



REVIEW ARTICLE

Local Anesthesia - Solution to Pain : An Overview

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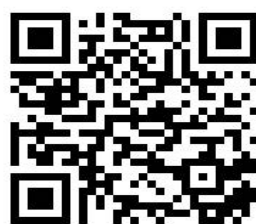
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Abstract

Local anesthetics have been used clinically for more than a century, but new insights into their mechanisms of action and their interaction with biological systems continue to surprise researchers and clinicians alike. Local anesthetics must traverse several tissue barriers to reach their site of action on neuronal membranes. In particular, the perineurium is a major rate-limiting step. Previously it was assumed that patients are rarely allergic to local anesthetic agents, but variation in individual patient's response to local anesthetics is larger than previously assumed adjuncts available to block sensory nerve are there, but these typically also prolong motor block.

Keywords: Anesthesia, Complication, Lignocaine, Toxicity



1 | INTRODUCTION:

Despite being in clinical use for more than a century, local anesthetics (LA) continue to surprise researchers and clinicians alike. (1) Various routes by which these drugs can be used are infiltration, nerve block, for neuraxial anesthesia and intravenously. Their clinical introduction profoundly changed perioperative medicine. Today, in parallel with advances in neurosciences, our understanding of LA has become much more detailed. (2) Local anesthetic agents are the most commonly used drugs

administered by dentist to relieve pain. These drugs when applied in sufficient concentration at the site of action prevent conduction of electric impulses by membrane of nerves and muscle. (3) The aim

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of this review is to highlight key aspects of LA pharmacology and toxicology and delineate current research.

Definition

It is defined as a loss of sensation in a circumscribed area of the body caused by depression of excitation in nerve endings or an inhibition of the conduction process in peripheral nerves (Stanley F Malamed, 1980). (4)

History (5, 6)

The 1st chemical local anesthetic came with discovery of cocaine in 1860 by Albert Nieman, but its anesthetic property was not realized until in 1862 when Schraff noted its local effect on tongue. William Halsted Steward carried out the 1st recorded inferior dental nerve block using cocaine in 1884. Modern chemical LA agents came of age when Alfren Einhorn achieved esterification of the base alcohol with benzoic acid to synthesize procaine in 1904-1905. Lofgren succeeded in synthesizing Lidocaine from a series of aniline derivatives in 1943. Bupivacaine became the longest acting amide LA in 1980's to be followed by Ropivacaine in mid 1990.

On the basis of myelinated and non myelinated, diameter and velocity, nerve fibres have been classified into different categories Table 1 (7)

Classification of LA (4)

Based on structure

(1) **Esters:** They possess an ester linkage between the benzene ring and the intermediate chain.

- Esters of Benzoic acid (ESTER GROUP) It includes Butacaine, Cocaine, Ethyl Amino Benzoate, Benzocaine, Piperocaine, Tetracaine
- Esters of paraamino benzoic acid: Chloroprocaine, Procaine, Propoxycaine.

(2) **Amide:** They possess an amide linkage between the benzene ring & intermediate chain. Various amide available are Articaine, Bupivacaine, Dibucaine, Etiodacaine, Lidocaine, Mepivacaine & Prilocaine.

(3) **Quinolone:** Centbucridine.

Based on potency and duration

Injectable:

A) Low potency, short duration: Procaine, Chloroprocaine

B) Intermediate potency & duration: Lidocaine, Prilocaine.

C) High potency & long duration: Bupivacaine, Tetracaine.

Surface anesthetic:

Soluble: Cocaine, Tetracaine. Benoxinate, Lignocaine.

Insoluble: Benzocaine, Oxethazine

Theories of regional anaesthesia (4, 8)

1. Electrical potential theory
2. Acetylcholine theory
3. Interference with nerve metabolism
4. Reversible coagulation theory
5. Plasma membrane expansion theory
6. Calcium gate theory
7. Specific receptor theory (most accepted): According to this theory the LA agent acts by binding to specific receptors that are present on the sodium channel. The action of the drug has been stated to be direct & involves the binding of the agent to the specific receptor & prevents the entry of sodium into the cell.

