Update on the Treatment of Psychosis

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Objectives

- Evaluate existing data in regards to the appropriate treatment of schizophrenia
- Review risks and benefits of antipsychotic therapy in the management of acute psychosis
- Discuss the monitoring of psychotic symptoms as well as the monitoring and management of short and long-term adverse effects associated with antipsychotic therapy

Symptoms of Schizophrenia

- Patients must have experienced > 2 of the following symptoms:
  - Delusions
  - Hallucinations
  - Disorganized speech
  - Disorganized or catatonic behavior
  - Negative symptoms

Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-5)

Symptoms of Schizophrenia

- At least 1 of the symptoms must be the presence of delusions, hallucinations, or disorganized speech
- Continuous signs of the disturbance must persist for at least 6 months, during which the patient must experience > 1 month of active symptoms, with social or occupational deterioration problems occurring over a significant amount of time. These problems must not be attributable to another condition

Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (DSM-5)

Symptoms of Schizophrenia

Positive Symptoms
- Hallucinations
- Delusions
- Disorganized speech
- Grossly disorganized behavior or catatonia

Negative Symptoms
- Apathy
- Lack of emotion
- Social withdrawal
- Poor social functioning

Cognitive Symptoms
- Difficulty maintaining/shifting attention
- Problems with memory
- Impaired executive function
- Deficits in skill acquisition

Diagnostic Evaluation

- Comprehensive history
  - Involve family/caregivers if necessary
- Physical exam
- CMP/BMP
- Electrocardiogram
- Chest X-Ray
- CBC
- LFT's
- Urinalysis
- Urine drug screen
- TSH
- Pregnancy Test

Clinical Course

- Lifetime Prevalence < 1 %
- Many have prodromal phase
  - Primarily negative and cognitive symptoms
- Typical onset late teens-early 30's
  - Women slightly later onset
- Chronic disease
  - Most have moderate to severe disability but can have periods of recovery
  - Adherence to treatment will improve patient functioning and outcomes

Schizophrenia Pathophysiology

- Pathophysiology Theories
  - Excessive dopamine (D2) in the mesolimbic pathway
  - Low dopamine in mesocortical area
    - Negative and cognitive symptoms
  - Low levels of serotonin (5-HT)
  - Low Glutamate
- Risk factors
  - Perinatal factors- hypoxia, fetal distress
  - Biological
  - Cannabis use

Treatment Considerations

- Some treatment guidelines recommend starting second-generation antipsychotic (SGA) as first-line therapy
  - Others guidelines recommend to start a SGA or first generation (FGA) antipsychotic
- Symptoms typically respond within 2 weeks but may take up to 4-6 weeks
  - Some data suggest switching AP if poor response in first 2 weeks
- Continually assess for reduction in positive symptoms, improvement in negative and cognitive symptoms, and medication adherence
- Continually assess for adverse effects and treat as needed (or change to an alternate AP)

Treatment Considerations

- Continue antipsychotic for at least 1 year for first-episode of schizophrenia
- Continue for at least 2-5 years if 2 or more episodes
- If > 2 episodes/5 years, patients may need to be on lifelong treatment*
- Consider changing patients to a long-acting antipsychotic (LAI) to improve medication adherence
  - Ensure patient can tolerate PO formulation

http://psychiatryonline.org/guidelines accessed 9/17*

First-Generation Antipsychotics (FGA's)

First-Generation Antipsychotics

Generic Name	Trade Name	FDA-approval Date
Chlorpromazine	Thorazine	1957
Perphenazine	Trilafon	1957
Trifluoperazine	Stelazine	1959
Haloperidol	Haldol	1967
Thiothixene	Navane	1967
Thioridazine	Mellaril	1962
Fluphenazine	Prolixin	1972
Loxapine	Loxitane	1975

