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Understanding the Impact of Concomitant Psychotropic Medication Use in Patients Also Receiving Physical And/Or Occupational Therapy

Enhancing pharmacological and rehabilitation therapies through understanding of meds

Rosanne Thomas PT, MS, PhD

Objectives

1) Given the name of a drug commonly prescribed for a patient with a psychiatric disorder, the participant will be able to list at least three side effects.
2) Describe at least three pharmacological interventions effect on PT treatment.
3) Describe at least three steps of performing a preliminary screening of a patients psychotropic medications, appropriate for an initial point of contact within the scope of PT practice.
4) Outline a list of at least five comprehensive on-line resources to continue to grow in ones knowledge of ever changing psychotropic medications.
Overview

- Pharmacology Review
- Pharm management of specific aims within dx
  - Effects that impact therapy
  - Effects that impact safety
  - Vulnerable population – the older adult
- Patient Problems
- Commonalities
- Finding Good Drug Websites

Pharmacology and non-prescribing Healthcare practitioners

Why???
Pharmacotherapeutics

Pharmacokinetics
- Drug absorption
- Distribution
- Metabolism
- Excretion

What does the Body do to the drug?

Pharmacodynamics
- Cellular effects
- Systemic effects

What does the DRUG do to the body?

Pharmacotherapeutics

Dose of Drug Administered
- Enteral
- Parenteral

Absorption

Drug concentration in systemic circulation

Drug concentration at site of action

Pharmacologic effect

Clinical Response

Summary

Pharmacokinetics
- Absorption
- Distribution
- Elimination

Pharmacodynamics
- Side effects/
- Toxicity
- Efficacy
Drug Mechanism of Action

The means by which the presence of a drug produces an alteration in function

Drugs usually must combine with a cellular receptor to produce an effect

[Diagram of extracellular environment and cellular receptors]

http://citadel.sjfc.edu/students/envi0216p2c02/pag/fig.htm

Mental Health Policy II
Mental Health Policy and Psychotropic Drugs
Recent Trends in the Use of Psychotropic Drugs

More Medicated
Americans’ use of mental health medications has been on the rise over the past decade.

<table>
<thead>
<tr>
<th>Year</th>
<th>Men</th>
<th>Women</th>
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<tbody>
<tr>
<td>2001</td>
<td>12%</td>
<td>6%</td>
</tr>
<tr>
<td>2010</td>
<td>19%</td>
<td>7%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Boys (ages 0 to 19)</th>
<th>Girls (ages 0 to 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>2010</td>
<td>7%</td>
<td>5%</td>
</tr>
</tbody>
</table>

[Graph showing trends over time]

http://image.slidesharecdn.com/06-mhpii-mentalhealthpolicy-psychotropics-drugs-6-638.jpg?cb=1446049164
The Older Adult and Psychotropic meds

• Age related changes
  • Pharmacokinetic changes
    • Altered absorption, distribution, changed hepatic metabolism, reduced renal excretion
    • Increasing co-morbidities which impact pharmacokinetics
  • Polypharmacy
  • Increasing risk of orthostatic hypotension
  • Increase morbidity and mortality with falls
  • Smaller doses important, especially when initiating

• Use of psychotropic meds common in older adults
  • More prevalent among community-dwelling older adults than any other age groups. (7 to 18 times more likely than middle-aged adults)
  • In acute care geriatric units – 87% of patients taking 1 psychotropic med, 66% - 2, 36%-3, 11% - 4 or more.
  • Older adults (>70) 3.5 times more likely than younger adults to be admitted to the hospital due to an Averse Drug Reaction associated with psychotropic drugs.

