Basics of Psychopharmacology

Anna Holen MD
Psychiatrist
VA Puget Sound Health Care System
Anna.Holen@va.gov

Learning Objectives

- At the end of this lecture, you will be able to:
  - Describe the common medications used to treat psychiatric conditions, including their various risks, benefits, and side effects.
  - Understand why/how these medications are used in different conditions/presentations.
  - Assist patients in understanding their medication regimens and provide basic education around medications.

Overview

- Basic Tenets of Psychopharmacology
- Antidepressants
- Antipsychotics
- Mood Stabilizers
- Anxiolytics/Sedatives
- Stimulants
- Medications for Substance Use

Basic Tenets of Psychopharmacology

- Medications are only part of the solution
  - While research indicates that people can gain significant benefit/improvement from medications, rates of full remission with medications alone are often low
  - Recommend focusing on a holistic approach to care

Basics of Psychopharmacology

- Medications take time
  - Do **not** rely on medications for immediate safety concerns (suicide, etc)
  - Medications typically take days to weeks to work
    - Most antidepressants: 4-6 weeks with ongoing improvement up to 12 + weeks out
    - Mood stabilizers: 7-12 days at therapeutic dose for mania
    - Antipsychotics: some benefits within a few days, but typically 4-6 weeks, may still see improvement for 3-6 mos out

Basics of Psychopharmacology

- Beware of Reactive Prescribing
  - Most of the factors affecting our patients' symptoms/distress are out of our control
  - Medical providers truly want to ease distress/pain and the 1 thing we can control are the medications we prescribe
  - It is easy to fall into a trap of prescribing/changing medications in response to acute distress
  - **BUT** far better to prescribe medications as part of a long-term, cohesive treatment plan

Basics of Psychopharmacology

- Take time with medications
  - Start low and go slow
  - Most titration schedules are written for ideal settings
  - Even if it takes longer to get to a therapeutic dose, the medication can only help if the pt keeps taking it
  - Taper even more slowly
  - Rebound symptoms are real
  - It is natural for symptoms to cycle/fluctuate. And natural for people to attribute any changes to their meds. Especially if stopping a med, need to allow enough time for the symptoms to cycle independent of the med change

Basics of Psychopharmacology

- Consider the psychological symbolism/role of medications
  - Stigma can be external and/or internal
  - Ambivalence about psychiatric medications is common
  - Watch for the no-cebo effect
  - Many communities (BIPOC) have very legitimate concerns about the medical establishment (including lack of inclusion in pharm studies)
  - Medications can also sometimes be seen as a validation of suffering (which makes tapering tricky)

Basics of Psychopharmacology

- Beware the influence of the pharmaceutical industry
  - New medications are **NOT** necessarily better than old ones
  - New medications **ARE** much more expensive
  - It is not unusual for side effects to emerge only after large numbers of people have taken medications for extended periods of time
  - Industry can influence practice at multiple levels
  - Statistical significance does not always equal clinical significance

Basics of Psychopharmacology

- How to choose a medication and starting dose?
  - Try to match expected effects/side effects to pt's symptoms/risk factors/concerns
  - Use past med history to guide
  - Consider fast vs. slow metabolizers
    - Genetic tests for this are of questionable clinical benefit
    - 20-40% of people from China, Korea, and Japan are slow metabolizers (mostly impacts studies in those countries); Latinx and African American populations can have higher rates of both fast and slow metabolizers

Antidepressants

- Most are also the primary pharmacologic treatment for anxiety disorders
- Need to be taken daily, typically result in gradual, slow improvement
- No good research on developing “tolerance”
- Common Types:
  - Selective Serotonin Reuptake Inhibitors
  - Serotonin-Norepinephrine Reuptake Inhibitors
  - Tricyclic Antidepressants
  - Other

Antidepressants - SSRIs

- Side effects:
  - Most are **TRANSIENT** (1-2 weeks) and **NOT DANGEROUS**
  - Common initial side effects include GI distress (nausea, diarrhea, constipation), dry mouth, headache, activation/akithesia
  - Black Box warning for increased suicidal ideation
  - Sexual side effects (30-50%)
  - Discontinuation symptoms – rebound depression/anxiety/agitation, flu-like symptoms, “electric shock” sensations – uncomfortable but not dangerous
  - Serotonin Syndrome
  - Teratogenicity

