Strategies To Improve Adherence: Understanding Schizophrenia, Weight Gain, and Associated Health Risks

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Supported by an educational grant from Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., administered by Ortho-McNeil-Janssen Scientific Affairs, LLC.
Strategies To Improve Adherence -
Understanding Schizophrenia, Weight Gain, and Associated Health Risks

Speaker:
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Speaker Disclosure: Dr. Montagnese has no actual or potential conflicts of interest in relation to this program.
Strategies To Improve Adherence—Understanding Schizophrenia, Weight Gain, and Associated Health Risks

Accreditation: Pharmacist-798-000-08-071-L01-P
Technicians- 798-000-08-071-L01-T

Target Audience: Pharmacists and Technicians

CE Credits: 1.0 Continuing Education hour or 0.1 CEU for pharmacists/technicians

Expiration Date 8/21/2011

Program Overview: This program will give pharmacists understanding of the underlying conditions, potential of currently available treatment options (along with their probable results and possible side effects) and the need to educate patients and family members on drug treatment strategies and the long-term medication and adherence problems commonly encountered with schizophrenia.

Objectives:
1. Outline the problems associated with medication noncompliance among patients with schizophrenia to include data on weight gain and metabolic abnormalities.
2. Compare and contrast second generation antipsychotics to include efficacy, dosing, safety, tolerability profiles and problems associated with metabolic abnormalities.
3. Describe the active role that pharmacists can play in collaboration with patients and physicians in setting patient goals, monitoring metabolic parameters, and other strategies to improve adherence to medication.

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What is schizophrenia?

- Theresa: 32 year old woman hospitalized at a State Mental Institution in PA
- Numerous acute hospitalizations in 2 previous years
- Her psychotic presentation
What is psychosis?

- What is real vs. fantasy
- Think of “A Beautiful Mind”
Hallucinations

- Think of 5 senses: visual, auditory, olfactory, gustatory, tactile
- Usually frightening, morbid, macabre
- Can be friendly, company
Delusions

- A fixed false belief
- Bizarre-illogical
- Non-bizarre: can really occur
What are the psychotic disorders?

- Schizophrenia- 5 types
- Schizoaffective Disorder
- Delusional Disorder
- Brief Psychotic Disorder
- Shared Psychotic Disorder
- Psychotic Disorder due to Medical Cond.
- Substance-induced psychotic disorder
- Psychotic Disorder NOS (common in kids)
DSM Criteria for Schizophrenia

- Two or more of following for 1 month: (A Criterion)
  - Delusions
  - Hallucinations
  - Disorganized speech
  - Disorganized behavior
  - Negative symptoms: flat affect, avolition, alogia

- Only 1 if delusions bizarre or voice keeping commentary or 2 voices conversing
DSM Criteria for Schizophrenia

- Social/occupational dysfunction
- Disturbance for at least 6 months with at least 1 month with criterion A
- Not due to substance, medical condition, mood disorder or PDD
Schizophrenia Subtypes

- Catatonic
- Paranoid
- Disorganized
- Undifferentiated
- Residual
Positive Symptoms

- Symptoms associated with
  - distorted reality
- Delusions
- Hallucinations

Things present in those with schizophrenia as compared to those without.
Negative Symptoms

- Affective blunting
- Poverty of speech
- Thought blocking
- Poor grooming
- Lack of motivation-apathy
- Anhedonia
- Social withdrawal

Things absent from those with schizophrenia as compared to those without.
Epidemiology

- How common? 1% of world’s population
- Across cultures, races
- M:F, 1:1
- Age of onset is earlier in men
- M: onset late teens, early 20’s
- W: onset mid to late 20’s
- Studies show overdiagnosis in African Americans, not higher incidence
Course of Disease

- Chronic illness
- No cure
- Very treatable
- Without treatment-downhill course
Cost of Schizophrenia

- 1990 accounted for 2.5% of health care expenditures + nondirect costs ($45 billion)
- 2002 accounted for $62.7 billion for direct and nondirect costs
- Unemployment rate is 70-80%
- 10% of those permanently disabled
Morbidity and Mortality

People with schizophrenia that are in the public mental health system die 25 years earlier than the general population!!

Schizophrenia can be lethal.
Social Aspects

- 1/3-2/3 are homeless
- 30-50% abuse alcohol
- Life style
- Poor access to care, both psychiatric and general medical care
- Poor diet
- Poor insight
- Most smoke (56-88%)
“Natural Causes of Death”

- 2.3X cardiovascular disease-related deaths
- 2.7X diabetes-related deaths
- 3.2X respiratory disease-related deaths
- 3.4X infectious disease-related deaths
Disease Aspects

- Increased prevalence of DM
- ? Genetic link
- ? Inherent increased risk of “Metabolic Syndrome” in schizophrenia
Metabolic Syndrome

- Abdominal Obesity: >40 in waist (M), >35 in waist (F)
- Triglycerides: >150 mg/dL
- HDL cholesterol: <40 mg/dL (M), <50 mg/dL (F)
- BP: ≥130 mm Hg
- Fasting blood glucose: >110 mg/dL
Weight Gain Alone

