Human beings have always sought ways to alleviate pain. The oldest medical text describing opium as a remedy for pain was written around 3000 BC in ancient Mesopotamia. The Ebers papyrus (1600 BC) describes several recipes against pain on the basis of dill (Anethum graveolens), mirtle and mandragora. The term «anesthesia» is derived from the Greek «deprivation of the senses» (1).

After Karl Koller started using cocaine as a local anesthetic in 1884, a large variety of anesthetics began to appear. Those exhibiting less toxicity are usually utilized in different techniques: general, retrobulbar, peribulbar, subtenon, subconjunctival and topical (2,3).

Local anesthetics are drugs that, when applied in sufficient concentration, inhibit the transmission of electrical impulses through the nerve membranes and the muscles in a temporary and predictable manner, causing the loss of sensitivity in a specific area. Nervous signals are transmitted by means of action potentials, i.e., quick changes in the potential of membranes which are rapidly extended throughout the nervous fiber. Under normal conditions, the cell membrane is at rest with a transmembrane voltage difference of \(-60 -90 \text{ mV}\) (idle potential), in which conductivity to K+ ions is 50-100 times above that of Na+ ions. In the presence of an electrical stimulation, the Na+ channels of the membrane become activated allowing the massive entry thereof, depolarizing the cell and reaching a positive potential of \(+10 +40 \text{ mV}\) (action potential). Subsequently, the permeability of the Na+ channel is reduced and K+ leaves the cell due to the concentration gradient (repolarization phase), which continues up to the point where the initial idle potential is reached by means of an active mechanism which depends on the Na+/K+ pump which introduces K+ ions and extracts Na+ ions (in the presence of ATP) at the cellular level.

Local anesthetics prevent the propagation of nervous inputs by reducing the permeability of the sodium channel, blocking the initial phase of the action potential. To achieve this, the anesthetic must penetrate the nervous membrane because its pharmacological action is based on its linking with the transmembrane receptor from its cytoplasmic side (4). The anesthetic action is extended over any excitable membrane and may act on non-specific points of a neuron or a group of neurons, including the muscle membrane and myocardium.

The action mechanism of an anesthetic is determined by (5):

– The type of fiber: anesthetics act on all nervous fibers, although those with smaller diameters are more susceptible (C fibers, in charge of pain) than those with larger diameters (A fibers, in charge of motility). A complete analgesia can be produced without affecting motor and tactile functions (differential action)

– The amount of local anesthetic available at the site of action: «minimum inhibiting concentration», i.e., the minimum concentration of local anesthetic that is necessary for inhibiting a specific nervous fiber.

– The pharmacological characteristics.

From the chemical viewpoint, all anesthetics have a common structure:

– An aromatic structure (benzoic or para-aminobenzoic acid), which is the lypophilic portion responsible for dissemination through the nervous membrane and fixation in the nerve axoplasm.

– An amino group which determines the water solubility of the molecule and therefore its dissemination and distribution in the blood. There are two
forms of amino groups: the non-ionized form (easier distribution through the nerve membrane) and the cationic form (less distribution, it joins the membrane receptor in the internal axoplasmic part).

- An intermediate hydrocarbonated chain which joins the aromatic nucleus through an ester or amide union. This type of link establishes the type of degradation and metabolization of the molecule and allows to divide local anesthetics in two large groups:
  1. The ester type: cocaine, procaine, tetracaine, benzocaine, which are metabolized through the pseudocolinesterase enzyme in the plasma. This type is of fast action and short duration. Their main metabolite is para-aminobenzoic acid (PABA), a powerful allergenic agent which accounts for anaphylactic reactions.
  2. The amide type: lidocaine, mepivacaine, bupivacaine and ropivacaine, which exhibit an enzymatic degradation by means of hepatic microsomes. This type is of longer duration and greater toxicity.

The objective of anesthesia is to produce an adequate level of nervous inhibition with a safe amount of local anesthetic. Accordingly, an adequate knowledge of the characteristics and toxicity of an anesthetic will facilitate an appropriate use, minimizing the risks of its application (6).

However, adverse reactions to local anesthetics are relatively frequent, although severe reactions are exceptional and account for under 1% of all reactions. Non-allergic adverse reactions can arise upon the administration of a local anesthetic. These can be toxic (not related to the drug, psychomotor and vasovagal, due to sympathetic stimulation, idiosyncratic, etc.) or of allergic nature (to the anesthetic itself or its preservatives and antioxidants). The risk of these reactions is directly proportional to its concentration in the bloodstream, mainly affecting the central nervous system and the cardiovascular system.

Accordingly, in the case of scheduled ophthalmological surgery, when an adverse reaction arises upon administration of the local anesthetic, the operation must be interrupted to perform an allergy study to determine the safest type of local anesthetic for the patient. If the surgery is urgent, the first option is general anesthesia and if it is contraindicated (and the cause of the adverse reaction is known) the following protocol should be followed: 1) if the local anesthetic is of the ester group, proceed to administer an anesthetic of the amide group; 2) if the cause of the adverse reaction is an anesthetic of the amide group, utilize another anesthetic of the same group or of the ester group (no crossed reactions arise between them). In this sense, it must be taken into account that some rare cases of allergy to amide derivatives have occurred, in which case lidocaine can be utilized because it is usually well tolerated; and 3) if the agent that causes the allergic reaction is not known, a local amide anesthetic shall be used but without containing vasoconstrictors or additional preservatives.

It is important to emphasize the need of knowing the type of local anesthetic to be utilized, as well as its characteristics and possible adverse reactions together with an early identification of symptoms to initiate therapeutic measures to prevent their progression.

REFERENCES