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Diploma in Pharmacy 2nd Year
Pharmacology
Chapter 2 : Drugs Acting On Peripheral Nervous System

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Drugs Acting On Peripheral Nervous System

- **CNS** : Includes the brain and spinal cord.
- **PNS** : It consists of the nerves branched out from the brain and spinal cord . These nerves form the communication network between the CNS and body parts.
 - **Somatic Nervous System** : It is a part of PNS and associated with the voluntary control of body movement via skeletal muscles . sensory and motor neurons found in it.
 - **Autonomic Nervous System** : It is a part of PNS also, and associated with Involuntary Physiological Process e.i. Heart rate , blood pressure , digestion etc.

Neurotransmitters

- Neurotransmitters are chemical compounds present in the brain.
- They are made up of amino acids and some of them are hormones.
- They transmit information from one neuron to the other.
- Major body functions like movement, emotional response, and the physical ability to experience pleasure and pain are controlled by neurotransmitters.
- Neurotransmitters are specific chemical signals allowing communication between nerve cell and effector cells/organs.

Substances acting as neurotransmitters can mainly be categorised into the following three classes:

- Amino acids (primarily glutamic acid, Gamma-Aminobutyric Acid (GABA). aspartic acid, and glycine).
- Peptides (vasopressin, somatostatin, neurotensin, etc.)
- Monoamines (NE, dopamine and serotonin) plus Ach

Classification of Neurotransmitters

The neurotransmitters can be classified:

On the Basis of Secretion Site: These are of two types:

1. **Neurotransmitters of Sympathetic Nervous System:** In this, two neurotransmitters are present:
 - Acetylcholine (ACh) (liberated at the ganglion) acts as a neurotransmitter for the preganglionic sympathetic nerves.
 - Nor-adrenaline (NA) acts a neurotransmitter for the postganglionic sympathetic nerves.

2. **Neurotransmitters of Parasympathetic Nervous System** : In parasympathetic nervous system, only Ach is released at the ganglion and it acts as a neurotransmitter for the preganglionic parasympathetic nerves. Acetylcholine (ACh) also acts as a neurotransmitter for the postganglionic parasympathetic nerves.

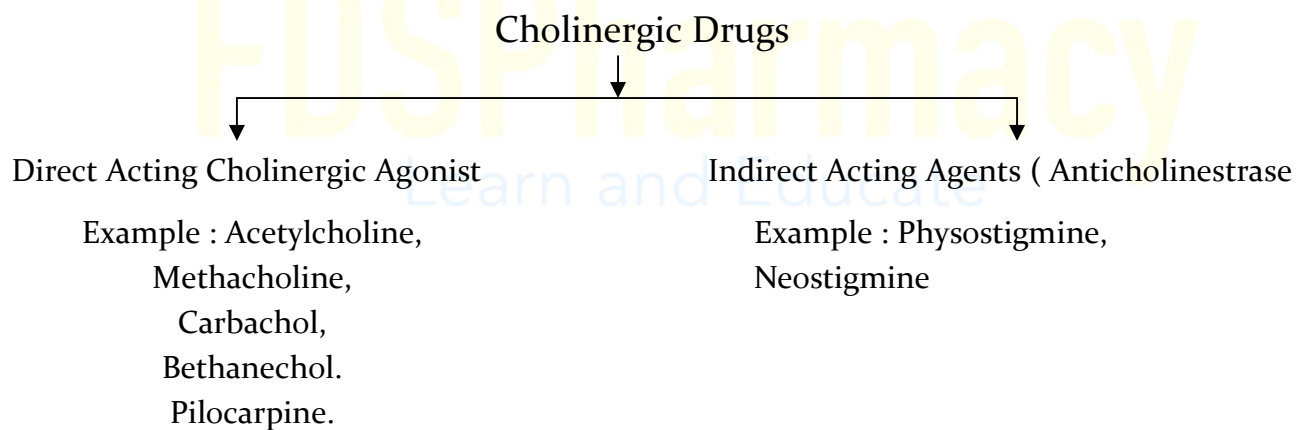
Steps Involved In Neurohumoral Transmission

- ⇒ Initiation Of an Action Potential and Axonal Conduction.
- ⇒ Arrival of an AP at nerve terminal , resulting in the release of the transmitter.
- ⇒ Events at the synaptic cleft and post - junctional sites.
- ⇒ Termination of effect of released Transmitter.