Antidepressants - SSRIs

- Fluoxetine/Prozac
  - Start at 10 mg q AM, usual dosing 20-60 mg/day (may go to 80)
  - Oldest of the SSRIs, very potent serotonergic med
  - Has the longest half-life of the SSRIs, good in questionable adherence
  - Typically more activating but may have more emotional blunting, can be helpful for people with a lot of reactivity/impulsivity
  - Preferred medication in OCD, possibly eating disorders
- Sertraline/Zoloft
  - Start at 25 mg, usual dosing 50-200 mg/day (can go as low as 12.5 mg to start)
  - Usually well tolerated, good 1st choice
  - Preferred medication in breastfeeding

Antidepressants - SSRIs

- Citalopram/Celexa
  - Start at 10 mg, usual dosing 20-40 mg/day
  - Well tolerated, used to be 1st choice but max dose was lowered due to cardiac effects
- Escitalopram/Lexapro
  - Usual dosing 10-20 mg/day
  - S-enantiomer of Citalopram
- Paroxetine/Paxil
  - Start at 10 mg, usual dosing 20-50 mg/day
  - More sedating, typically give at bedtime
  - Short half-life, more side effects

Antidepressants - SNRIs

- Side effects
  - Similar to SSRIs
  - Risks for high BP at high doses
  - Higher cardiac risk (higher OD risk)
  - Less known about teratogenicity
- Also helpful for pain (fibromyalgia, neuropathic pain) and possibly ADHD

Antidepressants – SNRIs

- Venlafaxine/Effexor
  - Use XR formulation, start 37.5 mg/day, usual dosing 75-225 mg/day
  - Generic and generally affordable, usually preferred by insurance programs
  - Very short half-life, can have big discontinuation sx

Antidepressants - SNRIs

- Duloxetine/ Cymbalta
  - Usual dosing 30-120 mg/day
  - Generic
- Desvenlafaxine/Pristiq
  - Usual dosing 50-100 mg/day
  - Active metabolite of Venlafaxine
  - Generic but not cheap
- Levomilnacipran/Fetzima
  - Usual dosing 20-120 mg/day
  - Not generic

Antidepressants - TCAs

- Side effects
  - Anticholinergic: sedation, dry mouth, constipation, urinary hesitancy, cognitive impairment, DELIRIUM
  - Cardiac conduction effects
  - Sexual side effects
- Narrow safety window – **DANGEROUS IN OD**!
- Also helpful for pain/sleep (at low doses)

Antidepressants - TCAs

- Amitriptyline
  - Usual dosing 50-200 mg/day
- Nortriptyline
  - Usual dosing 25-150 mg/day
  - Metabolite of Amitriptyline, may have less SE
- Imipramine
  - Usual dosing 25-300 mg/day
- Desipramine
  - Usual dosing 50-300 mg/day
  - Metabolite of Imipramine, may have less SE

Antidepressants - other

- Bupropion/Wellbutrin
  - Very activating, less helpful for anxiety
  - Lowest risk of sexual side effects and GI effects
  - Helpful for smoking cessation, often used for ADHD
  - Can increase seizure risk
  - Dosing:
    - IR 100-400 mg/day, divided 2-3x/day (avoid taking at bedtime)
    - SR 200-400 mg/day, divided 2x/day (avoid taking at bedtime)
    - XL 150-450 mg/day, once a day

Antidepressants - Other

- Trazodone
  - VERY sedating, mostly used for sleep
  - Usual dosing for depression is 300-400 mg/day, for sleep is 50-200 mg/day
  - Side effects: sedation, “hangover,” priapism
- Mirtazapine
  - Sedating, stimulates appetite (more at lower doses)
  - Usual dosing is 15-45 mg/day
  - Side effects: sedation, weight gain, few sexual SE

Antidepressants - Other

- Monoamine Oxidase Inhibitors (MAOIs)
  - Require strict dietary restrictions, serious med interactions
  - May help with treatment-resistant depression
  - Phenelzine/Nardil, Tranylcypromine/Parnate, Selegiline patch
- Vilazodone/Viibryd
  - Usual dosing is 10-40 mg/day
  - Expensive, not generic
- Vortioxetine/Trintellix
  - Usual dosing is 10-20 mg/day
  - Expensive, not generic
  - May have cognitive benefits
- Esketamine/Ketamine
  - Dissociative anesthetic
  - Potential for rapid results, but long-term effects not as clear
  - Requires close monitoring, difficult to administer in outpt settings
  - Lots of new (for profit/cash only) clinics offering this

