

Medications Affecting the Central Nervous System

- Antipsychotic Medications, Antianxiety, and Sedative Hypnotic Drugs
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Simplified Review of Neuro Transmission

- All of the psychopharmacological drugs produce their effects by altering the communication among neurons in the CNS by influencing synaptic transmission.

Steps in Synaptic Transmission

1. Synthesis- molecules of the transmitter must be present within the nerve terminal.
2. Storage-once the transmitter is synthesized, it must be stored until it is released. Storage takes place in vesicles, tiny packets in the axon terminals.
3. Release- a release of transmitters into the synaptic gap triggered by the arrival of an action potential.

Steps- Contd.

4. Receptor binding- transmitter molecules travel across the synaptic gap and bind to the receptors on the post synaptic neuron. Results in excitation or inhibition of the post synaptic neuron.
5. Termination- removal of free transmitters from the synaptic gap by: **reuptake** into the presynaptic neuron, enzymatic degradation, Diffusion away.

Effects of Drugs on Synaptic Transmission

- The drugs work on the level of change at one of these steps.
 1. Synthesis-increase or decrease of transmitters. Increases the amount stored in the presynaptic vesicles or decreases it.
 2. Transmitter storage-drugs that interfere with synaptic storage decrease the amount of transmitter available for release.

Effects of Drugs.....

3. Transmitter release-drugs can promote or inhibit release. Intensifying or suppressing transmission.

4. Receptor binding-Drugs acting at the receptors: bind to receptors and cause receptor activation, bind to receptors and prevent receptor activation by the natural transmitter, bind to the receptors and enhance the action of the natural receptors at the site.

The process is complex and we still do not know everything about how it works. Many things affect neuro transmission including diet, physical wellness of the person, immune function.

Psychoneuroimmunology

- Other things which effect neurotransmission are mind-body practices such as meditation (increases serotonin levels).

Antianxiety Agents

- Antianxiety agents- promote relaxation and and in larger doses the same drugs can promote sleep.
- Benzodiazepines- are the drugs most commonly prescribed for anxiety and or insomnia. Replaced the barbiturates in the 1960s.
- Barbiturates are less safe in that they are potent respiratory depressants and can be fatal in overdose, have a high potential for abuse, produce physical tolerance and dependence.

Benzodiazepines (Prototype is Valium)

Indications for Use:

- Anxiety and anxiety disorders
- Hypnotic agents- promote sleep
- Anticonvulsant agents- prevent seizures
- Pre-op sedation
- Prevention of Delirium tremens in alcohol withdrawal
- Muscle relaxant

Benzodiazepine

Indications for Use:

- Given concurrently with antidepressants, antipsychotics, and mood stabilizers to treat the manifestation of anxiety in psychosis, depression, and mania.

Symptoms of Anxiety:

- Worry (becomes classified as a disorder when meets the diagnostic criteria of DSM 4- worry about two or more circumstances and multiple symptoms for 6 months or longer).
- Restlessness, muscle tension, sleeplessness, difficulty concentrating, trembling, tachycardia

Benzodiazepines

- Method of Action- enhance the inhibitory effect of GABA to relieve anxiety, nervousness and produce sleep.
- Have a wider margin of safety (compared to barbiturates) between therapeutic doses and toxic doses. Rarely are lethal unless combined with other CNS depressants such as alcohol.

Benzodiazepines

Principles of therapy:

- Prescribed for short term use only to be coupled with teaching the patient life management skills for coping with anxiety, stress reduction techniques.
- Can cause physical and psychological dependence. Withdrawal symptoms will occur if stopped abruptly. Must taper.
- CNS depression, sedation, impairment of physical and mental abilities, respiratory depression.

Benzodiazepines

Contraindications:

- Severe respiratory disorders
- Severe liver or kidney disease(are metabolized in the liver)
- A history of alcohol or drug abuse (may trigger relapse). Ask patient and spell out that the drug may cause physical/psychological dependence and should only be used short term.
- Not to be used in combination with other CNS depressants

Side Effects of Benzodiazepines

- Excessive sedation
- Hypotension
- Paradoxical excitement
- Withdrawal or abstinence syndrome

Benzodiazepines

Dosage/Scheduling

- The lowest effective dose that does not cause excessive daytime drowsiness or impaired mobility. Short term
- The longer acting benzo's such as Valium (see table 8-2) can be given at HS to promote sleep. Shorter acting ones such as Xanax and Ativan have to be given TID or QID.
- If hospitalized patient has been taking them at home must not stop or patient will experience withdrawal(anxiety, agitation, insomnia, irritability, headache, tremors)

Management of Benzodiazepine Toxicity

- Accidental or intentional overdose and or reversal of sedation after diagnostic or therapeutic procedures.
- Romazecon (Flumazenil) a the antidote- competes at the benzodiazepine receptor sites and reverses sedation, coma, respiratory depression.
- It is short acting and if given to a patient who has taken a long acting benzo re sedation and hypoventilation will reoccur when Romazecon wears off (half life 60-90 minutes.)

Other Antianxiety Agents

- Buspirone-Buspar
- Acts with Serotonin and Dopamine receptors in the brain
- No muscle relaxant effect, no anticonvulsant effects, no physical/psychological dependence
- No increase in CNS depression if patient drinks alcohol (drug of choice for the patient with a history of substance abuse)
- No sedative effects
- Optimal effects may take up to 3-4 weeks. Not for quick effect. Must explain to patient.