Cholinergic Drugs (Parasympathomimetic Agents)

- Cholinergic Drugs are those drugs which give action similar to acetylcholine.
- They give their action by directly binding to the cholinergic receptors or by indirect process.

Classification



1. Direct Acting Cholinergic Agonist

- These drugs produced actions similar to ACh by directly interacting with cholinergic receptors . Acetylcholine , Methacholine , Carbachol , Bethanechol. Pilocarpine.

2. Indirect Acting Agents (Anticholinestrace)

- These drugs inhibit the enzyme cholinestrace , this enzyme inactivates the Acetylcholine . Physostigmine (this can cross blood brain barrier) Neostigmine (this can't cross blood brain barrier).

Pharmacological Actions

1. Muscarinic Action

- Heart : bradycardia (slow down heart rate)
- Blood Vessels : dilates blood vessels , lowers blood pressure
- Respiratory System : bronchoconstriction
- smooth muscles : contracts smooth muscles
- Exocrine Gland : Increase secretion (saliva ,HCL , Pancreatic Juice)
- GI Tract : Increase peristalsis Movement .
- Urinary Bladder : Contraction
- Eye : Contraction of Pupils

2. Nicotinic Action

- Skeletal Muscle : Contraction
- CNS : ACh does not cross BBB , but if injected directly into brain and stimulates initially and then depresses.

Indication

1. Acetylcholine is mainly used in experimental studies , and has limited clinical value because of following reasons.
 - It is rapidly hydrolysed by the Pseudocholinesterases.
 - It spread widely and diffuses in easily and thus does not produce a selective pharmacological action.
 - It can not be administered orally as it immediately hydrolysed and degraded by gastric enzymes.
2. Methacoline is not used nowadays.
3. Carbachol shows action on M and N receptors non selectively , so no longer in use.
4. Bethanechol Is in use as
 - In case of gastroparesis , postoperative abdominal distension.
 - In case of urinary bladder retention.

Dose

- Bethanechol : 5 or 10 mg tablets , 10-30 mg 3-4 times in a day.

Contraindications

- ◇ Hyperthyroidism : Choline ester may precipitate cardiac arrhythmias.
- ◇ Bronchial Asthma : Choline ester may precipitate bronchospasm.
- ◇ Peptic ulcer : Choline ester may increase gastric acid secretion.
- ◇ Myocardial Infarction : Choline ester may cause hypotension and form conduction block.

Pilocarpine

→ It is a alkaloid cholinergic drug , and it is a selective muscarinic agonist , therefore most of muscarinic effects can be predicted .

Pharmacological action

- Eye : miosis
- CVS : when administered intravenously a brief fall in blood pressure is seen.
- Sweat Glands : Excessive amount of sweat secret . (termed as diaphoresis)

Indication

▲ Pilocarpine is commonly used in glaucoma as eye drops.

Dose

✚ It is used 1-4 % pilocarpine nitrate in eye drops.

Contraindications

- During pregnancy and lactation
- In children because its safety and efficacy is not clear.
- In older people may cause diarrhoea , urinary frequency and dizziness.

