Metabolic Syndrome Secondary to Psychotropic Drugs

Satellite Conference and Live Webcast
Wednesday, March 16, 2011
2:00 - 4:00 p.m. Central Time

Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Objectives

- Define metabolic syndrome and its sequelae
- Discuss the link between second generation psychotropic drugs and metabolic syndrome/cardiovascular disease
- Discuss strategies for minimizing metabolic syndrome/cardiovascular disease in psychiatric patients

Introduction

- Metabolic Syndrome
  - Challenges treatment regimens, prescription drug use in clients who are seriously mentally ill
    - i.e. typical and atypical antipsychotics, mood stabilizers and antidepressants

Faculty

Debra Lett, PhD(c), MSN, MPA, RN
Assistant Professor
School of Nursing
Troy University

Cathy Russell, PhD, ACNS-BC, RN
Critical Nurse Specialist
Veterans Hospital
Tuskegee, Alabama

Objectives

- Discuss and provide updates on psychiatric drugs most frequently used in the mental health arena
- Identify compliance limitations of typical and atypical antipsychotics in mentally ill consumers

Introduction

- Presents as a constellation of symptoms
  - Hypertension, dyslipidemia, central obesity and insulin resistance
- Increased risk for the development of type 2 diabetes and cardiovascular disease

Typical vs. Atypical Antipsychotics

Typical Antipsychotic Drugs (Neuroleptics)
- Very strong antagonists of dopamine D2 receptors causing motor disturbances
  - i.e. tardive dyskinesia, akathisia, akinesia, dyskinesia, torticollis, pseudoparkinsonism, and oculogyric crisis

- Antagonists at muscarinic receptors for acetylcholine, α1 receptors for norepinephrine causing vasodilation, leading to orthostatic hypotension, ejaculatory failure and H1 receptors for histamine causing weight gain and sedation

- Reduces positive symptoms of schizophrenia
  - Delusions and hallucinations
- Causes anticholinergic side effects such as dry mouth, blurred vision, constipation and urinary hesitancy

- Prolactin elevation results in amenorrhea, glactorrhea, and gynecomastia


Atypical Antipsychotic Drugs
- Targets both negative and positive symptoms
- Antagonists at the 5-hydroxytryptamine 2 (5-HT2) receptors for serotonin, which may explain their efficacy in treating the negative symptoms of schizophrenia

- Produces less extrapyramidal side effects or motor disturbances with preferential binding of dopamine receptors occurring in the limbic system over the basal ganglia
- Decreased risk for suicide
- Improvement in cognition
Typical vs. Atypical Antipsychotics

- More effective in affective disturbances
- Greater efficacy in clients who pose a resistance to neuroleptics treatment regimen


Limitations of Typical Antipsychotic Drugs

- Only minimal improvement in activities associated with social and work behavior
- Increased potential for relapse and poor adherence in treatment regimens

- Less effective in symptoms associated with depression and suicidality
- When anticholinergic drugs are used in the management of EPS cognition does not improve with a potential for cognitive impairment

Limitations of Typical Antipsychotic Drugs

- Core negative symptoms only minimal improve
- Positive symptoms remain in 30% of patients
- EPS and Tardive Dyskinesia occur


Four Major Side Effects to Consider

- When prescribing Typical or First Generation Antipsychotics (FGA) or Atypical or Second Generation Antipsychotics (SGA) consider:
  - EPS and TD
  - Weight gain and metabolic effects
Four Major Side Effects to Consider
– Prolactin elevations and sexual side effects
– QTc prolongation

SGAs More Likely to Cause Metabolic Side Effects
• Certain SGAs are more likely to cause weight gain, glucose elevation and dyslipidemia which include Olazapine and Clozaril

SGAs More Likely to Cause Metabolic Side Effects
• Risperidone and quetiapine pose an intermediate risk for weight gain and elevated glucose levels
  – Palperidone appears to be similar to Risperidone in causing metabolic changes

SGAs More Likely to Cause Metabolic Side Effects
• Aripiprazole and Ziprasidone pose a lower risk for weight gain in the SGAs drug profiles
  – A newer atypical antipsychotic, Lurasidone does not cause weight gain or prolactin elevations

State of the Literature
• The Schizophrenia Patient Outcomes Research Team (PORT) examines evidence-based psychopharmacological treatment practices and recommendations from a systematic comprehensive and empirical review of the literature from January 2002 through March 2008 and other literature not reviewed in previous PORT studies

State of the Literature
• Algorithms and guidelines are developed for the treatment of schizophrenia
State of Literature

