Review Article

A REVIEW ON MODERATE AND LONG ACTING LOCAL ANASTHETIC AGENT FOR PERIODONTAL DELIVERY

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ABSTRACT

The practice of modern dentistry is inconceivable without the application of local anesthesia. The dentist has various devices and procedures available for achievement of local anesthesia. It is impossible to provide effective dental care without the use of local anesthetics. This drug class has an impressive history of safety and efficacy, but all local anesthetics have the potential to produce significant toxicity if used carelessly. The purpose of this review is to update the practitioner on issues regarding the basic pharmacology and clinical use of local anesthetic formulations. Pain control is an integral part of modern dentistry.

Keywords: Local Anasthetics, Mepivacaine, Bupivacaine, Anesthesia in dentistry.

INTRODUCTION

It is a well-established fact today that the many variants of periodontal disease are essentially infections of the periodontal structures with differing micro-organisms predominating in the different presentations of the disease. The current market offers a wide variety of products for the dentist to use a therapeutic material for local drug delivery in combating periodontal disease. The local anesthetic drugs presently available and used in dentistry represent the safest and most effective drugs in all of medicine for the prevention and management of pain[1].

Local anesthetics are valued for the ability to prevent membrane depolarization of nerve cells. Local anesthetics prevent depolarization of nerve cells by binding to cell membrane sodium channels and inhibiting the passage of sodium ions. The sodium channel is most susceptible to local anesthetic binding in the open state, so frequently stimulated nerves tend to be more easily blocked. The ability of a given local anesthetic to block a nerve is related to the length of the nerve exposed, the diameter of the nerve, the presence of myelination, and the anesthetic used. Small or myelinated nerves are more easily blocked than large or unmyelinated nerves.

Myelinated nerves need to be blocked only at nodes of Ranvier (approximately three consecutive nodes) for successful prevention of further nerve depolarization, requiring a significantly smaller portion of these nerves to be exposed to the anesthetic. Differential blockade to achieve pain and temperature block (A-D, C fibers) while minimizing motor block (A-a fibers) can be achieved by using certain local anesthetics and delivering specific concentrations to the nerve.

Local anesthetics bind directly within the intracellular portion of voltage-gated sodium channels. The degree of block produced by local anesthetics is dependent upon how the nerve has been stimulated and on its resting membrane potential. Local anesthetics are only able to bind to sodium channels in their charged form and when the sodium channels are open. Local anesthetics are compounds that have the ability to interrupt the transmission of the action potential in excitable membranes by binding to specific receptors in the Na+ channels. This action, at clinically recommended doses, is reversible. Conduction can still continue, although at a slower pace, with up to 90% of receptors blocked. All local anesthetics are potentially neurotoxic if injected intraneurally, especially if that injection is intrafascicular. The neuronal damage may be directly related to the degree of hydrostatic pressure reached inside the axoplasma. Local anesthetics injected around nerves could also be toxic as result of the concentration of the agent and the duration of the exposure (e.g., cauda equina after intrathecal local anesthetics)[2, 3].

HISTORY

Anesthesia by compression was common in the antiquity. Cold as an anesthetic was widely used until the 1800s. The native Indians of Peru chewed coca leaves and knew about their cerebral-stimulating effects and possibly about their local anesthetic properties.

The leaves of ***erythroxylon coca*** were taken to Europe where Niemann in Germany isolated cocaine in 1860.

Carl Koller, a contemporary and friend of Sigmund Freud, is credited with the introduction of cocaine as a topical ophthalmic local anesthetic in Austria in 1884. In 1888 Koller came to the United States and established a successful ophthalmology practice at Mount Sinai Hospital in New York until the year of his death in 1944. Recognition of cocaine's cardiovascular side effects, as well as its potential for dependency and abuse, led to a search for better local anesthetic drugs[1, 4]. Cocaine is a good topical local anesthetic that also produces

vasoconstriction and for this reason it is still used, by some, as a topical anesthetic in the nose and other mucous membranes. Cocaine blocks the reuptake of cathecolamines from nerve endings. Total dose should not exceed 100 mg (2.5 mL of a 4% solution), to avoid systemic effects like hypertension, tachycardia and cardiac arrhythmias.

