Anti-depressant drugs

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Introduction

Antidepressants are drugs that relieve the symptoms of depression. Classes of antidepressant agents are defined by their mechanism of action.

Definition

Anti-depressants are used in the treatment of depression to elevate mood, increase physical activity & mental alertness, improve appetite & sleep, and restore interest or pleasure in usual activities and things previously enjoyed.

Indications for Anti-depressants

- Major depressive disorder.
- Dysthymia.
- Anxiety disorders and obsessive compulsive disorder.
- Eating disorders.
- Dysmenorrhoea.
- Migraines.
- Attention-deficit hyperactivity disorder (ADHD).
- Substance abuse and sleep disorders.

Contraindications:

- Hypersensitivity.
- Impaired liver or renal function.
- Acute recovery phase in myocardial infarction.
- Respiratory disorders.
- Hypertension, Hyper thyrodism, Glaucoma, and diabetes mellitus
- Urinary retention or obstruction and benign prostatic hypertrophy.

Classifications of anti-depressants

Depending on when they were first introduced, antidepressants are sometimes described as:

- *First:* (tricyclic antidepressants (TCAs), or monoamine oxidase inhibitors (MAOIs)
- *Second:* selective serotonin reuptake inhibitors (SRRIs)
- *Third generation antidepressants:* known as serotonin-norepinephrine reuptake inhibitors (SNRIs).

Monoamine oxidase inhibitors (MAOIs)

The most common MAOIs are:

- Phenelzine (Nardil)
- Isocarboxazid (Marplan)
- Tranylcypromine (Parnate)
- Selegiline (Tonus)

Mechanism of action of MAOIs:

- MAO exists in two subtypes, A and B. The original MAOIs are nonselective, inhibiting both forms. The A form of MAO preferentially metabolizes serotonin (5-HT) and NE.
- Inhibition of the enzyme monamine oxidase, which is responsible for the decomposition of the biogenic amines, epinephrine, norepinephrine, dopamine, and serotonin. This action results in an increase in the concentration of these endogenous amines.

Drug-drug interaction Of (MAOIs)

MAOIs-drugs interaction:

- Serious, potentially fatal adverse reactions may occur with concurrent use of other CNS antidepressants.
- Hypertensive crisis may occur with amphetamines, methyldopa, levodopa, dopamine.
- Additive hypotension may occur with antihypertensives, thiazide diuretics, or spinal anesthesia.
- Hypertensive crisis may occur with ingestion of foods or other products containing high concentrations of tyramine.

Tyramine Reaction:

- Utilizing MAOIs has often been considered risky due to the potential of developing a hypertensive crisis.
- Ingesting high amounts of tyramine from the diet, Tyramine is a potent releaser of NE and can thus elevate blood pressure. Normally, NE cannot accumulate to dangerous levels, due to the efficient destruction of NE by MAO-A.

- When MAO-A is inhibited, the capacity to handle dietary tyramine is significantly reduced. A high-tyramine meal is sufficient to increase blood pressure when a substantial amount of MAO-A is irreversibly inhibited.
- 20 min to 1 hr. after ingestion tyramine has both direct and indirect sympathomimetic actions.

Hypertensive crisis:

- Is the most severe side effect. A sudden severe increase in blood pressure caused by high tyramine level, intracranial hemorrhage and death may result.

Signs and symptoms of hypertensive crisis:

- Sudden elevation of blood pressure higher than (170/110 mmHg).
- Explosive occipital headache.
- Head and face flushed and feel 'full'.
- Palpitation and chest pain.
- Sweating, fever, nausea, and vomiting.
- Dilated pupil and photophobia.

Treatment of hypertensive crisis:

- Stop MAOIs doses.
- Monitor vital signs frequently.
- Administer short acting antihypertensive medications as ordered by physician.
- Do not lie down.
- I.M chlorpromazine (antipsychotic) 100mg.
- I.V phentolamine, administer slowly in dose of 5 mg.
- Manage fever by external cooling technique.
- Evaluate diet adherence and teaching.

