Myorelaxants

Substances that relieve spasms and lead to relaxation of striated muscles. We divide them into substances that act through the CNS - **central myorelaxants** and substances that act through the neuromuscular plate - **peripheral myorelaxants** .

Central myorelaxants

The drug is used alone for painful contractures of the skeletal muscles or for central pain conditions with muscle spasms and spastic syndromes.

It acts at the level of the **spinal cord** or **brainstem** . They affect spasticity (myotonolytics). It suppresses mono- and polysynaptic reflexes. In pathological conditions, this system transmits painful stimuli that lead to increased muscle tension. Central myorelaxants dampen this transmission, thereby suppressing increased skeletal muscle tone, without loss of free contraction

Indication

Treatment of acute back pain caused by striated skeletal muscle spasms. They can also be used for chronic pain, but only if the pain worsens. They can also be used after brain trauma, cerebrovascular accident , multiple sclerosis and degenerative processes due to the formation of a brain tumor.

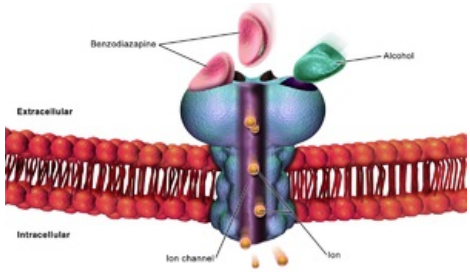
Adverse effects

Central muscle relaxants have a significant sedative and anxiolytic effect. Considerable differences in tolerability must be taken into account. It can lead to a general decrease in muscle tone, risk of **postural instability** , **drowsiness** , **confusion** , and general **CNS depression**.

Non-benzodiazepine

Baclofen

$GABA_B$-receptor agonist . It leads to the opening of K + channels, which leads to hyperpolarization of the membranes of synapses of spinal nerves or brainstem. This inhibits the release of the mediator, which leads to the release of pain (substance P release blockade). It reduces the frequency and intensity of flexor and extensor spasms. Antidepressants and alcohol increase the effect. Also effective in patients with a severed spinal cord. It can also be used in children.



$GABA_A$ receptor with bound benzodiazepine

Tolperisone

Symptomatic treatment of spasticity after CMP. It has an inhibitory effect at the reflex level of the spinal cord. It inhibits the descending control pathways. It reduces sodium influx through the nerve cell membrane, thereby reducing the amplitude and frequency of action potentials.

Symptomatická léčba spasticity po CMP. Působí inhibičně na úrovni reflexu míšních drah. Inhibičně ovlivňuje sestupné kontrolní dráhy. Snižuje influx natria membránou nervové buňky, čímž snižuje amplitudu i frekvenci akčních potenciálů.

Other substances used include **orphenadrine** , **thiocolchicoside** and **mefenoxalone** .

Benzodiazepines

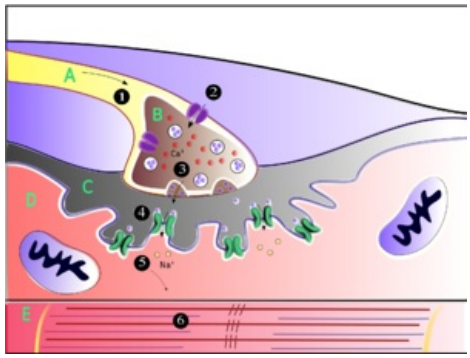
It helps the effect of GABA A , opens Cl- channels . It relaxes the muscles (myorelaxant) and the psyche (anxiolytic). Suitable for managing temporary painful muscle spasms (for fractures, vertebrogenic causes , lumbago , myalgia , after CMP). E.g. **diazepam** .

Their use for muscle relaxation is relatively disadvantageous due to **a large number of side effects** , such as a sedative effect (especially in higher doses). There is also a decrease in attention, memory disorders, etc. After stopping treatment, **withdrawal symptoms** may appear , including anxiety, agitation, irritability, motor restlessness, tremors, muscle twitching, epileptic seizures and psychosis. Symptoms can last up to several months.

See the Benzodiazepines page for more detailed information .

Peripheral myorelaxants

It acts on the **presynaptic nerve terminal** (release of ACh) or on the **postsynaptic membrane of the** neuromuscular plate . They do not affect the central nervous system. The main mechanism of action of peripheral myorelaxants consists in the binding of the drug to the receptor for acetylcholine, where it blocks neuromuscular transmission (binding of acetylcholine).



Neuromuscular disc

Indications: adjuvant drugs during general anesthesia in surgery where skeletal muscle relaxation allows access to the surgical site. We use short-acting muscle relaxants mainly in acute medicine to facilitate endotracheal intubation, laryngoscopy, endoscopy and other interventional examinations.