Highlights on local anesthesia

1850s Invention of the syringe and hypodermic hollow needle.

1884 Halsted, an American surgeon, blocks the brachial plexus with a solution of cocaine under direct surgical exposure.

1885 Wood, in the United Kingdom, is credited with the introduction of conduction anesthesia through a hypodermic injection.

1897 Epinephrine is isolated by John Abel at Johns Hopkins Medical School.

1897 Braun in Germany relates cocaine toxicity with systemic absorption and advocates the use of epinephrine.

1898 Bier is set to receive the first planned spinal anesthesia from his assistant Hildebrandt.

After CSF is obtained, the syringe is found not to fit the needle and therefore the spinal is not completed. Bier in turn successfully performs the first spinal anesthesia on Hildebrandt using cocaine. Subsequently both experienced the first spinal headaches.

1908 Bier introduces the intravenous peripheral nerve block (Bier block) with procaine.

1911 Hirschel performs the first percutaneous axillary block.

1911 Kulenkampff performs the first percutaneous supraclavicular block.

1922 Gaston Labat of France, a disciple of Pauchet, introduces in the US his book "Regional Anesthesia Its Technic and Clinical Application", the first manual of regional anesthesia published in America.

1923 Labat establishes the first American Society of Regional Anesthesia.

1953 Daniel Moore, practicing at Virginia Mason Clinic in Seattle, publishes his influential book "Regional Block".

1975 Alon Winnie, L. Donald Bridenbaugh, Harold Carron, Jordan Katz, and P. Prithvi Raj establish the current American Society of Regional Anesthesia (ASRA) in Chicago.

1976 The first ASRA meeting is held in Phoenix, Arizona.

1976 Regional Anesthesia Journal, volume 1, number 1 is published.

1983 Winnie introduces his book, Plexus Anesthesia, Perivascular Techniques of Brachial Plexus Block.

Chemical structure of local anesthetics[7, 8]

Local anesthetics are weak bases with a pka above 7.4 and poorly soluble in water. They are commercially available as acidic solutions (pH 4-7) of hydrochloride salts, which are hydrosoluble. A typical local anesthetic molecule is composed of two parts, a benzene ring (lipid soluble, hydrophobic) and an ionizable amine group (water soluble, hydrophilic). These two parts are linked by a chemical chain, which can be either an ester (-CO-) or an amide (-HNC-). This is the basis for the classification of local anesthetics as either esters or amides. Injecting local anesthetics in the proximity of a nerve(s) triggers a sequential set of events, which eventually culminates with the interaction of some of their molecules with receptors located in the Na+ channels of nerve membranes. The injected local anesthetic volume spreads initially by mass movement, moving across "points of least resistance", which unfortunately do not necessarily lead into the desired nerve(s). This fact emphasizes the importance of injecting in close proximity of the target nerve(s). The local anesthetic solution then diffuses through tissues; each layer acting as a physical barrier. In the process part of the solution gets absorbed into the circulation. Finally a small percentage of the anesthetic reaches the target nerve membrane, at which point the different physicochemical properties of the individual anesthetic become the factors dictating the speed, duration and nature of the interaction with the receptors.

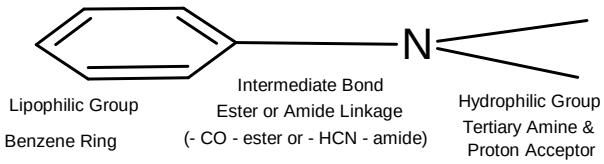
CHEMISTRY

The basic chemical structure of a local anesthetic molecule consists of 3 parts:

1. Lipophilic group- an aromatic group, usually an unsaturated benzene ring.

2. Intermediate bond- a hydrocarbon connecting chain, either an ester (-CO-) or amide (-HNC-) linkage. The intermediate bond determines the classification of local anesthetic.

