Al-Mustaqbal University College
Department of Pharmacy
5th stage
Clinical Toxicology
Lecture: 4

Cardiovascular Drugs Toxicity

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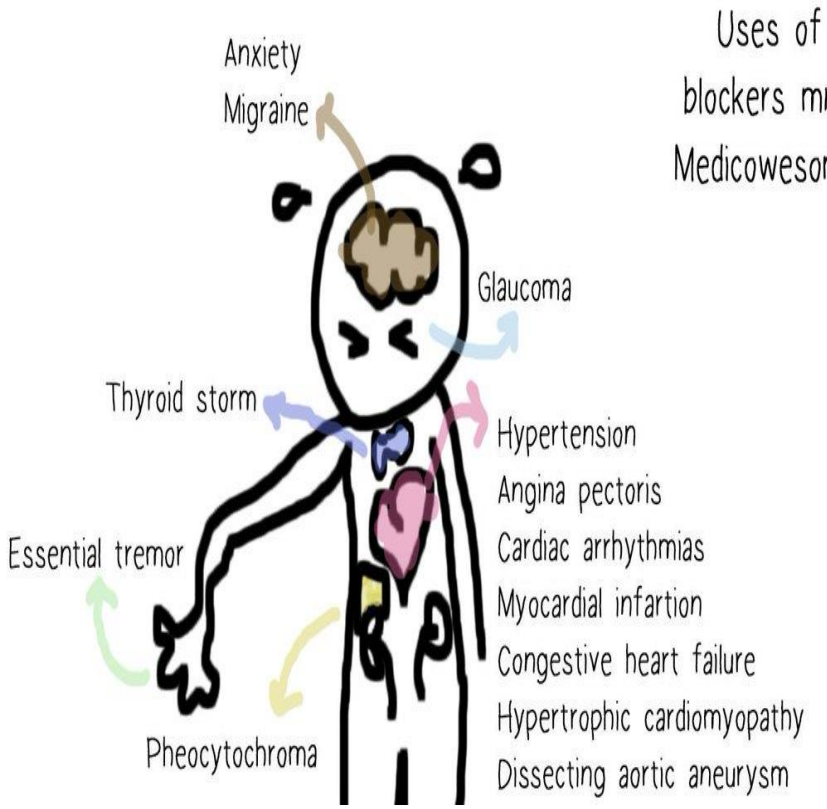
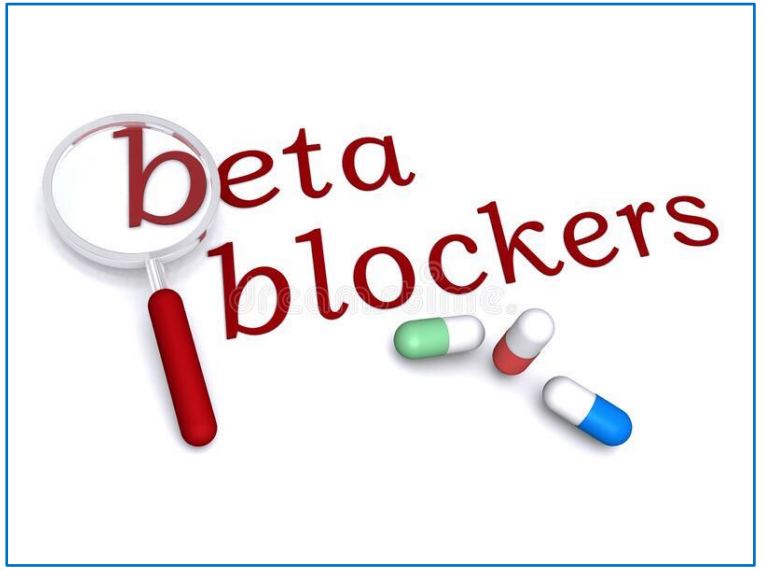
Beta Blockers Toxicity

- ✓**Beta-blockers have been in use for nearly 50 years.**
- ✓**It used in case of hypertension and other cardiovascular disorders.**
- ✓**Beta-blockers are also used for additional purposes such as migraine headaches, hyperthyroidism, glaucoma, anxiety, and various other disorders.**
- ✓**As a result of their expanded use, the incidence of overdose with these agents has also increased.**