- The 2009 Schizophrenia PORT Psychopharmacological Treatment Recommendations:
  - Found 16 treatment recommendations and 8 psychosocial treatments for schizophrenia

- Revised 11 previous recommendations and 5 treatment recommendations and eliminated 3 previous recommendations.
- Reviewed 3 large pragmatic studies

State of Literature

- Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), the Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia, Study (CUtLASS), and the European First-Episode Schizophrenia Trial (EUFEST)


State of Literature

- The CATIE and CUtLASS studies are representative of non-industry comparison of FGA and SGA in individuals who have multiepisodic schizophrenia
- The EUFEST reviewed individuals with multiepisodic and their use of Haloperidol and SGAs


State of Literature

- PORT 2009 Recommendations
  - Pharmacological Prevention and Treatment of Antipsychotic Associated Weight Gain in Schizophrenia

State of Literature

- Schizophrenic clients have higher morbidity and mortality rates in comparison to the general population which is thought to correlate with higher rates of obesity as a result of antipsychotic use
State of Literature
- Pharmacological interventions recommendations
  - Switch current antipsychotic medication to a medication with lower weight gain liability

State of Literature
- “Addition of a medication when an antipsychotic agent is initiated to prevent weight gain (p.85)
  - Addition of medication to prevent weight loss

State of Literature
- Insufficient evidence to support specific medication regimen to prevent or treat weight gain associated with antipsychotic use

State of the Literature
- Schizophrenia Patient Outcomes Research Team (PORT) Recommendations for Psychosocial Interventions
  - Assertive community treatment
  - Cognitive behavioral therapy
  - Skills training
  - Token economy intervention

State of the Literature
- Supported employment
- Family-based Services
- Interventions for weight management
- Integrated treatment for substance use disorders

Alternative Therapies
- PORT Recommendations-ECT and rTMS
  - ECT
    - Effective for the use of acute positive symptoms
    - There is no efficacy advantage over antipsychotic medications
**Alternative Therapies**

- Insufficient evidence to support use for core symptoms of schizophrenia
  - Transcranial Magnetic Stimulation (rTMS)
  - Recommended for acute treatment of auditory hallucinations

**Alternative Therapies**

- Use of low frequency over left temporoparietal cortex (1Hz)
  - Vagus Nerve Stimulation
    - Electrical stimulation boosts level of neurotransmitters, improving mood and antidepressant effects

---

**Did You Know?**

- An estimated 50 million Americans have metabolic syndrome
- Some studies estimate the prevalence in the US to be up to 25% of the population

**Did You Know?**

- Metabolic syndrome is also known as metabolic syndrome X, syndrome X, insulin resistance syndrome, Reaven’s syndrome, and CHAOS (Australia)

---

**Did You Know?**

- The dominant underlying risk factors for metabolic syndrome are abdominal obesity and insulin resistance
- People with metabolic syndrome are at increased risk for coronary heart disease, stroke, and peripheral vascular disease

---

**Fact or Fiction?**

Fact or Fiction?
• Patients with schizophrenia may have a predisposition to metabolic syndrome

Fact or Fiction?
• Psychiatric patients may have a predisposition to metabolic syndrome primarily due to their generally sedentary lifestyle, poor dietary habits, possible limited access to care, and antipsychotic-induced adverse effects

Fact or Fiction?
• 32% of persons with schizophrenia meet criteria for metabolic syndrome

Fact or Fiction?
• The prevalence of metabolic syndrome in schizophrenic patients is the same in women and men

Fact or Fiction?
• Children/adolescents receiving second generation psychotropic drugs are not at risk for developing metabolic syndrome

What is Metabolic Syndrome?
• Metabolic syndrome is the presence of 3 risk factors in one individual
• Risk factors for metabolic syndrome are:
  – Hypertension
  – Dyslipidemia
  – Abdominal obesity
What is Metabolic Syndrome?

– Insulin resistance/glucose intolerance
– Prothrombic factors
– Proinflammatory state
  • C-reactive protein

Clinical Identification of Metabolic Syndrome

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Obesity (waist circumference)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&gt;102 cm (&gt;40 inches)</td>
</tr>
<tr>
<td>Women</td>
<td>&gt;88 cm (&gt;35 inches)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&gt;150 mg/dl</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>&lt; 40 mg/dl</td>
</tr>
<tr>
<td>Women</td>
<td>&lt; 50 mg/dl</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>≥ 130/≥ 85 mmHg</td>
</tr>
<tr>
<td>Fasting Glucose</td>
<td>≥ 110</td>
</tr>
<tr>
<td>Prothrombic State</td>
<td>Alteration in coagulation, platelet abnormalities</td>
</tr>
</tbody>
</table>

Other Risk Factors

• Smoking
• Physical activity
• Age
• Race
• Gender
• Family history
• Hormonal imbalance

So How Is This Related to Psychotropic Drugs?

