Psychopharmacology: What the Pharmacist Needs to Know

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Learning Objectives

- Identify psychotropic medications by name and indication
- Describe expected outcomes of psychotropic medication use
- Manage the drugs interactions and monitoring parameters associated with psychotropic medication use
- Identify the roles of pharmacists in behavioral health

Mental Health in Georgia

- 1,405,000 adults have a mental health condition
- Last in the nation for access to mental health care
  - Disproportionately affects minority populations
- 1,569 lives lost to suicide in the last year
  - 103.81 per 100,000 in black men in 2022

Mental Health in Georgia. National Alliance on Mental Illness. February 2021. https://www.nami.org/NAMI/media/NAMI-Media/StateFactSheets/GeorgiaStateFactSheet.pdf
Valliant S, et al. Pharmacists as accessible health care providers: quantifying the opportunity. J Managed Care Spec Pharm. 2022 Jan; 28(1): 85–90.

Social Determinants of Health

Social Determinants of health are the non-medical variables that impact a person's health

Social factors make up 80-90% of a person's health

Social, economic, physical conditions that a person lives in, works in, grows in, and plays in that can affect health outcomes

Cobb CD et al. Social Determinants of Health in people Living with Psychiatric Disorders. The Role of the Pharmacists. Health Equity. 2023;7.1:223-234
Social Determinants of Health. Office of Disease and Health Prevention. 2023. Available: https://health.gov/healthypeople/priority-areas/social-determinants-health
SDOH-impact of psychiatric pharmacists [Internet]. [cited 2024 Mar 4]. Available from: https://aapp.org/psychpharm/sdoh

Psychotropic Medications

Use the provided sheet as guidance to the following case

- 56 year old female
  - Symptoms: low motivation, flat affect, auditory command hallucinations, passive SI
  - Vitals/Labs: BP 132/88 mmHg 5'8" 145 LBS CrCl 94 ml/min LFTs- WNL
  - PMH: Migraines with aura, T2DM (with neuropathy), Hypertension, Schizophrenia, Generalized anxiety
  - Current Medications: Quetiapine 25mg HS, Amitriptyline 25mg daily, Metformin 500mg BID, Sumatriptan 50mg at onset of migraine, Hydroxyzine 10mg TID PRN, Duloxetine 60mg daily, Lisinopril 10/12.5 mg daily, Aripiprazole 15mg daily

Question: What is the indication of each psychotropic medication? What does the dose or frequency of administration indicate?

Psychotropic Medications

- Medications used to treat mental health disorders
  - Antidepressants
    - SSRI, SNRI, TCA, MAOI, Atypical
  - Antipsychotics
    - FGA (typical), SGA (atypical)
  - Anxiolytics
    - Benzodiazepines
    - Buspirone
  - Mood Stabilizers
  - Stimulants
    - Amphetamine, Methylphenidate

Question: What other indications can the psychotropic medications be utilized for?

Psychotropic Medications - Indication

- Antidepressants (for depression)
  - First line SSRI, SNRI, Mirtazapine, Bupropion
  - Second line: Choose a different 1st line, TCA
  - Third line: Choose a different 1st, 2nd line, MAOI
    - Augmentation: Antipsychotics, Lithium, Folic Acid, Levothyroxine, Stimulants
    - ECT, TMS

Question: Which antidepressant works the best for depression?

SSRI – Selective Serotonin Reuptake Inhibitor, SNRI – Serotonin Norepinephrine Reuptake Inhibitor, TCA – Tricyclic Antidepressant, MAOI – Monoamine Oxidase Inhibitor, ECT – Electroconvulsive Therapy, TMS – Transcranial Magnetic Stimulation

Antidepressants – Efficacy

When will they work?

- Improvement within 1-2 weeks, max benefit in 4-8 weeks
  - Days: Anxiety, agitation decrease, sleep & appetite improve
  - 1-3 weeks: Increased concentration, activity, memory, self care
  - 2-4 weeks: Improvement in mood, subside SI thoughts, less hopelessness

Will they work?

