Practical Clinical Toxicology

Toxicity of β–adrenergic Blockers

Lab. 5

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by assistant lecturers

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- **Beta-blockers** antagonize beta-adrenergic receptors and are mainly used in the treatment of :
- Hypertension
- Heart failure
- Angina pectoris.
- Management of anxiety.
- Migraine headaches.
- Glaucoma.
- Tremors.
- Hyperthyroidism.
- Beta-blockers prevent remodeling of the heart after an ischemic event by reducing the effects of catecholamines on cardiac tissue.

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

	β_1-selectivity	Intrinsic sympathomimetic activity	Membrane stabilizing activity	Vasodilator effect	Lipophilicity	Elimination
First-generation						
Nadolol	0	0	0	0	Low	Renal
Pindolol	0	++	+	0	High	Renal/hepatic
Propranolol	0	0	++	0	High	Hepatic
Second-generation						
Acebutolol	+	+	+	0	Moderate	Hepatic
Atenolol	++	0	0	0	Low	Renal
Bisoprolol	++	0	0	0	Moderate	Renal/hepatic
Esmolol	++	0	0	0	Low	Renal
Metoprolol	++	0	+	0	High	Hepatic
Third-generation						
Betaxolol	++	0	+	+ (Blockade of calcium channel)	Moderate	Hepatic/renal
Bucindolol	0	+	0	+ (α_1-blockade)	Moderate	Hepatic
Carteolol	0	+	0	+ (α_1-blockade)	Low	Hepatic/renal
Carvedilol	0	0	++	++ (α_1-blockade)	Moderate	Hepatic
Celiprolol	+	+	0	+ (β_2 Agonism)	Moderate	Renal
Labetalol	0	+	+	++ (α_1-blockade)	Low	Hepatic
Nebivolol	++	0	0	++ (NO availability increases)	Moderate	Hepatic

+: Modest effect; ++: Strong effect; 0: Absence of effect; NO: Nitric oxide.

Pathophysiology

- beta-blockers are classified as selective and non-selective depending on the receptor specificity.
- Specificity is lost in cases involving overdose.

- To better understand the toxicity, beta-blockers are classified as lipophilic or lipophobic.

- Highly lipophilic beta-blockers can easily cross the blood-brain barrier and may cause various central nervous system (CNS) manifestations.

- Most of the beta-blockers are moderately lipophilic.

  Propranolol, the most lipophilic beta-blocker, can easily cross the blood-brain barrier and may cause seizures in overdose cases.

  The liver excretes beta-blockers most frequently, **Atenolol, carteolol, and nadolol** are the only exceptions that undergo renal excretion.

Various beta-blockers may cause sodium or potassium channel blockade and therefore cause prolongation in QRS and QTc intervals, respectively.

Sodium channel-blocking beta-blockers are said to possess “membrane stabilizing activity” which potentiates toxicity in overdose.

Bradycardia associated with hypotension may be the first clue to diagnose beta-blocker overdose. patients with BB toxicity have hypoglycemia and altered mental status.

While symptoms secondary to beta-blocker overdose usually appear early and are commonly observed within one to two hours.

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
	Seizures	
Shock	Respiratory depression	

Treatment / Management

1-Premedication with atropine may be necessary

2-Bronchospasm may be treated with oxygen and inhaled bronchodilators like albuterol.

3-Gastric lavage may be necessary for patients who present shortly after massive ingestions and/or with serious symptoms.

4-Administer activated charcoal.

5-Consider whole bowel irrigation with PEG in case of sustained-release preparations.

6-Benzodiazepines are the first line of treatment for seizures.

7-In the case of QRS widening, administer sodium bicarbonate while magnesium sulfate is administered for QTc prolongation.

8-glucagon is considered a useful treatment of choice.

9-Cases not responding to fluids, atropine, and glucagon are considered candidates for **high-dose insulin, euglycemia (HIE) treatment.**

High-dose insulin, euglycemia can cause profound hypokalemia and hypoglycemia that can potentiate cardiotoxicity in the setting of beta-blocker overdose.

Therefore, Potassium and glucose should be checked before initiation of high-dose insulin, euglycemia.

In general, 1 U/kg of regular insulin bolus along with 0.5 g/kg dextrose intravenously (IV) is administered.

Glucose should be monitored every 30 minutes initially for up to four hours to maintain strict glycemic control (glucose 100 mg/dL to 200 mg/dL)

Supportive treatment with vasopressors may be needed since the inotropic effect of high-dose insulin euglycemia may be delayed up to **15 min to 60 min**.

Phosphodiesterases such as inamrinone and milrinone increase the cAMP and may prove beneficial in increasing inotropy.

Hemoperfusion & and hemodialysis may be considered in cases involving nadolol & and atenolol.


Thank
you