Local Anesthesia in Clinical Dermatologic Practice

Essay

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Introduction

Dermatology is a medical and surgical specialty with a distinguished history in the development and advancement of diagnostic, therapeutic, and cosmetic procedures, many of these procedures frequently involve injections or surgery, and can cause pain and discomfort ***(Auletta, ١٩٩٤)***.

Knowledge of local anesthesia is critically important to dermatologist to perform successful dermatological procedures. Local anesthetics when used judiciously are extremely safe and allow dermatologists to perform a variety of procedures ***(Upadya and Upadya, ٢٠٠٥).***

Several different local anesthetic agents are available for dermatologic use. There are various methods of delivery and known toxicities associated with the use of these drugs. Thus a basic understanding of the pharmacologic properties of these agents, the potential adverse effects, and the different applications and techniques of administration is vitally important to the practicing dermatologic surgeon in order to maximize patient safety and comfort ***(Skidmore et al., ١٩٩٦).***

Aim of the Essay

The aim of this essay is to understand local anesthesia and its techniques which is an essential prerequisite to develop a successful dermatological surgery practice and to provide a baseline reference for future research work.

Spot Light on the Pharmacology of Local Anesthetics

Local anesthesia is defined as the reversible loss of sensation in a relatively small or circumscribed area of the body, achieved by topical application or injection of agents that either depress the excitation of nerve endings or inhibit the conduction of impulses along a peripheral nerve. While there are many ways of producing local anesthesia, such as topical application of ice or vapor-coolant ethyl chloride, local anesthetics are by far the most commonly used ***(Smith et al., ١٩٩٩a).***

Local anesthetic agents are drugs which used clinically to produce temporarily loss of sensation in a localized area of the body ***(Feyh, ١٩٩٣).*** The ideal local anesthetic agent should posses a number of properties; short onset of action, with a sufficiently long duration to complete any planned procedures, non irritating, cause no irreversible damage to nerves, and its potential systemic toxicity should be low ***(Covino and Giddon, ١٩٨٤).***

History of local anesthetics:

History of local anesthetics dates back to the time when the new world was discovered. After the conquest of Peru by Francisco Pizzaro in ١٥٣٠, it was brought to the attention of Europeans the properties of a wonderful plant whose leaves were described as stimulating when chewed. The indigenous

population of Peru regarded this plant as divine, and as a reflection of its importance in their economy, they called it *khoka*, meaning *the plant*, which resulted in the term *coca* in Europe ***(McAuley, ١٩٦٦).***

After description of the general and stimulant effects of coca by Europeans, the Austrian Carl von Scherzer imported a sufficient quantity of coca leaves for further analysis. He gave this material to the German chemists Albert Niemann. In the years ١٨٥٩-١٨٦٠ Niemann was able to isolate the main alkaloid of the coca plant, which he called cocaine ***(Niemann, ١٨٦٠).***

The frequency of central nervous and cardiovascular systemic toxic reactions grew as fast as the popularity of the use of cocaine. Local anesthesia entered a period of profound crisis. The medical community and the pharmaceutical industry were prompted to search for new and less toxic local anesthetics ***(Bardsley et al., ١٩٩٨).***

In ١٩٠٤ Procaine (An ester of para amino benzoic acid) was discovered. Procaine became the prototype for local anesthetics for nearly half a century because it does not have the severe local and systemic toxicities of cocaine. Following the introduction of procaine, hundreds of structurally related analogues were prepared and their local anesthetic properties are enhanced ***(Ruetsh et al., ٢٠٠١).***

In ١٩٣٠ Tetracaine the most widely used ester-type local anesthetic agents was developed. In ١٩٤٤ Lidocaine, was the first amide local anesthetic to be used clinically by Lofgren and

in ١٩٤٨ Lidocaine rapidly became widely employed because of its potency, rapid onset, and effectiveness for infiltration, peripheral nerve block, and for both epidural and spinal anesthesia ***(Ball and Westhorpe, ٢٠٠٤).***

In ١٩٦٠ Prilocaine was introduced, it is related to lidocaine. It is used for infiltration, peripheral nerve block, and epidural anesthesia. Its anesthetic profile is similar to that of lidocaine, although it produces less vasodilatation than lidocaine and has a lesser potential for systemic toxicity at similar doses. In ١٩٦٣ a very important step in the evolution of regional anesthesia was the appearance of bupivacaine. It was the first single long-acting amino amide drug ***(Steffen, ٢٠٠٢).***

In ١٩٧٢, Etidocaine was the next long-acting local anesthetic introduced. Ropivacaine and levobupivacaine are both new long acting aminoamide local anesthetics that may reduce cardiovascular toxicity, as evidenced by laboratory and clinical investigations they have been placed in clinical use where they remain today ***(Bardsley et al., ١٩٩٨)***.

