

# Indirect parasympathomimetics

## General Features

- Indirectly acting parasympathomimetics are substances that inhibit ACHE (they do not act on the receptor, but on ACHE – acetylcholinesterase).
- We distinguish:
  1. short-acting ACHE inhibitors (reversible);
  2. long-term ACHE inhibitors (irreversible).

## Effects and Uses

- ACh builds up as a result of ACHE inhibition.
- It is used in postoperative atonia, to induce miosis and reduce intraocular pressure, to increase stimulation on the neuromuscular disc (in the treatment of Myasthenia gravis) .

## Side effects

- Confusion, ataxia, convulsions and eventual coma can occur from excessive stimulation of the CNS by acetylcholine.
- From excessive stimulation of the *M* receptor in the sympathetic ganglia, a paradoxical increase in blood pressure, tachycardia can occur.

## Short-acting acetylcholinesterase inhibitors

They act on both the *N* *receptor* (*nicotinic*) and the *M* receptor (muscarinic).

### Therapeutic use

1. Myasthenia gravis.
2. Antidote for competitive peripheral myorelaxants.
3. Postoperative atony of the GIT and bladder.
4. Miotic and antiglaucomatic.

### Substances used

#### Physostigmine

- Natural alkaloid.
- Crosses the blood-brain barrier.
- Antidote for poisoning parasympatholytics (eg atropine).
- Used in ophthalmology - miosis, reduces intraocular pressure.

#### Neostigmine

- Does not cross the blood-brain barrier.
- Use in myasthenia gravis (increases ACh on the neuromuscular disc).
- Antidote to disc blockers (myorelaxants).

#### Edrophonium

- Very fast onset of effect.
- It is used to diagnose myasthenia gravis (the condition improves after administration, the patient was underdosed and the dose needs to be increased).

## Long-term acetylcholinesterase inhibitors

Today, they are no longer used therapeutically. They have only toxicological significance - organophosphates.

### Intoxication

- Proceeding quickly.
- Permanently phosphorylate ACHE.
- Manifests as nausea, convulsions, vomiting, increased salivation, bradycardia, lacrimation, anorexia, skeletal muscle weakness, decreased breathing and even death (respiratory arrest or circulatory collapse).

## Intoxication therapy

- Prevention of absorption.
- Controlled breathing, anticonvulsant treatment.
- Administration of atropine (block of *M* receptors).
- Preventive short-term inhibitors (Neostigmine).
- Cholinesterase reactivation – **oximes**'.

### Oximes

They are able to bind the organophosphate, which has all the side structures, and tear it away from ACHE. Once it loses them, it forms a covalent bond with ACHE, the bond is irreversible. Oximes must be administered in a timely manner (e.g. trimedoxime, pralidoxime).

### Substances used

Tabun, Sarin, Soman.

## Links

### Related Articles

- Parasympathomimetics
- Direct parasympathomimetics
- Sympathomimetics
- Sympatholytics

### Source

- HYNIA, Sixtus. *Pharmacology in a Nutshell*. 2. edition. Triton, 2001. ISBN 80-7254-181-1.