Psychotropic Medications and Adverse Side Effects

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Speaker Introduction

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Today’s Agenda

• Psychotropic Med use in the DDS Population
• Commonly Prescribed Psychotropic Meds
• Common Side Effects
• Managing Effects
• Adverse Effects
• Case Examples
• Questions
Psychotropic Med Usage
Polypharmacy in MA DDS Adults

• Approximately 60% of MA DDS adults are on 1 or more psychotropic medications.
• More medication use in older adults.
• Many adults experience long-term use of medications that affect the central nervous system (i.e. anti-seizure meds).
• Medication use may result in undesired or adverse side effects.
• Taking multiple medications increases the likelihood of having at least one side effect.
2011 Medicaid Claim Data

- Estimated 54%-60% of all adults on one or more psychotropic medication

Adult DDS Population - 2011 (Estimated Percentages)
Annual Meds Filled

Avg # Rxs per person

2008 Nonduals*, US: 6.8 (12 months)
2008 Duals*, US: 4.9 (12 months)
2011 MA DDS: 24.1 - 26.8 (7 months)

*Includes Children
## 2011 - Top Medication Categories

<table>
<thead>
<tr>
<th>Rank</th>
<th>Category</th>
<th>Est. of # MA DDS Adults with 1+ Rx in 7 months</th>
<th>All MA Duals&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vitamin/Supplement</td>
<td>35.1% - 39.0%</td>
<td>5.9%</td>
</tr>
<tr>
<td>2</td>
<td>Anticonvulsants</td>
<td>34.6% - 38.5%</td>
<td>9.1%</td>
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<tr>
<td>3</td>
<td>Antibiotics</td>
<td>32.4% - 36.0%</td>
<td>&lt;2.2%</td>
</tr>
<tr>
<td>4</td>
<td>Antidepressant</td>
<td>25.5% - 28.3%</td>
<td>3.4%</td>
</tr>
<tr>
<td>5</td>
<td>Cardiovascular</td>
<td>24.5% - 27.2%</td>
<td>3.4%</td>
</tr>
<tr>
<td>6</td>
<td>Analgesic (pain meds)</td>
<td>24.4% - 27.1%</td>
<td>4.4%</td>
</tr>
<tr>
<td>7</td>
<td>Laxatives/Cathartics</td>
<td>24.2% - 26.9%</td>
<td>Unk.</td>
</tr>
<tr>
<td>8</td>
<td>Antipsychotics</td>
<td>20.7% - 23.0%</td>
<td>1.7%</td>
</tr>
<tr>
<td>9</td>
<td>Gastrointestinal Drugs</td>
<td>20.2% - 22.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td>10</td>
<td>Anxiolytic</td>
<td>19.0% - 21.2%</td>
<td>18.2%</td>
</tr>
</tbody>
</table>
Most Common Medications

1. Vitamin D
2. Acetaminophen - Analgesic
3. Docusate - Laxative
4. Lorazepam/Ativan – Antianxiety
5. Prilosec/Omeprazole – Gastrointestinal
6. Divalproex sodium/Depakote - Anticonvulsant
7. Calcium
8. Loratadine – Antihistamine
Most Common Medications (cont.)

9. Polyethylene Glycol - Laxative

10. Levothyroxine Sodium – Thyroid Hormones

11. Risperdal – Antipsychotic

12. Clonazepam/Klonopin – Anticonvulsant

13. Simvastatin/Zocor – Cardiovascular

14. Ibuprofen – Analgesic

15. Citalopram/Celexa – Antidepressant
Side Effects
Common Side Effects

• Constipation
• Dehydration
• Increased falls risk
• Fatigue
• Sedation, which can include trouble swallowing
At a minimum

• Offer drinks frequently to prevent dehydration
• Manage bowel functioning
• Dietary interventions
• Environmental Scan
When to Intervene

• If you see something, say something.
• The person should probably be seen by a medical professional when:
  • There is a significant change in the person’s status (medical or physical)
  • “Something’s not right” with the person
Serious Adverse Effects

• Lithium Intoxication/Toxicity
• Anticholinergic Toxicity
• Serotonin Syndrome
• Neuroleptic Malignant Syndrome
Lithium Intoxication/Toxicity

- Lithium - 100% Kidney Excretion
- Excretion affected by changes in sodium & hydration
  - Negative sodium balance causes lithium retention
- Renal Insufficiency
- Drug Interactions
Risks for Increased Levels