Other Antianxiety and Sedative Hypnotic Drugs

- Hydroxyzine (Vistaril) an antihistamine used for anxiety, pre-op sedation, nausea and vomiting
- Diphenhydramine (Benadryl) antihistamine

Nursing Implications

Teaching:

- Teach patient to identify and avoid factors that cause or contribute to anxiety such as caffeine use, and any stimulant medications such as cold remedies and appetite suppressants.
- Assess patients knowledge and use of relaxation techniques. Be able to teach abdominal breathing, progressive muscle relaxation, imagery, and meditation techniques.
- What has patient tried? Is music a tool patient uses but is unaware of it's potential for anxiety reduction? How about prayer? Exercise? Humor?

Nursing Implications

- Has patient looked at life style issues such as working too many hours with no mental time off?
- Is patient able to “ shut off” his/her mind at night?
- Is patient getting enough sleep? Spending time with significant others in pleasurable activities?

Antipsychotic Medications

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Psychosis

Definition- a severe mental disorder characterized by disordered thought processes, bizarre thinking, blunted or unusual emotional responses, behavior ranging from hypoactivity to hyperactivity with agitation, autism (self absorption with no attention to other people or the environment), deterioration in previous level of functioning at occupational or social level. Difficulty with interpersonal skills and activities of daily living such as self care, cooking, eating.

Psychosis

- Hallucinations-sensory perceptions of people or objects that are not present in the environment. Hear, see, feel things that other people do not.
- Can not distinguish between false perceptions and reality
- Delusions-False beliefs that persist in the absence of reason or evidence. Can't present evidence and change the person's mind.
- May be due to Schizophrenia, delirium, toxic effects of medications or drugs, dementia, sleep deprivation, metabolic disorders, infection, drug withdrawal.

Psychosis

- Schizophrenia- etiology unclear. Thought to be related to increased dopamine activity in the brain . Other neurotransmitters such as serotonin may play a part.
- Antipsychotic drugs work by blocking dopamine, thereby decreasing dopamine activity.

Schizophrenia

Symptoms:

- Positive symptoms- Characteristics and behaviors that are present in the patient which are **not** present in people who do not have schizophrenia. Sometimes thought of as exaggeration or distortion of normal function. **Hallucinations, delusions, agitation.**

Schizophrenia

Symptoms:

- Negative symptoms-A lack of the characteristics or behaviors that people who do not have schizophrenia would have. A loss or diminution of normal function. Lack of motivation, poverty of speech,poor self-care,social withdrawal, blunted affect.
- Traditional antipsychotic medications have had a greater effect on the **positive symptoms. The newer atypical antipsychotics have been effective against the negative symptoms as well.**

Mechanism of Action

- Thought to block dopamine receptors in the brain and cause a decrease in arousal.
- Full therapeutic effects occur gradually over 1-2 months.
- Patient may experience a decrease in agitation, aggression, hostility in the first week and normalization of sleeping and eating.
- Full effect on symptoms such as hallucination, delusions may take longer.

Indications for Use

- Treatment of Schizophrenia- the goal is to treat the acute symptoms so that patients can participate in therapy, groups, return to community settings and their previous level of functioning.
- Want to increase the patients ability to cope and handle a degree of self care.
- Prevent exacerbations and frequent hospitalizations due to acute episodes.
- May be used in the manic phase of bipolar disorder until other drugs become effective.

Indications for Use

- Also used to treat psychotic symptoms in patients with brain impairment from head injury, CVA, brain tumors, alcohol withdrawal, over doses of CNS stimulants
- Also used in the treatment of nausea and vomiting (Phenergan and Compazine) and intractable hiccups (Thorazine)

Contraindication and Side Effects

- Contraindicated in patients with liver disease, CAD, Parkinsonism, bone marrow depression, cerebrovascular disease, coma, severe hypo or hypertension.
- Use with caution in patients with seizure disorder as they lower the seizure threshold.

Side Effects

- Anticholinergic Effects- dry mouth, blurred vision, photophobia, urinary retention, constipation, and tachycardia.
- Orthostatic hypotension
- Sedation
- Seizures
- Sexual dysfunction- suppression of libido. And impair the ability to achieve orgasm. A factor in non compliance
- Increased risk of sunburn- use sunscreen

Side Effects

- Agranulocytosis- rare , but can be fatal.
Monitor WBCs
- Gynecomastia and in men and amenorrhea in women due to blocking the usual inhibitory action of dopamine on prolactin.

Adverse Effects

- Extrapyramidal reactions are movement disorders. These drugs affect the extrapyramidal motor system (same tract involved in the disease of Parkinson's)
- Four types of extrapyramidal reactions: acute dystonia, parkinsonism, akathisia. These three occur early in therapy and can be managed with other drugs.
- The fourth one is Tardive Dyskinesia occurs late in treatment and can not be treated and is irreversible

Adverse Effects

- Neuroleptic Malignant Syndrome (NMS)
- Symptoms: Severe muscle rigidity, hyperpyrexia, tachycardia, diaphoresis, tachypnea, B/P fluctuations, altered mental status, coma, death.
- Notify MD, hold medication, assess V/S, LOC, muscle rigidity
- Parlodel or Dantrium may be given. ICU

Adverse effects

- Hyperglycemia and diabetes
- Especially with the atypical antipsychotics
- Monitor blood sugar

Categories of Antipsychotic Drugs

- Oldest group is the Phenothiazines- 1950's also called typical
- Thorazine, Mellaril, Trilafon see chart on page 169 of text.
- Can be given PO tablets, liquid concentrate (faster acting) IM.
- Prolixin and Haldol come in a longer acting form that is called decanoate and can be dosed once a month IM for the patient with difficulty in compliance with medications usually due to residual negative symptoms.