3. Hydrophilic group- a tertiary amine and proton acceptor.



Lipophilic Group Intermediate Bond Hydrophilic Group

Benzene Ring Ester or Amide Linkage Tertiary Amine & (CO- ester or –HNC- amide) Proton Acceptor Amide and ester local anesthetics follow different paths of metabolism. Ester local anesthetics are more likely to cause an allergic reaction. (See Biotransformation & Excretion). In the operating room we don't have the opportunity to examine the chemical structure[9, 10]. An

easy way to tell the difference between an ester and amide is to determine if the generic name has an "**i**" before the "caine". This „trick" will only work with generic name it will not work with the trade or commercial name. All amide local anesthetics contain an "**i**" in the name. For example, l**i**docaine, mep**i**vacaine, pr**i**locaine, bup**i**vacaine, rop**i**vacaine, and levo-bup**i**vacaine all contain an "**i**" before the "-caine". Esters such as procaine, chloroprocaine, and tetracaine do not contain an "**i**" before the "-caine".

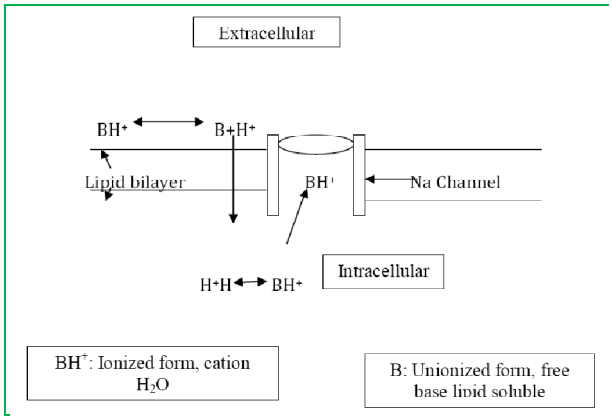
AMIDES	ESTERS
Bupivacaine	Benzocaine
Etidocaine	Chloroprocaine
Levobupivacaine	Cocaine
Lidocaine	Procaine
Mepivacaine	Tetracaine
Prilocaine	
Ropivacaine	

Structure activity relationships

- Local anesthetics (LAs) consist of a lipophilic and a hydrophilic portion separated by a connecting hydrocarbon chain.
- An ester (-CO-) or an amide (-NHC-) bond links the hydrocarbon chain to the lipophilic aromatic ring.
- The hydrophilic group is usually a tertiary amine, such as diethylamine, whereas the lipophilic portion is usually an aromatic ring, such as para-aminobenzoic acid.
- The nature of this bond is the basis for classifying drugs that produce conduction blockade of nerve impulses as ester local anesthetics or amide local anesthetics.

Mechanism of action[11, 12]

Local anaesthetics directly block transmission of pain from nociceptive afferents. Local anaesthetic agents are applied directly, and their efficacy results from action on the nerve where the inward Na+ current is blocked at the sodium ionophore during depolarization. LAs not only block Na+ channels but Ca2+ and K+ channels [16–18], transient receptor potential vanniloid-1 receptors, and other ligand-gated receptors as well. Local anaesthetics also disrupt the coupling between certain G proteins and their associated receptors. Through this action, LAs exert potent anti-inflammatory effects, particularly on neutrophil priming reactions. Local anaesthetics inhibit local inflammatory response to injury that can sensitize nociceptive receptors and contribute to pain and hyperalgesia. Studies have observed that local anaesthetics reduce the release of inflammatory mediators from neutrophils, reduce neutrophil adhesion to the endothelium, reduce formation of free oxygen radicals, and decrease edema formation. There are, in addition, a variety of other antithrombotic and neuroprotective actions of intravenous LAs that are independent of Na+ channel blockade but may account for many of the improvements in pain after surgery. Local anaesthetics can alleviate some types of neuropathic pain, and part of this effect may be related to sensitization of the antinociceptive pain pathways that occur in the neuropathic pain state; spinal glial cells have been shown to play some part in this as well.