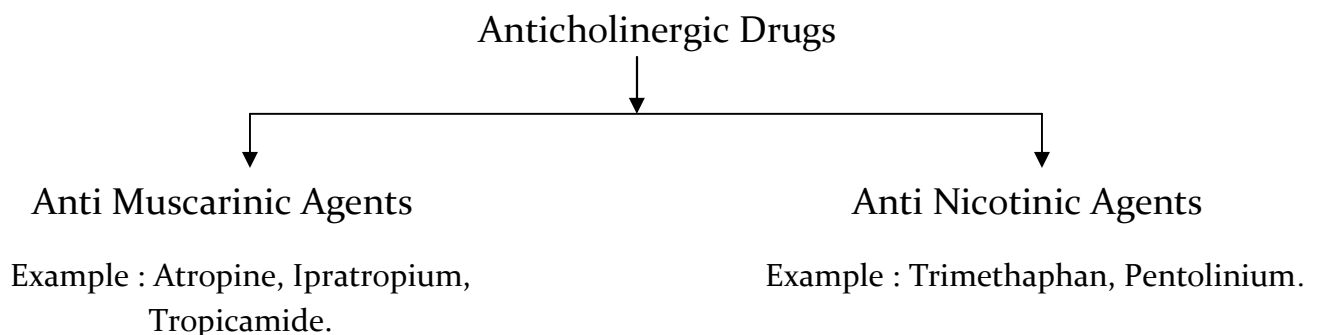
Anticholinergic Drugs

→ These are the drugs which occupy the ACh receptors and do not allow ACh to bind to the receptors .

→ Anticholinergic Drugs are also called " Parasympatholytic "

- AntiParasympathetic Agents "
- Cholinergic blocking Agents "
- Cholinergic antagonist

Classification



1. Anti Muscarinic Agents :

- These act by inhibiting the action of Ach by blocking the muscarinic acetylcholine receptors.
- Example : Atropine , Ipratropium , Tropicamide.

2. Anti Nicotinic Agents :

- These act by inhibiting the action of Ach at nicotinic acetylcholine receptors.
- Example : Trimethaphan , Pentolinium.

Atropine

→ It is most common anti muscarinic agent . It is an alkaloid and blocks the all types of muscarinic receptors.

Pharmacological Action

- CNS : Mild stimulation
- Eye : Mydriasis
- CVS : It cause bradycardia initially and then tachycardia.
- Respiratory System : Bronchodilation
- Secretion : Secretions of sweat , saliva , and gastric are reduced.
- GIT : Relaxation , decrease peristaltic movement so it used as antispasmodic and anti diarrhoeal drug.

Indication

- ▲ For dilation of pupil.
- ▲ Pre - Anaesthetic
- ▲ In bronchial Asthma and COPD.
- ▲ In hypersalivation.
- ▲ To treat diarrhoea
- ▲ As antidote for organophosphorus poisoning.
- ▲ To treat parkinsonism

Dose :

- ❖ It is given IV , IM and SC, routes.
- ❖ 0.4-0.6mg for preoperative and pre anaesthetic,
- ❖ 1% solution in eye drop for mydriasis

Contraindication

- ◇ In glaucoma condition
- ◇ In infants suffering from Down' syndrome (delay in development of body and brain)
- ◇ In patients are hypertensive with atropine .