First-Generation Antipsychotics

Medication	Dosage Forms	Starting Dose	Average Dose	Other
Chlorpromazine	PO/IM/IV	30-75mg/day div. in 2-4 doses	200-600mg/day Max < 1000mg/day	Reduce dose in liver disease
Perphenazine	PO	4-8mg/day div. in 3 doses	8-64mg/day Max 64mg/day	Reduce dose in liver disease
Trifluoperazine	PO	2-5 mg/day div. in 1-2 doses	20-40mg/day Max 40mg/day	Contraind. In liver disease
Haloperidol	PO/IM/IV/ oral soln.	1-15mg/day div. in 2-3 doses	< 30mg/day Max 100mg/day	
Thiothixene	PO	6-10mg/day div. in 2 doses	20-30mg/day Max 60mg/day	Reduce dose in liver disease
Thioridazine	PO	50-100mg/day div. in 3 doses	50-800mg/day Max 800mg/day	Reduce dose in liver disease
Fluphenazine	PO/IM/oral soln.	2.5-10mg/day div. Q6-8 hrs.	< 20mg/day; Max 40mg/day	Use with caution liver/kidney dis.
Loxapine	PO/INH	20-50mg/day div. in 2-4 doses	20-100mg/day Max 250mg/day	

Second-Generation Antipsychotics (SGA's)

Second-Generation Antipsychotics

Generic Name	Trade Name	FDA-approval Date
Clozapine	Clozaril	1989
Risperidone	Risperdal	1993
Olanzapine	Zyprexa	1996
Quetiapine	Seroquel	1997
Ziprasidone	Geodon	2002
Aripiprazole	Abilify	2006
Paliperidone	Invega	2006
Iloperidone	Fanapt	2009
Asenapine	Saphris	2009
Lurasidone	Latuda	2010
Brexpiprazole	Rexulti	2015
Cariprazine	Vraylar	2015
Pimavanserin	Nuplazid	2016

Second-Generation Antipsychotics

Medication	Dosage Forms	Starting Dose	Dosage Range	Other
Clozapine *Clozaril*	PO/SL/ PO susp.	12.5mg qday-BID	300-450mg/day	See separate slide
Risperidone *Risperdal*	PO/SL/ PO soln.	1-2 mg/day	4-6mg/day	
Olanzapine *Zyprexa*	PO/SL/IM	5-10mg/day	10-20mg/day	
Quetiapine *Seroquel*	PO/ER	25mg BID	400-800mg (divided in 2-3 doses)	
Ziprasidone *Geodon*	PO/IM	20mg BID	40mg-80mg BID	Give with food (> 500 kcal)
Aripiprazole *Abilify*	PO/SL/ PO soln.	10-15mg/day	15-30mg/day	

Second-Generation Antipsychotics

Medication	Dosage Forms	Starting Dose	Dosage Range	Other
Paliperidone *Invega*	PO	6 mg/day	6-12mg/day	Adjust dose in renal impairment
Iloperidone *Fanapt*	PO	1mg BID increase by 2mg/day	12-24mg/day	Dose titrate to reduce orthostasis/syncope; Decrease starting dose if on 2D6 or 3A4 inh.
Asenapine *Saphris*	SL	5mg BID	5-10mg BID	May need to decrease dose with 1A2 inhibitors; avoid water for 10 minutes
Lurasidone *Latuda*	PO	40mg/day	40-120mg/day	Take with food (at least 350 cal.); Contraindicated with strong 3A4 inhibitors/inducers

Newest Second-Generation Antipsychotics

Brexpiprazole (Rexulti®)

- Approved as monotherapy for adults with schizophrenia and as adjunctive treatment for adults with major depressive disorder
- Dose: Days 1-4 → 1mg/day; Days 5-7 → 2mg/day; Days 8+ → 2-4mg/day
  - Starter sample packs available
  - Half- dose of patients taking strong 2D6/3A4 inhibitors OR poor 2D6 metabolizers
- Mechanism of action:
  - Partial agonist at 5HT1A and D2 receptors and 5HT2A antagonism
  - Antagonist of alpha-receptors