Factors affecting onset, intensity, and duration of neural blockade[14]:

- Local anesthetics in solution exist in a chemical equilibrium between the basic uncharged form (B) and the charged cationic form (BH^+).
- At a certain hydrogen concentration specific for each drug, the concentration of local anesthetic base is equal to the concentration of charged cation. This hydrogen concentration is called the pKa.
- This relationship is expressed as, pH= pKa + log $[B]/[BH^+]$
- Lower pKa means greater fraction of the molecules exist in the unionized form in the body, so more easily cross nerve membranes leading to faster onset.
- The pKa of currently used local anesthetic compounds lies between 7.7 and 8.5.
- The commercially available solutions are always acid so that they contain more ionized molecules.
- Acidosis in the environment into which the local anesthetic is injected (as is present in an infected, pus tissue) further increases the ionized fraction of drugs. This is consistent with slower onset and poor quality of local anesthesia when a local anesthetic is injected into an acidic infected area.
- Local anesthetics with a higher degree of protein binding have a prolonged duration of action. Increased dose increases the duration of the block.
- The half-life of esters is only a few minutes due to their rapid hydrolysis in the plasma and liver, whereas the half-life of amides is a few hours.
- Patients with reduced cholinesterase activity (new born, pregnant) may have an increased potential for toxicity from ester local anesthetics.

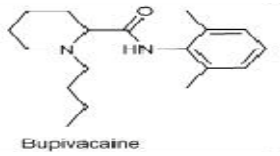
- Among the resulting metabolites from ester local anesthetics, the para-aminobenzoic acid is believed to be an antigen responsible for subsequent allergic reactions.
- Amides are mainly metabolized by the liver. Patient with severe hepatic disease may be more susceptible to adverse reactions from amide local anesthetics.
- Thin nerve fibers are more easily blocked than thick ones. However, myelinated fibers are more readily blocked than unmyelinated ones because of the need to produce blockade only at the node of Ranvier.
- In general, autonomic fibers (B and C fibers), small unmyelinated (C fibers), and small myelinated fibers (B and Aδ fibers) will be more readily blocked than thick, myelinated fibers (Aα and Aβ fibers).
- Thus, a differential block can be achieved where the smaller pain and autonomic fibers are blocked, while large touch and motor fibers are spared.
- This difference is due to the fact that nerve fibers containing myelin are relatively impervious to local anesthetic solutions compared to those which contain little or no myelin.
- The lipid solubility and pKa of the local anesthetic are the primary determinants of the degree of differential blockade.

IDEAL CHARACTERISTICS OF LOCAL ANASTHETICS

- Rapidly and completely block pain originating from the target area. Motor and other sensory functions are also lost, so anesthetic actions are not specific for pain.
- Act reversibly without causing any tissue damage. This is true of most local anesthetics.
- Possess large margin of safety expressed as systemic toxicity relative to anesthetic dose. Precise placement of drug reduces systemic toxicity in most applications, but accidental intravenous injection poses life-threatening risk with large doses via regional, spinal or epidural routes.
- Remain localized at the intended site long enough to complete the intended procedure. Addition of vasoconstricting α-adrenergic agents helps here.