Pharmacokinetics (4, 9)

Uptake: All LA produce vasodilatation of vascular bed into which they are deposited except cocaine which is a potent vasoconstrictor. A significant effect of it is vasodilatation, increased absorption of LA into blood leading to decreased duration and potential for toxicity. The rate at which LA is absorbed into the blood and reach their peak level vary acc. to the route of administration.

TABLE 1: Classification of nerve fibres

CHARACTERISTICS	A alpha	A beta	A gamma	A delta	B	C
MYELIN	+++	++	++	++	+	-
DIAMETER(μm)	12 to 20	5 to 12	5 to 12	1 to 4	1 to 3	0.5 to 1
CONDUCTION VELOCITY(m/sec)	70 to 120	30 to 120	15 to 35	5 to 25	3-15	0.7-3
ONSET TIME	6					
FUNCTION	Motor muscle proprioception	Touch, pressure proprioception	Touch, motor proprioception	Pain, temperature, pressure proprioception	Preganglionic autonomic (sympathetic) activity	Pain, temperature, pressure, itch postganglionic sympathetic

Distribution: Distributed to all tissues especially to highly perfused organs (brain, liver, kidney). But skeletal muscle (not among the highly perfused organ) which form the largest mass of tissue in body contains the greatest percentage of LA.

Metabolism

Ester LA : Hydrolysed in plasma by pseudocholinesterase. Faster the hydrolysis, lesser is toxic potential. Chloroprocaine (least toxic) & Tetracaine (most toxic). Allergic reactions in response to ester drugs are due to PABA (major metabolite of ester LA).

Amide LA : Liver is the primary site. Patient with lower than usual hepatic blood flow (hypotension, CHF, cirrhosis) are unable to biotransform amide LA at a normal rate leading to increase chance to toxicity. These conditions represent a relative contraindication to amide LA.

Excretion: Mainly excreted by kidney. % of a given dose of LA will be excreted unchanged in urine. Esters appear in small concentration. Amides are present in urine as parent compound.

Characteristics of an ideal local anaesthetic (10)

- Administration of agent is non irritating
- Little or no allergenicity
- A rapid onset & adequate duration
- Completely reversible.

- Minimal systemic toxicity.
- Anesthesia is selective to nociception pathway

Composition of LA (8)

- 1) **Local anesthetic agent:** Conduction blockade
- 2) **Vasoconstrictor:** Decrease absorption of local anesthetic into blood, thus increasing duration of anesthesia & decreasing toxicity of anesthetic.
- 3) **Sodium Metabisulfite:** Antioxidant for vasoconstrictor.
- 4) **Methyl paraben:** preservative to increase shelf life, Bacteriostatic
- 5) **Sodium chloride:** Isotonicity to solution.
- 6) **Sterile water:** diluents

Indications (11, 12)

- Extraction of teeth.
- Alveoloplasty and alveolectomy.
- Incision and drainage of abscesses.
- Cavity preparation especially in deep painful cavities.
- Pulp procedures like pulpotomy and pulpectomy.
- Periodontal surgery and gingival surgery.
- Cyst enucleation or marsupialization

Mechanism of action

The local anaesthetic weak base (BNHOH) must be combined with a strong acid like HCl to make soluble acidic salt (BNHCl)



BNHCl solution of local anaesthetic drug dissociates in the basic environment found in the tissues



The charged amino group (BNH⁺) further dissociates outside the nerve sheath yielding non-ionized lipophilic molecule (BN)



BN diffuses through nerve sheath and comes to lie in interstitial fluid space. Here it combines with H⁺ forming (BNH⁺)



After the reequilibration between the base & cationic form, at the cell membrane itself, the charged cation binds to a receptor site



Ultimately responsible for suppression of nerve transmission

- Removal of residual infection, small neoplastic growths and salivary stones etc.
- Sore spots as a result of denture get relieved
- Treatment of trismus and trigeminal neuralgia
- In patients who shows gagging especially during placement of film.
- For anesthesia of oral cavity and jaw bones for routine surgical procedures like treatment of fractures etc.

Contraindications (11, 12)

- Fearful and apprehensive patients who refuse for injection.
- Allergy to local anaesthetic solution.
- Acute infection.
- Mentally retarded and unco-operative children or very young children.
- Anatomic anomalies.