Con.

- An MAOI-induced hypertensive crisis can be treated with alpha adrenergic antagonists such as phentolamine or even chlorpromazine. This can lower blood pressure in few minutes.

Tyramine rich food that should be avoided:

- Aged cheeses. chocolate, colas, coffee, tea, sour cream, smoked and processed meats. which are meats treated with salt and nitrate or nitrite, such as dry-type summer sausages.
- Fermented cabbage.

- Soy sauce, fish sauce and shrimp sauce.
- Yeast-extract spreads, such as Marmite.
- Improperly stored foods or spoiled foods.
- Broad bean pods, such as fava beans.
- Tyramine amounts can vary among foods due to different processing, storage and preparation methods.

Side effects of MAOIs:

The most common side effects of MAOIs include:

- Dry mouth
- Nausea, diarrhea or constipation
- Headache
- Drowsiness, Dizziness or lightheadedness
- Insomnia
- Skin reaction.

- Involuntary muscle jerks
- Weight gain
- Difficulty starting a urine flow
- Muscle aches
- Prickling or tingling sensation in the skin (paresthesia)

Tricyclic antidepressants

Tricyclic antidepressants:

Tricyclic antidepressants are the second oldest class of antidepressant drugs. Tricyclics block the reuptake of certain neurotransmitters such as norepinephrine (noradrenaline) and serotonin. They are used less commonly now due to the development of more selective and safer drugs.

Generic name	***Trade name***
Amitriptyline	Elavil, Endep
Amoxapine	Asendin
Clomipramine	Anafranil
Desipramine	Norpramin, Pertofrane
Doxepin	Adapin, Sinequan
Imipramine	Tofranil
Nortriptyline	Pamelor, Aventyl

Mechanism of action of tricyclic antidepressants:

- Noradrenaline and serotonin are released from nerve cells they act to lighten mood. When they are reabsorbed into the nerve cells, they no longer have an effect on mood. TCAs work by preventing this reabsorption of noradrenaline and serotonin back into the nerve cells.

This prolongs the mood-lightening effect of any released noradrenaline and serotonin and in this way helps to relieve depression.

Side effects of tricyclic antidepressants

1- specific side effects:

- Sedation.
- Anticholinergic induced delirium.
- Amoxapine may cause neuroleptic malignant syndrome.
- The possibility of inducing manic episode and other psychotic disorders.

2- Non specific side effects:

1- Mild anticholinergic effects:

- Dry mouth, Blurred vision, Constipation
- Paralytic ileus, Urinary retention.
- Exacerbation of narrow angle glaucoma.

2- Cardiovascular effect:

- Increased heart rate, Arrhythmia.
- Low blood pressure, which can cause lightheadedness.

3- Endocrine and sexual effect:

- Impotence, glactorrea, amenorrea.
- Increased appetite, Weight gain.
- Ejaculatory dysfunction and Delayed orgasm and low sex drive, in men.

4- Allergic reaction:

- Skin rash or skin eruption.
- In Tricyclics, discontinuation syndrome symptoms include anxiety, insomnia, headache, nausea, malaise, or motor disturbance.

Selective Serotonin Reuptake Inhibitors (SSRIs)

- **SSRIs are recommended as first-line therapy in all depressions because:**
- Lower incidence of anti- cholinergic side effect.
- Less cardiac toxicity.
- Faster onset of action than the TCAs.
- The SSRIs seem to be effective on depressions with anxious feature and cause fewer side effects

SSRIs:

- Fluoxetine (Prozac).
- Sertraline (Zoloft).
- Paroxetine (paxil).
- Fluvoxamine (Faverin).
- Citalopram (Celexa)

SSRIs:

- SSRIs are called selective because they seem to affect serotonin significantly more than other neurotransmitters.
- Thus, the medications work by allowing the body to make the best use of the reduced amounts of serotonin that it has at the time.