BUPIVACAINE[15-17]

Bupivacaine is one of the most potent, long-acting local anaesthetics of the amide type. It prevents the generation and conduction of the nerve impulse by decreasing the permeability of the nerve cell membrane to sodium ions. As well as blocking conduction in nerve axons in the peripheral nervous system impermeable to the active (sodium permeable) state6. The increased duration of action of bupivacaine is due to its affinity to tissue. It has a relatively moderate-to-long duration of onset due to its moderate pKa. The transport of the amide local anesthetics across biological membranes is by passive diffusion. Because of bupivacaine's high affinity for protein binding, it is held in the neural membrane longer and more tightly than other local anesthetics, resulting in a longer and more profound sensory inhibition (Lenz *et al.,* 1992). Due to its ability to produce long duration local anesthesia, it is often employed to treat perioperative pain. Clinically Bupivacaine is utilized for intraoperative local anesthesia, post operative analgesia and in the treatment of chronic pain[6, 7]. It has also been noted that there is a period of analgesia that persists after the return of sensation, during which time the need for strong analgesic is reduced. In oral surgery, this drug provides excellent surgical anesthesia and extended post-operative analgesia. Bupivacaine is ideally suited for use in providing relief of severe dental pain when definitive treatment is to be postponed. Additionally, periodontal surgery as well as prolong dental restorative procedures would benefit from bupivacaine anesthesia.



Bupivacaine

Bupivacaine (Marcaine, Sensorcaine; both made by AstraZeneca, London, United Kingdom) has a p*K*a of 8.1. With an extensive history of successful use, bupivacaine is the long-acting local anesthetic to which others are compared. Although a bupivacaine block is long acting, it also has the longest latency to onset of block. Bupivacaine is noted for having a propensity for sensory block over motor block (differential sensitivity) at low concentrations. These factors, as well as the low cost of bupivacaine compared to newer long-acting local anesthetics, have established bupivacaine as the long-acting local anesthetic of choice in many institutions. When long-duration analgesia is required, the use of bupivacaine for low-volume infiltration or spinal anesthesia is well established.

The resion of the popularity of bupivacaine for regional anesthesia, its use for large-volume techniques such as epidural or peripheral nerve anesthesia may be problematic; prolonged resuscitation following accidental intravascular injection has been reported. The recommended dosages of bupivacaine are the lowest of any of the amide local anesthetics. If patient safety were the only issue (other than cost, convenience, or availability) involved in long-acting local anesthetic selection, less toxic options would likely be used for large volume blocks.

Mechanism of Action

Local anesthetics such as bupivacaine block the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the

action potential. In general, the progression of anesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) skeletal muscle tone. The analgesic effects of Bupivicaine are thought to be due to its binding to the prostaglandin E2 receptors, subtype EP1 (PGE2EP1), which inhibits the production of prostaglandins, thereby reducing fever, inflammation, and hyperalgesia.

Absorption

The rate of systemic absorption of local anesthetics is dependent upon the total dose and concentration of drug administered the route of administration, the vascularity of the administration site, and the presence or absence of epinephrine in the anesthetic solution.

Biotransformation / Drug Metabolism

Amide-type local anesthetics such as bupivacaine are metabolized primarily in the liver via conjugation with glucuronic acid. The major metabolite of bupivacaine is 2,6-pipecoloxylidine, which is mainly catalyzed via cytochrome P450 3A4.

Indications

Bupivacaine Hydrochloride is indicated for the production of local or regional anesthesia or analgesia for surgery, dental and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical procedures. Only the 0.25% and 0.5% concentrations are indicated for obstetrical anesthesia. Experience with nonobstetrical surgical procedures in pregnant patients is not sufficient to recommend use of 0.75% concentration of Bupivacaine Hydrochloride in these patients. Bupivacaine Hydrochloride is not recommended for intravenous regional anesthesia.

Dosage

The dose of any local anesthetic administered varies with the anesthetic procedure, the area to be anesthetized, the vascularity of the tissues, the number of neuronal segments to be blocked, the depth of anesthesia and degree of muscle relaxation required, the duration of anesthesia desired, individual tolerance, and the physical condition of the patient. The smallest dose and concentration required to produce the desired result should be administered. Dosages of Bupivacaine Hydrochloride should be reduced for elderly and/or debilitated patients and patients with cardiac and/or liver disease. The rapid injection of a large volume of local anesthetic solution should be avoided and fractional (incremental) doses should be used when feasible.