Beta Blockers Toxicity

- ✓**Beta-blocker toxicity** can produce clinical manifestations including **bradycardia**, **hypotension**, **arrhythmias**, **hypothermia**, **hypoglycemia**, and **seizures**.
- ✓**The clinical presentation of beta blockers toxicity may range from asymptomatic to shock.**



Beta Blockers Toxicity

Pathophysiology:

- ✓Beta-blockers act as competitive inhibitors of catecholamines, exerting their effects at both central and peripheral receptors.
- ✓Blockade of beta-receptors results in decreased production of intracellular cyclic adenosine monophosphate (cAMP) with an inhibition of multiple metabolic and cardiovascular effects of circulating catecholamines.
- ✓Beta1-receptor blockade reduces heart rate, blood pressure, myocardial contractility, and myocardial oxygen consumption.
- ✓Beta2-receptor blockade inhibits relaxation of smooth muscle in blood vessels, bronchi, the gastrointestinal system, and the genitourinary tract.
- ✓In addition, beta-adrenergic receptor antagonism inhibits both glycogenolysis and gluconeogenesis, which may result in hypoglycemia.

Beta Blockers Toxicity

Pathophysiology:

- ✓**Prognosis** is largely dependent on the **initial response** to therapy (**6-12 h** post ingestion) as drug levels are likely to have **peaked** at this time.
- ✓In addition, beta-blockers that are **lipid soluble** and have marked **antidysrhythmic** (ie, quinidine-like) effects are more **lethal** (eg, propranolol, sotalol).
- ✓**Underlying cardiac or pulmonary disease** places the patient at increased **risk for poor outcome**.

Beta Blockers Toxicity

History and Physical Examination:

- ✓ **Ideally, the clinician should determine the specific beta-blocker involved, the quantity, and the time of the overdose.**
- ✓ **Unfortunately, these details are often not immediately available.**
- ✓ **When a history of intentional overdose is lacking, beta-blocker toxicity can go unrecognized as a cause of bradycardia and hypotension.**

Beta Blockers Toxicity

Initial evaluation:

- ✓The initial evaluation of a patient that is in coma should include consideration of an overdose.
- ✓If a patient is suffering from bradycardia and hypotension, the clinician should consider a beta-blocker or calcium channel blocker overdose.
- ✓Other associated symptoms may include hypothermia, hypoglycemia, and seizures.

Beta Blockers Toxicity

Initial evaluation:

- ✓**Myocardial conduction delays with decreased contractility characterize the acute beta-blocker ingestion.**
- ✓**Cardiac output may diminish with resulting hypotension from bradycardia and negative inotropy.**
- ✓**Beta-blockers that are not sustained-release formulations are all rapidly absorbed from the gastrointestinal tract.**

Beta Blockers Toxicity

Initial evaluation:

- ✓The **first critical signs** of overdose can appear **20 minutes** post-ingestion.
- ✓In all clinically significant beta-blocker overdoses, symptoms develop **within 6 hours.**
- ✓Although the **half-life** of these compounds is usually short **(2-12 h),** half-lives in the overdose patient may be **prolonged** because of a **depressed** cardiac output, **reduced** blood flow to the liver and kidneys.

Beta Blockers Toxicity

Bradycardia

✓**Bradycardia with associated hypotension and shock defines severe beta-blocker toxicity.**

CNS symptoms

✓**A depressed level of consciousness and seizures may occur as a result of cellular hypoxia from poor cardiac output, a direct CNS effect caused by sodium channel blocking, or even as a result of hypoglycemia.**

The lipid-soluble agents have increased distribution into the brain, and these agents are associated with severe CNS toxicity.

Beta Blockers Toxicity

Bronchospasm

- ✓**Bronchospasm is a rare complication of beta-blocker therapy or overdose but is more likely in patients who already have bronchospastic disease.**
- ✓**Pulmonary edema had been reported to occur as a result of cardiac failure.**

Beta Blockers Toxicity

Treatment

- ✓ Administration of **charcoal** is indicated when the patient is alert and cooperative.
- ✓ Ipecac syrup is **contraindicated**.
- ✓ If the patient is **hypotensive**, administer (**20 mL/kg**) of isotonic **intravenous fluids**.

