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Recent Advances In Local Anesthesia: A Review

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Abstract

Achieving painless treatment is a breakthrough in the field of dentistry. This article reviews the newly introduced local anesthetic solutions in today's clinical dental practice over the past few decades such as levobupivacaine, ropivacaine, and articaine. Local anesthetics remain the safest and most effective in recent dental practice. It is imperative on our part to be updated with the knowledge and skills of newer pain controlling alternatives.

Keywords: Local Anesthetic Drugs, Lignocaine, Articaine, Phentolamine, Complications

Introduction

Local anesthesia clinically suggested to be used in order to achieve anesthesia and analgesia, which last probably for few minutes to few hours.[1] It was originated merely a century ago, when cocaine was extracted from coca leaves. After about forty-five years, a synthetic local anesthetic was prepared named as procaine.[2] Its use has completely changed the dreadful experience of the patient to a pleasant experience, making it a mandatory part of dentistry these days. As the history speaks, there are two discoveries to be mentioned, which played a significant role in the development of LA over the course of time, i.e.

- Braun's Discovery (includes addition of adrenaline in local anesthesia)
- Einhorn's Discovery (of Novacaine) [3,4]

As a matter of fact Lignocaine Hydrochloride has higher efficacy, low allergenicity with low toxicity, it I the Gold Standard and widely used regional anesthetic in the widest range of LA drugs.[5]

Year	Individual/Company	Events
1859	Niemann	Isolation of cocaine
1884	Koller	Cocaine topical anesthesia
1884	Halstead	Cocaine regional anesthesia
1885	Corning	Tourniquet to retard absorption
1903	Braun	Epinephrine as a chemical tourniquet
1904	Einhorn	Synthesis of procaine
1905	Braun	Clinical use of procaine
1920	Cook Laboratories	Anesthetic syringe and cartridge
1943	Lofgren	Synthesis of lidocaine
1947	Novocol	Dental aspirating syringe
1948	Astra	Lidocaine for dentistry
1959	Cook-Waite	Sterile disposable needle

Table 1: History Of Local Anesthetics [6]

Mechanism Of Action Of Regional Anesthesia

Local anesthetics acts by directly blocking pain transmission through the nociceptive afferents (pain receptors), mainly by inhibiting the sodium channels. They block the influx of Na^+ ions at the sodium ionophore during the depolarization phase. Furthermore, LA blocks Ca^+ and K^+ channels,[7,8] transient receptor potential vanniloid-1 receptors,[9] other ligand gated receptors.[10] LA disrupts the coupling between specific G proteins and their associated receptors, thus exerting anti-inflammatory effects on the neutrophils.[10,11]

Articaine

This widely accepted and newer local anesthetic first came into use clinically in 1976 in Europe and in 2000 in United States.[12] It consists of thiophene ring and falls under the amide group of local anesthetic agents, causing faster onset of action and longer duration of action by increasing the lipid solubility and protein binding capacity.[3,13,14,15] Articaine is eliminated exponentially with a half-life of 20 minutes an metabolism mostly in liver and plasma by unspecified eterases.[16]

The maximum recommended dose of articaine by FDA 4% with 1:1,00,000 epinephrine is half the number of cartridges than 2% lignocaine with 1:1,00,000 epinephrine (articaine- 72mg/cartridge, lignocaine- 36mg/cartridge). [13]

Advantages: [5,13,14,16,17,18]

- Onset of action is fast
- Duration of action is longer
- Success rate is higher
- 1.5 times more potency
- Systemic toxicity is low
- Safer drug
- Lipid solubility is lower
- Plasma protein binding rate is high
- Lower blood levels

Disadvantages: [14,16,19]

- Paresthesia associated to lingual nerve
- More neurotoxic

- May cause neuropathie or methemoglobinemia
- Ocular complications due to increased diffusion of drug through tissues (including bone)

Bupivacaine

Bupivacaine and mepivacaine are chemically similar in nature, yet the former is more potent as it is more lipid soluble than mepivacaine. Although, it is considered as more cardiotoxic than most other local anesthetic drug, due to the effect of dextrorotatory enantiomer on the cardiac tissues. It is rendered unsuitable for the maxillary infiltration due to slower onset time and slower diffusion by sequestration in mucosal tissues. It is available in cartridges of 0.5% solution with 1:2,00,000 epinephrine. Bupivacaine can cause a long-lasting anesthesia (8 hours).[6]

Centbucridine

It was the first local anesthetic synthesized in 1983 at the Centre for Drug Research of India, Lucknow.[20] It is a quinolone derivative and has vasoconstricting and anti-histaminic properties, with longer duration of action and an anesthetic potency (4-5 times) more than 2% lignocaine, useful for infiltration, nerve blocks and spinal anesthesia in concentration of 0.5%.[21,22]

It has been used successfully in the field of ophthalmology and other medical related specialties, though, the dental surgeons had encountered failure to authorize its use for pain management. Besides, it has only one study clamming for its use, which necessitates many more clinical trials.[23]

