Metabolic Syndrome Secondary to Psychotropic Drugs

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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

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

- 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

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
  - Chiles, C. & van Wattum. (2010 April). Psychiatric Aspects of the Obesity Crisis. Psychiatric Times. 47-51.

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

Typical vs. Atypical Antipsychotics

- 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

Typical vs. Atypical Antipsychotics

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

Typical vs. Atypical Antipsychotics

- Prolactin elevation results in amenorrhea, glactorrhea, and gynecomastia

– Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

Typical vs. Atypical Antipsychotics

- Atypical Antipsychotic Drugs
  - Targets both negative and positive symptoms
  - Antagonists at the 5-hydroxytryptamine α2 (5-HTα2) receptors for serotonin, which may explain their efficacy in treating the negative symptoms of schizophrenia

Typical vs. Atypical Antipsychotics

- 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

Typical vs. Atypical Antipsychotics

- Atypicals such as Risperidone, paliperidone, sulpride and amisulpride (used in Europe) increase prolactin elevation
  - Varcolis, E., Carson, V. Shoemaker, N. (2009) Foundations of Psychiatric Mental Health Nursing: A Clinical Approach. 6th ed. St. Louis: Sanders

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

Limitations of Typical Antipsychotic Drugs

- 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
  - Meltzer, H. (2010 November). Advances in Schizophrenia for Optimal Outcomes U.S. Psychiatric Congress

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

– Meltzer, H. (2010 November). Advances in Schizophrenia for Optimal Outcomes U.S. Psychiatric Congress

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

– Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

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

– Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

State of Literature

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

State of Literature

- 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)
  - Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

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
  - Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

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
  - Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

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
  - Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

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

– Buchanan, R., Kreyenbuhl, J., Kelly D., et al. (2009). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements Schizophrenia Bulletin 2009 , 36(1), 94-103.

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

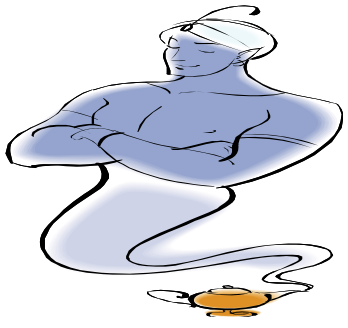
Did You Know?

- 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

Risk Factor	Defining Level
Abdominal Obesity (waist circumference)	
Men	>102 cm (>40 inches)
Women	> 88 cm (>35 inches)
Triglycerides	≥ 150 mg/dl
HDL Cholesterol	
Men	≤ 40 mg/dl
Women	≤ 50 mg/dl
Blood Pressure	≥ 130/ ≥ 85 mmHg
Fasting Glucose	≥ 110
Prothrombic State	Alteration in coagulation, platelet abnormalities

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

Generic Name	Trade Name
Risperidone	Risperdal
Clozapine	Clozaril
Olanzepine	Zyprexia
Quetipine	Seroquel
Ziprasidone	Geodon
Aripiprazole	Abilify

Link Between Psychotropic Drugs and Metabolic Syndrome

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

Atypical Psychotics Influence on Weight Gain and Glucose Levels

Drug Class and Drug	Weight-Gain Liability[a]	Glucose Metabolism Influence[b]
High-potency conventional antipsychotics	0/+	N/A
Haloperidol		
Low-potency conventional antipsychotics	+++/++	+/–
Chlorpromazine		
Atypical antipsychotics		++[c]
Clozapine	++++	
Olanzapine	+++	
Risperidone	++	
Quetiapine	++	
Ziprasidone	+/–	
Aripiprazole	+/–	

a ++++=unequivocal weight gain; +++=consistent weight gain; ++=some weight gain; 0/+=minimal weight gain; +/–=inconsistent weight gain/loss
b ++=increase in plasma glucose; +/–=inconsistent plasma glucose increase/decrease; N/A=not available
c Food and Drug Administration class labeling
Source: Adapted from McIntyre and Konarski (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 diurectics

Pharmacological Therapy for Blood Pressure

- Second Line Drugs
  - Alpha Blockers
  - Loop Diurectics
  - Central acting Adrenergic Agents

Pharmacological Therapy for Lipids

- Statins
  - Lipitor
  - Mevacor
  - Altacor
  - Lescol
  - Pravachol
  - Crestor
  - Zocor

Pharmacological Therapy for Lipids

- Bile Acid Binding Resins
  - Prevalite
  - Questran light
  - Welchol
  - Colestid

Pharmacological Therapy for Lipids

- Fibric Acid Derivitives
  - Tricor
  - Lopid

Pharmacological Therapy for Lipids

- Nicotinic Acids
  - Niacor
  - Niaspan
  - Advicor
- Zetia

Screening

- Fasting blood glucose
- Abdomial obesity

Challenges