- Hyperthyroidism, Liver disorders, Renal disorders, Cardiac problems, Diabetes mellitus.
- Internal hemorrhage.
- Major oral surgical procedure

Adverse effect of local anesthesia (13–18)

1. Caused by anesthetic solution.
2. Caused by vasoconstrictor drugs
3. Local reactions
4. Complications attributed to needle insertion

1. Caused by Anesthetic Solution

Sign and symptoms

Central Nervous System: All LA produces a sequence of stimulation followed by depression. Lidocaine toxicity may commence at concentrations $>5 \mu\text{g/mL}$, but convulsive seizures generally require concentrations $>8 \mu\text{g/mL}$.

Cardiovascular Reactions: These are cardiac depressants but no significant effects are seen at conventional doses. Bupivacaine is relatively more cardiotoxic & can produce ventricular tachycardia. Lidocaine has little effect on contractility & conductivity & is used as an antiarrhythmic agent.

Blood vessels: Cause fall in blood pressure. This is primarily due to sympathetic blockade, but high doses do cause direct relaxation of arteriolar smooth muscles.

Methemoglobinemia: A metabolite of prilocaine, *o*-toluidine, can oxidize the iron in hemoglobin from ferrous (Fe^{2+}) to ferric (Fe^{3+}). Altered Heme do not bind oxygen and normal hemes on the same hemoglobin molecule do not readily release their oxygen. This form of hemoglobin is called methemoglobin and when $>1\%$ of total hemoglobin is so

altered, the condition is called methemoglobinemia. Typical symptoms include cyanosis, dyspnea, emesis & headache. To reduce the risk clinician should take care to refrain from giving excessive dosages of local anesthetics.

Peripheral Nerve Paresthesia: Articaine is associated with fivefold higher incidence of paresthesia compared with lidocaine. as it can cause damage to inferior nerve or lingual nerve.

Allergic Reaction: The amide local anesthetics appear to have an extremely little immunogenic and therefore low rate of allergic reactions.

Reaction to Anesthetic Formulations containing a Sulfite Antioxidant: Allergic reactions like urticaria, bronchospasm & anaphylaxis. The use of local anesthetic without vasoconstrictors is a possible alternative with these patients.

2. Caused by Vasoconstrictor Drug

For prolong action of local anesthetic solution and to reduce its toxicity, vasoconstrictors have been added but its addition lead to contraindication of local anesthetic solution in various patients like in cardiac patients especially those suffering from refractory dysrhythmias, angina pectoris, postmyocardial infarction (6months) and uncontrolled hypertension. Other contraindications to vasoconstrictors are endocrine disorders such as hyperthyroidism, hyperfunction of the medullary adrenal (pheochromocytoma) and uncontrolled diabetes mellitus.

Symptoms: Palpitation, Tachycardia, Headache, Apprehension

Treatment: Brief duration reaction, so stop drug administration and reassure the patient.

3. Caused by local reactions

Infections caused by contaminated solutions are rare because of high standard of asepsis practiced by manufacturers.

Prevention: Use LA cartridges only once. Store cartridges as aseptically as possible. Before inserting needle into the cartridge, rubber diaphragm should be wiped with sterile disposable alcohol sponge.

4. Caused by Needle Insertion

(A) **Syncope:** Most frequent complication. It is a form of neurogenic shock caused by cerebral ischemia secondary to vasodilatation.

Sign and Symptoms

Pallor, Nausea, Vomiting, Patient may feel strange or different, Unconsciousness, Bradycardia and Hypotension

Treatment :

- Stop the dental procedure.
- Lower the chair back and elevate the legs of the patient.
- If patient is conscious, instruct him to take deep breath.
- Check patients BP, pulse rate and color.
- Ensure adequate oxygenation and CVS stability.

(B) Muscle Trismus

Common and mainly occurs after inferior alveolar nerve block.

Causes: Trauma to muscle during insertion, Infection (local), Hemorrhage.

Treatment

Mild: Slight exercises coupled with application of moist warm compresses for 15-20 min. /h, Mild analgesics, Physiotherapy consist of opening closing and side to side movement for 5-10 min. after every 3-4 hrs.