Beta Blockers Toxicity

Treatment

If the patient does not respond to the previous measures, the following interventions may be considered:

- ✓ **Inotropes & Chronotropes**
- ✓ **Glucagon**
- ✓ **Gastric decontamination**
- ✓ **Benzodiazepines (in patients with seizures)**
- ✓ **Hemodialysis**

Beta Blockers Toxicity

Treatment

✓**The pharmacotherapy of beta-blocker overdose may include a variety of inotropes and chronotropes, such as:**

1. **Epinephrine**
2. **Atropine**

✓**These agents indicated to reverse hypotension and bradycardia.**

✓**Doses of these agents should be titrated to response.**

Beta Blockers Toxicity

Treatment

- ✓**Glucagon** can enhance myocardial **contractility**, heart **rate**, and atrioventricular **conduction**.
- ✓ **Glucagon** consider it the drug of choice for beta-blocker toxicity.
- ✓**Because a glucagon bolus** can be **diagnostic** and **therapeutic**, the clinician can **empirically** administer glucagon and **check** for a **response**.

Beta Blockers Toxicity

Treatment

- ✓For gastric decontamination, gastric lavage (with appropriate protection of the airway) is preferred over emesis because of the rapid absorption and occasionally precipitous onset of toxicity that may place the patient at risk for aspiration.
- ✓Gastric lavage may be beneficial if the patient presents to the hospital within 1-2 hours of ingestion.

Beta Blockers Toxicity

Treatment

- ✓**Hemodialysis** may be **useful** in severe cases of **atenolol** overdoses because atenolol is **less than 5% protein bound** and 40-50% is excreted unchanged in urine.
- ✓Consider hemodialysis or hemoperfusion **only** when treatment with glucagon and other pharmacotherapy **fails**.

Beta Blockers Toxicity

Monitoring

Monitoring include repeat physical examinations, serial electrocardiograms, and continuous measurement of urinary output after placement of a Foley catheter.

- ✓ **End points Heart rate >60 beats per minute**
- ✓ **Blood pressure >90 mm Hg systolic**
- ✓ **Evidence of good organ perfusion (improved urine output)**

Beta Blockers Toxicity

Monitoring

- ✓The goal of therapy in beta-blocker toxicity is to restore perfusion to critical organ systems by increasing cardiac output.
- ✓This may be accomplished by improving myocardial contractility, increasing heart rate, or both.

Angiotensin-converting enzyme inhibitors (ACEIs) toxicity

✓ **ACEIs such as lisinopril, enalapril and captopril, block the conversion of angiotensin I to angiotensin II, thereby lowering arteriolar resistance and subsequently reducing blood pressure.**

✓ **Overdoses have been widely reported and mild toxicity may be produced with a single, supra-therapeutic dose, however, severe toxic effects and deaths rarely occur.**

Angiotensin-converting enzyme inhibitors (ACEIs) toxicity

- ✓**Overdose with ACE inhibitors may cause hypotension, tachycardia, and acute renal failure.**

- ✓**However, the majority of overdoses are asymptomatic and serious morbidity is rare.**

Angiotensin-converting enzyme inhibitors (ACEIs) toxicity

Mechanisms of toxic effects

- ✓These drugs **inhibit** angiotensin-converting enzyme (ACE) which converts angiotensin I to angiotensin II which is a potent **vasoconstrictor** and stimulator of **aldosterone** release.
- ✓In overdose these drugs do **not** seem to have any additional effects and the toxicity seen is very similar to that seen with the **first dose in therapeutic use**.

Angiotensin-converting enzyme inhibitors (ACEIs) toxicity

Clinical effects:

- ✓The principal adverse effect of ACE inhibitor overdose is hypotension, although hyperkaliemia and renal failure may occur.
- ✓Hypotension is generally not life-threatening and the renal failure is reversible.
- ✓It is possible some other acute adverse effects of ACE inhibitors, such as angioedema, cough, and bronchoconstriction may occur after overdose.

