



Effect of high concentration lidocaine for mandibular teeth anesthesia: Review literature

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Abstract

Inferior alveolar nerve block (IANB) is the most regularly used technique to anesthetize the mandibular teeth. Many authors have reported IAN block does not always result in completely success of pulpal anesthesia for the duration of the operation. The failure rates of pulpal anesthesia were reported from 10% to 39%. Many researches were manipulated several of ways to enhance the efficacy of local anesthetic use in dentistry. Many articles prove that high pH of local anesthetic enhances ionization property and provides sufficiency onset of local anesthetic. Furthermore, increasing concentration of lidocaine results in superior success rate compare to 2% lidocaine. To make a clear impression in effect of high concentration of lidocaine in mandibular anesthesia the further investigation should be encouraged. This review is to conclude ideas of related papers which studied in effect of increase concentration of lidocaine local anesthetic with vasoconstrictor in intraoral anesthesia.

Keywords: Efficacy, concentration, inferior alveolar nerve block, lidocaine hydrochloride, mandibular teeth, hemodynamic change

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Introduction

Local anaesthetic is used routinely in dental practise. It has been used in several of dental treatments to achieve painless operation¹⁻³. Those procedures such as: oral surgery, endodontic, periodontal invasive treatment and so on. However, even the right technique for nerve block has been provided, the anaesthesia effect is still not reaching a cheerful result and additional anaesthetic is recommended³⁻⁶. Moreover, inferior alveolar nerve block (IANB) is the most regularly used technique to anesthetize the mandibular teeth. Many authors have reported IAN block does not always result in completely success of pulpal anesthesia for the duration of the operation⁷⁻¹¹. The failure rates of pulpal anesthesia were reported from 10% to 39%⁶. Therefore, researchers have tried to manipulate a range of variables to improve the effectiveness of local anesthetic used an IAN block in a number of ways¹⁰⁻¹⁵. They have compared different volumes¹⁵⁻¹⁸, modified the concentration^{13, 19-23}, and buffered agent in the local anesthetic cartridge^{11, 22}. Those papers commonly reported on the onset of anesthesia, duration of anesthesia and success rate of pulpal anesthesia based on different methods^{6, 7, 11, 15, 16, 24-26}.

Objective of this review is to conclude ideas of related papers which studied in effect of increase concentration of lidocaine local anesthetic with vasoconstrictor in intra oral anesthesia.

Lidocaine with vasoconstrictor in local anesthetic

Lidocaine is known as Amino-Amide type which was formulated by Swedish chemist Nils Löfgren and Lundqvist in 1943²⁷. It is a tolerant local anesthetic, low toxicity and has been used in various groups of patient in practical dentistry²⁸⁻³¹. The pharmacodynamic of lidocaine local anesthetic is similar to other local

anesthetic agents, which deposit their action by inhabiting action potential of nerve. It is temporary blocking transmembrane of sodium ions into axon cell. Therefore, the action potential is transitory impeded then consequence of an electrical impulse cannot be transmitted from the stimulus part to the brain^{27, 30, 32, 33}.

Local anesthetic contained epinephrine is the most commercial preparation³⁴⁻³⁸. Common formula of epinephrine contained in local anesthetic are 1:50,000, 1:100,000, or 1:200,000³⁹. In reality, Epinephrine has been added to local anesthetic to prolong the duration of anesthesia and decrease rate of perfusion into the vascular system. High rate of perfusion into the vascular system may result in high plasma level of local anesthetic lead to have a consequent of systemic toxicity³⁶. Additionally, another advantage of epinephrine is providing a vasoconstriction activity, then it provides hemostasis at the operation site³⁰. The wildly used of epinephrine in dental practice seems to be safe^{36, 40}. However, the limited dose should be considered in patient with cardiovascular problem, ischemic heart disease, and patient who is taking some kind of drugs such as tricyclic antidepressants, nonselective β -blockers, cocaine and the general anesthetic (halothane, fluothane). These certain drugs may interact with epinephrine³⁹. In these situations, the dose of epinephrine is recommended to keep below 0.04 mg³⁹. It is approximately maximum 2 cartridges volume of epinephrine 1: 100,000 (2 cartridges \times 0.018 mg = 0.036 mg).