CYP450 Interactions

3A4 Inducers	Strong 3A4 inhibitors	Strong 2D6 Inhibitors
Carbamazepine	Indinavir	Bupropion
Efivarenz	Nelfinavir	Fluoxetine
Nevirapine	Ritonavir	Paroxetine
Phenobarbital	Clarithromycin	Quinidine
Phenytoin	Itraconazole	
Pioglitazone	Ketoconazole	
Rifampin	Nefazodone	
St. John's Wort	Saquinavir	
Rifabutin	Suboxone	
Pioglitazone	Telithromycin	
Troglitazone		

http://medicine.iupui.edu/clinpharm/ddis/main-table

CYP450 Interactions

Moderate 3A4 inhibitors	Moderate 2D6 Inhibitors
Aprepitant	Duloxetine
Erythromycin	Sertraline
Fluconazole	Terbinafine
Grapefruit juice	
Verapamil	
Diltiazem	

http://medicine.iupui.edu/clinpharm/ddis/main-table

Brexpiprazole (Rexulti®)

- Precautions/contraindications
  - Impairment in judgement, thinking, and motor skills
    - Caution driving or operating heavy machinery
- Adverse effects
  - Akathesia, increased weight, diarrhea, dyspepsia, tremor, increased CPK, sedation
- Cost: Approximately $1000/month

Cariprazine (Vraylar®)

- Approved for the acute treatment of manic or mixed episodes associated with Bipolar I Disorder and the treatment of Schizophrenia in adults
- Dosing:
  - Starting dose 1.5mg/day
  - Dosage range: 1.5-6mg/day
  - Not recommended for severe liver or renal disease
  - Dose should be reduced by half when using with strong 3A4 inhibitors
- Mechanism of action:
  - Partial agonist at 5HT1A and D2 receptors and a 5HT2A antagonist

Cariprazine (Vraylar®)

Precautions/contraindications

- Avoid use when patient taking 3A4 inducers

- Adverse effects
  - EPS, akathesia
- Cost: $770-1200/month

CYP450 Interactions

3A4 Inducers	Strong 3A4 inhibitors
Carbamazepine	Indinavir
Efivarenz	Nelfinavir
Nevirapine	Ritonavir
Phenobarbital	Clarithromycin
Phenytoin	Itraconazole
Pioglitazone	Ketoconazole
Rifampin	Nefazodone
St. John's Wort	Saquinavir
Rifabutin	Suboxone
Pioglitazone	Telithromycin
Troglitazone	

http://medicine.iupui.edu/clinpharm/ddis/main-table

Pimavanserin (Nuplazid)

- SGA approved for the treatment of psychosis and hallucination in patients with Parkinson's Disease
- Dosing: 34 mg PO daily
- Mechanism of action
  - Selective serotonin inverse agonist (SSIA) designed to target 5-HT2A and 5-HT2C receptors (not dopamine)

Pimavanserin (Nuplazid)

- Efficacy/tolerability
  - Decreased psychotic symptoms seen in 2-6 weeks
  - No change in motor control and ADR's vs. placebo
- Precautions/Contraindications: Caution use with drugs known to elevate QT interval, severe renal/liver impairment
- Adverse Effects: Peripheral edema, confusion, nausea
- Cost: > $2000/month

Long-Acting Injectable Antipsychotics (LAI)

LAI Dosing Considerations

- Ensure patient can tolerate oral version of preferred LAI prior to initiation
- Ideally wait until at least a partial positive response in addition to assessing tolerability prior to starting a LAI
- All LAI are available as an "IM" injection
  - Deltoid administration -All
  - Gluteal administration- Olanzapine only
- Review manufacturer product information if patient has missed dose(s)