Psychotropic Drugs

• Definition:

Psychiatric medicines that alter chemical levels in the brain which impact mood and behavior

• Most Common types in the U.S.:
  • Anti-anxiety medications
  • Antidepressants
  • Antipsychotics
  • Mood stabilizers
  • ADHD drugs – not covered in this webinar

Primary drug mechanism of action – Manipulate Neurotransmission
Manipulate neurotransmission

Treatable neurotransmitter diseases fall into 2 categories:

- Too MUCH neurotransmission
- Too LITTLE neurotransmission

General Mechanisms

**Too LITTLE neurotransmission due to:**
- Too few NT molecules binding to postsynaptic receptors (ex – PD, depression)
  - Rx - Drugs that cause release of NT stores from presynaptic terminals
  - NT precursors
  - Drugs that inhibit the enzymes that degrade NT
  - Agonist that act at postsynaptic receptors

**Too MUCH neurotransmission due to:**
- A focus of hyperexcitable neurons that fire in the absence of appropriate stimuli (ex- seizures)
  - Rx - \( \neg \) ing automaticity of these cells
- Too many NT molecules binding to post-synaptic receptors (ex- psychoses)
  - Rx – Administration of antagonists which block post-synaptic receptors
Manipulating transmission in a diseased pathway simultaneously affects synapses of normal neurons

Normal Synaptic Transmission

1. Presynaptic AP
2. Synthesis of NT
3. Storage of NT
4. Release
5. Reuptake
6. Degradation
7. Post synaptic receptor
8. Presynaptic autoreceptor
9. Membrane effects

https://clipartfest.com/categories/view/701152ab01a6d41f7d4cf7fd7f6e315e41a1cb3e/side-effects-of-drugs-clipart.html

http://people.fmarion.edu/tbarbeau/physio_neuro_supplements.htm
Neuronal Synapse Drug Manipulation Sites

1. Presynaptic AP
2. Synthesis of NT
3. Storage of NT
4. Release
5. Reuptake
6. Degradation
7. Post synaptic receptor
8. Presynaptic autoreceptor
9. Membrane effects

http://people.fmarion.edu/barbeau/physio_neuro_supplements.htm

Example Diagnoses with altered neurotransmission

- PD – too little dopamine
- AD – too little acetylcholine
- Schizophrenia -Too much dopamine?
- Bipolar – Na channels? Post-synaptic 2nd messenger overactivity?
- Depression – Serotonin/norepinephrine modulation?

http://www.brainbalancebook.com/neurotransmitters/what-are-neurotransmitters/
Neurotransmission modulation with psychiatric diseases

- Anxiety
- Depression
- Schizophrenia
- Bipolar

1. Sedative-hypnotics
2. Antidepressants
3. Antipsychotics
4. Mood stabilizers

1- Sedative Hypnotic Medications

Sedative – reduces anxiety & exerts calming effect with little or no effect on motor or mental function

Hypnotic – produces drowsiness & encourages the onset & maintenance of sleep

Hypnotic effects cause > depression of CNS than sedation effects
Neurotransmission modulation
1- Sedative-Hypnotics

Chemical Classification:
- Benzodiazepines – most important sedative-hypnotic
- Barbiturates - CNS depressants with potent sedative-hypnotic effects
  - Narrow Margin of Safety, overdose \( \rightarrow \) fatal
  - Addictive

Pharmacokinetics:
- Highly lipid soluble \( \rightarrow \) easily reaches the CNS
- Usually administered PO
- Metabolized in the liver – can be sequestered in adipose & other tissue \( \rightarrow \) slow release with prolonged effects

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Neurotransmission modulation
1- Sedative-Hypnotics

Mechanism of action:
Benzodiazepines-
- \( \uparrow \) inhibition present at CNS GABA synapses
- When \( \uparrow \) inhib effect @ GABA synapse in RF
\( \rightarrow \) arousal,
\( \uparrow \) relaxation, sleep

RF = Reticular Formation – an important collection of neurons in the brain stem that determine level of awake and arousal
Neurotransmission modulation
1- Sedative-Hypnotics

Mechanism of action:

**Barbituates –**
- May also own site on GABA receptor
- May directly inhibit NT release from presynaptic terminal
- Antagonistic-like effects on post-synaptic receptor
- Specificity for neurons in the midbrain reticular formation → generalized CNS depression

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Neurotransmission modulation
1- Sedative-Hypnotics- effects

1. Sedation - ↓ responsiveness
   - Anterograde amnesia – inability to remember events during drug’s action

2. Hypnosis – sleep
   - Disrupted sleep stages
     - More rapid onset
     - Prolongation of stage 2 NREM sleep
     - ↓ REM sleep
     - ↓ Slow-wave sleep

3. Anesthesia – at high dose
4. Anticonvulsant effects
5. Muscle relaxation
6. Respiratory & Cardiovascular function
   - Respiratory depression in patients with pulmonary disease
   - Dose-related
   - Over Dose → depression of medullary respiratory center

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https://basicmedicalkey.com/sedative-hypnotic-drugs-2/
Neurotransmission modulation
1- Sedative – Hypnotics - effects

**Tolerance:**
- ↓'ed responsiveness to a drug following repeated exposure (possibly due to receptor downregulation)

**Side Effects:**
- Daytime sedation/drowsiness
- Synergistic depression of CNS with other drugs (ETOH)
- Possibility of psychological & physiological dependence

**Influence on Physical Therapy:**
- Patient relaxed, less anxious +
- **Anterograde memory loss**, drowsiness –

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**Examples of Common Sedatives/ Hypnotics**

**Anxiolytics (reduces anxiety)**
- Chlordiazepoxide HCl (Librium)
- Alprazolam (Xanax)
- Diazepam (Valium)
- Promethazine HCl (Phenergan)
- Lorazepam (Ativan)

**Sedatives (sleep aids) > potency**
- Zolpidem tartrate (Ambien)
- Flurazepam HCl (Dalmane)
- Temazepam (Restoril)
- Triazolam (Halcion)

*Benzodiazepines often end in: -am*

Useful Handout:
https://education.ucsb.edu/sites/default/files/hosford_clinic/docs/Mental_Health_Medications.pdf
Sedative/ Hypnotics in the Older Adult

- Benzodiazepines most common anxiolytic meds prescribed for older adults
  - Alprazolam (Xanax)
  - Lorazepam (Ativan)
  - Clonazepam (Klonopin)
  - Diazepam (Valium)
- Increased magnitude of SE
  - Sedation
  - Memory
  - Psychomotor impairment
- ↑’d risk of falls & skeletal fx
- Long-term use (> 30d) contraindicated due to
  - Risk of cognitive decline
  - Poor functional autonomy
  - Addiction
- Use as a sleep aid may worsen sleep patterns in the older adult
- 10% of geriatric hospitalizations related to use of benzos

Patient Problem # 1

Your 34 y/o female patient sustained a spinal cord injury and has paraplegia at the T12 level. She receives 20 mg of Baclofen BID for her spasticity. She has experienced difficulty sleeping since arriving at your rehab facility and flurazepam (Dalmane) was prescribed as a sleep aid. You notice that her performance and level of attentiveness during morning PT sessions is very poor with poor carryover of training from the morning to the afternoon sessions.

- Hypothesize about why this may have occurred.
- What would you recommend and how could you modify PT?
Neurotransmission modulation – 2- Anti-Depressants

• Depression most prevalent form of mental illness in the U.S. 5% of Americans will experience major depression over a 1 year period
• Anti-depressant medications widely prescribed – at least 1 in 5 Americans on anti-depressants
• Therapeutic agents minimally changed in 40 years
  • Inhibition of monoamine reuptake & metabolism
  • Time lag of 2 - 4 weeks before drugs work due to latency period for compensatory cellular changes