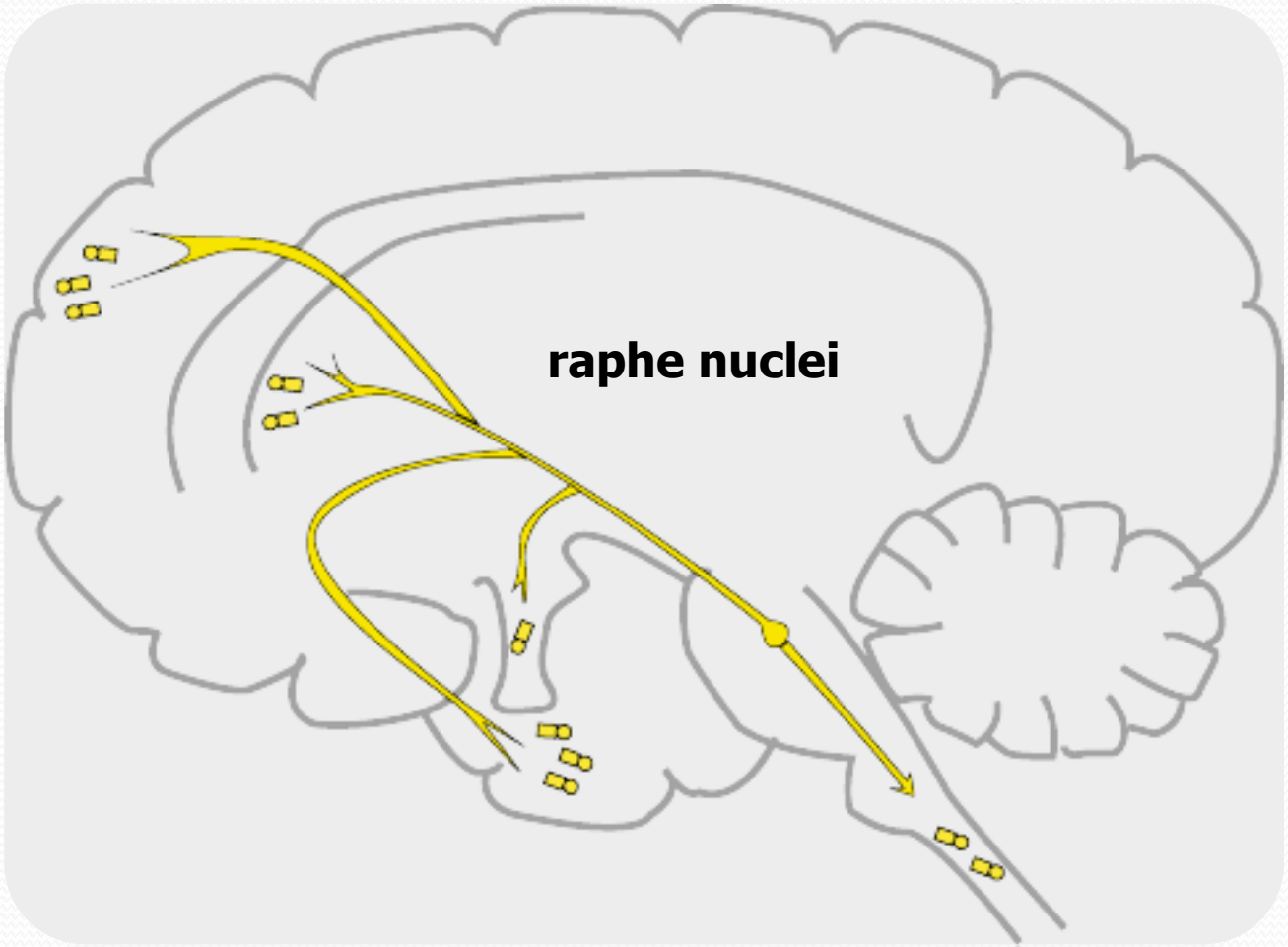
Con.