Long-Acting Antipsychotics

Name/ Year Approved	Monthly Cost*	Dosing Range	Other
Fluphenazine *Prolixin Decanoate* 1972	$220	6.25-100mg q2-3 wks. (usual 6.25-25mg)	Loading dose is approx. 1.25 x PO dose; Continue PO for at least 1 week; SS in 4-6 wks
Haloperidol *Haldol Decanoate* 1986	$25	20-450mg q3-4 wks	Cannot inject > 3mL IM ; SS in 2-4 mos.
Risperidone *Risperdal Consta* 2003	$460-1800	25-50 mg q2wks	Continue PO for 3 wks
Olanzapine pamoate *Zyprexa Relprevv* 2009	$1200-1800	300mg (given q4wks or split q2wks)-300 mg q2wks	Gluteal IM injection only; No PO overlap needed REMS program; Rare risk of post-delirium syndrome

**www.drugs.com-Accessed 9/17*

LAI Additional Information

- **Haloperidol decanoate**
  - Loading dose strategy – 10-20 x PO dose
    - Reduce PO dose if use loading dose
  - If initial dose > 100mg; give initial 100mg dose, followed by remainder in 3-7 days
- **Risperdone LAI**
  - Approximate equivalent doses:
    - < 3mg/day → 25mg q2wks
    - > 5mg/day → 50mg q2wks

LAI Additional Information

- **Olanzapine pamoate**
  - Can stop PO dose up to a week before 1st dose
  - Equivalent doses
    - 10mg/day = 150mg q2wks or 300mg q2wks
    - 20mg/day = 300mg q2wks
  - Rare risk of post-injection delirium syndrome
    - Caused by rapid increases of olanzapine serum concentrations
    - Dizziness, confusion, disorientation, slurred speech, elevated BP, mild-severe sedation, up to 3 hrs following injection
  - Drug only available by a ZYPREXA RELPREVV Patient Care Program
    - Prescriber, patient, healthcare facility, and pharmacy must be registered

Long-Acting Antipsychotics

Name/ Year Approved	Monthly Cost*	Dosing Range	Other
Paliperidone palmitate *Invega Sustenna* 2009	$420-2500	Day 1-234 mg followed by 156 mg in 7 days; Then 156 mg qmonth Dosage range 39-234mg qmonth	Discontinue PO with 1st dose
Aripiprazole *Abilify Maintena* 2013	$1500-2000	400mg qmonth	Continue PO for 14 days; Adjust dose if poor CYP2D6 metabolizers
Aripiprazole lauroxil *Aristada LAI* 2015	$1200-2900	441-882mg qmonth or 1064 mg q2mos.	Continue PO for 21 days; Adjust dose if poor CYP2D6 metabolizers
Paliperidone palmitate *Invega Trinza* 2015	$830-2500	273-819mg q3mos.	Switch after stabilized on *Invega Sustenna* for 4 mos.

**www.drugs.com-Accessed 9/17*

LAI Additional Information

- **Aripiprazole monohydrate**
  - Approximate equivalent doses
    - 10mg/day PO → 300mg qmonth
    - 20mg/day PO →400 mg qmonth
  - Reduce dose to 300mg qmonth if poor CYP2D6 metabolizer, and/or strong 2D6 or 3A4 inhibitors
  - Avoid medications that induce CYP3A4 for > 14 days
- **Aripiprazole lauroxil**
  - Approximate equivalent doses
    - 10mg/day PO → 441mg qmonth
    - ≥ 20mg/day PO → 882 mg qmonth
  - Can give 882 mg dose q6wks
  - Dose adjustments recommended for CYP450 interactions

