

CHAPTER

PHARMACOLOGY

(ADRENERGIC DRUG)

- ◆ Dopamine, Nor adrenaline and Adrenaline are endogenous catecholamine.
- ◆ These are chief Neurotransmitter of adrenergic system.
- ◆ Nor adrenaline (Nor epinephrine) is a neurotransmitter of most site.
- ◆ Catecholamine are biosynthesized by phenyl alanine (in liver).

Bio synthesis

Phenylalanine → Tyrosine → DOPA → Dopamine → Nor-Adrenaline → Adrenaline
(In liver)

- ◆ Endogenous catecholamine are metabolized in small intestine (COMT and MAO) and in liver (By MAO)

Action

- ◆ Dopamine act on α_1 , β_1 , D_1 and D_2
- ◆ Noradrenaline - α_1 , α_2 , β_1 , β_3 – Not action β_2 (very poor)
- ◆ Adrenaline - α_1 , α_2 , β_1 , β_2 and β_3

Adrenergic drug classification

(1) Directly acting

(a) Catecholamine:-

(i) Endogenous - ◆ Dopamine, Nor adrenaline and Adrenaline

(ii) Exogenous - ◆ Dobuta mine (β_1)

◆ Isoprenaline ($\beta_1\beta_2\beta_3$)

◆ Feneldopam (D_1)

(b) Non catecholamine:-

◆ Xylometazoline

◆ Phenyl Ephrine

◆ Clonidine

◆ Salbutamol

◆ Methoxamine

◆ Midodrine (Prodrug)

(2) Indirectly acting

(a) Reuptake inhibitor - ◆ Cocaine ,TCA, Tyramine

(b) Action by displacement - ◆ Amphetamine ,Modafinil ,Methyl phenidate

(3) Mixed action

◆ Ephedrine , Pseudo Ephedrine

Action of Adrenergic system

Heart - Positive inotropic, Positive chronotropic and positive dromotropic

Blood vessels - α_1 - cause - vaso constriction - \uparrow DBP

β_2 causes - vaso dilation - \downarrow DBP

Uninary system - Causes urinary retention due to relaxation of detrussor (β_2 action)
and contraction of trigone (α_1 action)

Bronchi - Bronchodilation (β_2 action)

Eye - Mydriasis (α_1 action)

Gland - Thick salivary secretion. \uparrow sweating

Metabolic action - Hyper glycemia due to glycogenolysis and gluconeogenesis (β_2 action)

\downarrow Release of Insuline (α_2 action)

◆ β_1 stimulation causes Renin release in kidney and β_2 causes tremor.

Action of catecholamine

(1) **Adrenaline** - DOC in Anaphylactic shock

◆ Dose 0.5 mg(IM/SC)

Indication	Route	Drug concentration
◆ Bronchial Asthma,	Inhalational	1 : 100
◆ Anaphylactic shock	I.M	1 : 1000
◆ Anaphylactic shock	SC	1 : 1000
◆ Anaphylactic shock	IV	1 : 10000
◆ Cardiac Arrest	Intra cardiac	1 : 10000
◆ With local anaesthetic	SC	1 : 200000

(2) **Dopamine** - DOC for cardiogenic shock with oligouric renal failure

◆ Dopamine act on D_1 , β_1 and α_1

◆ Dopamine causes renal vasodilation (D_1)

◆ Dopamine so dose related effect first on D_1 , β_1 then α_1

(3) **Nor Adrenaline** - Act on α_1 , α_2 , β_1 and β_3

◆ It does not have or have very poor action on β_2 .

◆ NA cause renal vaso constriction

◆ NA used in Hypotension

(4) **Dobutamine** - Selective β_1 agonist \uparrow Cardiac output

(5) **Fenaldopam** - D_1 agonist, used in Hyper tensive emergency

Non catecholamine

1) α_1 **Agonist** - used as nasal decongestant

Ex- Xylometazoline, Naphazoline, oxymetazoline

- ◆ Prolong use of α_1 agonist cause **Atrophic rhinitis (Rhinitis Medigamentosis)**.
- ◆ Phenyl ephrine used as mydriatic
- ◆ Midodrine (Prodrug) used for treatment of orthostatic hypotension (Postural hypotensen)

2) α_2 **Agonist** - Clonidine use for

- ◆ Managment of withdrawl symptoms of Alcohol, Nicotine and Opioid
- ◆ Prophylaxis of migraine,
- ◆ Prevent Diarrhea in diabetic
- ◆ Also used in ADHD
- ◆ Clodine have antihypertensive activity

Dexmeditomidine - Used for preanaesthetic medication and produce sedation in ventilated patients in ICU

α **Methyl dopa** - Produce false neurotransmitter that is methylnoradrenaline.

