



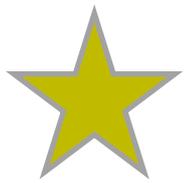
Treatment of schizophrenia and associated co-morbidities

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Disclosures

I will be discussing “off-label” uses of several medications.

Major Shareholder: Mental Health Alliance



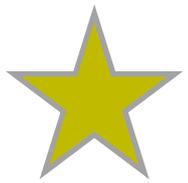
Outline

- Diagnostic criteria for schizophrenia
- Differential diagnoses
- Treatment options
- Barriers to treatment
- Co morbidities

Objectives

The goal of this program is to improve the management of comorbidities in patients with schizophrenia. After hearing and assimilating this program, the clinician will be better able to:

- Identify diagnostic criteria for schizophrenia and differential diagnoses.
- Identify psychiatric co-morbidities associated with schizophrenia.
- Discuss trends in lifespan and mortality among patients with schizophrenia in comparison to the general population.
- Address reasons for increased mortality in patients with schizophrenia.
- Manage cardiovascular (CV) morbidity and reduce CV mortality in patients with schizophrenia.
- Monitor and manage comorbidities seen in patients with schizophrenia.
- Weigh advantages and disadvantages of various antipsychotics in order to choose appropriate agent(s) in the management of schizophrenia and associated medical comorbidities in patients with schizophrenia



DSM-V Diagnostic criteria Schizophrenia

- Schizophrenia is characterized by delusions, hallucinations, disorganized speech and behavior, and other symptoms that cause social or occupational dysfunction. For a diagnosis, symptoms must have been present for six months and include at least one month of active symptoms.

DSM-V Diagnostic Criteria Schizophrenia

- Criterion A lists the five key symptoms of psychotic disorders:
 - 1) delusions
 - 2) hallucinations
 - 3) disorganized speech
 - 4) disorganized or catatonic behavior
 - 5) negative symptoms
- **two** of these five symptoms are required AND at least one symptom must be one of the first three (delusions, hallucinations, disorganized speech).

DSM-V Changes in Diagnostic criteria Schizophrenia

- Schizophrenia subtypes have been discontinued in the DSM-5 because of their “limited diagnostic stability, low reliability, and poor validity,”
- Previous subtypes:
 - Paranoid
 - Disorganized
 - Catatonic
 - Undifferentiated
 - residual type

Delusions

- Fixed beliefs
 - Persecutory (most common)
 - Belief one is going to be harmed, harassed, etc
 - Referential
 - Belief certain gestures, comments, environmental cues are directed at oneself
 - Somatic
 - Religious
 - Grandiose
 - Erotomaniac
 - Nihilistic

Delusions

- Thought withdrawal
 - Thoughts “removed” by some outside force
- Thought insertion
 - Thoughts have been put into one’s mind
- Delusions of control
 - Body or actions are being manipulated by some outside force
- Idea of reference
 - belief that casual events, people's remarks, etc. are referring to oneself when, in fact, they are not.
- Idea of influence
 - external forces or persons are controlling one's thoughts, actions, and feelings.

Hallucinations

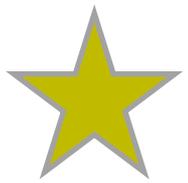
- Perception-like experiences that occur without an external stimulus
- Vivid and clear, with the full force and impact of normal perceptions, and not under voluntary control
- Auditory (most common)
- Visual
- Tactile (touch)
- Olfactory (smell) (more likely medical cause)
- Gustatory (taste) (Frontal lobe seizures, migraines)

Negative symptoms

- Diminished emotional expression
 - reductions in the expression of emotions in the face, eye contact, intonation of speech (prosody), and movements of the hand, head, and face that normally give an emotional emphasis to speech
- Avolition
 - decrease in motivated self-initiated purposeful activities
- Alogia
 - diminished speech output
- Anhedonia
 - decreased ability to experience pleasure from positive stimuli or a degradation in the recollection of pleasure previously experienced
- Asociality
 - apparent lack of interest in social interactions

DSM-V Diagnostic criteria Schizoaffective

- An uninterrupted period of illness during which there is a major mood episode (major depressive or manic) concurrent with Criterion A of schizophrenia.
Note: The major depressive episode must include Criterion A1 : Depressed mood.
- Delusions or hallucinations for 2 or more weeks in the absence of a major mood episode (depressive or manic) during the lifetime duration of the illness.
- Symptoms that meet criteria for a major mood episode are present for the majority of the total duration of the active and residual portions of the illness.
- The disturbance is not attributable to the effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.
- Bipolar type or Depressive type



Differential Diagnosis

- **Major depressive or bipolar disorder with psychotic or catatonic features.**
 - If delusions or hallucinations occur exclusively during a major depressive or manic episode, the diagnosis is depressive or bipolar disorder with psychotic features.
- **Schizoaffective disorder.**
 - requires that a major depressive or manic episode occur concurrently with the active-phase symptoms and that the mood symptoms be present for a majority of the total duration of the active periods.