CYP450 Interactions

3A4 Inducers	Strong 3A4 inhibitors	Strong 2D6 Inhibitors
Carbamazepine	Indinavir	Bupropion
Efivarenz	Nelfinavir	Fluoxetine
Nevirapine	Ritonavir	Paroxetine
Phenobarbital	Clarithromycin	Quinidine
Phenytoin	Itraconazole	
Pioglitazone	Ketoconazole	
Rifampin	Nefazodone	
St. John's Wort	Saquinavir	
Rifabutin	Suboxone	
Pioglitazone	Telithromycin	
Troglitazone		

http://medicine.iupui.edu/clinpharm/ddis/main-table

LAI Additional Information

- **Paliperidone Palmitate (*Invega Sustenna)***
  - Decrease dose in renal impairment (CrCl < 50mL/min)
  - Approximate equivalent doses:
    - 3mg/day PO → 39-78mg qmonth
    - 12mg/day PO → 234 mg qmonth
  - First injection should be give in deltoid; subsequent injections can be given in gluteal or deltoid muscle

LAI Additional Information

- **Paliperidone palmitate (*Invega Trinza)***
  - Equivalent doses of *Invega Sustenna* → *Invega Trinza*
    - 78 mg/mos. → 273 mg q3mos.
    - 117 mg/mos. → 410 mg q3mos.
    - 156 mg/mos. → 546 mg q3mos.
    - 234 mg/mos. → 819 mg q3mos.
  - Can be given up to 2 weeks early or 1 month late

FGA and SGA Adverse Effects

First-Generation Antipsychotics

Medication	ACH	Sedation	QTc Prolongation	EPS
Chlorpromazine	+++	+++	++	+
Perphenazine	+	+	++	++
Trifluoperazine	+	+	N/A	++
Haloperidol	Very low	Very low	++	+++
Thiothixene	+	+	N/A	++
Thioridazine	+++	+++	+++	+
Fluphenazine	+	+	++	+++
Loxapine	+	++	No	++

ACH= Anticholinergic side effects
EPS= Extrapyramidal side effects

Second-Generation Antipsychotics

Medication	Metabolic ADR	Sedation	QTc Prolongation	EPS
Clozapine *Clozaril*	+++	+++	+	Very low
Risperidone *Risperdal*	++	+	++	++
Olanzapine *Zyprexa*	+++	++	++	++
Quetiapine *Seroquel*	++	++	+++	+
Ziprasidone *Geodon*	very low	+	+++	+
Aripiprazole *Abilify*	+	+	+	+

Second-Generation Antipsychotics

Medication	Metabolic ADR	Sedation	QTc Prolongation	EPS
Paliperidone *Invega*	++	+	Very low	++
Iloperidone *Fanapt*	+	+	++	Very low
Asenapine *Saphris*	+	+	+	+
Lurasidone *Latuda*	Very low	+	No	+
Brexpiprazole *Rexulti*	++	+	No	+
Cariprazine *Vraylar*	+	++	No	++

Mortality Risk in Elderly Patients

- Black-box warning on all antipsychotic drugs increase the all-cause risk of death in elderly patients with dementia-related psychosis
  - Primarily SGA studied vs. placebo
  - Risk of death 1.6- to 1.7-times AP vs. placebo-treated patients
  - Death primarily attributed to cardiovascular and infectious disease causes

Antipsychotics Adverse Effects

- Serotonin syndrome
  - Risk with SGA's
- Neuroleptic malignant syndrome (NMS)
  - Hyperpyrexia, muscle rigidity, altered mental status, autonomic instability, elevated CPK, ARF, myoglobinuria
  - Immediately d/c medication and treat symptoms
- Increased risk of death in patients with dementia
  - Black box warnings with atypical antipsychotics but thought to occur with typical antipsychotics
- Increased suicidal thoughts/behaviors in patients aged 24 years old and younger
  - Black-box warning for SGA approved for the adjunctive treatment of depression

Extrapyramidal Side Effects (EPS)

- Most EPS due to blockade of the dopamine receptors in the basal ganglia
  - FGA > SGA
  - High-potency > Low-potency FGA
  - Dose-dependent risk
- Examples
  - Dystonic Reactions
  - Akathesia
  - Pseudoparkinsonism
  - Tardive dyskinesia