- 1/3 of patients reach remission. Each trial decreases efficacy

How do you dose?

- Elderly typically start at ½ adult dose
- Other indications may require higher or lower doses

How long should treatment last?

- 6 months – 1 year after remission

Antidepressants – What to Expect

Antidepressants are most commonly discontinued in the first 3 weeks

- Adverse effects occur before the benefit is noticed and are typically transient

Adverse Effects	
SSRI	Anxiety, sleep disturbance, headache, GI upset, sexual dysfunction, hyponatremia
SNRI	In addition to SSRI ADRs: cardiovascular complications
Atypical	Mirtazapine: Weight gain, appetite, sedation Bupropion: Insomnia, Seizures
TCA	Anticholinergic, sedation, cardiovascular complications weight gain
MAOI	Hypotension, weight gain **Serious**: Hypertensive crisis, Serotonin Syndrome

Question: When is the risk of suicidal ideation highest after antidepressant treatment

SSRI – Selective Serotonin Reuptake Inhibitor, SNRI – Serotonin Norepinephrine Reuptake Inhibitor, TCA – Tricyclic Antidepressant, MAOI – Monoamine Oxidase Inhibitor

Khawam E., et al. Side Effects of Antidepressants: An Overview. Cleveland Clinic Journal of Medicine. 2006;74(4):351-361

Psychotropic Medications - Indication

- Antipsychotics (for schizophrenia)
  - First line FGA or SGA
  - Second line: Choose a different FGA, SGA
  - Third line: Choose a different FGA, SGA, or Clozapine
  - Fourth line: Combination treatment

Question: Which antipsychotic works the best for psychotic symptoms?

FGA – first generation antipsychotic, SGA – second generation antipsychotic

Antipsychotics - Efficacy

- When will they work?
- Treatment begins as soon as indicated
  - Begin treatment as soon as indicated
  - Days: Acute symptoms decrease
  - 4 to 6 weeks: Psychotic Symptoms
- How do you dose?
  - Higher doses not associated with greater efficacy
  - Elderly, Renal/Hepatic impairment – begin at lower dose
- How long should treatment last?
- 1+ year after remission (indefinite)

Antipsychotics – What to Expect

All antipsychotics carry a BBW for increase risk of death & cerebrovascular events in elderly when used for dementia related psychosis

	Adverse Effects
FGA	Sedation, Anticholinergic Effects, **Movement Disorders**
SGA	Disturbance in sleep, Hypotension, Anticholinergic Effects, **Metabolic Syndrome**

Clinical Tip: FGAs cause more movement disorders depending on their potency. Clozapine, Olanzapine, and Quetiapine are the SGAs with the greatest risk of metabolic syndrome

FGA – first generation antipsychotic, SGA – second generation antipsychotic, BBW – Black Box Warning

Psychotropic Medications - Indication

- Anxiolytics (for anxiety)
  - Benzodiazepines - Place in therapy
    - Use as a bridge while waiting for maintenance treatment efficacy
    - Acute symptoms of anxiety
  - Non-Benzodiazepine – Hydroxyzine, Buspirone
    - Used as adjunct, augmenting agent

Question: What would you do if a patient was taking Alprazolam 0.5mg BID PRN and needed to take it consistently every day for the last 18 years

Anxiolytics - Efficacy

Benzodiazepines

- Provides immediate relief , scheduled duration not recommended past 4 weeks

Buspirone

- Efficacy similar to antidepressants, 2-4 week onset

Hydroxyzine

- 15-20 minute onset

FDA Approved/Onset of Action	
Alprazolam Rapid (short)	Clonazepam Intermediate (medium)
Chlordiazepoxide Intermediate (long)	Diazepam Very Rapid (long)
Lorazepam Intermediate (short)	Oxazepam Slow (short)