- All selective serotonin reuptake inhibitors have the same general mechanism of action. SSRIs seem to relieve symptoms of depression by blocking the reabsorption (reuptake) of serotonin by certain nerve cells in the brain.
- This leaves more serotonin available, which enhances neurotransmission and improves mood.

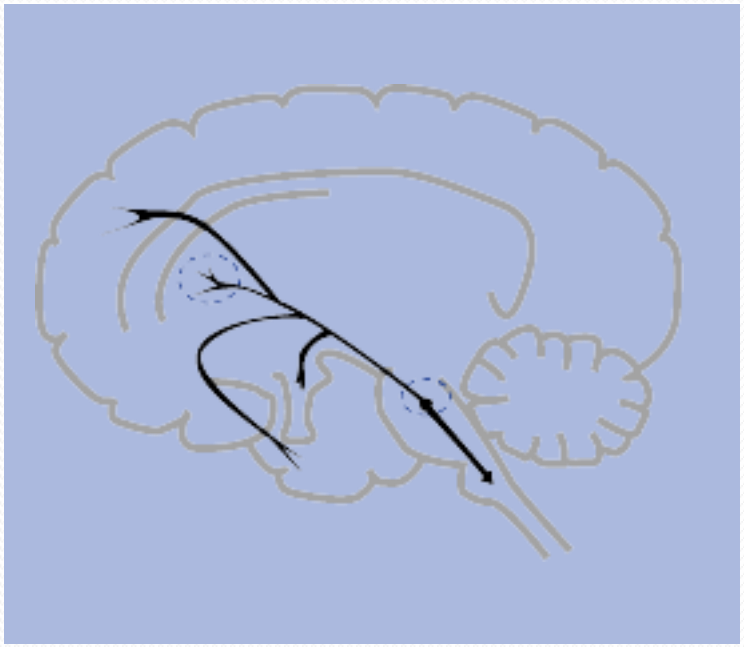
Con.

- The major site of serotonergic cell bodies in the brain is the **raphe nuclei** in the brainstem, from which fibers project to many brain structures, these include projections to:

