d/c
- No difference between 14 of 28 weeks
- Higher ABC predicted higher EPS symptoms
- Long-term follow at 26 & 40 weeks 16 great improvement and 7 worse
- Weight and BMI improved with any lowering
Little Side Effect Monitoring

SOLUTION

EMPOWER STAFF & CARGIVER TO ADVOCATE FOR MONITORING OF RISKS

Discontinue, evaluate need for medicines

• A rating scale developed for people with ID
• Researched and normed developed on an institutionalized population
• Covers a wide range of side effects associated with psychiatric medicines
• Professional interviews carer “informant interview scale”
• In addition to interview, medical information from chart is also incorporated

- **MEDS**: 90-item *informant-interview* scale: chart review also necessary
- Severity and duration the last 2 weeks
- 3- point scale *(severity: 0 = no problem, 1 mild/moderate, 2 severe/profound)* and *(duration: less, 1 mon., 1 month year, more than 1 year)*
- Inter-rater reliability 0.85 & internal consistency 0.99, test-retest 0.76 (Matson, Mayville, Bielecki, Barnes, Bamburg, & Baglio, 1998).
Areas with START programs or services based on START
START Medication Side Effects Project

- MEDS administered for individuals living in START Center programs
- Information shared with family, referral source, GP and psychiatrist
- Training for all staff on medications and side effects
- We are starting a conversation about efficacy and side-effects (informed consent)
Matson Evaluation of Drug Side Effects (MEDS)

9 categories, each 5-14 symptoms
(1) cardiovascular and hematological
(2) gastrointestinal
(3) endocrine/genitourinary
(4) eye/ear/nose/throat
(5) skin/allergies/temperature
(6) CNS-general
(7) CNS-dystonia
(8) CNS-parkinsonism/dyskinesia
(9) CNS-behavior/akathisia
MEDS Cardiovascular Subscale

- 1. A sudden loss of strength or fainting
- 2. Trouble breathing or shortness of breath
- 3. Rapid breathing (tachypnea)
- 4. Chest pain
- 5. Irregularity of the heartbeat
- 6. Abnormal frequency of heartbeat (Circle one: bradycardia / tachycardia)
- 7. Subnormal arterial blood pressure (hypotension)
- 8. Persistent high blood pressure (hypertension)
- 9. Abnormality in white blood cell count
Medications-Jim  57 yo Mild ID

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>quetiapine (Seroquel)</td>
<td>100 mg</td>
</tr>
<tr>
<td>levothyroxine</td>
<td>150</td>
</tr>
<tr>
<td>risperidone (Risperdal)</td>
<td>2 mg bid</td>
</tr>
<tr>
<td>benztropine (Cogentin)</td>
<td>5 bid</td>
</tr>
<tr>
<td>clonazepam (Klonopin)</td>
<td>4 tid</td>
</tr>
<tr>
<td>ranitidine (Zantac)</td>
<td>50 bid</td>
</tr>
<tr>
<td>antacid</td>
<td>500 tid</td>
</tr>
<tr>
<td>divalproex sod (Depakote)</td>
<td>125 tid</td>
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<tr>
<td>bupropion SR (Wellbutrin)</td>
<td>150 mg bid</td>
</tr>
<tr>
<td>alprazolam( Xanax)</td>
<td>0.5 tid</td>
</tr>
</tbody>
</table>
### Compared to non-treated controls

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cont</th>
<th>Jim</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) cardio /hematological</td>
<td>0.7</td>
<td>2</td>
</tr>
<tr>
<td>(2) gastrointestinal</td>
<td>0.13</td>
<td>3</td>
</tr>
<tr>
<td>(3) endocrine/genitourinary</td>
<td>0.0</td>
<td>2</td>
</tr>
<tr>
<td>(4) eye/ear/nose/throat</td>
<td>0.4</td>
<td>5</td>
</tr>
<tr>
<td>(5) skin/allergies/temperature</td>
<td>0.13</td>
<td>3</td>
</tr>
<tr>
<td>(6) CNS-general</td>
<td>0.87</td>
<td>22</td>
</tr>
<tr>
<td>(7) CNS-dystonia</td>
<td>0.0</td>
<td>1</td>
</tr>
<tr>
<td>(8) CNS-parkinsonism/dyskinesia</td>
<td>0.33</td>
<td>11</td>
</tr>
<tr>
<td>(9) CNS-behavior/akathisia</td>
<td>0.14</td>
<td>4</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>2.7</strong></td>
<td><strong>53</strong></td>
</tr>
</tbody>
</table>
APA five recommendations: www.choosingwisely.org

• Don’t prescribe antipsychotic medications to patients for any indication without appropriate initial evaluation and appropriate ongoing monitoring.
• Don’t routinely prescribe two or more antipsychotic medications concurrently.
• Don’t prescribe antipsychotic medications as a first-line intervention to treat behavioral and psychological symptoms of dementia.
• Don’t routinely prescribe antipsychotic medications as a first-line intervention for insomnia in adults.
• Don’t routinely prescribe antipsychotic medications as a first-line intervention for children and adolescents for any diagnosis other than psychotic disorders.
Rogers vs. Okin 1975

MEDICAL LAW-THE RIGHT TO REFUSE ANTIPSYCHOTIC DRUG TREATMENT: SUBSTANTIVE RIGHTS AND PROCEDURAL GUIDELINES IN MASSACHUSETTS

Rogers v. Commissioner of the Mental Health Department, 390 Mass. 489, 458 N.E.2d 308 (1983)