Anxiolytics – What to Expect

Benzodiazepines

- CNS Depression

Buspirone

- Dizziness, Headache, Sedation, Nausea, Nervousness, Excitement

Hydroxyzine

- Anticholinergic effects, sedation

Psychotropic Medications - Indication

Mood Stabilizers (for bipolar disorder)

- First Line: Lithium, Divalproex Sodium, Antipsychotics, Lamotrigine (depressive episode)
- Second Line: Carbamazepine
- Adjunct/Based on Episode: Antidepressant, Anxiolytic

Clinical Reminder: Mood stabilizers are consistently used regardless of episode. If patient is presenting with a manic episode assess regimen for antidepressant and discontinue

Mood Stabilizer - Efficacy

When will they work?

- Efficacy expected within 1-2 weeks

Choice of mood stabilizer dependent on episode

- Lithium – classic symptoms, depressive episode
- Divalproex sodium – classic symptoms, mixed episodes
- Lamotrigine – depressive episode

How long should treatment last?

- 1+ year after remission (indefinite)

Mood Stabilizer – What to Expect

Adverse Effects	
Lithium	Sedation, changes in weight, GI upset, **Narrow therapeutic window**
Divalproex Sodium	Sedation, GI upset, tremor, hair loss, fatigue, change in weight
Carbamazepine	Headaches, change in weight, GI upset
Lamotrigine	**Monitor for rash**, GI upset, sedation

Dosing Tip: Changing the formulation from IR to XR or splitting the dose may help reduce GI upset

Psychotropic Medications - Indication

Stimulants (for ADHD)

- 1st Line: Stimulants AMP or MPH
  - Failed 1st Line: Switch agents, Adjust Dose, Evaluate Diagnosis
- 2nd Line: Alpha 2 Agonist, Atomoxetine
- 3rd Line: Non-FDA approved agents/Off Label Agents

Question: What is the difference between AMP and MPH products?

Stimulant - Efficacy

When will they work?

- Failure of 1 does not rule out the class
- Equally efficacious
- Pharmacokinetics make them different
- Choice of agent: Severity of symptoms, time of day when symptoms are problematic

Stimulants – What to Expect

ADR	Management
Decreased Appetite	Eat a high calorie breakfast and dinner and assess for weight loss. Cyproheptadine in severe cases
Insomnia	Evaluate administration time, add a sedating agent
Stomach Ache	Take with food
Headache	Take with food, use an analgesic
Irritability/Jitteriness	Switch to longer acting formulation, assess for mood disorder , reduce dose, change to non-stimulant

Clinical Reminder: Secondary to their mechanism of action, amphetamine products may be associated with greater cardiovascular impacts

Monitoring Parameters

Antidepressants

- Weight Gain - Mirtazapine, MAOIs, TCAs, Paroxetine
- Blood Dyscrasias: Mirtazapine, Citalopram, TCAs
  - Not common. Monitor if indicated
- Electrolytes: SSRIs, SNRIs
  - Monitor sodium in higher risk patients
- Blood Pressure: SNRIs – Venlafaxine
  - Dose related, monitor routinely

Psychotropic Medication Monitoring

Use the provided sheet as guidance to the following case

- 48 year old male
  - PMH: Depression, Anxiety, Mood lability, AUD
  - Vitals: BP 140/77 mmHg, 5'4" 192 LBS

Chem7	Lipid panel	CBC	CMP	Misc Labs
Na 134 mEq/L K 4.0 mEq/L Cl 101 mEq/L CO2 30 mEq/L SCr 1.1 mg/dL BUN 15 mg/dL Glu 99 mg/dL	TC 195 mg/dL HDL 60 mg/dL TG 127 mg/dL LDL 139 mg/dL	WBC 5.2 x 10^6/L Hg 14.2 g/dL Hct 42.9% Plt 266 x 10^6/L RBC 4.81 x 10^6/mL	AST 57 IU/L ALT 41 IU/L eGFR >60 Urine Tox Amphet Neg Barb Neg Opi Neg Marijuana Pos Cocaine Neg EtOH Neg	Vit D 31.7 ng/mL A1C 5.4 Folate 7.9 ng/mL TSH 2.79 mIU/L