For specific techniques and procedures, refer to standard textbooks.

In recommended doses, Bupivacaine Hydrochloride produces complete sensory block, but the effect on motor function differs among the three concentrations.

Maximum dosage limit must be individualized in each case after evaluating the size and physical status of the patient, as well as the usual rate of systemic absorption from a particular injection site. Most experience to date is with single doses of Bupivacaine Hydrochloride up to 225 mg with epinephrine. 1:200,000 and 175 mg without epinephrine; more or less drug may be used depending on individualization of each case.

Contraindications

Bupivacaine Hydrochloride is contraindicated in obstetrical paracervical block anesthesia. Its use in this technique has resulted in fetal bradycardia and death.

Bupivacaine Hydrochloride is contraindicated in patients with a known hypersensitivity to it or to any local anesthetic agent of the amide-type or to other components of Bupivacaine Hydrochloride solutions.

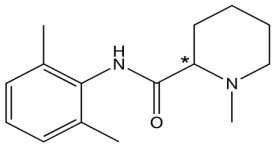
Significance of the bupivacaine

Bupivacaine, a long-acting amide local anesthetic, is a chemical analogue of mepivacaine with high lipid-solubility and protein-binding characteristics. These properties contribute to bupivacaine's greater potency and anesthetic duration as compared to other local anesthetics used in dentistry. The prolonged anesthesia it produces has been shown to limit postoperative pain following third molar extractions and endodontic procedures. Bupivacaine 0.5% with 1:200,000 epinephrines provides a safe and valuable alternative to the anesthetic agents presently available in dentistry.

MEPIVACAINE[18-20]

Description

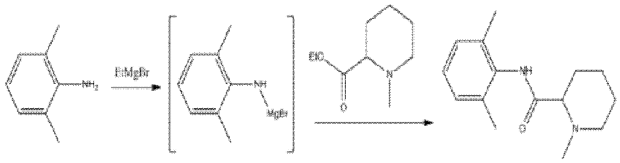
Mepivacaine hydrochloride, a tertiary amine used as a local anesthetic, is 1-methyl-2′,6′-pipecoloxylidide monohydrochloride with the following structural formula:



It is a white, crystalline, odorless powder soluble in water, but very resistant to both acid and alkaline hydrolysis.

Chemistry

Two primary methods of synthesis have been suggested. According to the first, mepivacaine is synthesized by reacting the ethyl ester of 1-methylpiperindine-2-carboxylic acid with 2,6-dimethylanilinomagnesium bromide, which is synthesized from 2,6-dimethylaniline and ethylmagnesium bromide.



Clinical pharmacology

Mepivacaine hydrochloride stabilizes the neuronal membrane and prevents the initiation and transmission of nerve impulses, thereby effecting local anesthesia.

Mepivacaine hydrochloride is rapidly metabolized, with only a small percentage of the anesthetic (5 to 10 percent) being excreted unchanged in the urine. Mepivacaine because of its amide structure is not detoxified by the circulating plasma esterases. The liver is the principal site of metabolism, with over 50 percent of the administered dose being excreted into the bile as metabolites. Most of the metabolized mepivacaine is probably resorbed in the intestine and then excreted into the urine since only a small percentage is found in the feces. The principal route of excretion is via the kidney. Most of the anesthetic and its metabolites are eliminated within 30 hours. It has been shown that hydroxylation and N-demethylation, which are detoxification reactions, play important roles in the metabolism of the anesthetic. Three metabolites of mepivacaine have been identified from adult humans: two phenols, which are excreted almost exclusively as their glucuronide conjugates, and the N-demethylated compound (2´,6´ - pipecoloxylidide).

The onset of action is rapid (30 to 120 seconds in the upper jaw; 1 to 4 minutes in the lower jaw) and mepivacaine hydrochloride 3% injection without vasoconstrictor will ordinarily provide operating anesthesia of 20 minutes in the upper jaw and 40 minutes in the lower jaw.