Serotonin Pathways

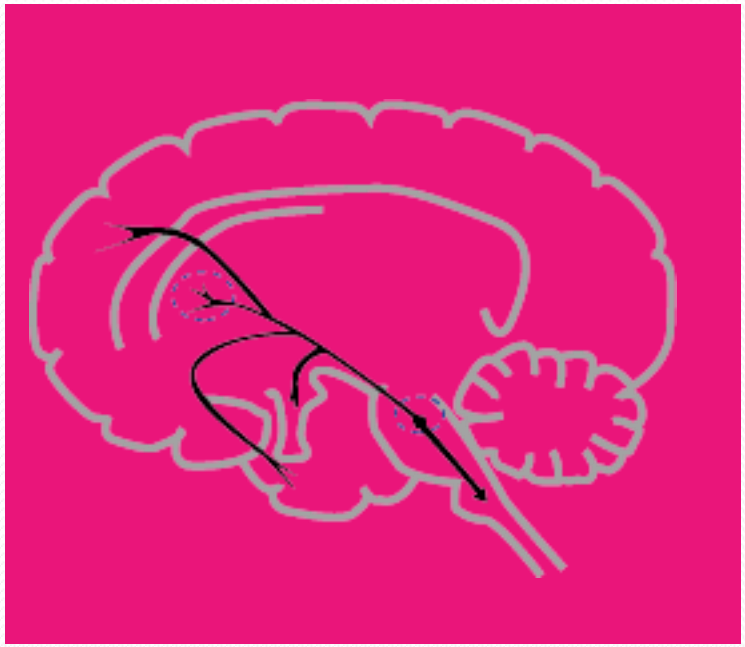


Frontal Cortex



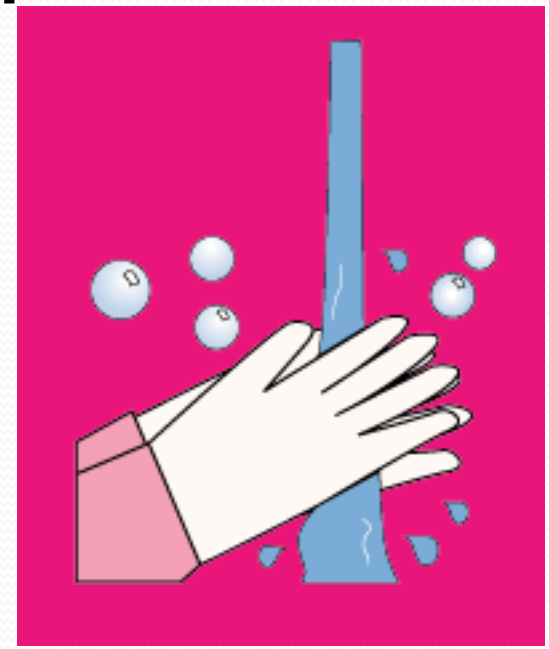
Mood

Basal Ganglia



Akathisia/ Agitation

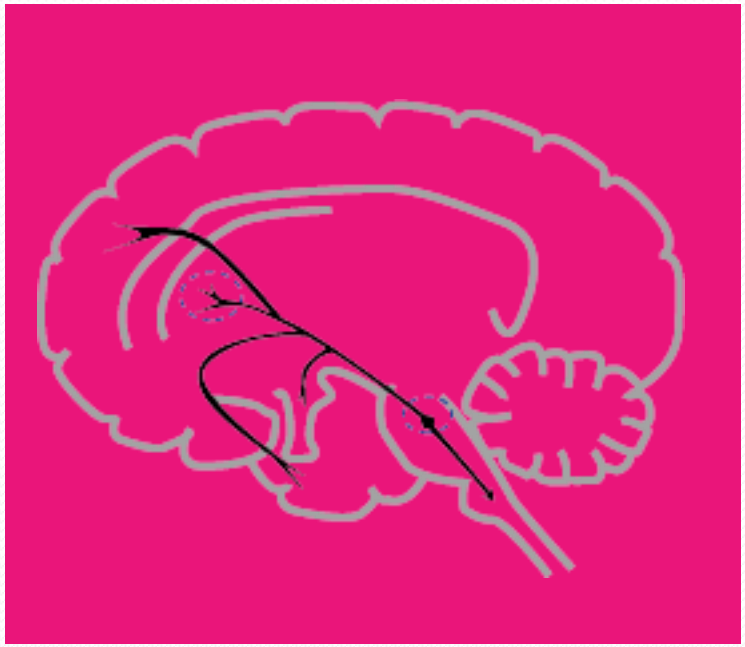
OCD



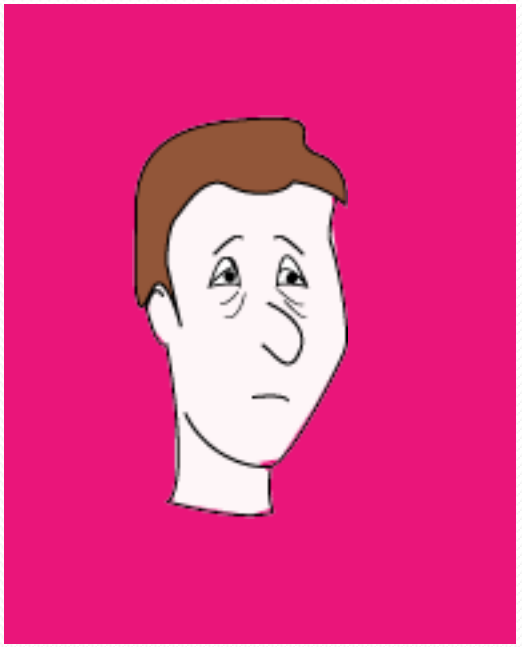
Limbic

Anxiety

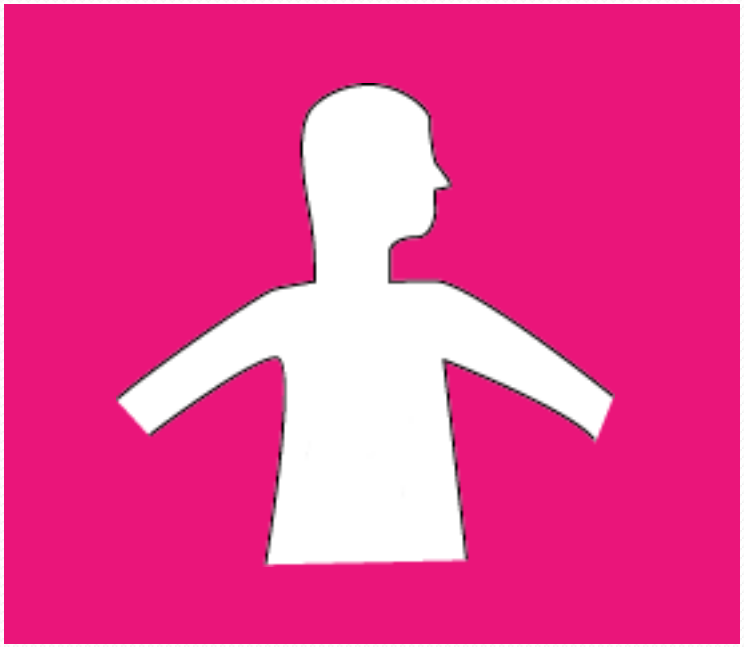
Sleep Centers



Insomnia



Gut



GI cramps/Diarrhea

- Frontal cortex: mood regulation (though presynaptic 5HTIA receptors).
- Limbic system: anxiety and panic feelings (5HT 2A-2C).
- Basal ganglia: movement control and compulsions (5HT2A).
- Hypothalamus: appetite and eating regulation (5HT3).

- Brainstem chemoreceptore trigger zone: vomiting (5HT3).
- Brainstem sleep centers: deep sleep (5HT2A) The ingestion of foods rich in tryptophan rapidly increases brain serotonin synthesis, which accounts for their mild sedating effects.
- Spinal cord: sexual spinal responses, orgasm (5HT2A).
- Periperal serotonergic receptors (5HT3-T4) in the intestine regulate intestinal motility.

Side effects of selective serotonin reuptake inhibitors

1- Serotonin syndrome:

- A rare but life –threatening adverse reaction to SSRIs that develops when blood level of serotonin elevated or it is occurs when there is an inadequate wish-out period between taking MAOIs and SSRIs or when MAOIs combined with SSRIs.

Signs and symptoms:

- Change in mental state (Anxiety, agitation and disorientation).
- Neuromuscular excitement (Muscle rigidity, tremors, weakness, sluggish pupils, shivering, muscle paralysis, cardiac collapse & death).
- Autonomic abnormalities (Hyperthermia, tachycardia, tachypnea, hyper-salivation & diaphoresis).

Treatment of Serotonin syndrome:

- Withdraw the offending agent.
- Supportive care: correction of vital signs.
- Benzodiazepines.
- 5HT2A antagonists: cyproheptadine, atypical antipsychotics, chlorpromazine (? mirtazapine – controversial reports).
- In severe cases neuromuscular paralysis and mechanical ventilation may be required.

2- Sexual effects:

- Inhibition of sexual orgasm.
- Decreased libido.

3- CNS effect:

- Insomnia and sedation.
- Vivid dreams and nightmares.
- Seizure.
- Extrapyramidal side effects.

4- GIT effects:

- Weight gain result from the drug use itself or from the increased appetite associated with better mood.
- Cramps and diarrhea.

Serotonin-norepinephrine reuptake inhibitors (SNRIs).

