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Pharmacology
Chapter 2 : Drugs Acting On Peripheral Nervous System

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Chapter 2

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

Cholinergic Drugs

Direct Acting Cholinergic Agonist	Indirect Acting Agents (Anticholinestrase
Example : Acetylcholine, Methacholine, Carbachol, Bethanechol. Pilocarpine.	Example : Physostigmine, Neostigmine

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 (Anticholinestrase)

➢ These drugs inhibit the enzyme cholinestrase , 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

- Pilocrpine 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.

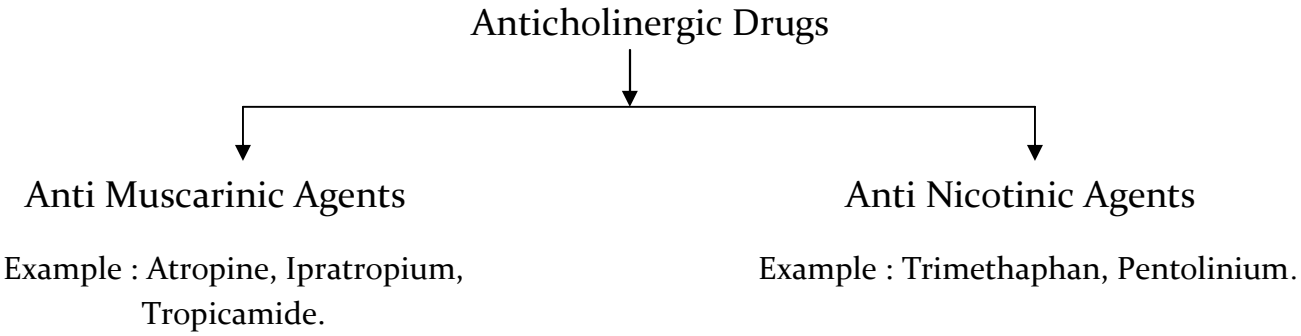
Anticholinergic Drugs

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

→ Anticolinergic 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

- → **Direct-Acting Sympathomimetic Agents**
  Example : Epinephrine or Norepinephrine.
- → **Indirect-Acting Sympathomimetic Agents**
  Example : Amphetamine.
- → **Mixed-Acting Sympathomimetic Agents**
  Example : Ephedrine.

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. α1 : Smooth muscles = Heart , , Bladder , spleen , Ureters, (contraction) eye (mydriasis)
2. α2 : Pancreas (decrease insulin)
3. ß1 : Heart (Increase heart rate)
4. ß2 : Smooth muscles = heart , bronchi , uterus , GIT , (relaxation)

Pharmacological Action

- **Cardiovascular system :** Stimulate the α1 receptor and increase the contraction force of heart and then output of blood.
- **Respiratory system :** Stimulate ß2 receptor and dilate the bronchi smooth muscles.
- **Pancreas :** Bind to α2 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

- α1 receptor agonist is contraindicated in hypertension .
- α2 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

Anti- Adrenergic Drugs

α - Adrenoceptor Blocking Drugs	**β - Adrenoceptor Blocking Drugs**
Example : Prazosin , Yohimbine , Phenoxybenzamine	Example : Atenolol , Butoxamine , propranonol

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 , propranonol

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
- Propanolol : 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. tubocuratine ,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) Anticolinesterases: Pridostigmine
2) Immunosuppression : Cyclosporine , Azthioprine
3) Intravenous Immune Globulin (IVIG)
4) Immunoabsorption : this procedure helps to remove anti AChR ABs (Acetycholine 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 :** Selecoxib , Rofecoxib
4) **Analgesic Antipyretics with poor Anti inflammatory Action** :
    - Paraaminophenol Derivatives : Paracetamol (acetaaminophen)
    - 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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