University of Mosul
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College of Veterinary Medicine
Date:
Unit of Scientific Affairs
Website:

Lecture title: ANTIADRENERGIC DRUGS (Sympatholytics)

Lecturer Affiliation: College of Veterinary Medicine

Summary:

ANTIADRENERGIC DRUGS (Sympatholytics)

Antiadrenergic drugs can be classified under two heads: -

(1) Direct acting adrenergic receptor blockers or adrenergic antagonists: These drugs interact with adrenergic receptors and by occupying these sites do not allow an adrenergic agonist access to the receptor.

Adrenergic blockers

I-Alpha adrenergic blockers:

- α 1 and α 2 nonselective blocker (Phenoxybenzamine , Phentolamine)
- selective α 1 blocker prazosin
- selective α 2 blocker yohimbine
- ergot alkaloids

Non selective α 1 and α 2 blocker:

1-Phenoxybenzamine:

Its blocker to α receptors, its bind to receptors irreversibly by covalent bond.

Long acting 4days

Uses

1- In pheochromocytoma with propranolol (which block β 1 and β 2).
2- In dog and cat reduce hypertonus at urethral sphincters
3- In horse: treat laminitis and secretory diarrhea.

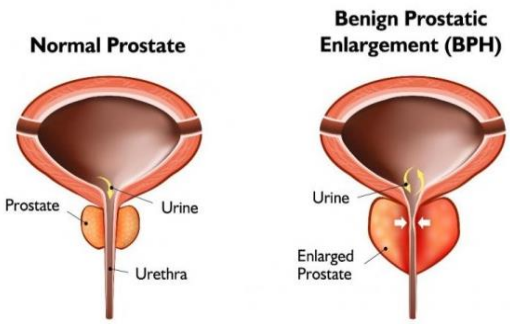
Adverse effect:

1- ↓BP with reflex tachycardia.
2- Miosis
3- Not use in horse with colic

2-Phentolamine

It's a competitive **α 1 and α 2** receptors antagonist.

Selective α 1 blocker:



1-Prazosin

Its act by block α 1 receptor

Effects

1-Vasodilation

2- Direct relaxation of smooth muscle of blood vessels

3- Don't affect RBF

4- ↓BP and lipid profile (cholesterol and triglyceride)

Uses:

1- Hypertensive patient with renal disease
2- Acute heart failure
3- Urine retention in benign prostate hypertrophy

Adverse effect:

F→ First dose syncope

F→ Fluid retention

U→ Urine incontinence

2-Tamsulosin:

Block α1A which located in the sphincter of UB, (α1B found in BV).

Uses

1- Symptom of BPH.

2- Allowing kidney stones to pass through ureter.

Selective α 2 blockers

Yohimbine and Atipamizole

Mechanism of action:

are competitive α 2 receptors antagonist.

Pharmacological effects:

1- CNS stimulation
2- Increase heart rate
3- Increase salivation

Uses:

Reverse the effect of xylazine

Ergot alkaloids

Natural	**Semisynthetic**
Ergotamine	Dihydroergotamine
Ergometrine	Methylergometrine
Ergotoxin (very toxic)	Dihydroergotoxin
Bromocriptine	

Note: all ergot alkaloids stimulate vomiting center

Caffeine increases the absorption

Drug	Properties	Effect	Uses
Ergotamine	Partial agonist for α 1 and 5HT receptor	Vasoconstriction of cerebral blood vessels	Migraine
Ergometrine	Agonist α 1	Vasoconstriction and uterine contraction	Post-partum hemorrhage
Dihydroergotoxin	Antagonism of α 1	Vasodilation of cerebral blood vessels	Cerebral insufficiency
Bromocriptine	Dopamine receptor agonist	↓ prolactin secretion	Treat Parkinson Treat hyperprolactinemia

Beta blocker

1- β 1 and β 2 blockers: Propranolol, Nadolol, Sotalol and Timolol

2- β 1 blockers: Atenolol, Esmolol, Metoprolol

3- β 1 blocker with direct vasodilator: carvedilol and labetalol

Pharmacokinetics:

1- absorbed well

2- extensive first pass metabolism

	Nonselective beta blockers	Selective beta blockers
1	Propranolol	atenolol
2	Lipophilic	Hydrophilic
3	CNS effect	no
4	↑ distribution	↓ distribution
5	Need liver metabolism to be more water soluble	no
6	Short duration	Long duration
7	Multiple dose	One tablet daily

Pharmacodynamics

1- Heart: decrease HR
2- Decrease blood pressure by the following mechanisms:
   - ↓↓ COP by their blocking β 1 receptor .
   - ↓↓ renin release from the kidney by their blocking β 1 receptor .
   - ↓↓ Norepinephrine release and central sympathetic outflow (by blocking presynaptic β 2).
   - Resetting the sensitivity of baroreceptor.
   - Increase vasodilator prostaglandins (PGI_2).
   - Some β blockers block also vascular α 1 receptor.

3- Respiratory system: bronchospasm.
4- Eye: decrease intraocular pressure
5- CNS: beta2 presynaptic → ↓ NE release → sedation →depression (antianxiety effect).

Beta blocker with special effect

1- Propranolol: membrane stabilization action so it has local anesthetic effect and antiarrhythmic action.
2- Pindolol: partial agonist---no Brady cardia
3- Esmolol: very short acting use during surgery to prevent arrhythmia.
4- Labetalol: beta and alpha 1 blocker ----pheochromocytoma.
5- Carvedilol : antioxidant action .

Uses:

1- Hypertensive patient.
2- Ischemic heart disease.
3- Cardiac arrhythmia
4- Hyperthyroidism
5- Glaucoma (betaxolol)
6- Pheochromocytoma. (timolol).
7- Migraine prophylaxis: Propranolol>Metoprolol
8- Anxiety.
9- Tremor.
10- Effective in asthma and may promote bronchodilation: Celiprolol
11- Augmentation therapy of depression: Pindolol

Adverse effects:

1- Fatigue due to ↓COP and ↓ blood supply of skeletal muscle
2- Bronchoconstriction.
3- Bradycardia
4- Peripheral ischemia.
5- Sleep disturbance (nightmare and vivid dream)
6- Cold extremities

(2) Indirect acting adrenergic neuron blockers: These drugs do not block receptors; instead, they act presynaptically at the nerve terminal to cause a decreased release of the endogenous neurotransmitter norepinephrine**.**

The adrenergic neuron blockers interfere with the transmitter function of adrenergic neurons by the following mechanisms:

(i) By interfering with the synthesis of catecholamines: e.g. Methyldopa and methyltyrosine.

(ii) By interfering with storage of norepinephrine: e.g. Reserpine (It depletes NE stores in adrenergic neurons).

(iii) By preventing the release of norepinephrine: e.g. Guanethidine

Adrenergic neuron blocker

- **α - methyldopa**

Mechanism of action: its act by enter in the NE synthesis as a false substrate which result in α - methylnorepinephrine (false transmitter) which act on α 2 receptor .

Uses: treatment hypertensive pregnant

Adverse effects

1- Sympathetic blocked→ postural hypotension, nasal congestion.
2- CNS signs→ sedation, depression and parkinsonian signs.
3- Increase prolactin hormone: due to inhibition of dopaminergic mechanism →gynecomastia in male and galactorrhea in female.
4- Allergy

- **Reserpine**

Mechanism of action:

This drug facilitates the NE release from the nerve ending and prevent reuptake 3 to the vesicle which result in destroyed by MAO leading to depletion of NE, D and 5HT.