Psychotropic Medications and Adverse Side Effects

July 1, 2015

UMASS MEDICAL SCHOOL | COMMONWEALTH MEDICINE
CENTER FOR DEVELOPMENTAL DISABILITIES EVALUATION AND RESEARCH

Eunice Kennedy Shriver Center
CDDER
UMASS MEDICAL SCHOOL
A Commonwealth Medicine Center of Distinction

Speaker Introduction

Edwin Mikkelsen MD

Today's Agenda

- Psychotropic Med use in the DDS Population
- Commonly Prescribed Psychotropic Meds
- Common Side Effects
- Managing Effects
- Adverse Effects
- Case Examples
- Questions

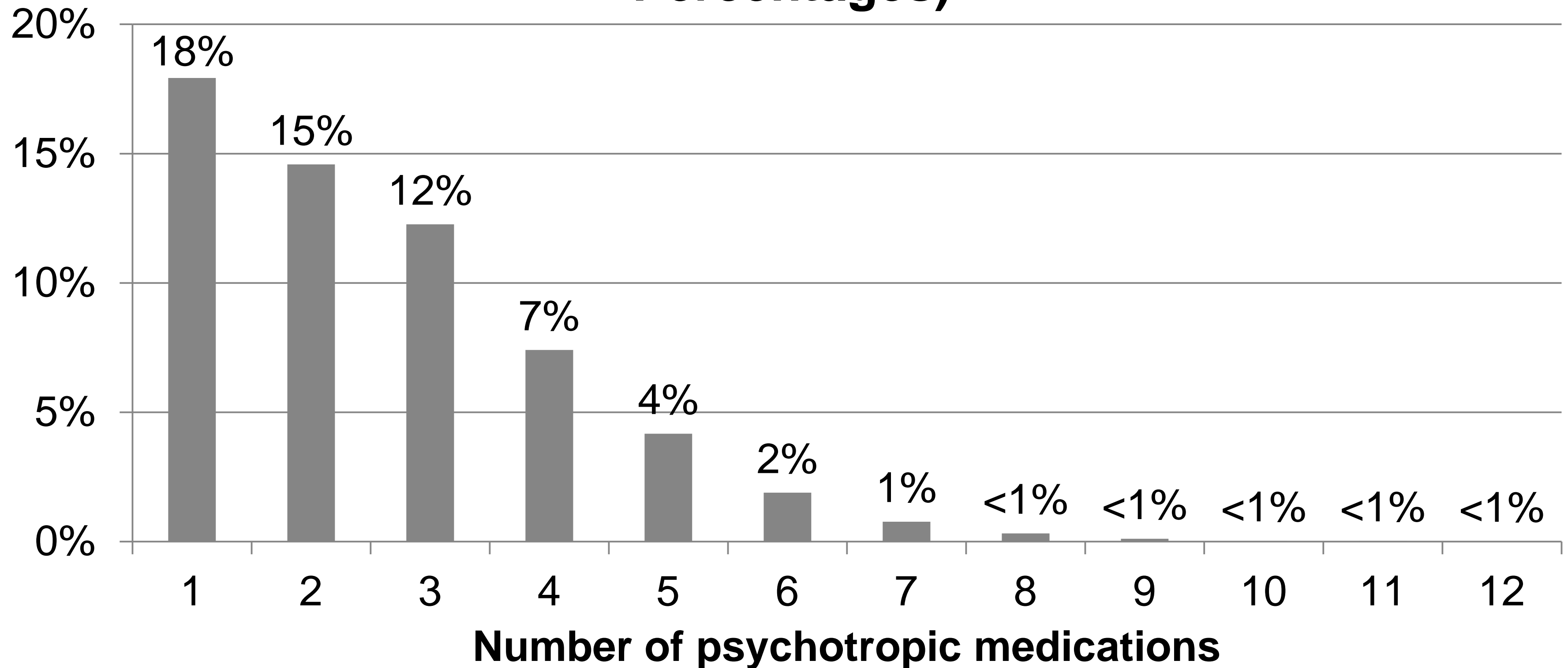
Psychotropic Med Usage

Polypharmacy in MA DDS Adults

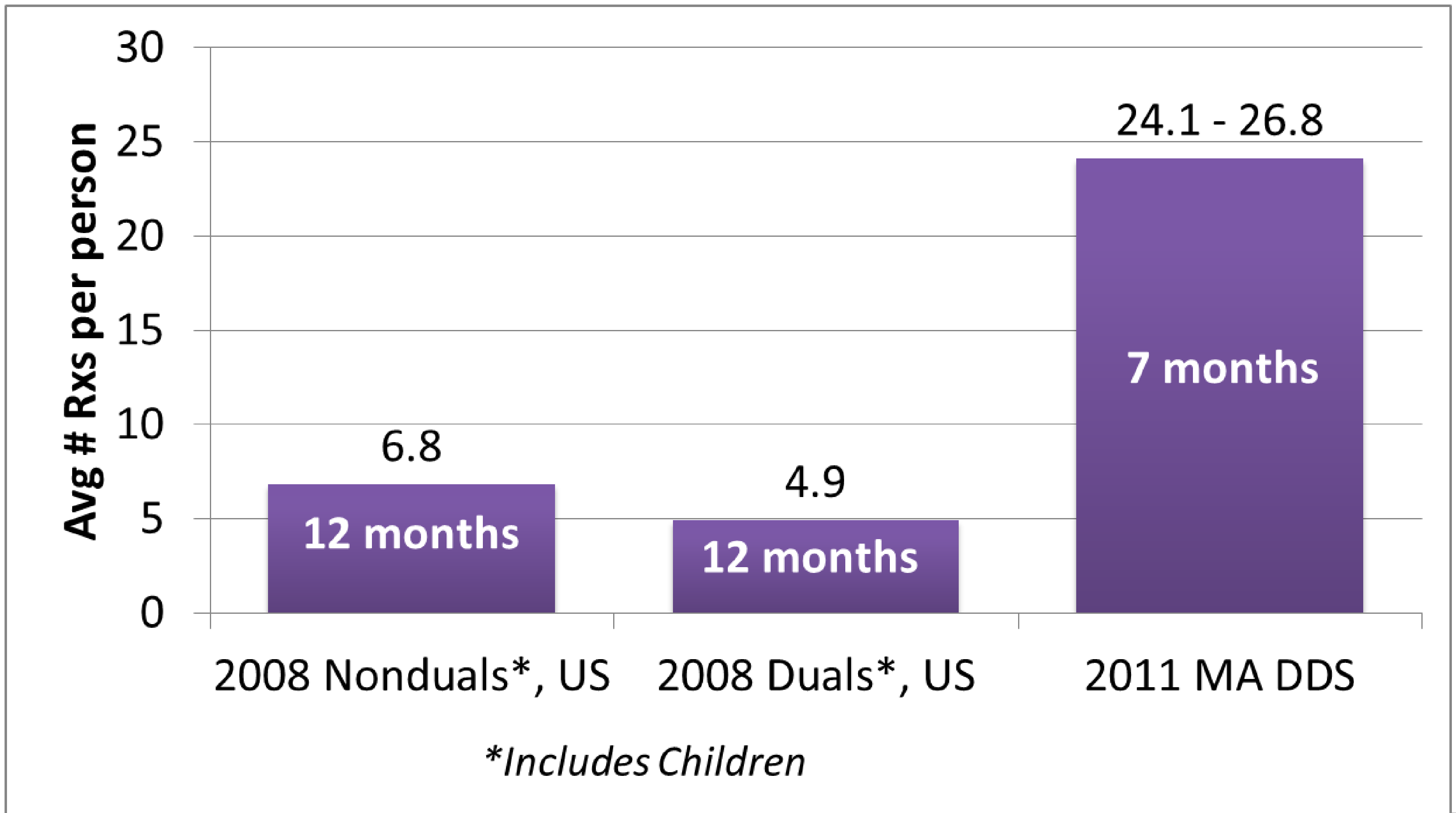
- Approximately 60% of MA DDS adults are on 1 <u>or more</u> psychotropic medications.
- More medication use in older adults.
- Many adults experience long-term use of medications that affect the central nervous system (i.e. anti-seizure meds).
- Medication use may result in undesired or adverse side 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



Annual Meds Filled



2011 - Top Medication Categories

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

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

<u>Inhibitors of Reuptake</u>

- 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

- 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-Trytophan
- 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 1st or 2nd visit
- Delay in diagnosis can be difference between life and death

Drug Resources

- Global RPH – lists of simple adverse reactions and dosing information. Free http://www.globalrph.com/
- RXList - part of WebMD http://www.rxlist.com/
- Clinical Pharmacology - drug compendium. User can register for a free trial. https://www.clinicalpharmacology.com/
- Micromedex – drug reference. Minimal fee for mobile devices. http://micromedex.com/

Questions and Answers