Differential Diagnosis

- **Schizophreniform disorder and brief psychotic disorder**
 - Shorter duration than schizophrenia. In schizophreniform disorder, the disturbance is present less than 6 months, and in brief psychotic disorder, symptoms are present at least 1 day but less than 1 month.
- **Delusional disorder**
 - Absence of the other symptoms characteristic of schizophrenia (e.g., delusions, prominent auditory or visual hallucinations, disorganized speech, grossly disorganized or catatonic behavior, negative symptoms).
- **Schizotypal personality disorder**
 - Subthreshold symptoms that are associated with persistent personality features.

Differential Diagnosis

- **Obsessive-compulsive disorder** and **body dysmorphic disorder**
 - Present with poor or absent insight, and the preoccupations may reach delusional proportions. But these disorders are distinguished from schizophrenia by their prominent obsessions, compulsions, preoccupations with appearance or body odor, hoarding, or body-focused repetitive behaviors.
- **Posttraumatic stress disorder**
 - Include flashbacks that have a hallucinatory quality, and hypervigilance may reach paranoid proportions. But a traumatic event and characteristic symptom features relating to reliving or reacting to the event are required to make the diagnosis.

Differential Diagnosis

- **Autism spectrum disorder or communication disorders**
 - Distinguished by their respective deficits in social interaction with repetitive and restricted behaviors and other cognitive and communication deficits. An individual with autism spectrum disorder or communication disorder must have symptoms that meet full criteria for schizophrenia, with prominent hallucinations or delusions for at least 1 month, in order to be diagnosed with schizophrenia as a comorbid condition.
- **Other mental disorders associated with a psychotic episode**
 - The diagnosis of schizophrenia is made only when the psychotic episode is persistent and not attributable to the physiological effects of a substance or another medical condition.

Differential Diagnosis

- **Delirium.** Hallucinations and delusions commonly occur in the context of a delirium; however, a separate diagnosis of psychotic disorder due to another medical condition is not given if the disturbance occurs exclusively during the course of a delirium. Delusions in the context of a major or mild neurocognitive disorder would be diagnosed as major or mild neurocognitive disorder, with behavioral disturbance.
- **Substance/medication-induced psychotic disorder.** If there is evidence of recent or prolonged substance use (including medications with psychoactive effects), withdrawal from a substance, or exposure to a toxin (e.g., LSD [lysergic acid diethylamide] intoxication, alcohol withdrawal), a substance/medication-induced psychotic disorder should be considered. Symptoms that occur during or shortly after (i.e., within 4 weeks) of substance intoxication or withdrawal or after medication use may be especially indicative of a substance-induced psychotic disorder, depending on the character, duration, or amount of the substance used. If the clinician has ascertained that the disturbance is due to both a medical condition and substance use, both diagnoses (i.e., psychotic disorder due to another medical condition and substance/medication-induced psychotic disorder) can be given.

Scales and Screening tools

- BPRS (Brief Psychotic Rating Scale)
 - <http://www.testandcalc.com/etc/tests/bprs.asp>
- AIMS (Abnormal Involuntary Movement Scale)
 - <http://www.testandcalc.com/etc/tests/aims.asp>
- PANSS (Positive and Negative Syndrome Scale)
 - Very extensive (31 pages)
- CDSS (Calgary Depression Scale for Schizophrenia)
 - http://www.mentaltests.com/mentaltests_demo/calg.html
- Screening tool for schizophrenia
 - <http://psychcentral.com/quizzes/schizophrenia.htm>

All, except CDSS, are available to download with this presentation

Schizophrenia Statistics

- Die significantly younger age (15 yrs in women-20 yrs in men)
- 20% shorter lifespan
- 50-60% increased mortality r/t Cardio-Vascular disease
- 6% death by suicide (10-fold higher)
- 62% smoke (50% higher)
- 3x greater risk diabetes
- Double incidence of hypertension
- Increase in high cholesterol
- 33% ≥ 3 medical comorbidities (3x greater than control)
- 50% increased risk of death from medical causes