Prior to starting a mental health medication, what labs values should be assessed or can be affected by the psychotropic medications utilized for hhiser mental health disorders

Monitoring Parameters

American Diabetes Association (ADA) – monitoring protocol for second generation antipsychotics (SGA)							
	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually	Every 5 Years
Personal/ Family History	X					X	
Weight (BMI)	X	X	X	X	X		
Waist Circumference	X					X	
Blood Pressure	X			X		X	
Fasting Plasma Glucose	X			X		X	
Fasting Lipid Profile	X			X			X

Clinical Pearl: Of the antipsychotics, Olanzapine, Clozapine, and Quetiapine have the greatest risk of metabolic syndrome. Prolactin levels should be monitored with Risperidone and FGAs

Clozapine Monitoring Guidelines

Clozapine is associated with agranulocytosis

- Agranulocytosis reported in 1% of patients
- All users are required to be registered in the Clozapine REMS program

One registry: www.ClozapineREMS.com

- ANC is the only value reported
  - General Population ≥ 1500 µL
  - Benign Ethnic Neutropenia ≥ 1000 µL
  - Monitoring frequency: Weekly x 6 months, Biweekly x 6 months, then monthly indefinitely

Pharmacists

- Pharmacy must be registered to dispense clozapine
- Blood work cannot be greater than 7 days old
- Do not dispense clozapine without receiving ANC

Question: What would you do if a patient came in with a prescription for Clozapine 300mg daily, but they did not have updated lab work?

Monitoring Parameters

Mood Stabilizers

Name	Weight	LFTs	Blood Dyscrasias	TSH	Electrolytes	Other
Lithium	X			X		
Valproic Acid	X	X	X			X
Carbamazepine		X	X		X	
Oxcarbazepine		X	X		X	
Lamotrigine	Does not typically require additional lab workup					

Monitoring Parameters

Stimulants

- Blood pressure, Heart Rate
  - Amphetamine products have a greater risk secondary to their mechanism of action
- Height, Weight
  - Lunch time appetite is most affected
  - Height may be decreased during childhood, conflicting data on affect of adult height

Wojnowski N, et al. Effects of Stimulants on Final Adult Height. J Pediatr Endocrinol Metab. 2022 Nov 25; 35(11): 1337–1344

Faraone S. The Pharmacology of Amphetamine and Methylphenidate: Relevance to the Neurobiology of Attention-Deficit/Hyperactivity Disorder and Other Psychiatric Comorbidities. Neurosci Biobehav Rev. 2018; 87: 255–270.

Pertinent Drug Interactions

Use the provided information to identify potential drug interactions for this patient

- 41 year old female
  - Presenting Symptoms: fatigued, poor concentration, hopeless mood
  - PMH: Deep Vein Thrombosis, Bipolar Disorder, Breast Cancer in remission
  - Vitals/Labs: BP 142/88 mmHg, 5’2” 145 LBS, CrCl 89 ml/min, LFTs- WNL
  - Current Medications: Tamoxifen 20mg daily, Ibuprofen 800 mg daily PRN pain, Carbamazepine 200mg daily, Warfarin 7.5 mg daily, Paroxetine 10mg daily, Multivitamin daily

What drug interactions are of concern?

Pertinent Drug Interactions

Drug Class	Watch Out For
Antidepressants	Fluvoxamine Paroxetine Fluoxetine Bupropion
Antipsychotics	Many are substrates of CYP 3A4
Mood Stabilizers/Antiepileptic	Carbamazepine Phenytoin Phenobarbital Lithium – ACEI, ARB, NSAID, Diuretics Caffeine
Stimulants	May affect efficacy of antihypertensive Monitor with cough/cold products
Anxiolytics	Additive effective with other CNS depressants Many are substrates of CYP 3A4

Question: How would you counsel a patient picking up a prescription for an oral contraceptive and Carbamazepine?