Antipsychotics

- Used to treat psychosis, also can help with bipolar d/o and depression
  - sometimes used “off label” as a sedative
- While there can be some effects within a few days, these typically take 2-4 weeks to see most benefit, may continue to see benefit 3-6 months out

Antipsychotics

- Side effects
  - Sedation
  - Sexual SE (hyperprolactinemia)
  - Metabolic – weight gain, diabetes, hyperlipidemia
  - Motor – Extrapyramidal Symptoms (EPS), akithesia, Tardive Dyskinesia (TD)
  - Teratogenicity

Antipsychotics - Typicals

- Older class, usually have more motor side effects (especially TD)
- Not prescribed as often but work as well as newer ones
- Include: Chlorpromazine/Thorazine, Haloperidol/Haldol (available in long-acting injection, IV, immediate acting injection), Perphenazine/Trilafon, Trifluoperazine/Stelazine, Fluphenazine/Prolixin (long-acting injection)

Antipsychotics - Atypicals

- Newer, fewer motor but more metabolic effects
- Risperidone/Risperdal
  - Usual dosing is 2-6 mg/day
  - Also available in long-acting injection (Consta)
  - Paliperidone/Invega is active metabolite, dosed 6-12 mg/day. Available in long-acting injection (Sustenna, Trinza)
- Aripiprazole/Abilify
  - Less sedating, lowest sexual SE
  - Usual dosing is 5-30 mg/day
  - Also available in long-acting injection (Aristada, Maintena)

Antipsychotics - Atypicals

- Olanzapine/Zyprexa
  - Very sedating, big metabolic effects (**not 1st line**)
  - Usual dosing is 5-30 mg/day
  - Also available in long-acting injection (seldom used due to side effects), new formulation with opioid antagonist Samidorphan (Lybalvi) to help with weight gain
- Clozapine/Clozaril
  - Usual dosing is 25-450 mg/day
  - **Only used in treatment-resistant psychosis** because of severe side effects, needs regular blood testing (every 1-4 weeks)

Antipsychotics - Atypicals

- Quetiapine/Seroquel
  - Very sedating, anticholinergic
  - Usual dosing is 200-1200 mg/day (2x/day unless XR formulation)
- Ziprasidone/Geodon
  - Less sedating, few metabolic effects
  - Usual dosing is 80-240 mg/day (2x/day)
  - Must be taken with at least 350 cal meal
- Lurasidone/Latuda
  - Similar to Ziprasidone
  - Usual dosing is 40-120 mg/day (also with meal)

Antipsychotics - Atypicals

- Asenapine/Saphris
  - 5-10 mg 2x/day (only in dissolving tab)
- Brexipiprazole/Rexulti
  - 1-4 mg/day
- Cariprazine/Vraylar
  - 1.5-6mg/day
  - May have added benefit for negative symptoms
- Iloperidone/Fanapt
  - 2-12 mg 2x/day
- Lumateperone/Calypta
  - 42 mg/day

Mood Stabilizers

- Most really are anti-manic agents (variable benefit for depression symptoms)
- Typically take 12 days (at therapeutic doses) to reach efficacy in acute mania
- Most antipsychotic medications (both typical and atypical) have antimanic properties. Many newer atypical antipsychotics have FDA approval for bipolar d/o (both acute and maintenance treatment)

Mood Stabilizers - Lithium

- Very effective antimanic but also good antidepressant – Gold standard treatment for bipolar
  - Has anti-suicide properties, strong evidence for treatment-resistant depression
- Side effects
  - Renal toxicity, thyroid dysfunction, cardiac conduction issues, elevated WBC, sedation, toxicity syndrome, teratogenicity
- Typical dosing is 300-1200 mg/day (2x/day), therapeutic blood level is 0.6-1.2
- Need to monitor renal function, blood count, thyroid function, and Li+ level after each dose change and then annually

Mood Stabilizers - Anticonvulsants

- Valproic Acid/Valproate/ Divalproex/Depakote
  - Effective anti-manic, may help with rapid cycling, mixed episodes, anger/impulsivity
  - Side effects: liver inflammation, pancreatitis, blood count changes (platelets and WBC), sedation, weight gain, PCOS, toxicity, teratogenicity
  - Usual dosing is 500-2000 mg/day (can do all bedtime dosing or 2x/day). Therapeutic blood level is 60-100.
  - Need to monitor liver function, blood count, and VPA level after each dose change, then every 6 mos