Factor correlated to the latency time of local anesthetic

On the injection side, Local anesthetic is converted to quaternary salt (BH⁺) and Tertiary base (B) by the action of pKa and the pH of physiological tissue. Once lipid soluble base (B) penetrated into the axoplasm, the amide

catches hydrogen ions and then become a quaternary form (BH⁺) that is important for the blockade of sodium channel^{11, 33} Figure (1). The proportion of drug administration that is converted to the tertiary base (B)/unionized lipid-soluble form is one of core factors enhancing onset of local anesthetic^{11, 33}.

To get rich of ionization property many studies have been manipulated in difference type of study's methodologies. For example the pH adjusting local anesthetic, they found that anesthetic formula with high pH has faster onset^{11, 41-43}. The pH value of dental local anesthetic ranged from 3.2 to 5.5 because of addition of epinephrine and preservation drug. Base on Henderson-Hasselbalch equation the ionization proportion is clearly related to the pH and pKa of local anesthetic.

Log (cationic form/uncharged form)= pKa-pH
 pKa of lidocaine= 7.8. So a simple way to understand the formula:

Example 1: Lidocaine pH= 5

⇒ Log(Ionize/Unionize)= 7.8 - 5

⇒ Log(Ionize/Unionize)= 2.8

⇒ Antilog. log(Ionize/Unionize)= Antilog

2.8

⇒ 1(Ionize/Unionize)= 630.95

⇒ (Ionize/Unionize)= 630.95

⇒ Ratio of Ionize 630 have 1 Unionize (630/1)

Example 2: Lidocaine pH= 6.04

⇒ Log(Ionize/Unionize)= 7.8 - 6.04

⇒ Log(Ionize/Unionize)= 1.76

⇒ Antilog. log(Ionize/Unionize)= Antilog 1.76

⇒ 1(Ionize/Unionize)= 57.54

⇒ (Ionize/Unionize)= 57.54

⇒ Ratio of Ionize 57 have 1 Unionize (57/1)

Therefore, high pH of local anesthetic enhances ionization property and provides sufficiency onset of local anesthesia. Furthermore, Whitcomb M et al (2010)¹¹ found that high pH adjustment local anesthetic to pH values 7.5 of lidocaine formula didn't have any negative effect.

Factor correlated to the profoundness and duration of action of local anesthetic

Lidocaine is considered as intermediate acting local anesthetic because of the moderate protein binding (64%)²⁷ if compared to long acting local anesthetic such as Bupivacaine (95%) and Levobupivaine (96%)²⁷. The greater protein binding, the longer potency of local anesthetic blocking the neuroplasm, but there are another factors have a correlation