Second Generation Psychotropic Drugs

• Major tranquilizers/neuroleptics
• Treatment of acute and chronic psychoses
• Block postsynaptic dopamine receptors in the basal ganglia, hypothalamus, limbic system, brain stem, and medulla

Second Generation Psychotropic Drugs

• Adverse effects
  – Anticholinergic effects
  – Nausea/GI upset
  – Skin rash
  – Sedation
  – Orthrostatic hypotension
Second Generation Psychotropic Drugs

- Photosensitivity
- Hormonal effects
- ECG changes
- Seizure threshold reduction
- Agranulocytosis
- Hypersalivation

Second Generation Psychotropic Drugs

- Extrapyramidal symptoms
- Neuroleptic malignant syndrome
- Hyperglycemia/diabetes

Second Generation/Atypical Psychotropic Drugs

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>Risperdal</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Clozaril</td>
</tr>
<tr>
<td>Olanzepine</td>
<td>Zyprexa</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroquel</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Geodon</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Abilify</td>
</tr>
</tbody>
</table>

Atypical Psychotics Influence on Weight Gain and Glucose Levels

Link Between Psychotropic Drugs and Metabolic Syndrome

- Hormonal changes/weight gain
- Impact on blood glucose levels

<table>
<thead>
<tr>
<th>Drug Class and Drug</th>
<th>Weight-Gain Likelihood</th>
<th>Glucose Metabolism Influence</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-potency conventional antipsychotics</td>
<td>D/±</td>
<td>N/A</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Low-potency conventional antipsychotics</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Typical antipsychotics</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Clozapine</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Risperidone</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>++/++; ++</td>
<td>++</td>
</tr>
</tbody>
</table>

* D/± = Idiosyncratic weight gain; ++ = Consistent weight gain; ± = Some weight gain.
* N/A = No information available.
* +/− = Inconsistent weight gain or glucose changes.
* Source: Adapted from McMillen and Kasen (23, 34).
Prevention/Management Strategies
• Screening for metabolic syndrome
• Prevent or minimize obesity
• Maintain therapeutic blood pressure, lipids, and glucose levels
• Consider alternate drug therapy

Prevent/Minimize Obesity
• Diet
  – Eating a diet low in fat, with a variety of fruits, vegetables, and whole-grain products
  – Losing weight so that your body mass index (BMI) is less than 25
  – Try to include fish, preferably oily fish, in your diet twice a week

Prevent/Minimize Obesity
• Exercise
  – Getting regular exercise, at least 30 minutes of moderate activity almost every day
• Pharmacotherapy
  – Diet pills
• Surgery

Target Glucose Levels
• Average A1C over 2-3 months should be 7
• Preprandial should be <110
• Average bedtime <120

Management of Blood Glucose
• Diet
  – Eating a diet low in fat, with a variety of fruits, vegetables, and whole-grain products
  – Losing weight so that your body mass index (BMI) is less than 25
  – Try to include fish, preferably oily fish, in your diet twice a week

Management of Blood Glucose
• Exercise
  – Get regular exercise, at least 30 minutes of moderate activity almost every day
### Management of Blood Glucose

- **Pharmacotherapy**
  - Oral hypoglycemic agents
    - Sufonylureas, metformin, ancillary
  - Insulin therapy
- **Surgery**

### Target Blood Pressure Level

- <130/85

### Target Cholesterol Levels

- **The good**
  - High density lipids
- **The bad**
  - Low density lipids
- **The ugly**
  - Triglycerides

### Nonpharmacological Therapy

- Dietary sodium restriction
- Weight loss
- Increased physical activity
- Smoking cessation
- Moderation of alcohol consumption

### Pharmacological Therapy for Blood Pressure

- **First Line Drugs**
  - Ace
  - ARB
  - B-Blockers
  - Thiazide diuretics

### Pharmacological Therapy for Blood Pressure

- **Second Line Drugs**
  - Alpha Blockers
  - Loop Diuretics
  - Central acting Adrenergic Agents
Pharmacological Therapy for Lipids

- Statins
  - Lipitor
  - Mevacor
  - Altacor
  - Lescol
- Bile Acid Binding Resins
  - Prevalite
  - Questran light
  - Welchol
  - Colestid
- Fibric Acid Derivitives
  - Tricor
  - Lopid
- Nicotinic Acids
  - Niacor
  - Niaspan
  - Advicor
  - Zetia

Screening

- Fasting blood glucose
- Abdominal obesity

Challenges