Lecture title: Noradrenaline

Lecturer Affiliation: College of Veterinary Medicine

Summary:

II-Noradrenaline

Mechanism of action: its potent agonist on α 1, α 2 and β 1 receptors

90% on α 1----------10% on β 1

Pharmacological effects:

1- Blood vessels: VC→ increase BP

2- Heart increase BP → reflex bradycardia

3- Uterus: contraction by activation α1 receptor.

Uses: acute hypotension in dogs

Administration: not SC or IM or IV but only intravenous infusion because of tissue necrosis.

III-Dopamine:

Dopamine receptors:

D1 (Gs) → **Renal**, mesenteric and coronary circulation → vasodilation

D2(Gi) →CNS (presynaptic nerve)

D3(Gi) →CNS

D4(Gi) →Heart and CNS

D5(Gs) →Lymphocyte

Pharmacodynamic:

Low dose →activate D1 →Vasodilation

Intermediate dose →activate β 1→ increase cardiac output

Large dose → activate α 1 →vasoconstriction

Uses

Shock state (septic shock) with impaired tissue perfusion

Dopamine used to combat reductions in renal blood flow that may contribute to acute renal failure. It also increases glomerular filtration and sodium excretion. is given as above, and furosemide is given at 1 mg/kg/hr, by IV bolus. If no improvement occurs within 6 hr, conversion is unlikely, and infusion should be discontinued. Dialysis (hemodialysis or peritoneal dialysis) may be required to maintain these animals.

Administration

IVI only

Dopamine	***Dobutamine***
Natural cat	Synthetic cat
D1 >β 1>α 1	β 1
Septic shock	Cardiogenic shock+CHF

Selective adrenoceptor agonist

I-Selective β1 agonist → dobutamine

II-Selective D1 agonist → fenoldopam: selective peripheral dopamine receptor D1 agonist, given by CRI to treat sever hypertension in hospitalized patient.

III-Selective α1 agonist:

- Phenylephrine
- Methoxamine

- Midodrine
  Non catecholamine

  Act as vasopressor

  Administration

  1. Injectable 2. Eye drop 3. Nasal drop 4. Tablet

  Uses

1. Red eye
2. Nasal decongestion
3. Mydriatic agent
4. Hypotension

Adverse effect:

1. Rebound congestion.

2. Stroke hypertension.

3. Atrophic rhinitis.

IV-Selective α2 agonist:

Xylazine, Medetomidine, Detomidine, Clonidine, Tizanidine

Chemistry: its non-catecholamine

Mechanism of action:

1) Stimulate presynaptic α_2 receptors →this binding decreases presynaptic Ca^{+2} levels and inhibit release of NE

2) Stimulate central α_2 receptors→ decrease sympathetic outflow → decrease NE and renin.

3) Stimulate I_1 (imidazoline) receptors → sympatho inhibitory action .

Clinical uses

1- Sedation

2- Anesthesia
3- Muscle relaxation
4- Analgesia
5- Emetic in cat
6- Hypertension
7- Treat withdrawal syndrome

Adverse effect

S→ Sedation, dry mouth

S→ Sudden withdrawal leads to sever hypertension

S→ Salt and water retention

Tizanidine: act specially on the α 2 receptor in the spinal cord leading to muscle relaxation so it used in muscle spasm.

Beta agonist

1- *Selective beta 2 agonist*
2- *Selective beta 1 agonist →dobutamine*
3- *Non selective beta agonist →isoprenaline Its synthetic cat act on β1 and β 2*

Selective β $_2$ agonists

Salbutamol, Ritodrine, Terbutaline, Salmeterol, Zilpaterol, Clenbuterol and Ractopamine.

- Its non-catecholamine
- Taken orally
- Have long duration
- Not destroyed by MAO and COMT

USES

1-Bronchial asthma.

2- Uterine relaxation (ritodrine). → premature labor

3- Clenbuterol, zilpaterol and ractopamine: used for increase the size of animals and efficacy of feeding them.

Off label uses:

1-Bodybuilding and animal feeding (fat burning and muscle gain).

2- Doping: increase performance in healthy athletes.

Adverts effects

T→ Tachycardia

T→ Tremors

T→ Tolerance

H→ Hypokalemia

Indirect sympathomimetic

These drugs cause release of NE from the sympathetic system.

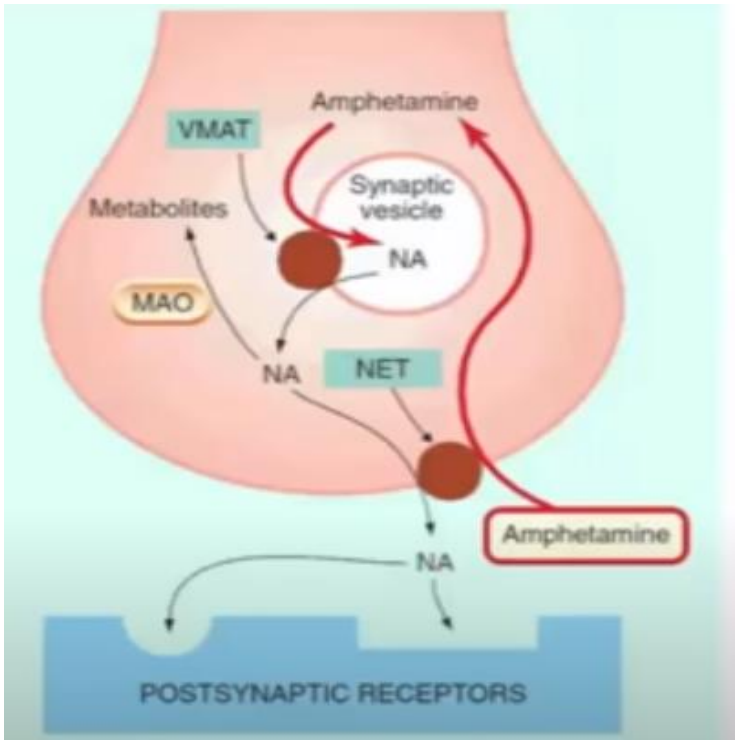
I-Amphetamine: its synthetic drug, not catecholamine, absorbed orally
Act on the nerve ending promote adrenaline release **and** inhibit the uptake leading to accumulation of NE, E, D and serotonin in the synaptic space.

Effects

- CNS stimulation
- Anorexia
- Euphoria
- Analgesic
- Hallucination

Adverse effects:

- Physical dependence
- Insomnia
- Nervousness
- Headache
- Seizure



Notes:

Amphetamine derivatives→ **Methylphenidate** uses in attention deficit – hyperactivity disorder.

Modafinil: used in narcolepsy, (Go pill)

II-Cocaine:

1. its plant alkaloids
2. **inhibit reuptake of E**
3. used as local anesthetic
4. toxicity of cocaine treated by benzodiazepine.

Mixed acting sympathomimetic

I-Ephedrine: act on the α and β receptor **and** stimulate the release of adrenaline from the nerve ending

Chemistry: its natural from plant alkaloid, its non- catecholamine.

Effects: CNS stimulation and bronchodilator.

II-Pseudoephedrine: available as eye drop and nasal drop to treat congestion

Off label uses:

1- Performance enhancing.

2- Treatment of depression.

3- Obesity treatment.

Notes: ephedrine cause urinary retention because it stimulate α 1and β 1 receptor in the bladder and contraction of the sphincter and because it have long duration of action (8h) unlike adrenaline which is catecholamine remain in the body for few min.