• Dehydration due to
  • Reduced fluid intake
  • Excessive sweating
  • Diarrhea
  • Vomiting
  • Excessive urination

• Dietary Changes
  • Substantial reduction in salt or caffeine

• Marked Weight Loss
Drugs Effecting Levels

• Numerous Interactions
• NSAIDs- ibuprofen, naproxen, etc
• COX-2 Inhibitors- celecoxib (Celebrex®), rofecoxib (Vioxx®)
• Thiazide Diuretics- hydrochlorothiazide
• ACE-Inhibitors- enalapril (Vasotec®), captopril, etc
Signs & Symptoms

- Mild Intoxication-Level < 1.5mEq/L
- Also initial transient effects
  - Fine hand tremor
  - GI upset- nausea, vomiting, diarrhea, anorexia
- Mild increase in urination, increased thirst and dry mouth
- Muscle weakness
Signs & Symptoms

• Moderate Intoxication: 1.5-2.5mEq/L
  • Course Tremor
  • GI upset
  • Slurred Speech
  • Vertigo
  • Confusion
  • Sedation/ Lethargy
  • Hyperreflexia—twitching movements
Signs & Symptoms

• Severe Intoxication: Level >2.5mEq/L
  • Seriously impaired consciousness
  • Stupor
  • Coma
  • Cardiovascular collapse
  • Death
• May simulate epileptic attacks or agitated psychotic stupor
Treatment

- Mild toxicity - increase fluids
- Contact physician immediately to determine if transport to ER required
- Stop lithium until lithium level has been determined and hold until symptoms have abated
- Severe toxicity may require hemodialysis
Lithium Toxicity

- Symptomatic improvement may lag behind fall in serum levels by several days to weeks
- Can be seen with therapeutic levels
- One study showed delirium to persist on average 11 days after DC of lithium
- Electrolyte imbalances can last for weeks
Lithium Toxicity

- Misdiagnosed as Flu Syndrome
- ER MD either not aware of lithium use or does not think to check levels
- Lithium has a narrow therapeutic index
Lithium Long Term Effects

- Hypothyroidism
- Decreased kidney function

After 10-20 years (course variable), kidney function as measured by GFR will begin to decline.

If Lithium is not tapered and removed, individual will progress to kidney failure.
Anticholinergic Toxicity

• Anticholinergic effects
  Dry mouth
  Pupil Dilation (Blurred vision)
  Inhibition of Sweating
  Difficulty in urination
  Constipation
  Alteration in heart rate
Anticholinergic Toxicity

- Sometimes confused with psychotic agitation
- Can develop rapidly
- Red as a Beet, Dry as a Bone, Blind as a Bat, Hot as a Hare, Mad as a Hatter
- Treatment is to remove AC meds increase fluids
- Will usually clear in 24-48H
Examples of Anticholinergic Medications

• Antihistamines- diphenhydramine
• Benztropine (Cogentin)
• Trihexyphenidyl (Artane)
• Antipsychotics- esp Clozapine, Thioridazine, Olanzapine & Quetiapine
• Amitriptylline & Imipramine
• Clomipramine
• Doxepin
• Paroxetine (Paxil)
Serotonin Syndrome

- Serotonergic Hyper stimulation
- Due to actions of multiple meds that act on Serotonergic System
- Meds act on this system in many ways
  - Inhibit reuptake; storage or metabolism
  - Enhance release
  - Direct receptor agonists
  - Serotonin precursors
- Non-specific increase in Serotonin Activity
Diagnostic Criteria
Sternbach’s Signs & Symptoms

Signs commonly seen in >20% of Cases

• muscle rigidity (51%)
• restlessness/hyperactivity (48%)
• Hyperthermia—high temperature (45%)
• tremor (43%)
• Tachycardia—fast heart beat (36%)
• Hypertension—high blood pressure (35%)
• Coma/unresponsiveness (29%)
• dilated pupils (28%)
• Tachypnea—rapid breathing (26%)
• nausea (23%)
Agents that increase Serotonergic activity

**Inhibitors of Reuptake**
- SSRIs (Paxil, Prozac, Zoloft, Celexa, Clomipramine)
- Effexor & Luvox
- Bupropion
- Serzone & trazadone
- TCA’s (Tricyclic antidepressant)
- Tramadol
- Cocaine
- St. John’s Wort

