Strategies to Improve Adherence—Understanding Schizophrenia, Weight Gain, and Associated Health Risk

Elizabeth Montagnese, M.D.
Adult, Child and Adolescent Psychiatrist, Medical Director of Family and Children Services of Central Pennsylvania, Private Practitioner

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

Speaker: Dr. Montagnese received her medical degree at Wayne State University in Detroit, Michigan. She completed her general psychiatry and child psychiatry training at the Penn State University Milton S. Hershey Medical Center. Dr. Montagnese is the medical director at Family and Children Services of Central Pennsylvania. This is a United Way-funded nonprofit agency that serves the greater Harrisburg, York and Lancaster areas. To contact her at this agency please call 717-238-8118.

Speaker Disclosure: Dr. Montagnese has no actual or potential conflicts of interest in relation to this program.

PharmCon is accredited by the accreditation council for Pharmacy Education as a provider of continuing pharmacy education.

Legal Disclaimer: The material presented here does not necessarily reflect the views of Pharmaceutical Education Consultants (PharmCon) or the companies that support educational programming. A qualified healthcare professional should always be consulted before using any therapeutic product discussed. Participants should verify all information and data before treating patients or employing any therapies described in this educational activity.

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
Expiration Date: December 31, 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 about 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.

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

**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- $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 (12.5-17.5 mg): 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 increased 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
Strategies to Improve Adherence—Understanding Schizophrenia, Weight Gain, and Associated Health Risk

Switching Agents
- Olanzapine/risperidone to ziprasidone/airpiprazole
- 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</th>
<th>Dose Equivalent</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>100-900</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Mesoridazine</td>
<td>Serentil</td>
<td>100</td>
<td>100-400</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Mellaril</td>
<td>150</td>
<td>200-800</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Perphenazine</td>
<td>Trilafon</td>
<td>8</td>
<td>16-64</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>Trifluoperazine</td>
<td>Stelazine</td>
<td>5</td>
<td>5-40</td>
<td>High</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>Prolixin</td>
<td>2</td>
<td>5-20</td>
<td>High</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Haldol</td>
<td>2</td>
<td>5-20</td>
<td>High</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Taractan</td>
<td>75</td>
<td>100-600</td>
<td>Low</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Thiothixene</td>
<td>Navane</td>
<td>5</td>
<td>5-60</td>
<td>High</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Luvox</td>
<td>15</td>
<td>25-200</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td></td>
</tr>
<tr>
<td>Molindone</td>
<td>Mobar</td>
<td>10</td>
<td>50-225</td>
<td>Intermediate</td>
<td>Intermediate</td>
<td></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

- Akathisia - 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
- Choreaathetoid
- Usually face, tongue, mouth
- Can involve trunk, arms
- Can occur after brief exposure
- Stop meds, lower dose
- Can be permanent
- Must get informed consent

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
Strategies to Improve Adherence—Understanding Schizophrenia, Weight Gain, and Associated Health Risk

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved. Reproduction in whole or in part without permission is prohibited.

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>
</tr>
<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>Paliperidone</td>
<td>Invega</td>
<td>6-12</td>
<td>tabs-D</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroquel</td>
<td>300-800</td>
<td>tabs-D, soln, INJ</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Risperdal</td>
<td>1-12</td>
<td>tabs-D</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Geodon</td>
<td>40-160</td>
<td>tabs</td>
</tr>
</tbody>
</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
Strategies to Improve Adherence—Understanding Schizophrenia, Weight Gain, and Associated Health Risk

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved. Reproduction in whole or in part without permission is prohibited.

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>
</tr>
<tr>
<td>Weight gain</td>
<td>+</td>
<td>+++</td>
<td>+/-</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Diabetes risk</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+ U</td>
<td>U</td>
<td>U</td>
<td>-</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+ U</td>
<td>U</td>
<td>-</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, Olan=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
Strategies to Improve Adherence—Understanding Schizophrenia, Weight Gain, and Associated Health Risk

© 2010 Pharmaceutical Education Consultants, Inc. unless otherwise noted. All rights reserved.
Reproduction in whole or in part without permission is prohibited.

Facing the Challenges Ahead

- Cost
- Access
- Coordination of care
- Resources
- Compliance
- Stigma

Addressing these will lead to a comprehensive model of care

References

- Diagnostic and Statistical Manual of Mental Disorders, fourth edition, Text Revision, American Psychiatric Association, 2000
- Physicians Desk Reference, 2008
- NIMH, Questions and Answers about the NIMH Clinical Antipsychotic Trials of Intervention Effectiveness Study (CATIE), http://www.nimh.gov/healthinformation/catieqa.cfm
- Baranger J., “Compliance with Treatment in Schizophrenic”, Medscape CME.
- Narasimhan, M., Bailey, S.B., “Schizophrenia, Metabolic Syndrome, and Antipsychotics Challenges, Controversies, and Clinical Management”, Medscape CME.