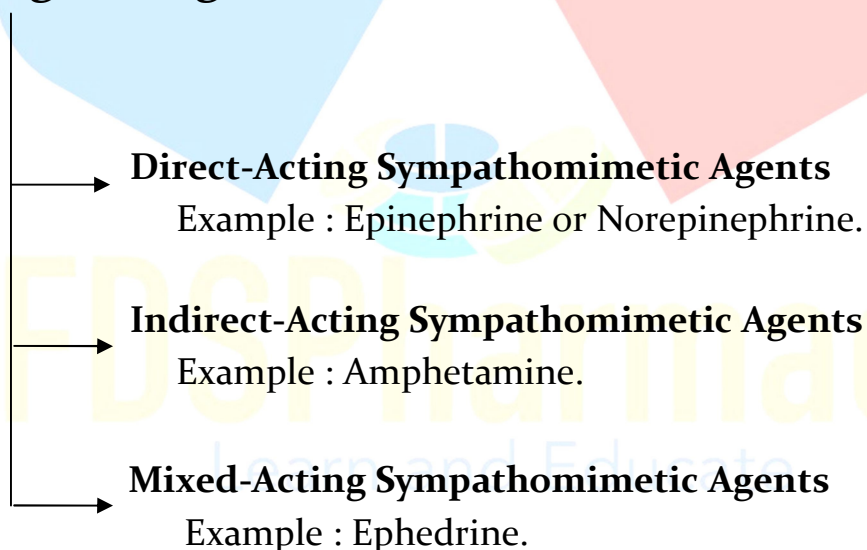
Adrenergic Drugs

- Adrenergic drugs or adrenergic agonists or sympathomimetic agents are drugs causing stimulation of the adrenergic receptors in the sympathetic nervous system.
- They are named so as they mimic the actions of major neurotransmitters of the sympathetic nervous system, i.e., epinephrine and norepinephrine.

Classification

- ⇒ On the basis of effects they produce on the organ cells, the sympathomimetic drugs can be categorised into three classes ;

Adrenergic Drugs



1. **Direct-Acting Sympathomimetic Agents** : They stimulate the adrenergic receptors directly, e.g., Epinephrine or Norepinephrine.
2. **Indirect-Acting Sympathomimetic Agents** : They act by stimulating the release of nor-epinephrine from the terminal nerve endings, e.g., Amphetamine.
3. **Mixed-Acting Sympathomimetic Agents** : They act both directly (stimulating adrenergic receptor sites) and indirectly (stimulating release of nor-epinephrine from the terminal nerve endings), e.g., Ephedrine.

Location of adrenergic receptors

1. α_1 : Smooth muscles = Heart , , Bladder , spleen , Ureters, (contraction) eye (mydriasis)
2. α_2 : Pancreas (decrease insulin)
3. β_1 : Heart (Increase heart rate)
4. β_2 : Smooth muscles = heart , bronchi , uterus , GIT , (relaxation)

Pharmacological Action

- **Cardiovascular system** : Stimulate the α_1 receptor and increase the contraction force of heart and then output of blood.
- **Respiratory system** : Stimulate β_2 receptor and dilate the bronchi smooth muscles.
- **Pancreas** : Bind to α_2 receptor of pancreas and decrease the release of insulin ,so give hyperglycemic effect.

Indication

- ▲ To control bleeding
- ▲ To slow the absorption of local anaesthetics.
- ▲ To increase blood pressure

Contraindication

- ◇ α_1 receptor agonist is contraindicated in hypertension .
- ◇ α_2 receptor agonist is contraindicated in low blood pressure .

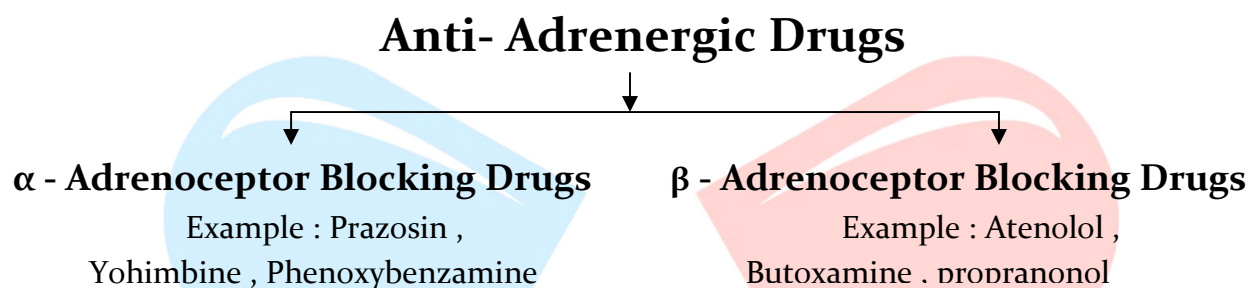
Dose

- ✚ Amphetamine 5-10mg tablet in the morning and midday
- ✚ Epinephrine in acute asthma 0.01ml/ml, in cardiac arrest 0.01ml/ml

Anti- Adrenergic Drugs

- The drugs block the effect or actions that occur by release of adrenaline are called antiAdrenergic Drugs.
- These drugs are also called " Adrenergic Blocking Agents " " Adrenoceptor antagonist " .