Clinically Significant Drug-Drug Interactions

- Hormone Contraceptives
  - Estrogen is metabolized by CYP3A4
  - Inducers may decrease estrogen component by 50%
    - Increased risk of unintended pregnancy
  - Clinical Recommendation
    - Utilize a backup method of contraception while using and 4+ weeks after discontinuing
    - Progesterone only contraceptive may be appropriate

Look Out For:

Carbamazepine

Phenobarbital

Topiramate

Oxcarbazepine

Clinically Significant Drug-Drug Interactions

- Lithium
  - Completely renally cleared
  - Cytochrome P450 enzymes, not a concern
  - Other medications may increase the risk of toxicity
    - ACE Inhibitors, ARBs, Diuretics, NSAIDs
  - Clinical Recommendations
    - Monitor lithium levels 12 hours post dose every 6 months, more if indicated
    - Stay well hydrated during summer months
    - Diet should be consistent, report changes

Look Out For:

ACE Inhibitor

ARBs

Diuretics

NSAIDs

Caffeine

Lithium Toxicity

- Mild Toxicity (1.5-2.0 mEq/L)
  - GI (N/V, loose stools, diarrhea)
  - CNS (lethargy, drowsiness, coarse hand tremor, muscular weakness)
- Moderate Toxicity (2.0 – 2.5 mEq/L)
  - GI (N/V diarrhea)
  - CNS (confusion, nystagmus, ataxia, myoclonic twitches, dysarthria)
  - Cardiac (EKG changes)
- Severe Toxicity (> 2.5 mEq/L)
  - GI (N/V diarrhea)
  - CNS (grossly impaired consciousness, seizures, syncope, coma)
  - Cardiac (EKG changes, death)
  - Kidney (renal insufficiency)

Treatment: Discontinue medication → Gastric Lavage → Supportive Care
Severe Toxicity: Hemodialysis (Goal Serum Concentration 1 mEq/L)

Gitlin, M. Lithium side effects and toxicity: prevalence and management strategies. *Int J Bipolar Disord*. 2016;4(27)

What Can You do – Behavioral Health

Estimated 20-72% of patients with schizophrenia are non-adherent [33]

Brand (generic)	Frequency of Administration
Abilify Maintena (aripiprazole)	4 weeks Requires 2 weeks of oral overlap
Aristada (aripiprazole lauroxil)	4 weeks or 6 weeks (882 mg dose) 8 weeks (1064 mg dose) Requires 3 weeks of oral overlap
Zyprexa Relprevv (olanzapine)	2 weeks (210 mg, 300 mg*) 4 weeks (300 mg, 405 mg)
Invega Sustenna, Trinza, Hafyera (paliperidone palmitate)	4 weeks
Risperdal Consta, Perseris (risperidone)	2 weeks Requires 3 weeks of oral overlap 4 Weeks
Haldol Decanoate (haloperidol)	4 weeks
Prolixin Decanoate (fluphenazine)	3 weeks

Leijala J, et al. Daily functioning and symptom factors contributing to attitudes toward antipsychotic treatment and treatment adherence in outpatients with schizophrenia spectrum disorders. BMC Psychiatry; 2021:37(21)

What Can You do – Behavioral Health

Smoking Cessation

- 40% of cigarette consumption in the US is by people with a mental health disorder

Olanzapine is a substrate of CYP 1A2

Chemicals formed in cigarette smoke is an inducer of CYP 1A2

Clinical Outcome: Patients who start or quit smoking may need a dose adjustment of olanzapine and clozapine. The chemicals cause olanzapine and clozapine to be metabolized from the body quicker

CDC. People With Mental Health Conditions. February 2023.

What Can You do – Behavioral Health

Assessment of Mental Health Disorders

- Depression
  - Patient Health Questionnaire 9
- Anxiety
  - Generalized Anxiety Disorder Scale 7
- Substance Use
  - CAGE Questionnaire
- Post Traumatic Stress Disorder
  - PC – PTSD 5

Questions

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