- First noticeable sign
- Most distressing to patients
- Worse with atypical antipsychotics compared to typicals
Weight Gain with Atypicals

**From baseline, weight gain at 1 yr**
- Olanzapine (all doses): 14 lbs
- Olanzapine (12.5-17.5mg): 25 lbs
- Clozapine: 11-12 lbs
- Quetiapine: 7-8 lbs
- Risperidone: 5 lbs
- Ziprasidone: 2.5 lbs
- Aripiprazole: 2.5 lbs
Mechanism of Weight Gain

- Meds stimulate the appetite
- Genetic Predisposition
- Sedentary lifestyle
- Impaired metabolic regulation: glucose transport, neuroreceptor effects
Hyperglycemia/Insulin Resistance

- Atypical antipsychotics increase the risk of hyperglycemia
- Schizophrenia has increase risk of DM-2 regardless of antipsychotic use
- Obesity is risk factor for impaired glucose regulation
- DM tends to occur in first few months of tx
Hyperlipidemia

- Antipsychotics affect serum lipid levels
- Olanzapine and clozapine cause greatest impairment
- Obesity is directly correlated
Cardiovascular Disease

- All these factors increase risk of CVD and death
- 2/3 of patients with schizophrenia die of CVD
- ½ of general population die of CVD
Monitoring for Metabolic Syndrome

- Check weight/BMI
- Waist circumference
- BP
- Fasting glucose
- Fasting lipid panel
- Personal/family history
Switching Agents

- Olanzapine/risperidone to ziprasidone/aripiprazole
- Significant weight loss
- Improvement of metabolic parameters
- Consider pt’s response
- Risk of relapse
- Cross taper over weeks
- Shared decision
Effect on Compliance

- Up to 75% rate of noncompliance
- Medication side effects
- Social factors: family support/attitudes
- Therapeutic alliance
- Stigma
- Paranoia about treatment
- Pleasant delusions
- Substance abuse
- Lack of access to meds/care
Effects of Noncompliance

- 40% of disease cost associated with noncompliance
- Relapse is almost inevitable
- Increased suicide risk
- Clinicians wrong about predicting compliance ½ of the time
Role of Pharmacists in Noncompliance

- Frontline providers
- Communicate with PCPs/Psychiatrists
- Patient Education
- Simplify dosing regimens
- Monitor for polypharmacy
- May be first to see EPS
Now, let’s get to the meds

- Antipsychotics revolutionized treatment
- Chlorpromazine (Thorazine) – 1952
- 1st of the “Typical” antipsychotics
- First used as an anesthetic
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dose Equiv.(mg)</th>
<th>Common Dose Range</th>
<th>Relative Potency</th>
<th>EPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>Thorazine</td>
<td>100</td>
<td>200-900</td>
<td>Low</td>
<td>Low</td>
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<tr>
<td>Mesoridazine</td>
<td>Serentil</td>
<td>50</td>
<td>100-400</td>
<td>Low</td>
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<tr>
<td>Thioridazine</td>
<td>Mellaril</td>
<td>100</td>
<td>200-800</td>
<td>Low</td>
<td>Low</td>
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<tr>
<td>Perphenazine</td>
<td>Trilafon</td>
<td>8</td>
<td>16-64</td>
<td>Intermediate</td>
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<tr>
<td>Trifluoperazine</td>
<td>Stelazine</td>
<td>5</td>
<td>5-40</td>
<td>High</td>
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<tr>
<td>Fluphenazine</td>
<td>Prolixin</td>
<td>2</td>
<td>5-20</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Haldol</td>
<td>2</td>
<td>5-20</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Chlorprothixene</td>
<td>Taractan</td>
<td>75</td>
<td>100-600</td>
<td>Low</td>
<td>Low</td>
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<tr>
<td>Thiothixene</td>
<td>Navane</td>
<td>5</td>
<td>5-60</td>
<td>High</td>
<td>Low</td>
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<tr>
<td>Loxapine</td>
<td>Loxitane</td>
<td>15</td>
<td>25-250</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Molindone</td>
<td>Moban</td>
<td>10</td>
<td>50-225</td>
<td>Intermediate</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>
How do these meds work?