Mood Stabilizers - Anticonvulsants

- Carbamazepine/Tegretol
  - Similar dosing, side effects, blood monitoring to VPA but higher risk of blood and allergic/autoimmune SE -> genetic testing recommended for people of Chinese descent
- Oxcarbazepine/Trileptal
  - Metabolite of Carbamazepine, fewer side effects, less blood monitoring
  - Usual dosing is 300-600 mg 2x/day

Mood Stabilizers (?) - Anticonvulsants

- Lamotrigine/Lamictal
  - Effective for bipolar depression but not a strong antimanic agent
  - Can cause a serious autoimmune reaction/rash so need to titrate very slowly, otherwise few SE
  - Usual dose is 200 mg/day (for mood)
- Gabapentin/Neurontin
  - Not effective for bipolar d/o
  - Used for neuropathic pain, also can help with anxiety/sleep
  - Low toxicity/side effects?

Anxiolytic Medications

- Prazosin
  - Old, generic BP medication (alpha-agonist)
  - Helpful for PTSD symptoms (nightmares, but also sleep quality, general PTSD symptoms)
  - Biggest side effect is dizziness/fainting (due to low BP)
  - Usual dosing is 2-14 mg at bedtime, can also do 1-4 mg mid-morning (need to build up doses slowly to avoid fainting)

Anxiolytic Medications

- Buspirone
  - Used for GAD
  - Few side effects
  - Usual dosing is 15-30 mg 2x/day
- Hydroxyzine
  - Antihistamine with anti-anxiety properties
  - Usually used on an as needed basis
  - Very anticholinergic (sedation, cognitive impairment, dry mouth, constipation, etc)
  - Dosing is 25-50 mg 2-4x/day

Anxiolytic Medications

- Benzodiazepines
  - Clonazepam/Klonopin, Lorazepam/Ativan, Alprazolam/Xanax, Diazepam/Valium
  - Risks for tolerance, dependence, withdrawal (can be life-threatening)
  - Also cognitive slowing, respiratory depression (esp with opiates), increased risks for falls, disinhibition (increased suicide risk)

Anxiolytic Medications

- Benzodiazepines
  - Typically do not recommend for long term use
  - Over time can create tolerance and increase anxiety levels
  - 1st symptom of withdrawal is rebound anxiety
  - Tapering can be very difficult, may help to move very slowly

Medications for Sleep

- Often use Trazodone, TCAs (Doxepin), Diphenhydramine, Hydroxyzine, Melatonin
- “Z-drugs”
  - Zolpidem/Ambien, Zaleplon/Sonata, Suvorexant/Belsomra
  - Can develop tolerance, risk for withdrawal symptoms
  - Cognitive impairment, amnestic sleep behaviors, driving impairment

Stimulants

- Used to treat ADHD/ADD
- High risk medications (abuse, addiction, psychosis, anxiety)
- Methylphenidate/Ritalin, Amphetamine Salts/Adderall, Dextroamphetamine/Dexedrine, Lisdexamfetamine/Vyvanse
- Non-stimulants used for ADD/ADHD: Atomoxetine/Strattera, Guanfacine, Bupropion

Medications for Substance Use

- Methadone
  - Long acting opiate used for opiate dependence/opiate replacement therapy
  - When prescribed for SUD, must be dispensed from specially designated methadone clinic
  - Typically dispensed every day
- Buprenorphine/Suboxone
  - Also long acting opiate for opiate dependence
  - Has mixed agonist/antagonist action so exhibits “ceiling effect” for intoxication/respiratory depression (when taken orally)
  - Usually mixed with Naloxone to prevent IV diversion
  - Able to be dispensed from regular clinics, up to a month at a time

Medications for Substance Use

- Naltrexone
  - Opiate antagonist used for opiate use d/o and EtOH use d/o
  - For opiates will block action of any used – can also cause acute withdrawal when administered
  - For EtOH is harm reduction techniques – decreases cravings, decreases reward experience of drinking
  - Available PO (50 mg/day) or long-acting Imq 4 weeks (Vivitrol)
  - Can cause liver inflammation/damage

Medications for Substance use

- Acamprosate
  - Treatment for EtOH use d/o – harm reduction
  - Typically dosed 666 mg TID
- Disulfiram
  - Aldehyde dehydrogenase inhibitor
  - Abstinence based treatment for EtOH – causes severe illness if taken with EtOH
  - Typically dosed 250-500 mg q Day

Thank you!

Questions?