- *Serotonin-norepinephrine reuptake inhibitors* (SNRIs) are a newer form of antidepressant that works on both norepinephrine and 5-HT.

The most common (SNRIs)

- Desvenlafaxine (Pristiq)
- Duloxetine (Cymbalta)
- Milnacipran (Ixel)
- Venlafaxine (Effexor)

Mechanism of action:

- They interfere with re-uptake process of serotonin and norepinephrine. The re-uptake process would prolong the effects of the neurotransmitter on the postsynaptic neuron. Changing the balance of serotonin and norepinephrine would help the brain cells send and receive messages; therefore boosting the mood. That also is the main reason why these types of medications are called dual re-uptake inhibitors.

Side effects of SNRIs:

- Nausea, Dry Mouth, Constipation
- Dizziness, Insomnia (numbness), Sleepiness
- Increased Blood Pressure, Excessive Sweating
- Tremor, Headache, Agitation
- Muscle Weakness

Nursing intervention for side effect of antidepressants.

- ***1- Anti-cholinergic side effect***
- *1- Dry mouth:*
- Provide client with sugarless candy, ice.
- Instruct client to frequent sips of water.
- Ensure that client practice strict oral hygiene.

- *2- Blurring of vision:*
- Advice client not to drive a car until vision clear.
- Clear small items from pathway to prevent falls.
- Explain that these symptoms will subside after few weeks.

- *3- Constipation:*
- Order food high in fibers.
- Encourage increase physical activities if not contraindicated.
- Encourage increase fluid intake.
- *4- Urinary retention:*
- Instruct client to report any difficulty urination.
- Monitor intake and output.
- Various methods to stimulate urination may be tried as water in the path room or pouring water over pernial area.

- ***2- Sedation:***
- Give the drug at bed time.
- Instruct client not to drive or use dangerous machine while experiencing sedation.
- Request that the physician decreased dose or ordered aless sedating drug.

- ***3- Orthostatic hypotension;***
- Instruct client to rise slowly from lying or sitting position.
- Monitor blood pressure before giving medication each shift, document and report significant changes.
- Avoid long hot shower or tub baths.
- ***4- Tachycardia and arrhythmia***;
- Monitor blood pressure, pulse and rhythm.

- ***5- Nausea:***
- Medication may be taken with food to minimize GIT distress.
- ***6- Insomnia and agitation:***
- Take dose early in day.
- Avoid caffeine containing food and drinks.
- Teach relaxation techniques to use before bed time.

- ***7- Weight gain:***
- Weight client every day.
- - Order caloric-controlled diet.
- - Provide opportunity for physical activity.
- ***8- Photosensitivity:***
- Ensure that client wear protective sunscreen clothes and sun glasses while outdoors.

Patient and family education related to antidepressants

- Continue to take the medication even though the symptoms have not subsided. The therapeutic effect may not be seen for as long as 4 weeks. If after this length of time no improvement is noted, the physician may prescribe a different medication.
- Use caution when driving or operating dangerous machinery.

- Do not stop taking the drug abruptly. To do so might produce withdrawal symptoms.
- Take frequent sips of water, chew sugarless gum, or suck on hard candy if dry mouth is a problem. Good oral care (frequent brushing,) i very important.

- Use sunblock lotion and wear protective clothing when spending time outdoors. The skin may be sensitive to sunburn.
- Report occurrence of any abnormal symptoms to the physician immediately.
- Rise slowly from a sitting or lying position to prevent a sudden drop in blood pressure.

- Avoid smoking while receiving tricyclic therapy. Smoking increases the metabolism of tricyclics, requiring an adjustment in dosage to achieve the therapeutic effect.
- Do not drink alcohol while taking antidepressant therapy. These drugs potentiate the effects of each other.

- Do not consume other medications without the physician's approval while receiving antidepressant therapy. Many medications contain substances that, in combination with antidepressant medication, could precipitate a life-threatening hypertensive crisis.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