Neurotransmitter Synthesis

• Monoamine neurotransmitters
  • Start with an amino acid:
    • Tyrosine OR
    • Tryptophan
  • End product → Neurotransmitter (NT):
    • Dopamine (DA)
    • Norepinephrine (NE)
    • Epinephrine (EPI)
    • Serotonin (5HT)
Mental Health and Monoamine NT

Neurotransmission modulation
Antidepressant Drug Classifications

- Reuptake inhibitors
  - Tricyclics (TCA) – prevent presynaptic reuptake of NE & Serotonin
  - **SSRI**
  - **SNRI**
- MAO Inhibitors (MAOI) – prevent breakdown of NE, Serotonin or Dopamine presynaptically
- Combinations
  - More than one Mech of Action
  - Effect > one NT
Common Antidepressants
Mechanisms of Action and Side Effects

Inhibits reuptake of NE and DA DNRI
Inhibits reuptake of NE and Serotonin
Potentiates synapses & Inhibits reuptake of NE
Inhibits presynaptic autoreceptors for NE & Serotonin
Serotonin antagonist & reuptake inhibitor

Antidepressant Problems & Adverse Effects

Tricyclics –
- Sedation
- Tachycardia, arrhythmia
- Hypotension (esp elderly)
- Anticholinergic properties – confusion, dry mouth, constipation, urine retention,
- **HIGHEST POTENTIAL FOR FATAL OVERDOSE**

Reuptake inhibitors –
- Not necessarily more effective
- Bupropion (Wellbutrin) – seizures

MAO Inhibitors –
- Produce CNS excitation ➔ restlessness, irritability, lack of sleep
- Anticholinergic effects but < tricyclics
- ↑ BP
- Interaction with food containing tyramine (stimulate release of EPI & NE ➔ HTN)
Neurotransmission modulation

Other Uses for Anti-depressants

- Depression – major depressive episodes
- Panic disorder
- Obsessive-compulsive disorder – esp SSRI’s
- Enuresis – incontinence
- Chronic pain – SSRI’s → sub P in S.C.
- Eating disorders
- ADD – esp Bupropion (Wellbutrin)

Useful Handout:
https://education.ucsb.edu/sites/default/files/hosford_clinic/docs/Mental_Health_Medications.pdf

Neurotransmission modulation

Examples of Common Antidepressants

Selective Serotonin Reuptake Inhibitors
- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Citralopram (Celexa)
- Fluvoxamine (Luvox)

Tricyclic Antidepressants
- Amitriptyline (Elavil)
- Desipramine (Norpramin)
- Nortriptyline (Pamelor)

Heterocyclic Antidepressants
- Mirtazapine (Remeron)
- Nefazodone (Serzone)
- Trazadone (Desyrel)

Monoamine Oxidase Inhibitors
- Phenelzine (Nardil)
- Tranylcypromine (Parnate)

Others
- Venlafaxine (Effexor)
- Bupropion (Wellbutrin)
Antidepressants in the Older Adult

- SSRIs the preferred first-line treatment for depression in older adult
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
  - Sertraline (Zoloft)
- Tricyclic antidepressants (TCA) > SE
  - Sedation
  - Psychomotor retardation
  - Orthostatic Hypotension
  - Anticholinergic effects
- Both - ↑ fall risk

Patient Problem # 2

Your patient is a 72 y/o male who is receiving in-patient rehab following a L CVA. He exhibits Brunnstrom Level 3 signs and symptoms (significant spasticity, movement within gross synergies) and moderate expressive aphasia. During his acute care stay, it was determined that he was severely depressed and he has now been receiving Amitriptyline (Elavil) for depression. He arrives for his therapy treatment in a W/C and, when you assist him to stand, he experiences a syncope episode.

