

Al-Mustaqbal University College
Department of Pharmacy
5th stage
Clinical Toxicology
Lecture: 5



Digoxin, TCA, & CNS Depressants Toxicity

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Digoxin Toxicity

- ✓ **Digitalis** is a **plant-derived** cardiac **glycoside** found in certain flowering plants (such as **oleander** and **lily of the valley**).
- ✓ Digitalis commonly used in the treatment of **chronic heart failure** (CHF), **atrial fibrillation**, and re-entrant **supraventricular tachycardia**.
- ✓ **Digoxin** is the available preparation of **digitalis**.



Digoxin Toxicity

- ✓ The **incidence** of digitalis toxicity has **declined** in recent years due to improved technology for **monitoring** of drug levels and increased awareness of drug **interactions**.
- ✓ Nevertheless, cardiac glycoside toxicity continues to be a **problem** because of its **wide use** and its **narrow therapeutic window**.

Digoxin Toxicity

- ✓ **Acute** digitalis toxicity can result from:
1. Unintentional or suicidal **overdose** of digoxin
 2. Accidental ingestion of **plants** that contain cardiac glycosides

Digoxin Toxicity

- ✓ **Chronic** toxicity in patients on **digoxin therapy** may result from:
 1. Deteriorating renal function
 2. Dehydration
 3. Electrolyte disturbances
 4. Drug interactions
- ✓ **Alterations** in cardiac rate and rhythm from digitalis toxicity may simulate almost **every known type of dysrhythmia**.

Digoxin Toxicity

Signs and symptoms: Digitalis toxicity produces:

- ✓ **CNS toxicity**
- ✓ **Visual toxicity**
- ✓ **GIT toxicity**
- ✓ **Cardiac manifestations**

Digoxin Toxicity

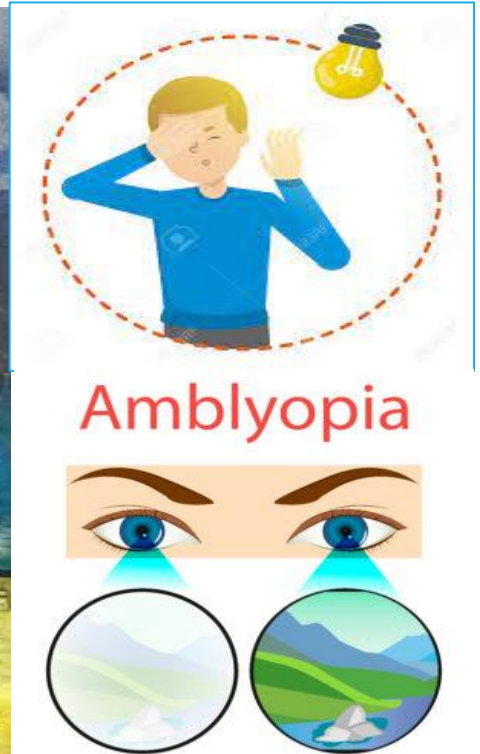
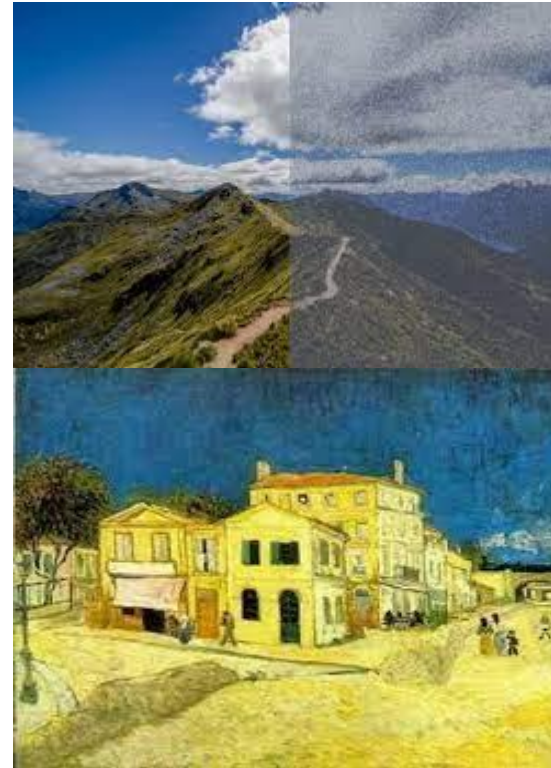
CNS symptoms of digitalis toxicity include the following:

- ✓ **Drowsiness, Lethargy, Fatigue, & Neuralgia**
- ✓ **Headache, Dizziness, Confusion, & Hallucinations**
- ✓ **Seizures (rare)**
- ✓ **Paresthesias and neuropathic pain**

Digoxin Toxicity

Visual symptoms include:

- ✓ Snowy vision
- ✓ Photophobia
- ✓ Decreased visual acuity
- ✓ Yellow halos around lights
- ✓ Transient amblyopia



Digoxin Toxicity

GIT symptoms in acute or chronic toxicity include :

- ✓ **Anorexia & Weight loss**
- ✓ **Failure to thrive (in pediatric patients)**
- ✓ **Nausea & Vomiting**
- ✓ **Abdominal pain & Diarrhea**



Digoxin Toxicity

Cardiac symptoms include:

- ✓ **Palpitations, Shortness of breath, & Syncope (temporary loss of consciousness caused by a fall in blood pressure)**
- ✓ **Swelling of lower extremities**
- ✓ **Bradycardia, Hypotension, & Dyspnea**

Digoxin Toxicity

Diagnosis:

- ✓ Serum digoxin level
- ✓ Electrolytes (In acute toxicity, hyperkalemia is common)
- ✓ Renal function test
- ✓ ECG (Digoxin toxicity may cause almost any dysrhythmia)

Digoxin Toxicity

Treatment:

Treatment of digoxin toxicity should be guided by the **patient's signs and symptoms** and the **specific toxic effects** and **not necessarily** by digoxin levels alone.

