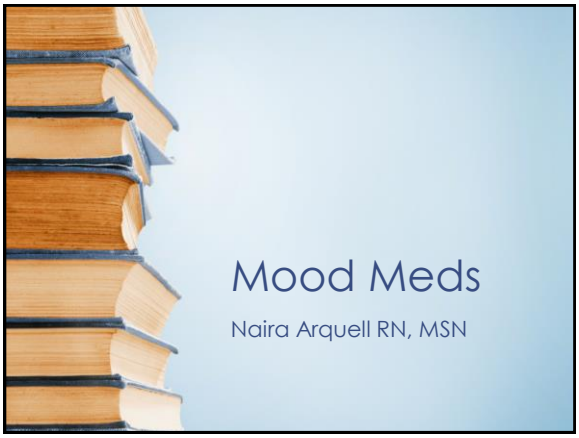


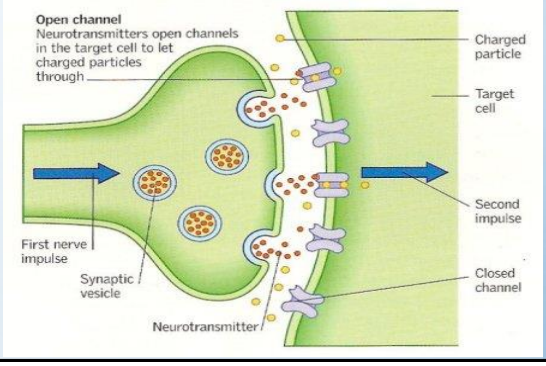
Objectives

- Identifies the general classifications of antidepressants
- Analyzes the implementation of the nursing process in the safe administration of antidepressants.
- Discusses the pharmacodynamics/ pharmacokinetics of antidepressants
- Describes the nursing implications with emphasis on the teaching points in the use of antidepressants

Objectives

- Discusses the pharmacodynamics/ pharmacokinetics of mood stabilizers
- Identifies commonly used mood stabilize
- Discusses the nursing implications with emphasis on the teaching points in the use of mood stabilizers
- Analyzes the implementation of the nursing process in the safe administration of psychotropic drugs: Mood stabilizers and Anti-depressants

Neurotransmitters



Neurotransmitters

- Scientists have theorized the depression results from a **deficiency** of biogenic amines in key areas of the brain:
  - Norepinephrine, Acetylcholine
  - Dopamine, GABA (gamma aminobutyric acid)
  - Serotonin, Glutamate
- Deficiencies of these neurotransmitters may develop for 3 reasons
  - Monoamine oxidase(MAO) may break them down
  - Rapid fire of neurons may lead to depletion
  - The number of sensitive receptors may increase depleting neurotransmitters level

Neurotransmitters

Acetylcholine (ACh)	It stimulates muscles, aids in sensory function, facilitates REM sleep, attention, motivation, learning, and memory. Too much ACh can lead to muscle spasms, tremors, and movement disorders. Insufficient ACh leads to a state of torpor(lethargy) or paralysis.
Dopamine	Dopamine is associated with brain reward mechanisms, arousal, and general physical motivation. Too much dopamine associated with Schizophrenia, while too little - Parkinson's disease and social anxiety disorders.

Neurotransmitters

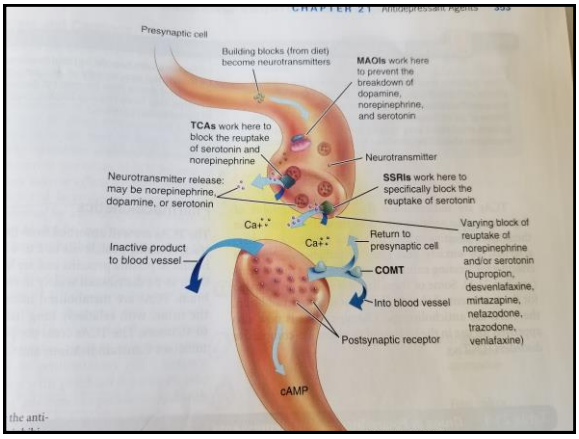
Endorphins (enkephalins)	Function similarly to opioids. Their presence reduces pain and effects pleasure, they tend to reduce stress, and enhance calm feelings.
GABA (gamma aminobutyric acid)	GABA slows the excitation that leads to anxiety. It's been linked to sleep and eating disorders. Too little GABA is associated with anxiety disorders and even epilepsy.
Glutamate	Glutamate is very important to memory function as well as how pain is perceived. Excess is associated with the destruction of brain cells, such as in ALS/ Lou Gehrig's disease.