The addition of adjunctive agents (adrenaline, opioids, clonidine) in epidural anesthesia may increase the duration, enhancing the quality and decreasing the risk of toxicity. Classically, the dose of levobupivacaine for spinal anaesthesia is 15 mg. In ambulatory surgery, small doses have been used (5-10 mg) with a rapid recovery rate. Recent trends suggests a potency hierarchy of bupivacaine > levobupivacaine > ropivacaine for epidurals in labour.[23]

Phentolamine

It is referred as anesthetic reversal drug (indicated to reverse the effect of local anesthesia). Phentolamine Mesylate is a non-selective alpha adrenergic blocking agent used for reversal of the anesthesia of soft tissue (lip/tongue region) and the effect of epinephrine/ nor-epinephrine on alpha one and alpha two adrenergic receptors, later causing vasodilatation resulting LA away from the injection site. The peak concentration is achieved after 20 minutes with the elimination half-life of 2-3 hours. Various adverse effects may include diarrhea, facial swelling, hypertension, jaw pain, oral pain, reaction at the injection site, tenderness and vomiting, many of them may be resolved in 48 hours. It is advised to be cautious for cardiovascular diseases/strokes.[1]

It is available in the form of cartridges of 0.4mg/1.7ml. The recommended dose is based on the number of cartridges of local anesthetic with vasoconstrictor administered.[1]

Indicated in patients above 6 years of age at the exact same site of previous injection. In pediatric patients (15-30kg) the maximum recommended dose is 0.2mg (half cartridge).[1]

Levobupivacaine

It is a pure S (-) enantiomer of bupivacaine, safer substitute for regional anesthesia than it's racemic parent. It comprises various properties such as less affinity, depressant effects on myocardial and central nervous system with a superior pharmacokinetic profile. Various clinical trials showed adverse effects similar to bupivacaine such as hypertension, nausea, postoperative pain, fever, vomiting, pruritus, back pain, headache, constipation, dizziness, foetal distress.[24]

It is seen that the dose of epidural levobupivacaine reaches 15mg/hour to achieve an effective postoperative analgesia.[23]

Ropivacaine

Ropivacaine is a long-acting enantiomerically pure (S-enantiomer) amide with the efficacy equivalent to that of bupivacaine. Additionally, due to its reduced central nervous system and cardiotoxic potential with lower propensity for motor block, it is indicative as an alternative for regional anesthesia. It displays less cardiotoxic properties than bupivacaine, although more than lignocaine with higher threshold for CNS toxicity as compared to bupivacaine. Epidural ropivacaine 0.2% is seen to be effective for the potential labour analgesia, acting as a pain relief after abdominal or othopaedic surgery when used in conjunction with opioids. However, the adverse effect profile is seen indistinguishable to that of bupivacaine.[24]

Structurally Different Newer Local Anasthetic Solutions

Efficacious groups of local anesthetics are available as an alternative (basic esters of phenylcarbamic acid). The basic esters of alkoxy-substituted phenylcarbamic acid possess higher LA potency and lower toxicity profile. Phenylcarbamic anesthetic bypass most other clinically used LA (100-300 times). The effectiveness of phenylcarbamic acid is inversely proportional to the pH of the external medium, which is significant while using LA in inflamed tissues.[25]

Furthermore, Butyl amino-benzoate an amino ester was discovered in 1923. Initially, it was thought to be unsuitable due to its extremely low pKa, low water solubility, poor dural permeability, rapid hydrolysis. However, following decades, after the manufacture of suspension preparations in polyethylene glycol and polysorbate-80, which were found to be long-lasting given epidurally to cancer patients as a substitute to alcohol or phenol neurolysis. During recent times it has also been successfully used in cancer as well as non-cancer patients for pain.[26]

Drug	Preparation
Lidocaine 2%	1:50,000 (epinephrine) 1:1,00,000 (epinephrine)
Mepivacaine 3%	Plain (no vasoconstrictor)
Mepivacaine 2%	1:20,000 (levonordefrin)
Prilocaine 4%	Plain 1:2,00,000 (epinephine)
Articaine 4%	1:1,00,000 (epinephrine) 1:2,00,000 (epinephrine)
Bupivacaine 0.5%	1:2,00,000 (epinephrine)

Table 2: Availability of Local Anesthetic In Cartridges [6]

Adverse Effects of Local Anesthetic Solution [1]

1. Tachycardia
2. Separation of the needle
3. Aspiration or ingestion of foreign body.
4. Pain, swelling caused due to overheating of bone and macerating of overlying soft tissue
5. Post-injection hyper-occlusion, pain, chewing soreness.
6. Dentinal tooth damage and osteonecrosis (which is rare)

Conclusion

Local Anesthesia being the foundation of painless treatment modality in dentistry, being the safest drug with efficiency to relieve intraoperative and postoperative pain. Hindrance in the path of pain free treatment is created by incomprehension in the advancements of these drugs in today's scenarios. The hunt for alternatives have bought up new areas of clinical research, enhancing todays dentistry.

Declaration of Patient Concent

The authors certify that they have obtained all the appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their/images and other clinical information to be reported in the journal. The patient(s) understand that their name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be granted.

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