Extrapyramidal Side Effects (EPS)

- Dystonic Reactions
  - Involuntary sustained muscular contractions occurring within first few days of treatment
    - Retrocollis, torticollis, oculogyric crisis, etc.
  - Higher risk in young males; FGA > SGA; dose-dependent
  - Treatment options
    - Diphenhydramine 25-50mg PO/IM q4-6 hrs
    - Benztropine 1-2 mg PO/IM q6hrs
    - Discontinue antipsychotic or decrease dose

EPS-Akathesia

- Most cases occur within 1-3 months of antipsychotic initiation
- Sensation of inner restlessness; patients cannot sit still
  - May be misdiagnosed as agitation/anxiety
- Highest risk with aripiprazole and cariprazine
- Treatment options:
  - Decrease dose or change antipsychotic
  - Propranolol 10-20mg PO 2-4 times daily
    - Most evidence for efficacy
  - Benzodiazepines
  - Anticholinergics

EPS-Pseudoparkinsonism

- Typically occurs within days/weeks of starting antipsychotic
- Includes slowed movements, masked facies, cogwheel rigidity, resting tremor, etc.
- Treatment options:
  - Decrease dose or change antipsychotic
  - Anticholinergics
    - Benztropine 1-6mg PO daily, diphenhydramine 25-300mg/day (divided)
  - Amantadine 100-400mg/day (divided)
  - Propranolol
    - Treatment resistant cases

Tardive Dyskinesia

- Irreversible drug-induced disorder that is characterized by involuntary choreoathetoid movements of the tongue, mouth, face, extremities, and/or trunk
- Risk increases with patient age, cumulative dose of AP, and duration of therapy
- Higher incidence with FGA vs. SGA
  - Highest risk with agents which have more potent dopamine blockade

Tardive Dyskinesia

- Chronic anticholinergic treatment have been associated with higher risk of developing tardive dyskinesia
- Treatment options include
  - Discontinue antipsychotic
  - Vitamin E supplementation
    - Conflicting data
  - Pyridoxine (vitamin B6) 400-1200mg/day
  - Deep Brain Stimulation
    - Treatment resistant cases

Valbenazine (Ingrezza™)

- Approved for the treatment of tardive dyskinesia
- Dosing:
  - Starting dose 40 mg/day x 1 week, then increase to 80mg/day if needed
  - Dose should be reduced by half when using with strong 3A4 inhibitors
- Mechanism of action:
  - Selectively inhibits VMAT2 in presynaptic neurons which reversibly reduces dopamine in synaptic cleft and reduces the amount of dopamine available to postsynaptic D2 receptors

www.ingrezza.com

Valbenazine (Ingrezza™)

- Precautions/Contraindications
  - Somnolence (counsel patients), potential QT prolongation
  - Do not use if patients on strong 3A4 inducer, MAO inhibitors, or in severe renal dysfunction (CrCl < 30ml/min)
  - Reduce dose to 40mg/day if on strong 3A4 inhibitors, or in patients with moderate-severe liver disease
- Adverse Effects
  - Somnolence, anticholinergic adverse effects, balance disorders, headaches, akathesia, nausea, vomiting, arthralgia
- Cost >$5000/month

Metabolic Adverse Effects

- Includes drug-induced weight gain, diabetes risk, and dyslipidemia
- Thought to be caused by ….
  - Seen more with SGA vs. FGA
- Weight gain
  - Highest with olanzapine and clozapine
  - Monitor weight at baseline and periodically thereafter

Metabolic Adverse Effects

- Hyperlipidemia
  - Higher risk with olanzapine
  - Obtain fasting lipid profile prior to initiation and periodically thereafter
- Hyperglycemia
  - Check BS prior to starting a SGA