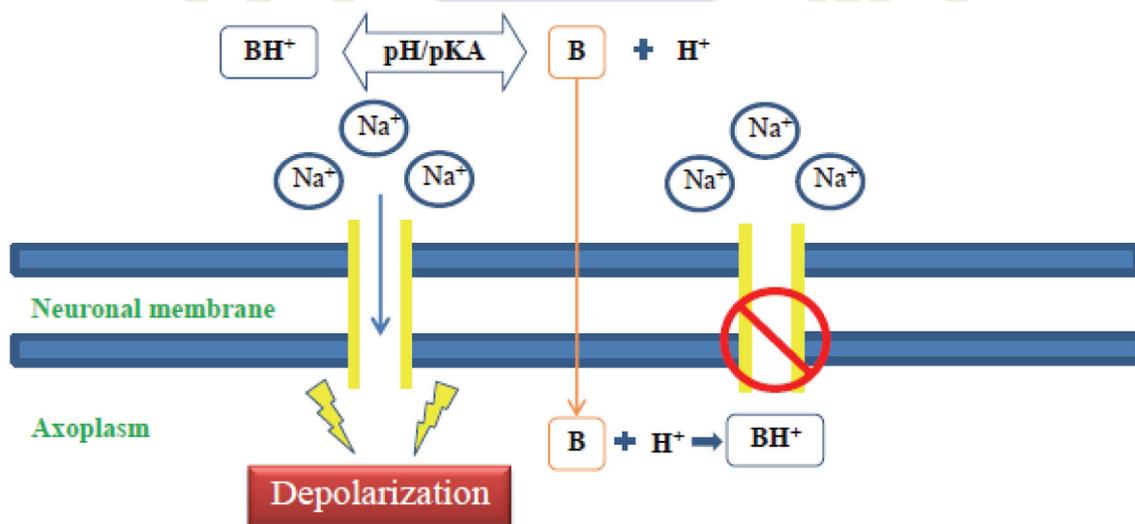


Figure 1 Local anesthetic action.

effect on duration of anesthesia as well. Such as, dose of administration, vascularity at the site of injection and addition of vasoconstrictor^{8, 27}.

There are studies in volume or concentration of lidocaine effect the efficacy of local anesthetic^{13, 15-23}. Rood JP et al (1976)¹⁹ demonstrated a study in patients participate in routine dental treatment by comparing repeated of IAN block after failure of initial block by 2% lidocaine with epinephrine 1: 80,000. The study evaluated in 5% lidocaine with epinephrine 1:8,000 for an experiment group and 2% lidocaine with epinephrine 1: 80,000 for a control group. The result was higher success rate in 5% lidocaine (95%) than 2% lidocaine (6%). Then, the studies about the efficacy of 5% lidocaine have started to be challenge. Many studies were done, all have been concluded that increasing concentration to 50mg/ml of lidocaine will be more effective, while not causing any systemic toxicity or delaying the healing process if within a safe dosages administration^{13, 20, 21}. Later, a study of Vreeland DL et al (1989)²³ evaluated the effect of volumes and concentrations of lidocaine in inferior alveolar nerve block. The study prove that increasing in volume of lidocaine to 3.6ml or increasing concentration of lidocaine to 40mg/ml didn't show any different in success rate of IAN block. These controversial ideas should be disentangled by further investigation in high concentration of lidocaine compare to the normal dose.

Moreover, other investigation by Smith S et al (2013)²² evaluated the effect of adding

1.82ml of 0.5 M mannitol to 4% lidocaine local anesthetic with 50µg epinephrine in asymptomatic teeth, the result showed that lidocaine solution with 0.5 M mannitol provide a significant greater effect of pulpal anesthesia than the lidocaine without mannitol.

Base on Backer DE et al (2012)⁸, Haas DA (2002)³⁹, and Thomas PD et al(1973)²⁹ showed duration of action of lidocaine local anesthetic in table 1.

Hemodynamics

The use of excessive dose of lidocaine with epinephrine prone to have high blood levels that may rises in cardiac output (CO) total peripheral resistance (PR) and mean arterial pressure (MAP). These effects maybe because of epinephrine in the local anesthetic acts direct depressant in cardiovascular system and the beta-adrenergic receptors. There is a report significant increase systolic blood pressure (5-12 mmHg) in patient underwent scaling and root planning using lidocaine with 1: 100,000 epinephrine⁴⁴. Dionne et al (1984)⁴⁵ reported that 5.4ml of 2% lidocaine with 1: 100,000 epinephrine increased in heart rate 19% of cases and cardiac output as much as 30%. The use of high dose of local anesthetic 18ml contained 1:100,000 epinephrine reported excessive energy used, that is not appropriate for medical compromise patients⁴⁶. However, de Morais HH (2012)⁴⁷ administrated 2.7ml of local anesthetic with epinephrine 1:100,000 or 1:200,000 in surgical removal impacted third molar. The study showed absence of