Barriers to Diagnosis & Treatment

- Less likely to have complete physical exam
- Less likely to seek treatment (even when insured)
- Treatment non-compliance
- More likely to have more severe symptoms and complications
- Failure of medical providers to treat medical conditions
- Failure of psychiatric providers to ask about medical issues

Medical Comorbidities

- Cardiovascular (2.3 times greater risk)
 - Hypertension
 - High cholesterol
- Diabetes (2.7 times greater risk)
- Other metabolic disorders
- Liver disease
- Respiratory conditions (3.2 times greater risk)
- Infectious disease (3.4 times greater risk)

Physical disease with increased frequency in schizophrenia

- Tuberculosis
 - **HIV ***
 - Hepatitis B/C
 - Osteoporosis/decreased bone mineral density
 - Poor dental status
 - Impaired lung function
 - Sexual dysfunction
 - Extrapyrarnidal side effects of antipsychotic drugs; motor signs in antipsychotic-naive patients
 - **Obstetric complications***
 - Hyperprolactinemia-related side effects of antipsychotics (eg irregular menses, galactorrhea)
 - **Cardiovascular problems ***
 - Hyperpigmentation (side effect of chlorpromazine)
 - **Obesity***, diabetes, hyperlipidemia, metabolic syndrome
 - Thyroid dysfunction
- * Very good evidence of increase risk*

Management of Comorbidities

Treatments for schizophrenia

- Properties and side effects of available meds
- Choosing a treatment
- Managing side effects

First generation antipsychotics

- Chlorpromazine (Thorazine)
- Fluphenazine (Prolixin)
- Haloperidol (Haldol)
- Perphenazine (Trilafon)

Second generation (atypicals)

- Aripiprazole (Abilify)
- Asenapine (Saphris)
- Clozapine (Clozaril)
- Iloperidone (Fanapt)
- Lurasidone (Latuda)
- Olanzapine (Zyprexa)
- Paliperidone (Invega)
- Quetiapine (Seroquel)
- Risperidone (Risperdal)
- Ziprasidone (Geodon)

Long acting Injectibles

- Fluphenazine (Prolixin) decanoate
- Haloperidol (Haldol) decanoate
- Olanzapine (Zyprexa) Relprevv
- Paliperidone (Invega) Sustenna
- Paliperidone (Invega) Trinza
- Risperidone (Risperdal) Consta
- Aripiprazole (Abilify) Maintena

Receptor Profiles

- **D2 antagonism**-Positive sx efficacy, EPS, endocrine effects
- **5HT2A**-Negative sx efficacy, reduced EPC, Prolactin
- **5HT1A**-Antidepressant, anxiolytic, improved cognition, reduced EPS
- **5HT2C**-Antidepressant activity
- **5HT6**-Antidepressant activity
- **5HT7**-Antidepressant activity, improved cognition
- **Alpha 1 antagonism**-postural hypotension
- **Alpha 2 antagonism**-Antidepressant activity, improved cognition
- **H1**-Weight gain, sedation
- **M1**-Anticholinergic side effects, sedation, cognitive impairment

Receptor overview



	D2	5HT2A	5HT1A	5HT2C	5HT6	5HT7	Alpha 1	Alpha 2	H1	M1
asenapine	+++	++++	++	++++	++++	++++	+++	+++	+++	++
clozapine	+	++	+	++	++	++	+++	++	+++	+++
olanzapine	++	+++		++	++	+	++	+	+++	++
quetiapine	+	++	+	+	+	+++	+++	+	+++	++
iloperidone	+++	+++	++	+	++	++	+++	+	++	
lurasidone	+++	+++	+++	+		++++	++	++		
paliperidone	+++	++++	+	++		+++	+++	++	++	
risperidone	+++	++++	+	++		+++	+++	++	++	
ziprasidone	+++	++++	++	++	++	+++	++	++	++	
aripiprazole	+++	++	+++		+	+++	++	++	++	
	partial									

Choosing a treatment

- Pharmacogenomics
- Side effects
- Cost
- Compliance
- Other co-morbidities

Managing side effects

- Monitor vital signs
- Monitoring labs
- Weigh benefits vs side effects

Questions?