Classification



1. **α - Adrenoceptor Blocking Drugs** : The effects of catecholamine facilitated via α receptors are blocked by these agents. Furthermore, depending on the ability of these drugs to dissociate from the receptors, they may either be reversible or irreversible.
 - **Example** : Prazosin , Yohimbine , Phenoxybenzamine
2. **β - Adrenoceptor Blocking Drugs** : The effects of catecholamine facilitated via the β - adrenoceptors are blocked by β - adrenoceptor blocking drugs. They can further be categorised as selective or non-selective β - adrenoceptor blocking agents.
 - **Example** : Atenolol , Butoxamine , propranolol

Pharmacological Actions

- ▲ On Eye : miosis
- ▲ Decrease the heart rate
- ▲ Bronchodilation
- ▲ Vasodilation .
- ▲ Lower blood pressure
- ▲ Increase intestinal motility .

Indication

- ◇ To treat hypertension
- ◇ In congestive heart failure
- ◇ In migraine
- ◇ Angina pectoris

- ◇ Anxiety
- ◇ Parkinson's disease

Contraindication

- Hepatic and renal disease
- Peptic ulcer
- Any drug allergy
- Coronary artery disease

Doses

- ✚ Atenolol : 25 - 100mg daily
- ✚ Propranolol : 80 - 240 mg 12 hourly
- ✚ labetalol : 200 -600 mg 12 hourly

Neuromuscular Blocking Agents (Skeletal Muscle Relaxant)

- The drugs are used to block the transmission of nerve impulses at the skeletal neuromuscular junction and cause skeletal muscle relaxation are called Neuromuscular Blocking Agent.
- They are used to reduce spasm and pain in skeletal muscles.

Classification

Drugs Acting Peripherally at the Neuromuscular Junction

1) Non Depolarising Agents

- a) long acting (60 - 120 minutes) e.g. tubocurarine ,Dexacurium
- b) Intermediate acting (20 -50 minutes) e.g. Atracurium
- c) Short Acting (10 -20) e.g. Mivacurium

2) Depolarising Agents : Succinyl Choline

Pharmacological Action

- ⤴ Skeletal muscle : parental Administration of Tubocurarine results in weakness of Motor Impulses .
- ⤴ CVS : These agents produce Hypotention and cardiac arrhythmia (increase or decrease in heart rate)

Indications

- ❖ Adjuvant (helping) to general Anaesthesia : Neuromuscular Blocking Agents are use with general anaesthesia to achieve adequate (as need) muscle relaxation.
- ❖ In Convulsant : These drugs are used for muscle relaxation in epileptic condition.
- ❖ In sever tetanus : Tetanus cause a painful muscle contraction , these drug are used only in severe case of tetanus.

Contraindications

- ⤴ Heart patients : These are contraindicated in heart patients .
- ⤴ Asthma patients ; These are contraindicated in asthma patients .

Dose

- d -tubocurarine 0.5 - 0.6 mg/kg
- Dexacurium 0.03 -0.05 mg / kg
- Atracurium 0.4 -0.5 mg / kg
- mivacurium 0.15 -0.2 mg/kg
- Succinyl Choline 1.0 -1.5

Drugs Used in Myasthenia Gravis

Myasthenia Gravis

- It is an autoimmune disorder in which antibodies are produced that blocks od destroy Muscles receptors
- Patients with Myasthenia show severe muscular weakness.
- Breakdown in communication between nerves and muscles.

Drugs used In Myasthenia Gravis

- 1) Anticholinesterases: Pridostigmine
- 2) Immunosuppression : Cyclosporine , Azthioprine
- 3) Intravenous Immune Globulin (IVIG)
- 4) Immunoabsorption : this procedure helps to remove anti AChR ABs (Acetylcholine Receptor Antibodies)
- 5) Plasma Exchange : It helps to remove the abnormal antibodies .

Local Anaesthetic

→ The drugs are used to block the sensation in a limited area are call Local anaesthetics .

Or

→ we say The drugs are used to abolish the sensory perception over a local area are called local anesthetics.

