Cholinergic system
(Parasympathetic system)
Part 1

By
Dr. Shaymaa F. Abbas
Msc pharmacology
Learning objectives

• This system is covered in three lectures

1. Identify the neurotransmitter and the receptors on which it acts

2. Classify the drugs acting on parasympathetic system according to their mechanisms of action

3. List their main side effects

4. Correlate between the pharmacological effects of drugs and their main clinical uses and contraindications

5. Recognize the most common utilized drugs in clinical practice
Autonomic nervous system (physiological view)

• The autonomic nervous system ANS is a part of peripheral nervous system
• It control the involuntary body function
• ANS has two divisions
  1. Parasympathetic system (cholinergic system)
  2. Sympathetic system (adrenergic system)
• Both sympathetic and parasympathetic systems consist of

1. Preganglionic fiber: originate from brain and spinal cord

2. Autonomic ganglia

3. Post ganglionic fibers
• The following fibers release acetylcholine as a main neurotransmitter

1. All preganglionic fibers (sympathetic and parasympathetic)
2. All postganglionic parasympathetic fibers
3. Only postganglionic sympathetic fibers to sweat glands
4. Somatic nerve fibers at neuromuscular junction
Cholinergic system
parasympathetic system

• The neurotransmitter: acetylcholine ACh

• The receptors

1. Muscarinic receptors (M1-M5); present in CNS and other organs supplied by parasympathetic system

2. Nicotinic receptors (Nn,Nm); in CNS, autonomic ganglia, adrenal medulla and neuromuscular junction
Acetylcholine

Choline acetyl transferase

Botulinum toxin inhibit ACh release

Spider venom enhance release

Cholinesterase
• Most cholinergic synapses are richly supplied with cholinesterase so half-life of Ach is very short (seconds).

• Cholinesterase enzyme is of 2 types

  1. **True**- found at cholinergic nerve endings & in RBC

  2. **False***(pseudo cholinesterase)*- has lower specificity for Ach & found in blood plasma, liver & many other tissues.
Effects of acetylcholine

1- CNS
Contains both muscarinic & nicotinic receptors causing stimulation followed by depression.

2- Eye
1. Contraction of circular muscles of iris----miosis
2. Contraction of ciliary muscles---accommodation for near vision
3. Decrease intraocular pressure IOP
Pupil constricts as circular muscles of iris contract (parasympathetic)

Bright light

Pupil

Normal light

Pupil dilates as radial muscles of iris contract (sympathetic)

Dim light

Anterior views
Diagram of eye & outflow of aqueous humor (arrow) which drains at Schlemm's canal.
• Intra-ocular pressure decrease by
  1. miosis- the iris is pulled away from the angle of the anterior chamber
  2. by contraction of ciliary muscle, the trabecular meshwork on the base of the ciliary muscle is opened

  Both these effects facilitate aqueous humor flow into canal of Schlemm.
3- **Bronchi**- bronchoconstriction & increase bronchial secretion (Bronchorrhea)

4- **GIT**

1. increased tone and peristalsis of the gut and may cause **colicky pain and diarrhea**.
2. increased exocrine secretions mainly of salivary & gastric glands
3. Relaxation of sphincters
   - anal sphincter (causes defecation)
   - esophageal sphincter (causes regurgitation)
5. CVS
On the heart: Causes bradycardia with AV block & eventually cardiac arrest.
On blood vessels—vasodilation through release of nitric oxide----hypotension

6- GUT
Contraction of detrusor muscle with relaxation of trigone & sphincter muscles ------micturition.
7. **Exocrine glands**- increase secretions mainly salivary, lacrimal, bronchial & sweat glands.

**Sweat glands** are cholinergic, but anatomically part of sympathetic system, **axillary sweat glands are adrenergic.**
Cholinergic drugs
(Parasympathomimetic drugs)

They have acetylcholine-like effects, include:

1. Directly acting (act directly at cholinergic receptors)
   a. cholinesters
   b. alkaloids

2. Indirectly acting drugs (cholinesterase inhibitors) influence cholinergic receptors indirectly by preventing the breakdown of ACh including:
   a. reversible anticholinesterases
   b. irreversible anticholinesterases
Direct acting cholinomimetic drugs

• Cholinesters

1. Acetyl choline; not suitable as drug because of its very short duration of action and wide range of activity (lack of selectivity)

2. Synthetic esters of choline
  • Bethanecol
  • Carbachol
Bethanechol and carbachol

- Both resist hydrolysis by choline esterase
- Act mainly on GIT and GUT
- Used mainly for treatment of intestinal and bladder atony
- Can be used for treatment of glaucoma
Alkaloids

1) Nicotine - is absorbed through mucous membranes

- At low dose—stimulate *autonomic ganglia
  * NMJ (fasciculation)

- In large doses - blocks *autonomic ganglia
  * NMJ causing paralysis.

- CNS is stimulated (including vomiting center, tremor, convulsion) & followed by depression.

*Clinical use* - is a social drug used as an adjunct to stopping its own abuse as tobacco.
2) *Muscarine-* is of no therapeutic use.

*it has role in discovery of cholinergic receptor subtypes

*has toxicological significance because of its presence in certain poisonous mushrooms.*
3) Pilocarpine

Is a direct acting muscarinic agonist

**Clinical uses**

1. **Glaucoma**, it decreases IOP by miosis & contraction of ciliary muscle

2. Used orally for treatment of xerostomia (dry mouth) following irradiation of head & neck tumors
Adverse effects –

Local effects: decreased visual acuity, eye irritation & pain

rarely is absorbed in amounts sufficient to cause systemic effects (bradycardia, bronchospasm, hypotension, urinary urgency, diarrhea, hyper salivation & sweating)

*Its systemic toxicity is reversed by atropine
Questions

• The following effects result from action of acetylcholine on muscarinic receptors except
  • A- miosis
  • B- sweating
  • C- bradycardia
  • D- skeletal muscle contraction

• What are the effects of acetylcholine on GIT?

• By which mechanism pilocarpine decrease intraocular pressure?