



Lecture 7

Drugs used in anxiety and panic disorders

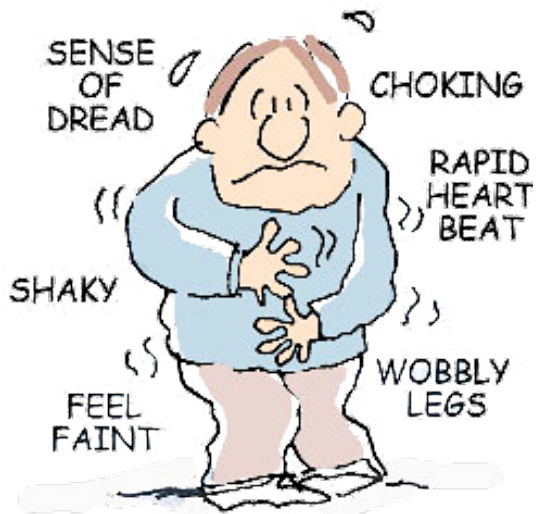
Objectives:

1. Define different types of anxiety disorders
 2. Classify types of drugs used for treatment of anxiety
 3. Recognize the pharmacokinetics & pharmacodynamics of different classes of anti-anxiety drugs.
 4. Identify the specific clinical applications of each class of anti-anxiety drugs.
 5. Know side effects of different classes of anti-anxiety drugs.
- Additional Notes
 - Important
 - Explanation –Extra-

What is anxiety? Physical and emotional distress which interferes with normal life. It starts as emotional distress and progresses till it becomes physical.

Symptoms of anxiety

Emotional or psychological symptoms.	Physical or somatic symptoms.
<ol style="list-style-type: none"> 1. Feeling tense 2. Trouble concentrating 3. Irrational and excessive fear and worry 4. Irritability 5. Restlessness 	<ol style="list-style-type: none"> 1. Sweating 2. Tachycardia 3. Shortness of breath 4. Stomach upset 5. Frequent urination or diarrhea. 6. constipation may occur 7. Sleep disturbances (Insomnia) 7. Fatigue



Types of anxiety

Generalized anxiety disorder (GAD)	Post-traumatic stress disorder (PTSD).	Obsessive-compulsive disorder (OCD).	Panic disorder	Phobias
<p>Patients are usually and constantly worried about health, money, work <u>with no apparent reasons.</u></p>	<p>An anxiety disorder that affects people who have experienced a severe emotional trauma, such as rape or dramatic car accident, or even war.</p>	<p>An anxiety disorder in which people cannot prevent themselves from unwanted thoughts or behaviours that seem impossible to stop as Washing their hands .</p>	<p>Sudden, intense and acute attacks of anxiety in certain situations. Panic attacks cannot be predicted.</p>	<p>An intense, uncontrolled fear of a specific situation such as open spaces and heights.</p>

Antianxiety drugs

Drugs that can relieve anxiety without interfering with mental or physical function. If psychotherapy is not enough the patient uses anxiolytics.




Treatment of anxiety

1. Psychotherapy (cognitive behavioral therapy).
2. Anxiolytics.

Classification of anxiolytic drugs

1. Benzodiazepines (BDZ).
2. 5HT reuptake inhibitors.
3. 5HT_{1A} agonists.
4. Antidepressants
5. Beta-adrenergic blockers
6. MAO inhibitors

Drug interactions (Benzodiazepines (BDZ).)

Drugs	Examples
CNS depressants e.g. alcohol & anti-histaminic (1 st generation)	 effect of benzodiazepines (Additive effect) We do not give alcohol & antihistamines with benzodiazepines (because both are CNS depressants)
Cytochrome P450 inhibitors e.g. cimetidine & erythromycin	 t _{1/2} of benzodiazepines
CYT P450 inducers phenytoin & rifampicin (In general, antiepileptic drugs are p450 enzymes inducers)	 t _{1/2} of benzodiazepines