Classification Of Local anaesthetics

1. Injectable Anaesthetics
 - Short duration : procaine
 - Intermediate duration : Lignocaine (lidocaine)
 - Long duration : Tetracaine
2. Surface Anaesthetics : Cocaine , Lignocaine

Pharmacological Action Of Local Anaesthetics

The local anaesthetic have the following two types of actions :

- Local Action
- systemic action

1) Local Action

- They block the nerve ending
- They block the neuromuscular junction
- They delay the release of acetylcholine from motor neuron.

2) Systemic Action

a) CNS

- They stimulate the CNS in starting and then depress
- They produce restlessness , mental confusion.

B) CVS

- Heart : Cardiac depression
- Blood Vessels : Vasodilation
- Lower Blood pressure

Indications

- ◇ These are used for infiltration anaesthetics (anaesthetic of an operative site by local injection)
- ◇ These are used as antiarrhythmic agents.
- ◇ These are used to treat status epilepsy.

Contraindications

- ▲ These are contraindicated in coronary disease.
- ▲ These are contraindicated in heart failure.
- ▲ These are contraindicated in heart block.
- ▲ These are contraindicated in liver disease.

Dose

- ✚ Lignocaine : 4mg/ kg and should not exceed 300 mg or 500mg
- ✚ Procaine : 12mg/kg and should exceed 1000mg

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

- ➔ The drugs are used to treat Inflammation , and mild to moderate Pain and fever are called Non steroidal anti Inflammatory drugs .

Analgesic

- Analgesic are those drugs which used in the treatment of pain.
- NSAIDs reduce only slow pain
- These drugs can not used in severe pain.
- Eg : Aspirin etc,

Anti-Pyretics

- Antipyretics are those drugs which to reduce the high blood temperature.
- These drugs reduce only high body temperature not normal body temperature.
- Mainly antipyretics drugs used in the treatment of fever
- Eg : Paracetamol etc.

Anti-Inflammation Agent

- Anti-inflammatory are those drugs which used to reduce the inflammation in the body.
- Eg :Ibuprofen

Classification of (NSIADs)

1) Non -Selective COX inhibitors

- Salicylates : Aspirin
- pyrazolone Derivatives : Phenylbutazone
- Indole Derivatives : Indomethacin
- Propionic Acid Derivatives : Ibuprofen
- Aril Acetic Acid Derivatives : Diclofenac
- Oxycame Derivatives : Piroxicam

2) Preferential COX 2 inhibitors : Nimesulide , meloxicam

3) Selective COX - 2 inhibitors : Celecoxib , Rofecoxib

4) Analgesic Antipyretics with poor Anti inflammatory Action :

- Paraaminophenol Derivatives : Paracetamol (acetaminophen)
- Pyrazolone Derivatives : Metamizol .

Indications

- Analgesia : NSIADs are used to eliminate or treat mild to moderate pain like :
 - Headache
 - Toothaches
 - Muscle aches
 - Arthritis
 - Migraine
 - Dysmenorrhea
- Antipyresis : NSIADs are used to treat fever / to normalize body temperature .
- Anti Inflammation : NSIADs are used to stop inflammation and pain like :
 - ▲ Rheumatoids
 - ▲ Osteoarthritis
 - ▲ Ankylosing spondylitis
 - ▲ Bursitis

Contraindication

- ❖ With NSIADs hypersensitivity (an exaggerated response by immune to a drug).
- ❖ In peptic Ulcer,
- ❖ In children suffering from chicken pox or influenza.
- ❖ In chronic liver disease
- ❖ In during pregnancy.
- ❖ In breastfeeding mother.

Dose

1) Aspirin :

- Adults : 325 -650mg orally 4 -6 Hours as need and should not exceed 3.9 g/day
- Children under 12 years : 10-15mg/kg

2) Paracetamol

- Adults : 500- 650 mg , duration 4-6 hours , and should not exceed 4000mg/day
- Children under 18 years : 15mg/kg duration 6 hours.



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