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)
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 Duals1</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>
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<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>
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<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>
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</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

- 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
  o 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

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

• **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

- 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
- Benzotropine (Cogentin)
- Trihexyphenidyl (Artane)
- Antipsychotics- esp Clozapine, Thioridazine Olanzapine & Quetiapine
- Amitriptyline & 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 & trazodone
- TCA’s (Tricyclic antidepressant)
- Tramadol
- Cocaine
- St. John’s Wort

**Serotonin granular uptake & storage Inhibitors**
- Reserpine
- Meperidine (demerol)
- Dextromethorphan
- Fenfluramine

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

**Serotonin Release Enhancers**
- Amphetamines
- Cocaine
- Lithium
- Mirtazapine (Remeron)

**Serotonin precursors**
- L-Tryptophan
- 5-hydroxytryptophan

**Direct Serotonin receptor Agonists**
- Buspirone
- Sumatriptan
- Ergotamine
- LSD
- Psilocybin
- Mescaline
- Yohimbine

**Non-Specific Increase in Serotonin Activity**
- Lithium
- ECT (Electroconvulsive therapy)
**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 at 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, 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 (Risperdone?/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 1st or 2nd visit
- Delay in diagnosis can be difference between life and death

Drug Resources

- RXList - part of WebMD http://www.rxlist.com/

Questions and Answers