- What would you do?
- Hypothesize about why this may have occurred.
- How would you prevent future occurrences?
Neurotransmission modulation
3- Anti-Psychotic Drugs (APD)

**Psychosis** = Loss of touch with reality

- Not a specific disorder
- Psychotic symptoms can occur in many types of mental illness

<table>
<thead>
<tr>
<th>+ Symptoms</th>
<th>- Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired sense of reality</td>
<td>Delusions</td>
</tr>
<tr>
<td>Disturbance of thought &amp; emotion</td>
<td>Blunted/ Inappropriate Affect</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Attentional deficits – can’t ignore irrelevant stimuli</td>
</tr>
</tbody>
</table>

Theory as to Cause of Psychosis

- “Too much” dopamine in the brain
- Antipsychotic medications block dopamine receptors (DA R) in the brain

- **Typical antipsychotics**
  - Older ~ First Generation
  - Varied potency ~ ability to bind to DA R

- **Atypical antipsychotics**
  - Newer ~ 2nd Generation (1989)
  - Targeted DA R AND other NT R
  - Less Side Effects (SE)

Neurotransmission modulation
APD Pharmacokinetics

- Readily but incompletely absorbed with significant 1st pass effects
  - Bioavailability 25 – 60%
- Highly lipid soluble & 92 – 99% bound to protein
- Accumulates in brain, lung, fat – tissue with high blood supply
  - Longer duration of action than T1/2 due to sequestration in fat
- Metabolized in the liver

- Blocks D2 receptors
- Can reverse + s/s of Schizophrenia
- Have high risk of producing extrapyramidal SE

Neurotransmission modulation
APD Clinical Effects may take several weeks for optimal effect

1. Prominent sedative effect – especially early in rx
2. Anti-anxiety effects
3. Suppression of spontaneous mov’t & complex behavior (Spinal reflexes intact)
4. ↓ initiative, interest in environment, emotional expression & affect
5. With continued rx → ↓ agitation, aggression, impulsive behavior
6. Autistic → ↑ communication

http://video.astarc/i socioeconomic-effects-of-antipsychotic-meds-nysphp

The Ideal Antipsychotic Agent

Well tolerated
Easy to use – desire, switching, isolated
No EPS or TD
Improve positive, negative, and mood symptoms
Improves cognitive function and prevents cognitive deterioration

The goal is to get the patient well and keep them well

continued
Neurotransmission modulation
APD Side Effects - General

- Anticholinergic effects ABCDS
  - Agitation
  - Blurred vision
  - Constipation
  - Dry mouth
  - Stasis (urinary retention)
- Orthostatic hypotension (alphadrenergic)
- Neuroendocrine effects
  - Diabetes
  - Weight gain
  - Cataracts
  - Dyslipidemia
  - Cardiac disease
    - Prolongation of QT interval
    - Myocarditis

Neurotransmission modulation
APD Neurological SE - Neurological

- Extrapyramidal Motor System – due to DA receptor blockade in the Basal Ganglia
  - Acute Dystonia – uncontrollable movements & distortions of the face, head, neck
    - Develop in 5% of pts esp with high potency APDs
    - Most common in males, young and with older drugs
    - ↑ Dose → symptoms
  - Akathesia – intense motor restlessness
    - 20% of pts
    - Often confused for agitation → ↑ dose which worsens symptoms
  - Tardive Dyskinesia – involuntary mov’t of face, trunk, extremities
    - Often irreversible
    - 20% of pts on long-term APD (esp haloperidol)
    - Most common in elderly females with long term use
  - Parkinsonism
  - Malignant syndrome – rare but can be fatal
    - Catatonia, rigidity, stupor, flux PD, fever, dysarthria
  - Rx – D/C drugs, give bromocriptine (DA agonist)
Onset of Neurological Side Effects w APD

SE onset Varies dependent on:
- Duration of drug use
- Type of APD used

Typical APD SE > Atypical

Side Effect Risk Perception

http://video.aster.id/30c/side-effects-of-antipsychotics-medica/my.php
Neurotransmission modulation
Examples of Common APD