- ◆ It is safest antihypertensive drug for the treatment of Aclampsia.

3) β_1 **Agonist** - Prenaltrenol, Dobutamine (usde in cardiac shock)

4) β_2 **Agonist** - Salbutamol, salmeterol, Fenotelol Terbulaline use in bronchial Asthma.

◆ **Ritodeine and Isoxsuprene** are tocotytic (uterine relaxant) used in premature delivery.

Indirectly acting

- ◆ Tyramine causes cheese reaction patient taking MAO inhibitor
- ◆ Methyl Phenidate used in ADHD
- ◆ Amphetamine is addictive substance can cause Tolerance and dependance.
- ◆ It is also produce **Kick** effect with sodium bicarbonate
- ◆ Modafinil used in **narcolapsy** in shift worker

Mixed action

- ◆ Ephedrine and Pseudo ephedrine are anticold, used in Asthma.
- ◆ **Ephedrine vesso pressure of choice in pregnancy**

Anti Adrenergic(Sympatholytic Drugs)

1) **Non selective** α - Blocker

1) **Irreversible** α **Blocker** - Phenoxy benzamine

2) **Reversele** α **Blocker** - Phentolamine and Tolazoline

- Both type of drug causes vasodilation and Postural Hypotension

◆ **Phenoxybenzamine** - DOC for prevention of hypertension episode during operation of pheochromo cytoma (Adrenal tumor)

◆ **Diagnosis of pheochromocytoma done by phentolamine**

◆ **Phentolamine and Tolazoline** - are preffered drug for the treatment of hypertensive crisis in **clonidine withdrawal** and **cheese** reaction

2) α_1 Blocker - Prazosin, Terazosin, dexazosin

Tamsulosin, silodosin, Indoramine. urapadil

- ◆ α_1 Blocker - \downarrow LDL, \downarrow VLDL, \uparrow HDL
- ◆ α_1 Blocker - are Doc for Patient of hypertension with BHP (Benign Hyperplasia of prostate)
- ◆ Prazosin is Doc for scorpion Bite
- ◆ Tamsulosin and silodosin most effective for BHP patient

ADR

- ◆ Postural Hypotension (Initial Doses)
- ◆ Tolerance (continous use)
- ◆ Inhibition of ejaculation
- ◆ Causes floppy Iris syndrome

3) α_2 Blocker - yohimbine, Idozoxan

4) Non selective β Blocker (First generation β - Blocker)

EX.- Propanolol (Max. membrane stabilizing)

- ◆ Temolol used in glucoma
- ◆ Nadolol (longest acting , lipid insoluble)
- ◆ Metinoprolol, pindolol, Alprenolol

Effect of Non selective β Blocker

- ◆ Causes \uparrow Broncho constriction (Contraindicated in Asthma)
- ◆ \uparrow LDL and VLDL, \downarrow HDL
- ◆ \downarrow Myocardial oxygen demand (can be used in classical angina)
- ◆ Coronary vasoconstriction can occur (β_2 action) so contraindicated in variant Angina
- ◆ \downarrow Production of Aqueous humor (used in glucoma)
- ◆ Causes Hypoglycemia for diabetic taking insulin and oral hypoglycemia

Drug for Glucoma

- ◆ Glucoma is progressive damage of optic nerve that raise intra ocular tesion (IOT)
- ◆ In Glucoma IOT $>$ 21 mm Hg
- ◆ Normal IOT - 10 - 21 mm Hg

Glucoma

- 1) Primary open angle glucoma (POAG)- \uparrow IOT and \uparrow Aqueous humour \downarrow Drainage
- 2) Acute angle closure gloucoma

Drug for glucoma

(1) Drug for primary open angle glucoma (POAG)

- (a) β Blocker (Timolol and Betaxolol), \downarrow Aquous humor
- (b) Levubunolal and Betaxalol - are safe in asthmatic, diabetic, hyperlipidimic
- (c) Prostaglandin - Increase outflow (Drainage)

Prostaglandin are Doc for POAG

Ex. Latanoprost, unoprostone

(d) α **Agonist**- Apraclonidine , bromonidine Depivefrine, Adrenaline - \downarrow Aqueous humor

(e) **Carbonic Anhydrase inhibitor** - \downarrow IOT and \downarrow Aqueous humor

◆ Acetazolamide (Oral), Dorzelamide and Brinzolamide - Topical

(f) **Mitotic** - Pilocarpine (Short acting) and physostigmine (Long acting)

(2) Drug for acute angle closure glaucoma (Acute glaucoma)

◆ Primary treatment is **Surgery**

◆ **Drug** - Mannitol 20% (IV infusion), 10 % glycerol, pilocarpine, acetazolamide (oral), dorzolamide, brinzolamide