Benzodiazepines

classified according to duration of action into:	<ol style="list-style-type: none">1. Short acting (3-8 hours): triazolam- Oxazepam.2. Intermediate (10-20 hours): "LATE":Alprazolam – Lorazepam -Estazolam - Temazepam.3. Long acting: (24-72 hours):Diazepam - Chlordiazepoxide – Flurazepam.
Mechanism of Action:	by binding to BZ receptors in the brain → enhance GABA action on brain "opening of Chloride channels" (BZ R are adjacent to GABA receptors but separated from them) → ↑ chloride influx to the cell → hyper- polarization → more difficult to depolarizes → reduction of neural excitability. (more inhibition that's why these drugs can induce sedation)
Pharmacokinetics:	lipid soluble "Fetal depression" (depression of cardiovascular and respiratory centers), widely distributed, absorbed well orally, excreted in milk (neonatal depression). Metabolized in the liver to active metabolites" long duration of action" (The Long duration of action by the drug itself and its active metabolites), cumulative effect, excreted in urine. <ul style="list-style-type: none">• be careful when use it with patient with hepatic problems cause they accumulate.• Chlordiazepines + diazepam are given through IV route because with IM route absorption is less.
actions	CNS depressants, Anxiolytic action ,Sedation ,Hypnotic action (given as sleeping pills), Anterograde amnesia, Depression of cognitive and psychomotor function "workers in factory or driving a car "minimal depressant effects on cardiovascular system & respiratory system. some have skeletal muscle relaxing effect (diazepam). Some have anticonvulsant effect e.g. clonazepam, diazepam, lorazepam.
Therapeutic uses	<ul style="list-style-type: none">• Anxiety disorders: short term relief of severe anxiety, General anxiety disorder, Obsessive compulsive disorder, Panic disorder with depression Alprazolam (antidepressant effect).<ul style="list-style-type: none">• Benzodiazepines are fast acting—typically bringing relief within thirty minutes to an hour.• Sleep disorders (Insomnia): Triazolam, Lorazepam, Flurazepam (short to intermediate duration of action)• Treatment of epilepsy: Diazepam – Lorazepam• Alcohol withdrawal syndrome (diazepam). (we give the patient a depressing drug other than alcohol)• In anesthesia:<ol style="list-style-type: none">1. Pre-anesthetic medication (diazepam). (indicated because patients have fear before surgeries)2. Induction of anesthesia (Midazolam, IV)
Adverse Effects	Risk of withdrawal symptoms: Rebound insomnia, anorexia, anxiety, agitation, tremors & convulsion). Respiratory & cardiovascular depression in large doses only (toxic effects). (should not be given to a driver)
Precautions	Pregnant women or breast-feeding (They are highly distributed, thus it is contraindicated to use them in pregnant women due to placental crossing). Dose reduction is recommended in :Liver disease and Old People. (We should adjust the dose in old aged patients because they may take extra dose by mistake and the drug has long duration of action (cumulative effect) (Accumulation of the drug can occur with liver disease).

Serotonin 1A agonists & Selective serotonin reuptake inhibitors (SSRIs) “Slow onset of action”.

	5HT _{1A} agonists “ Buspirone ”	Selective serotonin reuptake inhibitors (SSRIs) “ Fluoxetine ”
Acts on	a partial agonist at brain 5HT _{1A} receptors	acts by blocking uptake of 5-HT
Administration	orally	Orally
T_{1/2} + pharmacokinetics	2 – 4 hour, rapidly absorbed orally. delayed onset of action in comparison with benzodiazepines.	long half life. given orally.
use	<ul style="list-style-type: none"> - We use this class of anxiolytics more in OCD = obsessive compulsive disorder. - As anxiolytic in generalized anxiety disorders. “Only anxiolytic”. - No hypnotic effect or muscle relaxant effect or anticonvulsant action or alcohol additive effect (can be given with alcohol). it doesn't impair memory and Coordination, Minimal risk of dependence it has no withdrawal symptoms 	<p>Considered the first line of treatment for most anxiety disorders (panic disorder, OCD, GAD, PTSD, phobia) because they are well tolerated, have low risk for dependency and abuse and low potential for overdose.</p>
Disadvantages	<ul style="list-style-type: none"> -Slow onset of action (delayed effect). -GIT upset, dizziness, drowsiness. -Not effective in severe anxiety/panic disorders. -Drug interactions with CYT P450 inducers and inhibitors 	<ul style="list-style-type: none"> - EXPENSIVE. - Delayed onset of action (weeks). - Nausea, diarrhea - Weight gain - Sexual dysfunction - Dry mouth - Sleep disturbance or insomnia - Seizures