- Target dopaminergic neurons
- Increase dopamine = psychosis
- Dopamine blockers
- Typical agents affect nigrostriatal tract and mesolimbic tract
- Nigrostriatal area also affects involuntary movements
- Reason for EPS
Extra Pyramidal Symptoms

- Akathesia - uncontrolled restlessness
- Dystonic reactions - muscle spasms, usually eyes, neck, back and tongue
- Parkinsonism - shuffling gait, stiffness, tremor, masked faces
- Can be intolerable, very frightening
- Common reason for medication noncompliance
EPS (Cont)

- Higher incidence with higher potency
- Higher incidence at start of tx
- Risk factors for EPS: young age, male, IM administration
- Treat with anticholinergic or antihistaminergic
- Prevent with anticholinergic or antiparkinsonian drugs
Tardive Dyskinesia

- Tardive dyskinesia
- Abnormal involuntary movements
- Dyskinetic
- Choreoathetoid
- Usually face, tongue, mouth
- Can involve trunk, arms
- Can occur after brief exposure
- Stop meds, lower dose
- Can be permanent
- Must get informed consent

- Risk increases with longer use (4%/yr tx)
- Risk increases with age, female gender, affective disorder, GMC, high doses
- Can be disfiguring
- Clozapine may help
- Vit E, lithium, amantadine
Atypical Agents

- Newer
- Affect D2 and 5HT(2A) receptors
- Reason for increased efficacy
- Affects positive (D2) and negative (5HT) symptoms
- Don’t effect nigrostriatal tract as much-less EPS
- Affect mesolimbic and mesocortical tracts
# Atypical Agents

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Daily Dosage (mg)</th>
<th>Forms available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Abilify</td>
<td>10-30</td>
<td>INJ, soln, tabs-D</td>
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<tr>
<td>Clozapine</td>
<td>Clozaril</td>
<td>25-900</td>
<td>tabs-D</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Zyprexa</td>
<td>5-20</td>
<td>INJ, tabs-D</td>
</tr>
<tr>
<td>Palipaeridone</td>
<td>Invega</td>
<td>6-12</td>
<td>tabs</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroquel</td>
<td>300-800</td>
<td>tabs</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Risperdal</td>
<td>1-12</td>
<td>tabs-D, soln, INJ</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Geodon</td>
<td>40-160</td>
<td>tabs</td>
</tr>
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</table>
How do we choose an atypical?

- Side effect profile - make them work for patient
- Any absolute contraindications or medical risks
- Other meds: drug-drug interactions
- Cost!!!
- Insurance
- Patient/family perceptions
- Doctor’s own perceptions about meds
General Side Effects of Atypicals

- Less likely to cause EPS or TD
- Prolactin elevation-galactorhea, gynecomastia
- Sedation
- Anticholinergic
- Weight gain
- Also seen with typicals
Risperidone (Risperdal)

- 1993
- Only depot form of atypical
- Depot form q 2 weeks
- Weight gain, sedation and high prolactin most common
- Above 6 mg daily—↑EPS
Olanzapine (Zyprexa)

- Very sedating
- Excessive weight gain
- Metabolic syndrome
Quetiapine (Seroquel)

- Moderate for weight gain
- Slit lamp eye exam recommended - cataracts, not often done
- Very sedating
- Used in low doses for sleep-off label
Ziprasidone (Geodon)

- 2001
- Short acting injectable available
- Can be used for acute agitation
- More weight neutral than other atypicals
- Lower incidence of metabolic syndrome
Aripiprazole (Abilify)

- Not a full DA agonist
- "Dopamine stabilizer"
- Agonist in areas of low activity
- More weight neutral
- Low incidence of metabolic syndrome
Clozapine (Clozaril)

- 1989
- Weight gain
- Agranulocytosis - serious, fatal
- Weekly WBC count
- Specific protocol - complex to manage
- Used in refractory cases
- Seizures
- Excessive salivation
Palipaeridone (Invega)

- 2007
- Active metabolite of risperidone
- Slow release over 24 hours
## Comparison of Atypicals

<table>
<thead>
<tr>
<th></th>
<th>Typicals</th>
<th>Cloz</th>
<th>Arip</th>
<th>Olan</th>
<th>Risp</th>
<th>Que</th>
<th>Zip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin elev</td>
<td>+ / ++</td>
<td>-</td>
<td>+ / -</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Weight gain</td>
<td>++</td>
<td>+++</td>
<td>+ / -</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+ / -</td>
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<tr>
<td>Diabetes risk</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>U</td>
<td>U</td>
<td>-</td>
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<tr>
<td>Dyslipidemia</td>
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<td>-</td>
<td>+</td>
<td>U</td>
<td>U</td>
<td>-</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>+</td>
<td>+ / ++</td>
<td>+++</td>
<td>+ / -</td>
<td>+ / -</td>
<td>+</td>
<td>+ / -</td>
</tr>
<tr>
<td>Sedation</td>
<td>+ / ++</td>
<td>+++</td>
<td>+ / -</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+ / -</td>
</tr>
</tbody>
</table>

Cloz=clozapine, Arip=aripiprazole, Olanz=olanzapine, Risp=risperidone, Que=quetiapine, Zip=ziprasidone, U=uncertain
Are Atypicals Worth It?

- CATIE-Sept 2005
- NIMH study in NEJM
- Ground breaking
- Outcome stated typicals = atypicals in efficacy
- Cost of atypicals may not always be justified
- Patients stopped both meds at a high rate
Facing the Challenges Ahead

- Cost
- Access
- Coordination of care
- Resources
- Compliance
- Stigma
- Addressing these will lead to comprehensive model of care
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