Digoxin Toxicity

Supportive care of digitalis toxicity includes the following:

- 1. Hydration with IV fluids**
- 2. Oxygenation and support of ventilatory function**
- 3. Discontinuation of the drug, and, sometimes, the correction of electrolyte imbalances**
- 4. GI decontamination : Activated charcoal is indicated for acute overdose**

Digoxin Toxicity

Treatment digitalis toxicity includes the following:

1. Treatment of electrolyte imbalance

- ✓ **Treat hyperkalemia** by using **sodium bicarbonate** to correct metabolic **acidosis** and **insulin plus glucose** to enhance **potassium** uptake by cells.
- ✓ Treatment with **digoxin Fab** fragments is indicated for a **potassium level** greater than 5 mEq/L.
- ✓ **Hemodialysis** may be necessary for **uncontrolled hyperkalemia**.

Digoxin Toxicity

Treatment digitalis toxicity includes the following:

2. Digoxin immune Fab (Digibind)

- ✓ Digoxin immune Fab is considered the **first-line** treatment for **significant** dysrhythmias from digitalis toxicity.
- ✓ Digoxin immune Fab is an **immunoglobulin** fragment that **binds** with digoxin.
- ✓ Digoxin immune Fab is packaged in a **40-mg vial** and must be reconstituted with **4 mL** of sterile water for **IV** injection.

Tricyclic Antidepressant (TCA) Toxicity

- ✓ The **toxic effects** of TCAs are results of the following **4 main** pharmacologic properties :
1. **Inhibition** of norepinephrine and serotonin **reuptake** at nerve terminals.
 2. **Anticholinergic** action
 3. Direct **alpha-adrenergic** blockade
 4. Membrane **stabilizing** effect on the myocardium by blocking the cardiac myocyte **fast sodium channels**

Tricyclic Antidepressant (TCA) Toxicity

✓ **Physical findings are:**

- 1. Tachycardia and Hypotension**
- 2. Fever, Altered mental status, and Rigidity**
- 3. Ileus (severe intestinal spasm with vomiting), and Absent bowel sounds.**
- 4. Dry skin and mucous membranes.**
- 5. Mydriasis**

Tricyclic Antidepressant (TCA) Toxicity

✓ Treatment:

1. **GIT decontamination** may be helpful within the **first several hours** post-ingestion because TCAs can **slow gastric emptying** through the anticholinergic activity.
2. **Gastric lavage.**
3. **Activated charcoal** reduces the absorption of CAs. It should be administered **only** in patients who are able to protect the airway.

Tricyclic Antidepressant (TCA) Toxicity

✓ **Treatment:**

4. Administer **intravenous fluid** if the patient is hypotensive.
5. For hypotension **refractory** to intravenous saline, **vasopressors may be used**

Tricyclic Antidepressant (TCA) Toxicity

✓ Treatment:

4. Administer **intravenous fluid** if the patient is hypotensive, for hypotension **refractory** to intravenous saline, **vasopressors** may be used.
5. **Benzodiazepines** are recommended for TCA-associated convulsions.
6. **Serum alkalinization** with intravenous **sodium bicarbonate** has been the mainstay of therapy in TCA-induced **cardiovascular toxicity**.

CNS Depressant Toxicity

- ✓ **Sedative-hypnotics** are a group of drugs that cause **CNS depression**.
- ✓ **Benzodiazepines** and **barbiturates** are the most commonly used agents in this class.
- ✓ **Barbiturates** include:
 1. **Ultrashort** acting - thiopental
 2. **Short and intermediate** acting - Amobarbital, pentobarbital
 3. **Long acting** - Phenobarbital

CNS Depressant Toxicity

✓ **Nonbarbiturates include:**

- 1. Benzodiazepines**
- 2. Meprobamate**
- 3. Chloral hydrate**
- 4. Glutethimide**

CNS Depressant Toxicity

Pathophysiology:

- ✓ **All** the sedative-hypnotics are general **CNS depressants**.
- ✓ **Most** stimulate the activity of **GABA**, the principal **inhibitory** neurotransmitter in the CNS.
- ✓ **Mild** Barbiturates toxicity is characterized by **ataxia, incoordination, nystagmus, slurred speech, and altered level of consciousness**.

CNS Depressant Toxicity

- ✓ **Pathophysiology:**
- ✓ **Moderate poisoning leads to respiratory depression and hyporeflexia.**
- ✓ **Severe poisoning leads to areflexic coma, apnea, and hypotension**
- ✓ **Miosis is common.**
- ✓ **Hypotension is usually secondary to vasodilation and negative cardiac inotropic effects.**

CNS Depressant Toxicity

Treatment:

- ✓ Establish **ABCs**, obtain **IV** access, provide **oxygen**, and perform aggressive **supportive care** with airway protection as necessary .
- ✓ **Ipecac** syrup is **not recommended** for home use because of the fear of **emesis** after onset of respiratory depression .
- ✓ **Ensure** adequate airway and ventilation. Consider and reassess the need for **endotracheal intubation** .

CNS Depressant Toxicity

Treatment:

- ✓ **Flumazenil** competitively and reversibly binds **benzodiazepine** receptors.
- ✓ **Gastric lavage** may be performed if the patient presents within **1 hour** of ingestion .
- ✓ The use of **activated charcoal** .
- ✓ **Alkaline diuresis** enhances elimination of phenobarbital and other long-acting barbiturates. It is recommended for **all symptomatic patients** with long-acting barbiturate toxicity

**THANK YOU
FOR YOUR ATTENTION**