Table 1 Duration of action of lidocaine with/without epinephrine in inferior alveolar nerve block

Formulation	Duration of anesthesia	
	Pulpal	Soft tissue
2% lidocaine (plain)	-	2h
2% lidocaine with epinephrine 1:100,000 or 1:50,000	80-90min	3-5h

hemodynamic change comparable to previous study by Santos et al (2007)⁴⁸. All in all, dose limitation of using local anesthetic contained epinephrine must be considered in special patients such as: cardiovascular problem, ischemic heart disease, and patient who is taking some kind of drugs included nonselective β - blockers, tricyclic antidepressants, cocaine and the general anesthetic (halothane, fluothane) that these certain drugs may interact with epinephrine³⁹

Pharmacokinetic and metabolism

Lidocaine completely absorbs following parenteral administration via tissue perfusion and vascular absorption into the system circulation. Absorption rate depends on many factors such as the vascularity at site of injection and the presence or absence of a vasoconstrictor agent in the local anesthetic.

The first step of biotransformation of lidocaine involves hydroxylation, N-dealkylation and methylation, followed by second step where the metabolites are conjugated with amino acids into degradation stage of its action and deactivation stage. Dealkylation reaction happens while the ethyl group is cut from the tertiary amine. However, this metabolism of

Amidno-amide type local anesthetic occurred by enzyme degradation call microsomal enzymes (CYP450), which occurs in the liver.²⁷ Therefore, clearance of amide local anesthetic is significantly depends on hepatic perfusion, hepatic extraction, hepatic enzymatic function, and plasma protein binding³³. Half-life of lidocaine is approximately 90 min for normal liver function but it is slower in hepatic insufficiency. Additionally, it proves that biotransformation appears to be slightly slower in the newborn than in the adult.³³ Moreover, metabolite of the amino-amides group occurs by renal excretion, the uncharged drug least than 5% was excreted into urine. Overall, local anesthetics with superior level of clearance are greater considered safety³³.

In 1986, Tucker GT (1986)⁴⁹ had reported the pharmacokinetic parameters of local anesthetic in adult as showed in Table 2.

Indication of use

Lidocaine hydrochloride with epinephrine is used as local anesthetic for dental procedure by infiltration or injection for the nerve block. It has disposed in various groups of patient as show in table (3) base on the report of Thomson PD, et al²⁹

Table 2 Pharmacokinetic of lidocaine use in adults patients

Local Anesthesia	Elimination Half-Life (T ½) (min)	Volume Distribution (Vd) (Liters)	Clearance (Cl) (L/min)	Hepatic Extraction
Lidocaine	96	91	1.0	0.7

Table 3 Lidocaine use in various group of patients

Group	Haft-life (min)	Mean total body clearance (ml/kg/min)
Normal	108	10
Heart failure	114	6.3
Hepatic disease	294	6
Renal disease	78	13.7

Contraindication

Lidocaine is considered as safe drug but within high number of injections given yearly adverse reaction is seen. It is contraindication for the subjects who are allergic to Amide type local anesthetic.

Doses of administration

The dosage of lidocaine hydrochloride with epinephrine depends on clinical status of the patients, the area of anesthetize in the oral cavity, and the application technique. Lesser dose of solution that adequate for treatment should be recommended.

Additionally, Practitioners should apply an effective injection technique to avoid unnecessary excessive doses administration which tends to overdoses occurs. The maximum recommended doses of local anesthetic shows in Table 4^{8, 39}.

Precaution

Lidocaine is usually well tolerated. Nevertheless, toxic effects of local anesthetics may occur due to hypersensitivity, faulty technique, over dosage and accidental intravascular injection.

Lidocaine should be used with caution in patient with severe shock or heart block, impairment cardiovascular function or cardiovascular diseases because exaggerates of vasoconstrictor response may result ischemic injury or necrosis.⁵⁰

By the way, patient with hepatic disease should be caution in using this drug as well. Because patient with severe hepatic impairment

has lacked of ability to metabolize lidocaine in a normal clearance rate, that is hazardous to toxic plasma level⁵⁰. Resuscitate equipment such as, oxygen and resuscitated drug should be available for the emergency situation.

