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Toxicity of β -adrenergic Blockers	عنوان المحاضرة باللغة الانجليزية
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9th Edition, edited by Curtis D. Klaassen, McGraw-Hill Education, 2019.	
12th Edition, McGraw-Hill Education, 2023	

محتوى المحاضرة

Introduction:

- β -adrenergic blockers are widely used for treatment of many disease states, including hypertension, arrhythmia, angina, glaucoma & migraine prophylaxis.
- They have significant pharmacologic & pharmacokinetic differences (Table 1).
- These differences influence their therapeutic applications, incidence of side effects, & type & severity of toxic reactions when taken in overdose.

Table 1. Pharmacologic & pharmacokinetic properties of β -adrenergic blockers.

Drug	Adrenergic receptor blocking activity	Membrane stabilizing activity	Intrinsic sympathomimetic activity	Lipid solubility	Half-life (hr)	Elimination
Acebutolol	B ₁	+	+	Low	3-4	Hepatic, renal, bile
Atenolol	B ₁	0	0	Low	6-9	Unchanged (50%)
Betaxolol	B ₁	+	0	Low	14-22	Hepatic
Bisoprolol	B ₁	0	0	Low	9-12	Unchanged (50%)
Esmolol	B ₁	0	0	Low	0.15	Esterases in RBCs
Metoprolol	B ₁	0	0	Moderate	3-7	Hepatic, renal
Carteolol	B ₁ , B ₂	0	++	Low	6	Unchanged (50-70%)
Nadolol	B ₁ , B ₂	0	0	Low	20-24	Unchanged
Penbutolol	B ₁ , B ₂	0	+	High	5	Hepatic
Pindolol	B ₁ , B ₂	+	+++	Moderate	3-4	Renal, unchanged
Propranolol	B ₁ , B ₂	++	0	High	3-5	Hepatic
Sotolol	B ₁ , B ₂	0	0	Low	12	Unchanged
Timolol	B ₁ , B ₂	0	0	Low to moderate	4	Hepatic
Labetalol	B ₁ , B ₂	0	0	Moderate	5.5-8	Hepatic, unchanged

Toxicity of β -adrenergic blockers:

- Most of the toxicity of β -adrenergic action of catecholamines at cardiac β -adrenergic receptors.
- A membrane depressant effect likely contributes to the cardiac depressant effects of propranolol.
- Most poisonings involve propranolol.
- High doses of β -adrenergic blockers with intrinsic sympathomimetic activity (ISA) (e.g., acebutolol & pindolol) can cause tachycardia & hypertension.
- The high lipid solubility of certain β -adrenergic blockers, especially propranolol accounts for the CNS effects.
- In overdose, pharmacokinetic parameters may change drastically due to decreased cardiac output with subsequently reduced hepatic & renal blood flow.
- Blood drug level determination alone is unreliable for assessing possible overdose because clinical symptoms might persist beyond the drug's half life.

Characteristics of poisoning:

- The most commonly reported signs & symptoms of β -adrenergic blocker poisoning are listed in (Table 2).

- **Electrographic changes consist of first-degree AV block (prolonged PR interval), widening of the QRS complex, absence of P waves, & prolongation of the QT interval.**
- **Sotalol & acebutolol prolong the QT interval. The prolonged QT interval by sotalol predisposes to torsades de pointes (Figure 1), & ventricular dysrhythmias may complicate the therapeutic use of sotalol.**

Table 2. Clinical manifestations of β -adrenergic blocker toxicity.

Cardiac	CNS	Other
Arrhythmias	Sleepiness	Bronchospasm
Bradycardia	Dizziness	Pulmonary edema
Atrioventricular block	Unconsciousness	Hypoglycemia
Hypotension	Coma	Hyperkalemia
Shock	Seizures	
	Respiratory depression	

- **Cardiac changes do occur most frequently with drugs that have membrane-stabilizing action.**
- **Propranolol possesses the most membrane stabilizing QRS prolonged conduction, AV impaired bradycardia interval.**

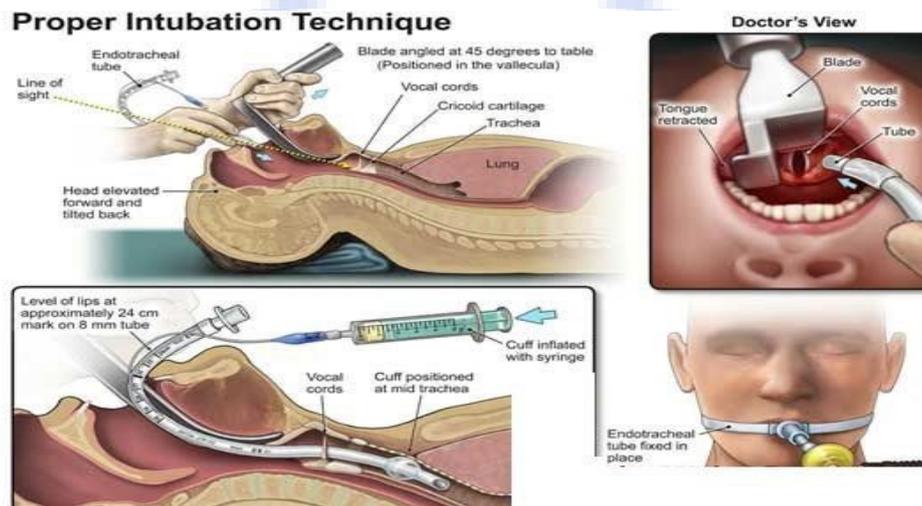
Management of poisoning:

- **The airway ventilation should be maintained with endotracheal intubation (Figure 2) if necessary.**

It is reasonable to give atropine before intubation of patients with bradycardia

- **Orogastric lavage is recommended for patients with significant symptoms such as seizures, hypotension, or bradycardia if the drug is still expected to be in the stomach.**

Before performing orogastric lavage, it is reasonable to pretreat patients with standard doses of atropine.



- **Activated charcoal can be given repeatedly during the first 24 hours**
- **Whole bowel irrigation with polyethylene glycol should be considered in patients who have ingested sustained release preparations**
- **Other areas of general management include giving glucose for hypoglycemia, diazepam for convulsions, monitoring potassium levels.**
- **In the treatment of bradycardia if the patient is compromised hemodynamically atropine may be given.**
- **The hypotensive patient may respond to fluids in the absence of pulmonary edema.**
- **Patients who fail to respond to atropine & fluids require management with the inotropes.**
- **When time permits, it is preferable to introduce medications sequentially. It is recommended to give:**

1. **Glucagon,**
2. **followed by calcium, high dose insulin euglycemia therapy, a catecholamine (isoproterenol, epinephrine, & dobutamine), & if this fails, then give**
 - **phosphodiesterase inhibitors**