Indications and usage

Mepivacaine hydrochloride injection, USP, 3% is indicated for production of local anesthesia for dental procedures by infiltration or nerve block in adults and pediatric patients.

Contraindications

Mepivacaine hydrochloride injection, USP, 3% is contraindicated in patients with a known hypersensitivity to amide type local anesthetics. Mepivacaine hydrochloride does not ordinarily produce irritation or tissue damage.

Adverse reactions

Systemic adverse reactions involving the central nervous system and the cardiovascular system usually result from high plasma levels due to excessive dosage, rapid absorption, or inadvertent intravascular injection. A small number of reactions may result from hypersensitivity, idiosyncrasy or diminished tolerance to normal dosage on the part of the patient. Reactions involving the central nervous system are characterized by excitation and/or depression. Nervousness, dizziness, blurred vision, or tremors may occur followed by drowsiness, convulsions, unconsciousness, and possible respiratory arrest. Since excitement may be transient or absent, the first manifestations may be drowsiness merging into unconsciousness and respiratory arrest.

DISCUSSION

Bupivacaine is a long acting local anesthetic that is becoming extensively used in clinical practice. The potency to toxicity ratio (anesthetic index) is favorable when compared to other currently used local anesthetics.

In oral surgery, this drug provides excellent surgical anesthesia and extended post-operative analgesia. Bupivacaine is ideally suited for use in providing relief of severe dental pain when definitive treatment is to be postponed. Additionally, periodontal surgery as well as prolong dental restorative procedures would benefit from bupivacaine anesthesia. The possibilities for self-mutilation must always be considered when contemplating the use of a long acting perioral local anesthetic. The excellent results with bupivacaine underscore its clinical efficacy and motivate continued use and evaluation in oral surgery.

Mepivacaine has a number of potential advantages over lidocaine including: (i) intrinsic vasoconstrictor effects, thereby reducing the rate at which drug is cleared away from peripheral (skin) sites of pain generation and (ii) the lowest potential for neurotoxic effects on developing or regenerating primary cultured neurons with lidocaine having the highest neurotoxic potential in this model.

Previously it was proven that Bupivacaine and mepivacaine are effective anesthetic agents. They can be incorporated in high viscosity hydro miscible vehicle such as hydrophilic gels which are useful for controlled and site specific anesthetic drug delivery. In recent year's poloxamers a class of polymer has attracted particular interest in the design of dermal transdermal, oral, mucosal delivery system with a view to promoting, improving site specific drug delivery through the skin.

CONCLUSION

Local anesthesia forms the backbone of pain control techniques in dentistry, and local anesthetics are the safest and most effective drugs in all of medicine for the prevention and management of pain.

Local anaesthetic are widely used to manage acute, chronic, and cancer pain, for anaesthesia, and for diagnostic purposes. Local anaesthetics may have similar chemical structures, but differing pharmacokinetic properties and spectra of pharmacodynamic effects. This influences the selection of agents for use in various clinical situations. New innovations pertaining to LA formulations lead to prolonged action or to novel delivery approaches. Decades after the introduction of local anaesthetics for analgesia/anaesthesia, new properties may still be discovered. New applications of this class of drugs may still be anticipated. The development of new effective delivery systems should suitably modulate the release rate of these drugs, extend their anaesthetic effect, and enhance their localisation; this should reduce problems of systemic toxicity.

The development of safe and effective local anesthetic agents has possibly been the most important advancement in dental science to occur in the last century. The agents currently available in dentistry are extremely safe and fulfill most of the characteristics of an ideal local anesthetic. These local anesthetic agents can be administered with minimal tissue irritation and with little likelihood of inducing allergic reactions. A variety of agents are available that provide rapid onset and adequate duration of surgical anesthesia. This article provides a brief update of the clinical pharmacology of bupivacaine and mepivacaine as local anesthetic agents in dentistry at present.

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