Severe: Add centrally acting muscle relaxant

(C) Pain or Hyperesthesia

Most commonly occur due to carelessness of dentist.

Prevention: Use Sharp needle, No multiple traumas, Needle insertion should be Atraumatic and slow, LA should be forced into the tissue slowly.

(D) Broken Needle

Most annoying and depressing complication of anesthesia.

Prevention : Do not force needle against resistance, Do not change the direction of the needle while

embedded in tissue, Do not use needle of too fine a gauge, Do not use resterilized needle & Inform the patient before inserting the needle

(E) Hematoma

It is associated with posterior superior alveolar nerve block and infraorbital nerve block. Occurs because of improper technique.

Treatment

Immediate: Direct pressure to the bleeding site for at least 2 minutes.

Subsequent: Do not apply heat to the area for 6 to 8 hours after the incident. Application of ice to the region immediately and reassure the patient.

Techniques of Local Anesthesia

1. *Topical Anesthesia (4, 19, 20) : For obtaining the anesthesia of mucosa prior to injection, a suitable agent is applied to an area of either the skin or mucous membrane which it penetrates to anesthetize superficial nerve endings.*

(a) Sprays: Sprays are useful because of their rapidity of action. The active ingredient is 10% lignocaine hydrochloride in a water miscible base, which is expelled in small quantities from an aerosol container. The onset time of anesthesia is approximately 1 min & the duration about 10 min.

(b) Ointments & Jelly: Ointments containing 5% lignocaine hydrochloride can be used for a similar purpose, but it takes 3-4 min to produce surface anesthesia. It is occasionally used to produce surface anesthesia prior to incision of fluctuant abscesses.

(c) EMLA (Eutectic Mixture of Local Anesthetics) : EMLA cream (composed of lidocaine 2.5% & prilocaine 2.5%) is an emulsion in which the oil phase is a eutectic mixture of lidocaine & prilocaine in 1:1. Usually anesthetic solutions work on abraded skin but it provides anesthesia to intact skin

Indication: In pediatrics, Vein puncture, Suture removal, Split thickness skin graft, Pulpal anesthesia and Needle phobic patients

Contraindications : Patients with congenital/ idiopathic methemoglobinemia, Infants under the age of 12 months and Patients allergic to local anesthesia

2. Local Infiltration: In this, local nerve endings in the area of surgery are flooded with local anesthetic

solution, rendering them insensitive to pain or preventing them from becoming stimulated & creating an impulse. Incision is then made into the same area in which the local anesthetic has been deposited. (4)

3. *Field Block*: Solution is deposited near the larger terminal nerve branches so the anesthetized area will be circumscribed. An incision is made away from the site of injection. (4)

4. *Nerve Block*: Local anesthetic is deposited close to main nerve trunk, usually at a distance from the site of operative intervention. (4)

5. *Intrapulpal*: It is utilized in cases of pulp therapy where the other techniques have failed. The needle is bent for the purpose of proper positioning. Also a sufficient amount of pulp tissue needs to be engaged for the solution to be injected into it. (21)

6. *Intraosseous*: When the anesthetic is injected in the bone through a hole in the cortical plate, the tissue will not affect it & it anesthetizes only the area of treatment, not the quadrant. (21)

Maxillary Anesthesia (4, 21–23)

1. *Posterior Superior Alveolar Block*: For several molar teeth in one quadrant.

2. *Middle Superior Alveolar Block*: For management of premolars in one quadrant.

3. *Anterior Superior Alveolar Block*: For management of anterior teeth in one quadrant.

4. *Maxillary Nerve Block*: For extensive buccal, palatal & pulpal management in one quadrant.

5. *Greater Palatine Nerve Block*: For palatal & soft osseous tissue treatment distal to canine in one quadrant.

6. *Nasopalatine Nerve Block*: For palatal & osseous tissue management from canine to canine bilaterally.

7. *Supraperiosteal Injection*: For obtaining pulpal anesthesia in maxillary anterior teeth when treatment is limited to one or two teeth.