- Chlorpromazine (Thorazine)
- Risperidone (Risperdal)
- Thioridazine (Mellaril)
- Haloperidol (Haldol)
- Clozapine (Clozaril)
- Olanzapine (Zyprexa)

Red = older, typical APD
Blue = newer, atypical APD


SE vary significantly & are present in both typical & atypical APD

### Table 3. Comparative Risk of Adverse Effects of Antipsychotic Medications

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>Low-potency FGAs</th>
<th>High-potency FGAs</th>
<th>Atypical atypicals</th>
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</thead>
<tbody>
<tr>
<td>EPS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuroleptic malignant syndrome</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Sedation</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Seizures</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Weight gain</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

### Notes:
- 0 = rare; + = lower risk; ++ = medium risk; +++ = higher risk.
- FGAs = first-generation antipsychotics; SGAs = second-generation antipsychotics.
- Effects are approximate, and relative to other antipsychotic medications rather than absolute risk of an adverse effect occurring.
- FGAs with lower potency dopamine D2 receptor blockade include chlorpromazine and thioridazine.
- FGAs with higher potency dopamine D2 receptor blockade include fluphenazine, haloperidol (Haldol), thiothixene (Navane), and trifluoperazine. Perphenazine is considered to have intermediate dopamine D2 receptor blockade, with an adverse effect profile between the low- and high-potency FGAs.
- Thioridazine has a higher risk of prolonged QT interval and should be used only when no other appropriate options are available.


Muench J, Hamer AM. Am Fam Phys, 18:5. 2010
APD in the Older Adult

• Frequently administered to manage disruptive behavior in older adults with cognitive impairment
• Older at greater risk for all APD SE
• Weight gain common
• Atypical APD – warning by FDA - ↑’d cerebrovascular, cardiac and mortality risks in patient with dementia.

Patient Problem # 3

Your patient is a 26 year old woman who has been receiving physical therapy intermittently throughout her recent pregnancy for TMJ dysfunction. Today is her first appointment with you after giving birth 2 weeks ago to her son. She presents to the outpatient clinic with her crying infant in her arms, appearing highly disorganized and disheveled (beyond the normal post-partum expectations.) As you talk with her, she accuses you of trying to steal her son and appears to be having a conversation with someone who is not actually present.

• What is happening?
• What will you do?
Patient Problem #3 continued

• The patient is eventually admitted to a psychiatric hospital where she and her infant stay for 2 weeks. She was diagnosed with post partum psychosis and put on a gradually increasing dose of risperidone to which she responded well.

• Three weeks later, she has a physical therapy appointment with you. This time, her 6 week old infant is in a stroller and the patient appears well groomed and better rested. She states she has been allowed to continue breastfeeding while on the risperidone. She also complains of not being able to lose any of her prenatal weight gain to date.

1- Is the lack of weight loss related to her medication? What SE is she susceptible to while on risperidone?

2- Is there evidence regarding nursing with APD?

Neurotransmission modulation

4- Anti-manic or Mood Stabilizing Drugs

Mania = mood disorder characterized by disordered or delusional thinking & perceptions

• Excessive elation/ exuberance
dysphoria/irritability

• Insomnia

• Hyperactivity

• Uncontrolled speech & activity
(impulsive)

• Impaired judgement (feelings of
grandiosity)

Manic/ Depression swing

• Severe mania

• Hypomania (mild to moderate mania)

• Normal/balanced mood

• Mild to moderate depression

• Severe depression
Triggers for Bipolar Episode

- Stress – good or bad
- Substance abuse –
  - cocaine, ecstasy, amphetamines \(\rightarrow\) mania
  - Alcohol, sedatives \(\rightarrow\) depression
- Medication –
  - SSRIs, OTC cold med, appetite suppressants, caffeine, corticosteroids, thyroid med \(\rightarrow\) mania
- Seasonal changes –
  - Manic episodes common in summer
  - Depressive episodes common in fall and winter
- Sleep deprivation \(\rightarrow\) mania

Neurotransmission modulation

4. Anti-manic or Mood Stabilizing Drugs

The different faces of bipolar disorder

- **Bipolar I Disorder (mania or a mixed episode)** – The classic manic-depressive form of the illness, with at least one manic episode or mixed episode. Usually—but not always—involves at least one episode of depression.