**Serotonin granular uptake & storage Inhibitors**
- Resperpine
- Meperidine (demerol)
- Dextromethorphan
- Fenfluramine
Agents that increase Serotonergic activity

- Inhibitors of Serotonin Metabolism
  - MAO-I’s
    - Phenylzine (nardil)
    - Tranylcypromine (parnate)
    - Isocarboxid (marplan)
  - Selegiline

- Serotonin Release Enhancers
  - Amphetamines
  - Cocaine
  - Lithium
  - Mirtazapine (Remeron)
Agents that increase Serotonergic activity

- Serotonin precursors
  - L-Tryptophan
  - 5-hydroxytryptophan

- Non-Specific Increase in Serotonin Activity
  - Lithium
  - ECT (Electroconvulsive therapy)

- Direct Serotonin receptor Agonists
  - Buspirone
  - Sumatriptan
  - Ergotamine
  - LSD
  - Psilocybin
  - Mescaline
  - Yohimbine
Prevention & Recognition

- No lab test will confirm and elevated blood levels not required for syndrome
- Develops rapidly- usually 24 hrs of change in serotonergic med
- Some cases show mild symptoms days to weeks before severe syndrome occurs
- Often resolves in 24h after stopping medications
- Rarely results in death
- Fever >105 indicates severe process with increase risk of complications
Treatment

• Stop all serotonergic meds
• Supportive measures depend on severity of symptoms
• Lorazepam
• Cooling measures for hyperthermia
• Serotonin antagonists like propranolol & Cyproheptidine (Periactin) have been used in mild cases
Neuroleptic Malignant Syndrome

• Potentially lethal form of drug-induced hyperthermia (high temperature)
• Rare- 1% of patients on antipsychotics
• Likely due to depletion of dopamine
• Can occur with any dopamine blocking medication
  • metoclopramide (Reglan)
  • antidepressants that affect dopamine
  • compazine
NMS symptoms

• Severe muscle rigidity
• Fever - seen in 95% of cases 101°F-103°F common with as high as 108°F reported
• Elevated creatine kinase levels
• Elevated White blood cell count
• Altered mental status
NMS risks

• Rapid antipsychotic titration
• High-potency or high dose antipsychotics
• History of NMS- Patients who have developed NMS have a higher risk of recurrence
• Concurrent dehydration
• Can occur any time- however 96% of cases within 4 weeks of starting therapy with dopamine blocker
Differentiating NMS from other Medical Diagnoses

• Malignant Hyperthermia- occurs after anesthesia
• Heat stroke – hot dry skin- absence of rigidity
• Severe EPS (extrapyramidal side effects) – absence of rigidity, fever, increased White blood cells
• Central Nervous System Infection – absence of rigidity
• Elevated CPK (Creatine phosphokinase) level is essential
• Serotonin Syndrome
NMS treatment

- Stop all meds affecting dopamine
- Maintain hydration & monitor renal status
- Begin bromocriptine if able to swallow
- Bromocriptine will reduce symptoms in over 90% of cases, but may worsen psychotic features
- Cooling measures
Final thoughts on other commonly prescribed medications
Valproic Acid

- Connection between VPA and bruising often overlooked
- Risk of Hemorrhage
- Allegations of abuse due to bruising
Clozapine

• Problems with white blood count almost always detected due to strict protocols
• When problem noted; withdrawal of clozapine immediate which leads to withdrawal reactions
• Very difficult to find adequate replacement
Seroquel-Risperdal-Zyprexa

• Metabolic effects
  • Weight gain
  • Increase in triglycerides (Seroquel)
  • Increase in prolactin (Risperidone?/Reisperdal?)
  • Increased risk of developing Type II Diabetes Mellitus

• Very Rare, but lethal rapid increase in blood glucose leading to fatal diabetic ketoacidosis (Primarily with Zyprexa)
Systems Issues and Case Examples
Systems Issues & Case Examples

- NMS
- 3-5 trips to ER before correct diagnosis
- Misdiagnosed as Flu Syndrome
- CPK can be helpful but often not done on 1\textsuperscript{st} or 2\textsuperscript{nd} visit
- Delay in diagnosis can be difference between life and death
Drug Resources


• RXList - part of WebMD [http://www.rxlist.com/](http://www.rxlist.com/)

• Clinical Pharmacology - drug compendium. User can register for a free trial. [https://www.clinicalpharmacology.com/](https://www.clinicalpharmacology.com/)

Questions and Answers