8. *Posterior Superior Alveolar Nerve Block*: Nerve anesthetized: Posterior superior alveolar nerve. Regions anesthetized: 1st, 2nd, 3rd maxillary molars & their investing tissue except palatal mucosa.

9. *Greater or Anterior Palatine Nerve Block*: Nerves anesthetized: Greater palatine nerve. Region anes-

thetized: Posterior portion of hard palate & its overlying soft tissues anteriorly till 1st premolar.

10. Infraorbital Nerve Block

Nerves anesthetized: Anterior superior alveolar nerve, Middle superior alveolar nerve, Infraorbital nerve, Inferior palpebral branch, Lateral nasal branch Superior labial branch

Regions anesthetized: Maxillary central incisors upto maxillary premolars, MB root of 1st molar & buccal investing tissues.

11. Nasopalatine Nerve Block

Nerves anesthetized: Nasopalatine nerves bilaterally.

Regions anesthetized: Anterior portion of hard palate from 1st premolar to 1st premolar.

12. Maxillary Nerve Block

Nerves Anesthetized: Maxillary nerve & its branches.

Area anesthetized: Maxillary teeth, overlying bone & mucosa on the affected side, Hard & soft palate, Upper lip, cheeks, side of the nose & lower eyelid.

Supplemental Anesthesia Techniques

1. *Supraperiosteal (Infiltration)*: recommended for limited treatment protocols

2. *Periodontal Ligament Injection*: recommended as an adjunct to other techniques or for limited treatment protocols

3. *Intraseptal Injection*: For periodontal surgical techniques.

4. *Intraosseous*: for single tooth when other techniques have failed.

Mandibular Anesthesia (4, 19, 22, 24, 25)

1. Mental & Incisive Nerve Block

Nerves anesthetized: Mental & incisive nerves.

Regions anesthetized: Lower lip, Mucosa anterior to mental foramen, teeth anterior to second premolar.

2. Classical Inferior Alveolar Nerve Block

Nerves anesthetized: Inferior alveolar, incisive, mental & lingual nerve.

Regions anesthetized: Mandibular teeth & buccal soft tissues anterior to 1st molar & anterior 2/3rd of tongue & floor of the mouth.

3. Closed Mouth Approach (Vazirani-Akinosi Block)

Nerves anesthetized: Inferior alveolar, incisive, mental, lingual & mylohyoid nerves.

4. Gow-Gates Nerve Block: It is an intraoral mandibular nerve block given at neck of condyle & provides hard & soft tissue anesthesia of mandible upto the midline. Mandibular nerve & its branches are blocked including its auriculotemporal subdivision.

Preanesthetic evaluation (26)

Preanesthetic evaluation should be done before administering any anesthetic drug. It is done to secure pertinent information to evaluate and not to diagnose or treat the patient for any medical problem. It is done to determine the following:

- Patients general and psychological condition.
- Need for medical consultation.
- History of any previous unpleasant esthetic experience.
- Specific drug sensitivity of the patient.
- The need for premedication or intraoperative sedation.
- The time to be allotted for procedure.
- The technique or method to be used.
- Choice of an anesthetic solution.
- The need and quantity of vasoconstrictor.

On first visit patients pulse rate and blood pressure should be taken. Brief medical history should be taken. It involves:

- CVS Status
- Any respiratory difficulties, nervous system disorder, metabolic deficiencies, endocrine imbalance, hematological pathologies & iatrogenic conditions

- Presence of allergy, patient's size and age, emotional or psychological problems.
- Medications the patient may be taking

CVS status: Conditions concerned to dentists are Congenital heart disease, Acquired heart disease, Rheumatic heart disease, Atherosclerotic heart disease, Hypertension, CHF, Valvular heart disease Arrhythmia(conduction system defect).

Precautions

- Consultation with patient physician taken when indicated.
- Procedure should be planned to fit the individual patient condition.
- If patient is anxious, he should be moderately premedicated or sedated during appointment.
- He should be given short appointment to prevent undue tiring.
- Least possible amount of anesthesia should be used.
- Vasoconstrictors, although not contraindicated, should be kept at a minimum dose or eliminated if necessary.
- Patient may be given oxygen by nasal cannula during procedure.
- Prophylaxis with appropriate antibiotics should be given if indicated

Respiratory System: Bronchitis, Bronchiectasis, Emphysema, Asthma

Precautions

- Treatment should be given in afternoon.
- Preoperative medications such as adhesives, hypnotics and narcotics should be used with extreme caution as they interfere with cough reflex and depress ventilation.