Angiotensin-converting enzyme inhibitors (ACEIs) toxicity

Treatment:

1. Supportive care:

- ✓Patients should be given adequate **fluids**, if necessary with IV fluids, to maintain a **satisfactory blood pressure** and a **good urine output.**
- ✓If patients are well **after 6 hours**, they should be medically fit for **discharge**.

2. GI Decontamination:

- ✓Oral activated **charcoal** may be given to patients who have ingested a large overdose if they present within **1-2 hours**.

Angiotensin-converting enzyme inhibitors (ACEIs) toxicity

Treatment of specific complications

1. Hypotension

- ✓ **Hypotension should be treated with IV fluids (normal saline).**
- ✓ **Small doses of vasoconstrictors (e.g. adrenaline) may be given if the patient fails to respond.**

2. Bronchoconstriction

- ✓ **If bronchoconstriction occurs, beta 2 agonists such as salbutamol are indicated.**

Calcium Channel Blocker (CCB) Toxicity

✓**The different classes of CCBs cause decreased myocardial contractility and peripheral arterial vasodilation by inhibiting calcium influx.**

✓**Overdoses of immediate-release CCBs are characterized by:**

1. **Rapid progression to hypotension**
2. **Bradydysrhythmia**
3. **Cardiac arrest,**

Calcium Channel Blocker (CCB) Toxicity

✓**While overdoses of extended-release formulations can result in:**

1. **Delayed onset of dysrhythmias**
2. **Shock**
3. **Sudden cardiac collapse**
4. **Bowel ischemia**

Calcium Channel Blocker (CCB) Toxicity

Signs and symptoms:

✓**Signs and symptoms of CCB toxicity may include any of the following:**

1. **Temporary loss of consciousness caused by a fall in blood pressure, Lightheadedness, Chest pain, and Palpitations.**
2. **Severe sweating, Flushing, Weakness, Peripheral edema, and Dyspnea.**
3. **Confusion, Seizure, Dizziness, Headache, Nausea, Vomiting.**

Calcium Channel Blocker (CCB) Toxicity

Physical examination findings may include the following:

1. **Slowed heart rate**
2. **Hypotension**
3. **Depressed level of consciousness**

Calcium Channel Blocker (CCB) Toxicity

Management:

- ✓**Basic supportive care** is the most important mode of management for CCB toxicity: **Stabilize airway**, **breathing**, and **circulation** (ABCs).
- ✓**Correction of acid-base disturbances** and **electrolyte abnormalities** is also important, to optimize cardiac function.

Calcium Channel Blocker (CCB) Toxicity

Management

- ✓ Activated charcoal has been demonstrated to significantly adsorb immediate-release medications within 1 hour of ingestion and extended-release medications as long as 4 hours after ingestion.
- ✓ Before administration of activated charcoal, protect the patient's airway to prevent vomiting and aspiration.

Calcium Channel Blocker (CCB) Toxicity

Management

- ✓**Ipecac syrup** is always **contraindicated** in CCB toxicity because the patient may rapidly **lose consciousness** and may develop **seizures**.
- ✓**Gastric lavage** is especially important for patients who may have taken a **large dose** of medication or for those who have ingested **sustained-release** preparations.

Calcium Channel Blocker (CCB) Toxicity

Specific agents used in treatment include the following:

1. **IV volume expansion (Blood pressure can be augmented with isotonic sodium chloride solution or Ringer lactate solution, both are efficient volume expanders)**
2. **Calcium (administered IV to patients who present with symptomatic hypotension or heart block)**

Calcium Channel Blocker (CCB) Toxicity

Specific agents used in treatment include the following:

3. **Glucagon (Glucagon promotes calcium entry into cells via stimulation of a receptor that is considered to be separate from adrenergic receptors)**
4. **Vasopressors (eg, dopamine, epinephrine, norepinephrine they stimulate myocardial contractility and cause vasoconstriction, thus supporting blood pressure and cardiac output)**

THANK YOU
FOR YOUR ATTENTION