Neurotransmitters

Norepinephrine (noradrenalin)	(Nobel Prize). This is the "high alert" transmitter- increasing heart rate and blood pressure to deal with stress or danger. It prompts physical and mental arousal, and can elevate the mood, also important for forming lasting memories.
Serotonin	Not enough serotonin accompanies depression, excessive carbs cravings, sleep troubles, anger control issues, migraines, irritable bowel syndrome, fibromyalgia, obsessive-compulsive disorder, and an increase in suicide related thoughts and acts

Medications affecting mood include Antidepressants and Mood stabilizers

- Herbal remedies- St. John's wort and ginkgo biloba
- Antidepressants
  - Tricyclic antidepressants (TCA)
  - Monoamine oxidase inhibitors (MAOI)
  - Selective serotonin reuptake inhibitors (SSRI)
  - Non-selective serotonin reuptake inhibitor (NSRI)
- Mood stabilizers
  - Lithium
  - Off label use of anticonvulsants



Herbal remedies- St. John's wort and ginkgo biloba

- Caution
- Self treating
- Drug-herb interactions
- Need for collaboration

Tricyclic Antidepressants (TCA)

- Antipruritic(itching)
- Antibulemic
- Antineurotic
- Antinarcolepsy adjunct -periods of excessive daytime sleepiness that usually last from seconds to minutes and may occur at any time.
- Antipanic
- Anti OCD(obsessive-compulsive disorder)
- Anticataplexic (muscle weakness)
- Antineuralgic(nerve pain)
- Antiulcer

Tricyclic Antidepressants (TCA)

- Amitriptyline (Elavil)
  - Depression with or without melancholia
- Clomipramine HCL (Anafranil)
  - Depression and obsessive-compulsive disorder
- Doxepin HCL (Sinequan)
  - Depression and anxiety r/t bipolar disorder

Tricyclic Antidepressants (TCA)

- TCA in the brain block the re-uptake of
  - Norepinephrine-
  - Serotonin-
  - Leads to accumulation of this neurotransmitters in the synaptic cleft and increases stimulation of post-synaptic receptors

TCA Contraindication and cautions

- Allergic reaction- risk for hypersensitive reaction
- Recent MI- can get worse
- Preexisting CV – can exacerbate anticholinergic side effects (glaucoma, urinary retention, BPH, etc.)
- Myelography- possible drug-to-drug interaction
- Concurrent use with MAOI- potential for toxic reaction
- BBW- increased suicidality (children, adolescents, and young adults)

Anticholinergic side-effects

- Dry as a bone
- Blind as a bat
- Hot as a hare
- Red as a beet
- Mad as a Hatter

Anticholinergic side-effects

ABCDE

Agitation and hallucinations

Blurred vision and mydriasis

Convulsions

Dryness(skin, constipation, urinary retention)

Elevated temperature and HR

Anticholinergic syndrome

Can be caused by:

- Anticholinergics
- Antihistamines
- Antipsychotics
- Antispasmotics
- Cyclic antidepressants
- Mydriatics
- Plants e.g. Datura

TCA toxicity

- **TCA overdose** is **poisoning**
- **Symptoms** may include
  - elevated body temperature, blurred vision,
  - dilated pupils, sleepiness,
  - confusion, seizures,
  - rapid heart rate, cardiac arrhythmias, and cardiac arrest. …

  The **toxic** dose depends on the specific **TCA**.

TCA drug to drug interaction

- TCA and anticoagulants lead to an increase serum level of anticoagulants- **risk for bleeding**
- Concurrent administration with clonidine- increased **risk for arrhythmias and hypertension**
- TCA and MAOIs leads to increased risk of severe hyper pyretic crises with severe convulsions, hypertensive episodes, and death.
- Please check drug book for additional drug to drug interaction

TCA nursing considerations

- **Assess for :** - Known allergies, history of seizures and psychiatric or suicidal thoughts, impaired kidney and liver function(which could alter metabolism and excretion of the drugs), cardiac dysfunction, recent MI, GI obstruction, and pregnancy and lactation
- Full patient assessment-to determine baseline before therapy
- **Monitor** lab work(liver and kidney function), obtain EKG, monitor adverse and side effects
- Evaluate the effectives of TCA therapy

Nursing implications for TCA toxicity

- A – B – C
- GI decontamination
- ECG abnormality – sodium bicarbonate
- Control agitation
- Fever control
- Physostigmine…umh

Monoamine Oxidase Inhibitors (MAOI)

- Monoamines (norepinephrine, dopamine, serotonin, histamine) and mood
- MAO and COMT (Catechol-o-methyl-transferase)
- MAOI – as a medication
  - phenelzine (Nardil)
  - isocarboxazid (Marplan)
  - tranylcypromine (Parnate)

Therapeutic action and Indication (MAOI)

