Local anesthetics (pharmacology)

Local anesthetics are substances that block the conduction of excitation by sensitive neurons. This leads to **loss of pain perception** in a certain area, control of movements is preserved. This condition is called *local anesthesia*.

Mechanism of action

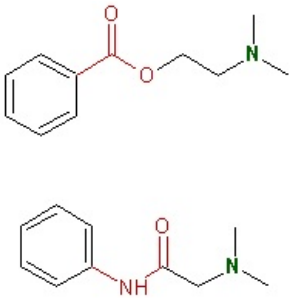
The essence of the effect of local anesthetics is interaction with voltage-controlled **Na^+ channels**.

In the *normal state* the channels open when excited. This allows influx of Na^+ into the cell and causes membrane depolarization. Channels respond to depolarization by closing and entering an inactive state. After a change in the membrane potential, their conformation returns to the resting state.

When the anesthetic acts there is an **intracellular** interaction between the drug and the channel and the ***entry of sodium ions into the cell is blocked.*** This results in an increase in the threshold for excitation, a slowing down of impulse conduction and a reduction in the amplitude of action potentials until their complete disappearance.

Chemical Structure

The average local anesthetic consists of a lipophilic benzene core, an ester or amide bond, and a basic nitrogen in the side chain, and, as already stated, the essence of its action is the intracellular blockade of Na^+ channels.



General structure of local anesthetics

The ionized form of the anesthetic is important for blocking the channels, but the anesthetic penetrates into the cell in a non-ionized form. It follows that the effectiveness of local anesthetics depends on their pK_a and also on the ***pH of the environment.***

Thread Types

Pain sensations are conducted by unmyelinated C fibers and myelinated A-δ fibers. During the application of an anesthetic, depending on the concentration, first the perception of pain, then temperature, touch and finally motor function is lost. Preganglionic sympathetic fibers are most sensitive to the effects of local anesthetics. As a result of their blockade, vasodilation occurs. Some anesthetics can be used to affect the propagation of the excitation in the fibers of the heart muscle.

Pharmacokinetics

The pharmacokinetics of local anesthetics is very specific. Absorption and distribution are not important for the pharmacological effect, but they are significant from the toxicological point of view. The effect is terminated by enzymatic cleavage. Ester anesthetics are split by esterases (primarily pseudocholinesterase) already in the blood plasma, amides are then split by amidases in the liver. There are no esterases in the cerebrospinal fluid.

The rate of absorption is dependent on the concentration of the anesthetic, not on the amount administered, and also on the blood supply to the tissue. This can be reduced by using vasoconstrictor additives. These slow down the flushing of the anesthetic into the systemic circulation and thereby prolong its effect and reduce toxicity. Adrenaline is mainly used as a vasoconstrictor additive, more recently vasopressin analogues can be used.

Side effects

Typical side effects are most pronounced on the CNS and cardiovascular system.

CNS

Effects on the CNS paradoxically begin with stimulation. Confusion, tremors, restlessness, convulsions or CNS depression leading to respiratory arrest may also occur.

Cardiovascular System

Anesthetics have a dysrhythmic effect on the cardiovascular system. This is due to the inhibition of pacemaker activity as well as a reduction in the conductivity of the conduction system. This effect can be used therapeutically - some antidysrhythmics.

A decrease in Na^+ concentration leads to a decrease in Na-Ca antiport. This results in lower cellular calcium levels and lower contractility.

It also causes vasodilation in the area of arterioles. All these effects can lead to a dangerous drop in pressure.

Other

Other side effects may include, for example, hypersensitivity reactions. Methemoglobinemia may also occur with high doses of prilocaine.

Types of Local Anesthesia

Surface anaesthesia - in most cases it is anesthesia of mucous membranes, only EMLA (a non-crystalline mixture of 2.5% lidocaine and 2.5% prilocaine) is effective on the skin; side effects are also possible with surface anesthesia.

Infiltration anaesthesia - the anesthetic is introduced into the tissues, mostly in the areas of minor surgical procedures; a vasoconstrictor additive is often used, the risk of side effects is considerable.

Seductive anesthesia – the anesthetic is applied near the nerve trunk; the onset of effect tends to be delayed, the advantage is lower consumption; often in dentistry.

Intravenous regional anesthesia – the blood flow is stopped with the cuff and the anesthetic is applied distally from the cuff; for surgical procedures on the limbs, there is a risk of systemic effects.

Spinal (spinal, subarachnoid) anesthesia – application to the subarachnoid space, affects the spinal roots and spinal cord; suitable for procedures in the abdominal cavity, pelvis or lower limbs; risks: bradycardia, hypotension, respiratory depression and urinary retention.

Epidural anesthesia – anesthetic is applied to the epidural space; unlike spinal anesthesia, it requires a larger amount of anesthetic but is not as risky.

Medications

Esters

- ***Cocaine*** *- the first local anesthetic, no longer registered;*
- ***benzocaine*** - insoluble in water - for surface anesthesia (e.g. as a powder in dentistry for alveolitis after extraction or as an emulsion to facilitate swallowing for stomatitis after radiotherapy);
- ***procaine*** - short-term and weak effect - metabolized to PABA, poor tissue penetration, low toxicity, NEODENTICAIN preparation;
- ***tetracaine*** - for all types of anesthesia, toxicity is higher than procaine due to slow metabolism.

Amides

More modern and less allergenic than ester anesthetics.

- ***Lidocaine*** - the most widely used local anesthetic with a fast onset of action, can be used for all types of anesthesia, preparations XYLESTEZIN spr 15%, XYLONOR spr 15%, XYLONOR gel 5% (injection site anesthesia) , XYLOCAIN spr 10%, EMLA cream 5% / EMLA patch with prilocaine;
- ***trimecain*** - similar in structure and effects to lidocaine, the preparations MESOCAIN inj 1% (for procedures in certain high-risk patients) and MESOCAIN gel 2% (used, for example, in vascularization);
- ***prilocaine*** - can induce methemoglobinemia, but is used with lidocaine in EMLA mixture for surface anesthesia;
- ***mepivacaine****- preparations MEPIVASTEZIN inj 3% and SCANDONEST inj 3%*
- ***bupivacaine, levobupivacaine, ropivacaine*** - have a slower onset of action, but long-term action, are suitable for epidural and seductive anesthesia, MARCAIN inj 0.5%;
- ***cinchocaine*** - the strongest and longest-acting anesthetic, but only for surface anesthesia.

Amido-esters (thiophenes)

They contain both types of bonds in the molecule.

- ***artikain*** - for seductive and infiltration anesthesia in dentistry (0.6 lidocaine toxicity; 0.8 procaine toxicity), preparations SUPRACAIN inj 4% (with adrenaline 1:200,000), UBISTEZIN inj 4% (with adrenaline 1:200,000), UBISTEZIN FORTE inj 4% (with adrenaline 1:100,000), SEPTANEST inj 4% (with adrenaline 1:200,000/1:100,000).

Links

Related Articles

- Regional anesthesia
- Local and Seductive Anesthesia
- Anesthetics (Dentistry)
- General anesthetics (pharmacology)

References

- MLADĚNKA, Přemysl. *Lokální anestetika – seminář* [lecture for subject Farmakologie, specialization Farmacie, FaF HK UK v Praze]. Hradec Králové. 17.5.2011.
- DAGMAR, Lincová – HASSAN, Farghali. *Základní a aplikovaná farmakologie.* 2. edition. Praha : Galén, 2007. ISBN 978-80-7262-373-0.