Pharmacology of local anesthetics:

The pharmacology of local anesthetics is an integration of the basic physiology of excitable cells and the mechanism by which local anesthetics are capable of interrupting conduction of neural messages. The common characteristics of the molecules have been identified and can explain the properties of the agents. These same chemical characteristics also explain toxicity of these agents and differences that exist between local anesthetics with similar structure ***(Tetzlaff, ٢٠٠٠).***

Physiology of nerve conduction:

The function of excitable tissue is based on the presence of a cell with a lipid membrane, axoplasm, membrane-integrated ion specific channels, and ion gradients maintained by energy dependent enzymes ***(Hollmann et al., ٢٠٠١).***

Potassium moves freely through the membrane, whereas sodium moves in a semi permeable manner, controlled by gates on the sodium channels (Fig.١) ***(Tetzlaff, ٢٠٠٠)***. Sodium is restricted to the extracellular space, except when specific ion channels are open. Potassium selectively accumulates inside the nerve cell to preserve electrical neutrality ***(Olschewski et al., ١٩٩٨).***

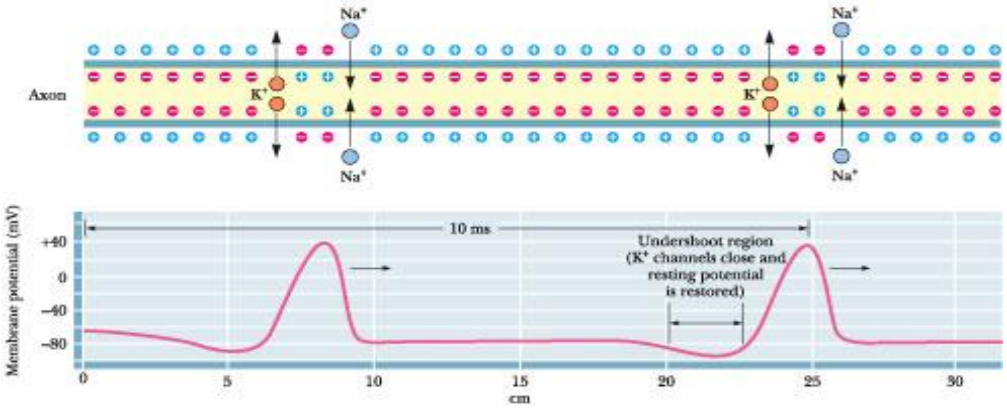

Fig. (١): Action and Resting potential of the nerve cell membrane ***(Tetzlaff, ٢٠٠٠).***

In an unexcited state, the electrical potential inside the cell is negative in reference to the outside of the cell and very close to the potential that would be determined by potassium alone (Fig.١). This is the resting potential of the nerve cell membrane. During conduction of an impulse (action potential),

sodium channels open and sodium ions move into the cell, depolarizing the cell. The gate that opens and closes these channels is present on the axoplasmic side of the nerve cell membrane. In the open state, this channel is susceptible to the action of local anesthetic molecules that cause it to remain inactive and prevent subsequent depolarization. This is the basis for conduction blockade ***(Tetzlaff, ٢٠٠٠).***

Chemical structure:

Local anesthetics possess a basic chemical structure that gives it amphipathic characteristics. Its structure can be divided into three distinct parts: an aromatic portion (lipophilic), intermediate chain, and amine group (hydrophilic) (Fig. ٢). The intermediate chain connects the aromatic group to the amine group. It is also the basis of local anesthetic classification as either esters or amides ***(Heavner, ٢٠٠٧).***

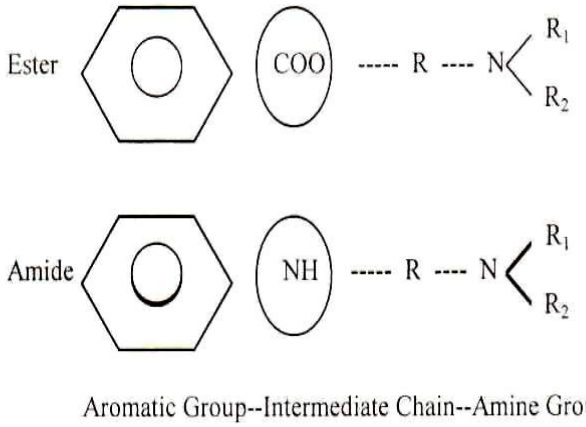

Fig. (٢): Local anesthetic Structure ***(Heavner, ٢٠٠٧).***

Esters:

Ester local anesthetic agents have an esteric bond (-coo-) between aromatic and amino components. As the esteric bond is relatively unstable these solutions are liable to degradation and thus are disadvantaged by a relatively short half life. They are hydrolysed in the plasma by pseudocholinestrase which make them of short duration. Commonly used esters include tetracaine, procaine, chloroprocaine, cocaine, and benzocaine. Ester group is less frequently used because of a higher incidence of allergy ***(Feyh, ١٩٩٣).***

Amides:

They have a much stronger intermediate bond (-NHCO-) than esters. They are therefore, stable in solution and little affected by changes in pH. In contrast to esters, amide local anesthetic agents do not undergo plasma hydrolysis but are usually metabolized in the liver by combination of oxidative dealkylation and hydroxylation. Amide group is more frequently used because of a less incidence of allergy. Commonly used amides include lidocaine, mepivacaine, prilocaine, bupivacaine, etidocaine, and dibucaine ***(Boren et al., ٢٠٠٧).***

Physiological activity:

Physiologic activity of local anesthetics is a function of their lipid solubility, diffusibility, affinity for protein binding, percent ionization at physiologic pH, and vasodilating properties ***(Revis et al., ٢٠٠٥).***

١. **Lipid solubility:** It is an important characteristic as potency is directly related to it, because ٩٠٪ of the nerve cell

membrane is composed of lipid. Increased lipid solubility leads to faster nerve penetration and blockade of sodium channels ***(Covino and Wildsmith, ١٩٩٨).***

٢. **Diffusibility**: After local anesthetic is injected, its movement then occurs through the process of diffusion. Local anesthetic is diluted by absorption into tissues, blood and lymph. The diffusibility of the local anesthetic depends to large extent on pKa, the concentration of the anesthetic and possibly the lipid solubility (local anesthetic with high lipid solubility is more diffusible) ***(Burm, ١٩٨٩).***

٣. **Protein binding**: It is related to the duration of action. The more firmly the local anesthetic binds to the protein of the sodium channel, the longer the duration of action ***(Beker and Reed ٢٠٠٦).*** Protein binding may vary, increasing in trauma, major surgery, chronic inflammation, cancer, and uremia. Conversely, protein binding decreases during pregnancy, in the newborn and with use of the contraceptive pills ***(Tucker, ١٩٩٤).***

٤. **PH:** Local anesthetics exist in ionized and non ionized forms, the proportions of which vary with the pH of the environment ***(McLure and Rubin, ٢٠٠٥).*** A decrease in pH shifts equilibrium toward the ionized form, delaying onset of action. This explains why local anesthetics are slower in onset of action and less effective in presence of inflammation, which creates a more acidic environment with

lower pH. The increase in the pH produces the reversed effect ***(Strichartz, ١٩٩١).***

٥. **Vasodilating properties**: Local anesthetics, with the exception of cocaine, are vasodilators. This occurs via direct relaxation of peripheral arteriolar smooth muscle fibers. Greater vasodilator activity of a local anesthetic leads to faster absorption and, thus shorter duration of action. To counteract this vasodilatation, epinephrine often is included in local anesthetic solutions ***(Revis et al., ٢٠٠٥).***

Mechanism of action of local anesthetics:

Local anesthetics block nerve conduction by reversibly binding with the intracellular portion of voltage-gated sodium channels in the nerve membrane. As this site of action is intracellular, it requires the local anesthetic to diffuse across the lipophilic lipoprotein membrane ***(Olschewski et al., ١٩٩١).***

Local anesthetic is administered in an acidic solution that maintains the majority of the drug in the ionized soluble form. Once injected into the tissue it must be converted into the neutral unionized form in order to enter the nerve cell. The proportion of drug that is converted will depend upon the local anesthetic pKa and the tissue pH. Once inside the cell the lower intracellular pH regenerates the ionized form, which blocks the receptor within the sodium channel. Sodium influx is reduced and the upsurge in the membrane potential slows. If a sufficient number of sodium channels are blocked the threshold potential will not be reached and impulse conduction stops. The resting

membrane and threshold potential remain the same, but the action potential is temporarily halted ***(McLure and Rubin, ٢٠٠٥).***

In addition to the action of ionized local anesthetic on the intracellular portion of the sodium channel, the unionized local anesthetic also disrupts the intra-membrane portion of the channel. The local anesthetic action is augmented by blockade of potassium channels, calcium channels and G-protein-coupled receptors. As the block proceeds different sensory modalities are lost in the order of pain, temperature, touch, deep pressure then motor function ***(Day et al., ١٩٩٨).***

Administration of local anesthetics:

For proper administration of local anesthetics, consider the individual characteristics of the patient, dose of local anesthetic to be administered, presence or absence of epinephrine, speed of administration, local tissue vascularity, and technique of administration ***(Mikesell et al., ٢٠٠٥).***

In each case, physicians should strive to find the smallest dose possible administered over the longest period of time that achieves adequate anesthesia ***(Tetzlaff, ٢٠٠٠)***.