Discussion

Lidocaine have been wildly used in medical and dental fields. 2% lidcaine with epinephrine is the most favorable used in dentistry that provides intermediate acting local anesthesia due to its moderate protein binding approximate 64%. Beside of 2% formula in dental cartridge another solution of 3% Lidocaine with norepinephrine (32.01mg+ 0.08mg) have been commercially manifested by Septodont in French⁵¹.

To enhance successful of pulpal anesthesia in mandibular teeth, high concentration of lidocaine should be considered for using in IAN block as many studies have been stated higher success rate compared to 2% lidocaine with epinephrine. This prediction is based on researches that have been carried out in the medical and dental fields as the following.

Raj’s textbook of Practical Management of Pain Fourth Edition (2008)³³ wrote that lidocaine has been used intravenously during the operative and post-operative period. Intravenous lidocaine provides an improvement in analgesic and anti-inflammatory properties³³. A recent study showed that it not only decreased pain intra-operation and post-operation, but also enhanced healing after surgery, reduced time in hospital and improved

Table 4 Maximum recommended doses

Formulation	Maximum dose Mg/kg (Total)	Maximum no. of cartridges
2% Lidocaine (plain)	4.5mg (300mg)	
2% Lidocaine with epinephrine 1:100,000 or 1:50,000	7mg (500mg)	13

the quality of life for the patients. The authors reported that during studies the infusion intravenously of low dose of lidocaine at 1 to 2 mg/kg/hr while monitoring plasma levels there were no clinical signs of systemic toxicity⁵².

Another experiment in dentistry by Rood and Sowray (1980) demonstrated that 5% lidocaine improved analgesia whereas 2% lidocaine was poor in its effectiveness. This clinical experience of 5% lidocaine with 1:80,000 epinephrine has confirmed its clinical safety for the adult patient in a study group of over 200 healthy patients¹³.

Sandy and Rood (1980) used 5% lidocaine in a group of 115 patients aged between 6 and 15 years for varieties of clinical dental procedures including: surgical procedures, pulpectomy, pulpotomy, replacement of root filling, and restorative procedures using either the IAN block or infiltration technique. They found that 100 patients who had conservative restorations placed, 90 were in permanent teeth with clinical evidence of inflammatory lesions. The teeth with acute pulpal inflammation were often painful to treat despite the use of 5% lidocaine solution. This study showed that using a 1.8ml volume of 5% lidocaine solution, analgesia was achieved in the children without any clinical adverse effects²⁰. They concluded that if the concentration of lidocaine in local anesthetic is increased to 50mg/ml it will be more effective, while not causing any systemic toxicities (if within safe dosages) or delaying the healing process. However, Vreeland DL et al (1989)²³ proved that increasing in volume of lidocaine to 3.6ml or increasing concentration of lidocaine to 40mg/ml didn't show any differences in success rate of IAN block. The used to high concentration of lidocaine have been reported by some authors in laboratory work that may product neurotoxicity⁵³. Contraversally, there is no reported of neurotoxicity in human⁵⁴. Moreover,

lidocaine has been used intravenously as an antiarrhythmic drug or to control postoperative pain³³. Minimum dose of intravenous injection of 1-2mg/kg/h while monitoring plasma level showed no clinical signs of systemic toxicity⁵². These showed a remarkable safe of lidocaine while accidentally intravenous injection in nerve block administrated. However, as all drug remained toxicity if careless procedure is manipulated. Therefore, the fulfilled knowledge of using local anesthetic is considered morally need.

Based on our knowledge there were a few studies related to high concentration of lidocaine used in IAN block. To make a clear impression in effect of high concentration of lidocaine in mandibular anesthesia the further investigation should be encouraged.

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