Other Adverse Effects

- Hyperprolactinemia
  - Associated with sexual dysfunction, gynecomastia, irregular menstrual periods
  - More common with risperidone and paliperidone
- Orthostasis/syncope
  - Quetiapine
  - Seen when initiating or increasing dose
- Seizures
  - All seizures decrease seizure threshold
- Anticholinergic adverse effects
  - Constipation, blurry vision, dry mouth, urinary retention

QTc Prolongation

- All antipsychotics can increase QTc interval
  - Highest risk with thioridazine and ziprasidone
  - Avoid/caution use with other medications that can increase QT prolongation (assess risk vs. benefit)
  - Avoid if history of cardiac arrthymias, symptomatic bradycardia, hypomagnesemia, hypokalemia, underlying elevated QT interval
    - Use low-risk AP's
    - Monitor EKG regularly

Other Adverse Effects

- Increased impulse-control disorders
  - Warning added to aripiprazole labelling in 2016
  - ? Possible with brexpiprazole and cariprazine?
- Dizziness
  - Titrate dose of iloperidone

Other Adverse Effects

- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
  - FDA warning added to labeling of olanzapine-(2016) and ziprasidone-(2014) containing products
  - Rare adverse effect
  - Symptoms include new-onset fever with a rash and swollen lymph glands, and/or swelling in the face; symptoms can progress to other parts of the body

Clozapine Adverse Effects

- Drug-induced neutropenia
  - Rare but life-threatening
    - < 3 cases/1000 patient years
    - Typically seen within first 6 months of therapy
  - Severe neutropenia
  - Agranulocytosis
    - Absolute Neutrophil Count (ANC) of < 500/mm3
      - ANC= Total WBC count X Neutrophil % (Segs % + Bands %)

Clozapine Adverse Effects

- Federally-mandated REMS program created in 2015
  - www.clozapineregistry.com
  - Prior to that individual manufacturers had individual registries to monitor WBC and ANC results
  - Patient's prescribed clozapine need have ANC drawn every 2 weeks upon initiation
    - Less often after 6 months of clozapine therapy
  - REMS Program has specific instructions of monitoring recommendations following abnormal lab results
    - Specific guidelines for patients with Benign Ethnic Neutropenia (BEN)

Conclusion

- Patients diagnosed with schizophrenia should be started on a SGA or FGA
- Consider clozapine after trials of 2 antipsychotics from different classes
- Consider long-acting antipsychotic provided patient tolerates PO form to improve adherence
- Assess for improvement in positive, negative, and cognitive symptoms
- Assess and treat adverse effects or consider changing AP as needed

Review Questions

1. Which of the following are symptoms seen in schizophrenia?

   a) Grossly disorganized speech and/or behavior
   b) Delusional thoughts
   c) Lack of emotion
   d) Impaired executive functioning
   e) All of the above

Review Questions

2. Dosage adjustments are necessary with brexpiprazole (Rexulti®) in patients also prescribed strong cytochrome p450 3A4 and 2D6 inhibitors.

   a) True
   b) False

Review Questions

3. Cariprazine (Vraylar®) is considered safe to use in the treatment of psychosis in elderly patients with dementia.

   a) True
   b) False

Review Questions

4. Which of the following statements are true for valbenazine (Ingrezza ™)?

   a) FDA approved for the acute treatment of manic or mixed episodes associated with Bipolar I Disorder and the treatment of Schizophrenia in adults following knee/hip replacement
   b) The dose should be doubled when used with strong cytochrome p450 3A4 inhibitors
   c) It works by selectively inhibiting VMAT2 in presynaptic neurons which reversibly reduces dopamine in synaptic cleft and reduces the amount of dopamine available to postsynaptic D2 receptors
   d) The monthly cost is less than $1000/month

Review Questions

5. The most effective treatment for antipsychotic-induced tardive dyskinesia is oral anticholinergics prescribed daily (vs. PRN).

   a) True
   b) False