	Tricyclic Antidepressants Doxepin- imipramine Delayed onset of action (weeks).	Monoamine oxidase inhibitors (MAOIs) Phenelzine	Beta Blockers Propranolol – atenolol
Act on	act by reducing uptake of 5HT & NA. - Delayed onset of action (weeks).	act by blocking the action of MAO enzymes.	act by blocking peripheral sympathetic system.
Use	<ul style="list-style-type: none"> - anxiety especially associated with depression. - Effective for panic attacks. <p>Tricyclic antidepressants are nonselective antidepressants . SSRIs are selective antidepressant.</p>	for panic attacks and phobia.	<ul style="list-style-type: none"> • Reduce somatic symptoms of anxiety. (symptomatic relievers) • Used in performance or social anxiety. (are less effective for other forms of anxiety.)
Side effect	<ul style="list-style-type: none"> • Atropine like actions (dry mouth-blurred vision, tachycardia, urinary retention). • α-blocking activity (Postural hypotension). • Sexual dysfunction. • Weight gain. 	<ul style="list-style-type: none"> - Dry mouth, constipation, diarrhea, restlessness, dizziness. - Require dietary restriction. - Avoid wine, beer, fermented foods as old cheese that contain tyramine (hypertensive crisis) → severe vasoconstriction. (Tyramine releases adrenaline). 	<ul style="list-style-type: none"> - Hypotension. - should be used with caution in asthma (because it cause vasoconstriction), cardiac failure, peripheral vascular disorders. <p>(When beta-2 receptors are inhibited alpha receptors action will take the upper hand leading to vasoconstriction)</p>

CLASSES OF ANXIOLYTICS	USES	Adverse effects
Benzodiazepines	Generalized anxiety disorders, OCD, phobia, panic attack	Ataxia, confusion, dependence, tolerance, withdrawal symptoms,
SSRIs (Fluoxetine)	Generalized anxiety disorders, OCD, phobia, panic attack	Sexual dysfunction atropine like actions
Tricyclic antidepressants (doxepin, imipramine)	anxiety with depression panic attacks	weight gain, sexual dysfunction, atropine like actions, arrhythmia
5HT1A agonists (Buspirone)	Mild anxiety Not effective in panic attack	Minimal adverse effects
Beta blockers (propranolol, atenolol)	Phobia (social Phobia)	Hypotension

Which one of the following drugs has skeletal muscle relaxant effect:

- a) Lorazepam
- b) Diazepam
- c) flurazepam
- d) Alprazolam

Answer : B

A 37 year old female was referred to the clinic as she had depression for the past 4 weeks .she also explained to the doctor that she has experienced episodes of feeling afraid with shortness of breath and tachycardia without any reason. Which of the following drugs is best for her condition.

- a) Alprazolam
- b) Triazolam
- c) Lorazepam
- d) Flurazepam

Answer: A

A 45 year old male who works in an industrial factory in Riyadh has difficulty sleeping insomnia for the past 5 days he said I slept about 1 hour a day without felling rest. Which of the following drugs is best for him

- a) Diazepam
- b) Alprazolam
- c) Triazolam
- d) Non

Answer: c

An Indian 34 year old male was prescribed rifampicin for his chronic T.B. he also was prescribed benzodiazepines as he had anxiety.

Which of the following statements is correct:

- a) Rifampicin has no effect of the $t_{1/2}$ of the benzodiazepines.
- b) Rifampicin will lower $t_{1/2}$ of the benzodiazepines.
- c) Rifampicin will increase $t_{1/2}$ of the benzodiazepines
- d) Rifampicin and benzodiazepines have the same effect (additive effect)

Answer: b

Which one of the following is an use for Buspirone ?

- a) Panic disorder
- b) Sever generalized anxiety
- c) Skeletal muscle relaxant
- d) Mild anxiety

Answer :D

Good luck!

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