- Bronchodilators, nebulizers and expectorants can be given preoperatively.
- Choice of local anesthetic or vasoconstrictor is not of utmost importance provided there are no other complicating pathologies.
- Oxygen can be given by nasal cannula if required during dental procedure.

Metabolic diseases

(1) Diabetes Precautions Severity of diabetes.

- Evaluate the patient treatment whether diabetes is controlled by diet/hypoglycemic agents/insulin.
- Patient controlling diabetes by diet pose no problem.
- Patient on insulin should be treated between 9.00 am – 12pm because as a result of food and insulin intake, it is during these hours that they are best able to tolerate stressful situations.

(2) Hypothyroidism

These patients do not metabolize drug as well as the normal individual therefore doses of vasoconstrictors in drug should be kept minimum because of relative CVS conditions.

(3) Hyperthyroidism

Physician consultation

- Well premedication/sedation
- Vasoconstrictor should be reduced.

Local Anesthesia in Pregnancy & Postpartum (27)

Local anesthetics can be safely used when treating pregnant & postpartum patients if careful guidelines are followed. Because teratogenic risks are highest in the first trimester, the 2nd trimester is usually the period chosen for routine dental care. Lidocaine is least associated with medical complications.

LA Consideration in Endodontics

Effect of Inflammation on LA (2): Inflammation and infection lowers the tissue pH, altering the ability of a LA to provide clinically adequate pain control. There are two methods of obtaining adequate nerve block are:

1. Administer LA away from the area of inflammation: It helps in preventing the spread of infection to uninvolved regions. It also provides adequate pain control because of presence of more normal tissue condition. Regional nerve block anesthesia is the major factor in pain control for pulpally involved teeth.

2. Deposit a larger volume into the region: It will provide a greater no. of uncharged base molecule to diffuse through the nerve sheath to give satisfactory nerve block. Some patients respond unfavorably to instrumentation of their root canal, even when canals are debrided thoroughly.

Solution: Infiltration, Intrapulpal anesthesia & Topical anesthesia: Can apply a small amount of topical anesthetic ointment onto the file or reamer prior to inserting it into the canal.

Recent Advances in Local Anesthetics and some Additions in Lidocaine to Improve its Properties

Centbucridine: It is quinolone derivative which is 5-8 times potent than Lidocaine. It does not effect CNS or CVS adversely except when higher doses administered. (28) **Vacharajani et al (1983)** proved that efficacy of 5% of Centbucridine is same as that of 2% Lidocaine. (29)

Oraqix: A recently introduced locally applied anesthetic gel, is a eutectic mixture of prilocaine & lidocaine each in a 2.5% concentration. It was approved by FDA in 2004. (30)

Ropivacaine: It is a long acting amide having lower arrhythmogenic potential than Bupivacaine. It has low toxicity and available in 0.75%, 0.2% concentration. (31)

Electronic Dental Anesthesia: Anesthesia (Electronic Dental Anesthesia or EDA) which works by transcutaneous electrical nerve stimulation (TENS) was introduced to the dental profession. (32) One

study has favored its use as its efficacy in pain control has been described as comparable to local anaesthesia while at the same time avoiding the possible side effects associated with commonly used local anaesthetic agents and the inconvenience of post-operative anaesthetic effect. (33) Another study suggested EDA could be indicated for needle-phobic children; however, studies that have tested its effectiveness in children are few. (34)

2 | SUMMARY & CONCLUSION:

The science of LA is an active research field and LA will continue to be one of the mainstays of contemporary perioperative medicine. Anxiety, fear & apprehension should be recognized & managed before administration of a local anesthetic. Vasoconstrictors should be included in all local anesthetics unless specifically contraindicated. Partial resistance to LA may be more frequent than previously thought. LA are toxic on many tissues but clinically apparent nerve damage is very rare and LA-induced toxicity after peripheral nerve block has a good prognosis overall.

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