ADRENERGIC DRUGS - I

I Differences b/w α_1 and α_2 Receptors.

	α_1	α_2
Location	Post. junctional on effector organs	Prejunctional on nerve endings (α_{2A}) also post-junctional in brain, pancreatic β cells & extra junctional on certain blood vessels, platelets.
Functions.	Vasoconstriction. Gut smooth muscle contraction Gland - secretion CVT - relaxation eye - contraction of Radial muscles of Iris - mydriasis Urin - constriction Blood vessels - vasoconstriction Liver - Glycogenolysis Heart - Arrythmia.	Inhibition of Transmitter release vasoconstriction Decd central sympathetic flow. Decd insulin release platelet aggregation
Selective Agonist	Phenylephrine	Clonidine.
Selective Antagonist	Prazosin	Yohimbine.
Coupling Protein	G_q	G_i / G_o

Effector pathway	IP_3 / DAG ↑ Phospholipase A_2 ↑, Ph release	cAMP ↓ K^+ channel ↑ Ca^{2+} channel ↓ or ↑ IP_3 / DAG ↑

II Difference b/w B_1, B_2, B_3 receptors.

	B_1	B_2	B_3
Location	Heart, JG cells in kidney	Bronchi, bld vessels, Uterus, Liver, Grit, Urinary tract, etc	Adipose tissue, Detrusor muscle of bladder.
Selective Agonist	Dobutamine	Salbutamol	Mirbegron.
Selective Antagonist	Metoprolol	α-methyl propranolol	—
Functions	Cardiac stimulations ↑ce in force, rate, contraction, velocity, Renin release from kidney	Dilation of arterioles & veins; bronchodilation Intestine ↓ Relax^n Uterus ↓ Relax^n eyes - Alt secretion Glycogenolysis; Lipolysis, insulin, Glucagon secretion	Lipolysis Relax detrusor muscle

ADRENERGIC DRUGS - II

---

① NASAL DECONGESTANTS.

→ Are α_2 receptor agonist which on topical application as dilute solution (0.05 - 0.1%) produce vasoconstriction in nasal mucosa which primarily expresses α receptors.

the imidazoline compounds [xylometazoline and oxymetazoline] are relatively selective α_2 agonists. (like clonidine) with longer duration of action (12 hr) than ephedrine.

After congestion in nasal mucosa is claimed to be less likely than that with ephedrine or phenylephrine. They may cause initial stinging sensation.

Regular use of these agents for long periods should be avoided because mucosal ciliary function is impaired; atrophic rhinitis and anosmia can

develop due to persistent vasoconstriction. These drugs can be absorbed from the nose and produce systemic effects, mainly CNS depression and rise in BP

Nasal decongestants should be used cautiously in hypertensives and on those receiving MAO inhibitors.

② DRUG OF CHOICE IN ANAPHYLACTIC SHOCK.
- ADRENALINE (Reason)

Adrenaline 0.5 mg injected intramuscularly promptly is the DOC in anaphylatic shock. It not only raise BP, but also counteracts bronchospasm and laryngeal edema that may accompany. [Also, Adr should not be injected i.v. (can itself be fatal) unless shock is immediately life threatening. Because of this peculiar mode of action as well as rapidity of onset, Adr is the only life saving measure.

③ DRUG OF CHOICE IN CARDIOGENIC SHOCK - DOPAMINE

Dopamine action: dopaminergic [D_1 & D_2] + weaker adrenergic β_1 + very weak α receptor agonist.

* The D_1 receptors in renal & mesenteric bed vessels are the most sensitive; IV infusion of low dose of DA dilates these vessels [by raising intracellular

cAMP]. Increased renal flow rates GFR. In addn. DA exerts natriuretic effect through D_1 receptors on proximal tubular cells

Moderately high doses produces a positive ionotropic [derived β_1 & D_1 action + that due to NA release], but little chronotropic effect on heart. Vasoconstriction [α_1 action] occurs only when large doses are infused.

* At clinically employed dose, it raises CO and systolic BP with little effect in diastolic BP.

→ Dopamine is used in patients of cardiogenic shock / septic shock & acute heart failure where it increases BP & urine outflow. It is administered by IV infusion [0.2 – 1 mg/min] which is regulated by monitoring BP & rate of urine outflow.

(4) RATIONALE FOR COMBINING ADRENALINE WITH LIGNOCAINE.

Addition of a vasoconstrictor like Adr has several advantages :-

- Prolongs duration of action of Local Anesthetic Lignocaine by slowing rate of removal from local site into circulation; contact time of lignocaine with nerve fibre is prolonged.
- Enhances intensity of nerve block
- Reduces systemic toxicity of lignocaine; rate of absorption slowed & metabolism keeps plasma conc. lower.
- Provides more bloodless field for surgery

[Also, lignocaine 2% with Adr 1:80000 in 1.5ml cartridge. for dental anesthesia]

[As local vasoconstrictor (Adr) 1 in 2,00,000 to 1 in 8000 added to lignocaine]

⑤ USES AND ADVERSE EFFECTS OF ADRENALINE.

* Adverse effects & contraindications.

transient nervousness, headache, palpitation, anxiety, tremor & pallor may occur after S.C / IM injection of Adr

* Hazards of large doses or inadvertent IV injection of Adr are Marked rise in BP leading to cerebral hemorrhage, ventricular tachycardia / fibrillation, angina, MI.
* Adr is contraindicated in Hypertensive, Hyperthyroid & angina patients.
* Adr should not be given during anesthesia with halothane (milk of magnesia) and to patients receiving β blockers (marked rise in BP can occur due to unopposed α Action.

Actions of Adr

the peripheral actions of Adr in most tissues have been clearly differentiated into those mediated by α or β receptors depending on predominant receptor type present in a given tissue.

[Adr : $\alpha_1 + \alpha_2 + \beta_1 + \beta_2$ + weak β_3 action]

α - Actions	β - Actions.
* Constriction of arterioles & veins → rise in BP. [$\alpha_1 + \alpha_2$]	* Dilation of arterioles & veins → fall in BP [B_2].
* Heart : Little action	* Cardiac stimulation (B_1), ↑ rate, Force & conduction velocity.
*	* Bronchodilation (B_2)
* Contraction of radial muscles of iris → mydriasis (α_1), ↓ed aq. secretion.	* No effect on iris, slight relaxation of ciliary muscle, enhanced aq. secretion.
* Intestinal relaxation, contraction of sphincters	* Intestinal relaxation.
* Bladder trigone, prostate - contraction (α_1)	* Detrusor - relaxation (B_2, B_3)
* Uterus contraction (α_1)	* Relaxation (B_2)
* Neuromuscular transmission facilitated, ↑ Ach release	* Active state - prolonged in fast contracting muscle, abbreviated in slow contracting muscle; tremors (B_2)
* Insulin secretion inhibited (α_2) (dominant)	* Augmented insulin (mild) & glucagon secretion (B_2)
*	* Liver glycogenolysis (B_2) → Hyperglycemia Muscle - glycogenolysis (B_2). → Hyperlactatemia. Fat - lipolysis ($B_1 + B_2 + B_3$) → ↑ed b/d FFA calorigenesis.
* Renin release ↓ (α_2)	* Renin release ↑ (B_1) dominant
* Male sex organs - ejaculation (α_1)	*
* Salivary gland - K⁺ & H_2O secretion (α_1)	* Pancreatic secretion.

* Adrenergic nerve-inhibits NA release terminals

* ADH secretion from post-pituitary (β_1)

* Facilitates NA release (mild action).

ANTIPLATELET DRUGS