- Blocking the breakdown of nor-epinephrine, dopamine and serotonin
- Accumulate neurotransmitters in synaptic cleft and in neuronal storage vesicles

Monoamine Oxidase Inhibitors Indication

- Depression
- No the first choice for treatment. However is still being used for depression that does not respond to other antidepressants especially atypical depression
- **Adverse effect**-allergy, CV emergency, stroke, renal/hepatic impairment,⬆ suicidality(BBW)
- MAOI poisoning
  - Overdose
  - Drug-food interaction
  - Drug-drug interaction

Drug-food interaction

- Tyramine containing foods ⬆ BP-HTN crisis
  - High – avoid
  - Moderate –occasionally
  - Low – limited quantities
  - Aged cheese, raisins, fava beans, Chinese pea pods, red wine, pickled herring, soy sauce, brewer's yeast, smoked/processed meats, caviar, chicken or beef liver, MSG, gouda cheese, processed American cheese, mozzarella, yogurt, sour cream, avocado, bananas, beer, white wine, coffee, colas, tea, hot chocolate, pasteurized cheeses

Drug-drug interaction

- Sympathomimetic effect will increase if given with methyldopa
  - Diet pills
  - OTC
- Dextromethorphan
- Other antidepressants(hypertensive crisis, coma, severe convulsions, and serotonin syndrome with SSRIs) 6 week must relapse after stopping SSRI to start patient on MAOI
- Combination with insulin or oral antidiabetic agents increases hypoglycemic effect

MAOI Poisoning

- Hypertensive crisis
- Severe toxicity – hyperthermia, Seizure, respiratory depression

Nursing consideration and intervention

- Nursing
  - Vital signs(BP, HR, Neuro, Cardiac, Respiratory, Elimination obstruction), known allergies
  - Cooling measures
  - Determine whether female pts are pregnant, breastfeeding
  - Teaching and Patient Safety
- Collaborative
  - IV fluids
  - Benzodiazepines
  - Short acting antihypertensive

SSRI and other antidepressants

- Selective Serotonin Reuptake Inhibitor(SSRI)- citalopram(Celexa), escitalopram (Lexapro), fluoxetine (Prozac),paroxetine(Paxil), sertraline (Zoloft)
- Serotonin norepinephrine re-uptake inhibitor(SNRI)- desvenlafaxine (Pristiq), duloxetine(Cymbalta), venlafaxine (Effexor), venlafaxine XR(Effexor XR)
- Noradrenergic and Specific Serotonergic Antidepressant- mirtazapine(Remeron)

Selective Serotonin Re-uptake Inhibitor (SSRI)

- The action is to block the reuptake of **serotonin** and increase level at synaptic cleft
- Indicated for the treatment of Depression, OCDs, panic attacks, bulimia, posttraumatic stress disorders, social phobias, and social anxiety disorder
- Takes up to 4 weeks to get full therapeutic effect
- The choice of drugs depends on the indication and patient's response

Selective Serotonin Re-uptake Inhibitor (SSRI)

- Contraindications
  - Allergy hypersensitivity
  - Impaired renal and liver function
  - Diabetic patients(exacerbation)
  - Increased risk for suicide
  - Possible congenital defects – weigh the benefits and risks
- Adverse effects- assess neuro, CV, Respiratory, GI and GU, Liver, and etc.

SSRI- drug to drug interaction

- Avoid combining with MAOI(2-4 weeks between them)
- SSRI and ATC- increased therapeutic and toxic effects
- Serotonin syndrome when combined with any drugs that increase serotonin level
  - Other SSRI, SNRI, St. John's wort, and etc.
  - Risk for bleeding combined with Aspirin, NSAIDs, antiplatelet

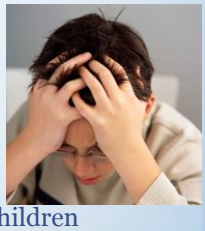
SSRI- Nursing consideration

- Nursing
  - Arrange for lower dose for elderly and those with impaired kidney and liver function
  - Monitor the patient for up to 4 weeks before adjusting the dose
  - Suicide screening and precautions
  - Suggest to use barrier contraceptives due to serious fetal abnormalities
  - Comfort measures- bowel and bladder program, take medication with food, environmental control
  - Patient teaching

Serotonin Norepinephrine re-uptake inhibitors (SNRI)

- Combining the system arousal effects of increased norepinephrine with the positive mood benefits of serotonin may be a good combination for some clients struggling with depression.
- SNRIs also tend to have a weak dopamine reuptake effect.
- Safety and tolerability of the SNRIs are similar to the SSRIs, although monitoring is warranted for an uncommon sustained rise in blood pressure.