- **Bipolar II Disorder (hypomania and depression)** – The person doesn’t experience full-blown manic episodes. Instead, the illness involves episodes of hypomania and severe depression.

- **Cyclothymia (hypomania and mild depression)** – A milder form of bipolar disorder that consists of cyclical mood swings, with less severe symptoms than full-blown mania or depression.

**Medications – purpose: control emotion and behavior**

1. Lithium
2. Selected anti-convulsant meds
3. Selected APD with
4. Selected antidepressants

Acute rx – benzodiazepine often added for rapid symptom control
Lithium

- Historical drug of choice
- 60 – 80% effective
- Therapeutic for manic phase
- Helps prevent transition into depressive phase
- Helps prevent recurrence of mania
- Less effective in seriously ill
- More effective in mild mania
- Serum NA can alter response

Mechanism
- Unknown
- Monovalent cation included in alkali metal group
- Small size & + charge \(\rightarrow\) able to pass thru open neuronal Na channels (may directly influence neuronal excitation)
- Altered ionic distribution & membrane conductance - stabilizes neuronal membrane \(\rightarrow\) excitability \(\rightarrow\) transmission in overactive aminergic pathways

Neurotransmission modulation
Lithium

<table>
<thead>
<tr>
<th>Pharmacokinetics:</th>
<th>Acute Li Toxicity (Above 2 meq/L):</th>
<th>Chronic Li Toxicity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral absorption erratic</td>
<td>Fatigue, weakness, tremor</td>
<td>Decreased thyroid function (\rightarrow) goiter</td>
</tr>
<tr>
<td>Kidney excretion</td>
<td>Diarrhea, N &amp; V, ataxia, mental confusion</td>
<td>Polydipsia &amp; polyuria (Diabetes insipidus)</td>
</tr>
<tr>
<td>Narrow therapeutic window</td>
<td>LOC, coma</td>
<td>Chronic interstitial nephritis</td>
</tr>
<tr>
<td></td>
<td>Rx: (\downarrow) dose, saline drip, dialysis, osmotic diuretic (mannitol)</td>
<td>Edema (from Na retention)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Some transfer of Li in breast milk</td>
</tr>
</tbody>
</table>
Common Drug Combinations for Bipolar Disorder

- **Anticonvulsants**
  - Unknown mechanism but ↑'s duration of inactive state of Na channel
  - May be used alone or combo with Li
  - Valproic Acid (Depakote)
  - Carbamazepine (Tegretol)
  - Lamotrigine (Lamictal)
  - Oxcarbazepine (Trileptal)

- **Atypical APD**
  - Olanzapine (Zyprexa)
  - Aripiprazole (Abilify)
  - Risperidone (Risperdal)
  - Ziprasidone (Geodon)
  - Clozapine (Clorazil)

- **SSRI – Antidepressants**
  - If used as monotherapy, tends to induce mania- need to use w/ a mood stabilizer
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)

Rx Combinations Side Effects (SE)

- **Anticonvulsants SE**
  - Changes in weight
  - Loss of appetite/ anorexia
  - Nausea/ stomach pain/vomiting
  - ↑ testosterone in teenage girls → polycystic ovarian syndrome
  - FDA Warning - ↑ risk of suicidal thought/action

- **Atypical APD**
  - Olanzapine (Zyprexa)
  - Aripiprazole (Abilify)
  - Risperidone (Risperdal)
  - Ziprasidone (Geodon)
  - Clozapine (Clorazil)

- **SSRI – Antidepressants**
  - If used as monotherapy, tends to induce mania- need to use w/ a mood stabilizer
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)