Factors affecting anesthetic activity:

١-Dosage of local anesthetic solutions:

As the dose of local anesthetic is increased, the quality of anesthesia is improved. This can be achieved either by using a large volume of a less concentrated local anesthetic solution, or a small volume of a more concentrated local anesthetic solution ***(Singh and Erwin, ١٩٩٨).***

٢-Site of injection:

The site of injection can influence the onset time and duration of nerve blockade of the local anesthetic. For example, bupivacaine, when used for intercostal nerve block, has an onset time of approximately ٥ minutes and duration of effect of approximately ٤ hours, and when used for brachial plexus block has an onset time of approximately ٣٠ minutes and duration of around ١٠ hours. These differences can partly be explained by differences in anatomy, and variable rate of vascular uptake from the site of injection ***(Drake et al., ١٩٩٥).***

٣-Addition of vasoconstrictors:

Adrenaline (epinephrine) is the most commonly used vasoconstrictor, at a concentration of ١:٢٠٠,٠٠٠ (٥ mg/mL), it is employed with local anesthetics because its vasoconstrictive effects, so it decreases blood flow at the procedure site. As a result; bleeding is reduced, the absorption of anesthetic is decreased, the amount of anesthetic necessary is lessened, the effects of the drug are prolonged, and the risk of systemic toxicity is diminished. Epinephrine may potentially induce adverse effects (Table ٢). Therefore its use must be carefully considered in patients with heart disease and in those patients concomitantly taking B-blockers ***(Wahl et al, ٢٠٠١).***

Other vasoconstrictors, such as noradrenaline (norepinephrine) and phenylephrine, have also been used in conjunction with local anesthetic solutions. However, studies were unable to demonstrate superiority of these agents to adrenaline ***(Becker and Reed, ٢٠٠٦).***

Table (١): Adverse effects of lidocaine with epinephrine ***(Wahl et al., ٢٠٠١).***

Symptoms	Treatment
١-Central nervous system: **Lidocaine** Drowsiness, circumoral Numbness, tingling of tongue, Metallic taste, diplopia, Blurred vision, tinnitus, Slurred speech, muscle Twitching, shivering, seizure, **Epinephrine** Nervousness, tremors, Headaches.	Intravenous diazepam, oxygen.
٢-Cardiovascular system: **Lidocaine** Progressive myocardial Depression, prolonged. Conduction time, Arteriovenous block, Bradycardia, Hypotension, Hypoxia, acidosis. **Epinephrine** Tachycardia, palpitations, Chest pain, hypertension.	Cardiopulmonary resuscitation, oxygen, vasopressors, intravenous fluids. Vasodilators (hydralazine, clonidine, sublingual nifedipine).
٣-Allergic Reactions: **Lidocaine** Urticaria, angioedema, Anaphylaxis.	Antihistamines, subcutaneous epinephrine, oxygen, steroids.
٤-Psychogenic: Vasovagal response.	Cold compresses on forehead and neck, trendelenburg position, ammonia ampoule.

٤-Use of additives with local anesthetics:

In order to improve the onset of action or to prolong the duration of nerve blockade, adding sodium bicarbonate (١ mmol/١٠ mL local anesthetic solution) to lidocaine decreases the onset time after injection by increasing the amount of non-ionized drug (because of the more alkaline medium) ***(Mather and Chang, ٢٠٠١)***.

٥-Mixtures of local anesthetics:

The advantages of mixing two local anesthetics in theory is to allow the use of a smaller amount of any one drug, thus limiting its toxicity, and to combine the rapid onset of one drug with the long duration of the other. At present it appears to be no significant clinical advantage in using mixtures of local anesthetics ***(Covino and Wildsmith, ١٩٩٨).***

Toxicity and adverse effects of local anesthetics:

Local anesthetics are safe drugs, but they have the potential to cause serious harm if used without caution ***(Boren et al., ٢٠٠٧).*** In ***١٩٧٩ Albright*** drew the attention of the anesthetic community to the risks of intravascular injection of etidocaine and bupivacaine. He highlighted the unreliability of the aspiration test, the fact that cardiovascular collapse could occur without preceding hypoxia and that resuscitation may be difficult. Such severe reactions are rare, but can follow absorption of an inappropriately high dose, or accidental intra-vascular injection of an appropriate dose. The magnitude of the effect will depend on the toxicity of the drug, the dose administered, the speed and site of administration, as well as the physical status of the patient in terms of age, medical conditions and pregnancy ***(McLure and Rubin, ٢٠٠٥).***