SSRI AND SNRI cost - benefit



- Expensive
- Tolerable side effects
- Sexual dysfunction
- Wide margin of safety
- Increased suicide rates in children

- *Did somebody say NO grapefruit ?*

Mood stabilizers

- Mood stabilizers are medications that buffer the dramatic emotional rollercoaster ride which accompanies
  - **Bipolar Affective Disorder**
  - **Schizoaffective**
  - **Manic**
  - **Major Depressive Syndromes**

Mood stabilizers

- Mood stabilizers are the mainstay treatment for acute mania
- Used to induce remission in those individuals experiencing symptoms of hypomania, manic episodes
- Aid to stabilize mood swing cycles into a maintenance range closer to what that person's normal would be
  - Lithium
  - Anticonvulsants- off label use

Lithium

- Lithium (Lithobid) is a mainstay and consistently effective treatment for mania
- Indication - Bipolar disorder
- Inhibits the release of norepinephrine and dopamine from stimulated neurons
- Increases sensitivity of serotonin receptors (we think)
- Absorbed from GI tract, peaks in 30 min-3 h
- Competes with Na - low Na in the system...more Lithiu being reabsorbed by the kidney-→ lithium toxicity

Cost and Benefit

- Very effective and cost is around $16 per month
- Disabling adverse effects
- Narrow therapeutic range
- Drug-drug interaction
- Decreases thyroid
- Diet restriction

Pros and Cons

- A first-line, long-term treatment for bipolar disorder. Effective at stabilizing mood and preventing relapse.
- For manic episodes (acute mania), more effective when taken together with an antipsychotic medicine.
- Lowers the risk of suicide, possibly because it lowers aggressiveness and impulsivity.
- Has many short- and long-term side effects.
- Small therapeutic range, get help immediately if you accidentally take too much.
- Not safe if you have kidney, cardiac problems, pregnant or breastfeeding.
- Requires routine blood tests to see how the medicine is affecting your body

Lithium toxicity

- Therapeutic level 0.6-1.4 mEq/L- lethargy, slurred speech, muscle weakness, giddiness, fine tremor, polyuria(renal toxicity), beginning of GI toxicity with N/V/D
- 1.5 - 2.0 mEq/L- intensification of all problems with ECG changes
- 2.0 – 2.5 mEq/L- progression of CNS effects to ataxia, muscular rigidity, convulsions, psychomotor retardation, confusion, excessive diluted urine, CV9 severe ECG changes and hypotension
- > 2.5 mEq/L- complex multi-organ toxicity with a significant risk of death

Patient teaching

1. Therapeutic action and indication
2. Contraindications
3. Adverse effects
4. Clinically important drug to drug interaction

So the low sodium diet is for his heart failure !?!

Anticonvulsants as mood stabilizer

- Valproic acid (e.g. Depakote, Depakene)
- Carbamazepine (Tegretol)
- Lamotrigine (Lamictal)
- Gabapentin (Neurontin)
- .....e.t.c....

Valproic acid

- Serious adverse effects- toxicity
- Therapeutic range
  - acute mania 50 – 125 mcg/mL
  - MAX recommended dose 60 mg/kg/day

Valproic acid

- Toxicity
- → 200mcg/mL → CNS depression
- → 400 mcg/mL → Multi-organ toxicity
- ANTIDOTE : L-Carnitine
- > 750 mcg/mL →

Drug therapy across the lifespan

- Adults
  - Rule out all other medical causes prior to therapy
  - Effects of drug therapy may not be seen for 4 weeks, need to take meds for at least 1 month
  - Has potential for adverse effects on Fetus (CV, respiratory, neurological)

Drug therapy across the lifespan

- Older Adults
  - More susceptible for adverse effects
  - Doses need to be reduced and client monitored closely
  - Patients with hepatic and renal impairment should be screened carefully and closely monitored

Drug therapy across the lifespan

- Children
  - Child response is unpredictable and long term effects are not clearly understood
  - TCA's- established doses for children >6 y, closely monitor for adverse side effects, change dose as needed based on age and weight
  - MAOI's-should be avoided at all if possible9drug-to-grug and severe adverse effects)
  - SSRI's- can cause serious adverse effects, should be monitored closely for suicide ideation

Name (Generic)	Brand Name	Normal Serum Level	Weight Effect
Carbamazepine	Epitol, Tegretol	4-12mcg/mL	Neutral
Divalproex sodium	Depakote	50-125 mcq/mL	Increase
Lamotrigine	Lamictal	n/a	Neutral
Lithium carbonate	Eskalith, Lithobid	0.5-1.2mEq	Increase
Oxcarbazepine	Trileptal	n/a	Neutral
Valproic acid	Depakene	50-125 mcq/mL	Increase