Side effects:

- Release of histamine from mast cells – leads to bronchoconstriction, increased bronchial secretion and a drop in blood pressure.
- Blockade of the sympathetic ganglia and adrenal medulla, whose action leads to bradycardia and a drop in blood pressure.
- Ionic imbalance (*suxamethonium – succinylcholine*).
- Respiratory paralysis in case of overdose (as an antidote we administer ACHE inhibitors – *neostigmine*).
- *Malignant hyperthermia (we administer dantrolene as an antidote)*).

Drug interactions: Increasing the effect of substances that inhibit the release of ACh from the presynaptic terminal (*aminoglycosides , tetracyclines , calcium channel blockers*). Increasing the effect of substances that depolarize the postsynaptic membrane (cardiac glycosides). Inhalation anesthetics stabilize the postsynaptic membrane, thereby increasing the activity of non-depolarizing myorelaxants (dose reduction).

Dantrolene before dilution in a 20mg package. The drug is used in the treatment of malignant hyperthermia.

Substances acting presynaptically

They reduce the release of ACh from the presynaptic terminal into the synaptic cleft. This is followed by myorelaxation, even paralysis. Blockade of ACh release is caused, for example, by **botulinum toxin** or **aminoglycosides**.

Botulinum toxin

A natural bacterial toxin produced by the sporulating anaerobic bacillus *Clostridium botulinum* . This toxin **prevents the release of ACh at presynaptic terminals** , thereby disabling the function of the neuromuscular plate. The effect becomes apparent **after 2-3 days** after application, the maximum release of muscle tone occurs in 2-3 weeks. The effect of botulinum toxin **lasts for 3-4 months** until new signal connections are formed between the nerve ending and the muscle.

It is administered in a solution IM into selected muscles according to clinical intent. **Dermatological indications** are most often disorders of the skin and subcutaneous tissue (hyperhidrosis , cosmetic surgery). The most common **use in neurology** is in the treatment of spasms after a stroke, cerebral palsy, spasm of facial muscles. Also for focal spasms in patients with cerebral palsy , blepharospasm or as prevention of headaches in adults with chronic migraine . **Urological indications** are bladder dysfunction (hyperactivity , incontinence).

The advantage of the treatment is a minimum of side effects. There may be pain at the injection site, swelling or, rarely, a hematoma.

See the Botulism page for more detailed information .

Substances acting postsynaptically

NM receptors are affected .

Non-depolarizing

Competitive antagonists of ACh at the NM receptor . They reversibly bind to nicotinic receptors, thereby blocking the binding of ACh and thus the depolarization of the postsynaptic membrane. They do not cause conformational changes of the receptor. When using them, controlled ventilation is required with constant monitoring and the use of an **antidote - acetylcholinesterase inhibitors** .

A well- known representative is the alkaloid **d-tubocurarine** , which is part of the arrow poisons of the Indians. Myorelaxation occurs in a typical sequence - from the head down, and the diaphragm relaxes last (manifested by a short-term apneic pause). Intubation and full pulmonary ventilation are required during use . It does not penetrate the blood-brain barrier, consciousness and perception of pain is preserved. The effect starts within 5 minutes and lasts about 80 minutes.

The poisons of some snakes (cobra, aquarius, mamba, etc.) can also be included in this group.

Today, substances with a faster onset and longer effect are used (**mivacurium** , **rocuronium** , **atracurium**).

Depolarizing

ACh agonists that are resistant to the action of ACHE. They produce a longer-lasting membrane depolarization followed by a delayed repolarization , which prevents the contractile effects of acetylcholine . The result of their action is a temporary activation of the muscle, which is followed by muscle paralysis. At the time of maximum effect, a temporary apnoeic pause appears (required controlled breathing). They have no antidote.

Depolarizing muscle relaxants include **suxamethonium** (succinylcholine). It is very short-acting because it is rapidly hydrolyzed by pseudocholinesterase. For longer-term effects, it can be given by infusion. After the injection of a muscle myorelaxant, the small muscles (eyes, fingers and toes, tongue) relax first, followed by the muscles of the limbs, trunk, neck and larynx. Lastly, it paralyzes the diaphragm and intercostal muscles. The block is removed in the reverse order.

⚠**In the case of a genetic polymorphism for pseudocholinesterase, its levels may be low in plasma and liver, significantly prolonging the elimination of succinylcholine, which increases the risk of prolonging the apneic pause.**

Substances affecting skeletal muscle by a different mechanism

Blockade of Ca^{2+} release from the sarcoplasmic reticulum. This mechanism reduces heat generation during contraction, thereby preventing hyperthermia. A representative is **dantrolene** . Used in the therapy of malignant hyperthermia (adverse effect of peripheral myorelaxants based on succinylcholine) and the therapy of malignant neuroleptic syndrome .

Links

External links

- Neuromuscular monitoring – interactive algorithm + test (https://www.akutne.cz/algorithm/cs/325--/)
- Myorelaxation (Czech Wikipedia) (https://cs.wikipedia.org/wiki/Myorelaxans)

Source

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- ŠVIHOVEC, Jan, et al. *Pharmacology.* 1st edition. Prague: Grada, 2018. ISBN 978-80-271-2150-2 .