- **Common SE with COMBOS**
  - Restlessness, anxiety
  - Anticholinergic SE – dry mouth, tachycardia
  - Acne
  - Intolerance to cold
  - Joint or mm pain
  - Heartburn
  - Sun sensitivity
Bipolar in the Older Adult

• 90 % of Bipolar dx occurs before age 50
  • peaks between 20- 40 y/o
  • 10% Late Onset
• Must rule out other causes for new onset s/s including
  • Medication
  • Organic brain disease
  • Infection
• Antidepressants seem to exacerbate mania more in older adults
• Mood stabilizer may be sufficient for symptom management though toxicity levels are more easily reached with age
• Long-term use of lithium may lead to kidney failure

Patient Problem # 4

• Your patient is a 59 y/o female receiving home health PT following B TKA. Her past medical history is significant for bipolar disorder for which she has been receiving lithium for many years. As you evaluate her ability to perform functional activities, the patient reports that tremors have recently made hand activities difficult. You notice that the tremors are present both at rest and during activity.
  • Hypothesize about why this may be occurring.
  • What would you do?
Common Side Effects of Psychotropic Meds

CNS
- Extrapyramidal
  - Esp with typical APD
  - When start new APD
  - When rapidly increase dose of APD
  - Major change – surgery, trauma that changes blood levels of drug
- Sleep disturbances
  - CNS activating → Insomnia, restlessness – some SSRIs
  - CNS sedating → Somnolence, daytime sedation- some APD
  - Nightmares – some atypical APD
- Seizures
  - All APD ↓ seizure threshold
  - Wellbutrin - antidepressant

Systemic/Metabolic
- Metabolic syndrome – common in Atypical APD
  - Weight gain
  - Insulin resistance
  - Dyslipidemia
- Hypersalivation – older APD
- Anticholinergic- APD, tricyclic antidep
- Cardiovascular
  - Orthostatic hypotension
  - Tachycardia – more common in males & young
  - Cardiac Arrhythmia- all APD
    - Prolongation of QT interval
    - Sudden cardiac death
  - Agranulocytosis – rare – Clozapine (APD)
    - Asian female at greater risk

Finding Accurate Drug information

- Anyone can post information
- Don’t waste time on unreliable/ inaccurate sites
- Suggestions
  - What is the site’s domain? Don’t make this your only criteria!
    - .gov, .edu – almost always reliable
    - .org – often nonprofit, less reliable
    - .net, .com – least reliable
  - Who wrote/sponsored/ published the site? Check for biases or ulterior motives
  - When was the site last updated? Is it current?
  - What links connect with the site? Are they reputable?
  - Who is the site’s audience?

Example – Drug Referencing

- *Acute treatment* – medically stable patient, 1 week post-op R TKA.
- *Example – Fluoxetine x 20 y*, post-op TKA. *Concomitant use of warfarin, vicodin*


<table>
<thead>
<tr>
<th>Check Drug</th>
<th>Check Interactions</th>
<th>Precautions</th>
<th>Rehab Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="http://www.pdr.net/drug-summary/Prozac-fluoxetine-hydrochloride-3205.2826">http://www.pdr.net/drug-summary/Prozac-fluoxetine-hydrochloride-3205.2826</a></td>
<td><a href="http://www.webmd.com/interaction-checker/">http://www.webmd.com/interaction-checker/</a></td>
<td>• SSRI • Boxed warning – suicidal ideation</td>
<td>• Incision site • Bleeding • Easy bruising • (Coumadin – INR monitoring) • Synergy possible w/ Prozac &amp; Coumadin</td>
</tr>
</tbody>
</table>

Keep in mind -

- We’re not the expert
- There are multiple sources of information available
- Be pro-active and ready with information *before* its needed
- Be responsible and *always* screen your patient’s meds
- Establish relationships with prescribing healthcare professionals
References


