Comparison of Alkalinised and Non-alkalinised Lignocaine on Pain and onset of Anesthesia during Intra-oral Injection

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ABSTRACT

Introduction: The acidic nature of commercial local anaesthetics (LAs) can cause pain during injection and delay the onset of anaesthesia. It is suggested that adjusting the pH of anaestheticagent could minimize these effects. The aim of the study is to assess the efficacy of alkalinised lignocaine on pain and onset of anesthesiaduring intraoralnerve block injection.

Materials and Methods: An experimental comparative study was carried out in patients requiring extraction visiting the department of Oral and Maxillofacial Surgery at Kantipur Dental college and hospital. Patients will be randomly divided into two groups of 40 each usingsimple random sampling technique. All patients will be given standard nerve blocks: inferior alveolar, lingual, and long buccal. The study was designed to assess the effect of alkalinisation of the lignocaine solution with sodium bicarbonate. One group of patients were given 2% lignocaine hydrochloride with adrenaline 1:80,000 and the another group of patients were randomly allocated to be given 8.4% sodium bicarbonate in a 1/10 dilution. Pain was measured on a Visual Analogue Scale (VAS).

Result: 26 Patients given the injection with sodium bicarbonate complained of no pain, 12 patients complained of mild pain and 1 patient with moderate pain compared with 34 patients complained with moderate pain and 6 patients with severe pain who were not given sodium bicarbonate ($p < 0.0001$). The mean (SD) time (seconds) to onset of local anaesthesia in the group given sodium bicarbonate was 1.39 compared with 3.33 in the control group ($p < 0.001$).

Conclusion: Our results have confirmed the efficacy of the alkalinised local anaesthetic solution in reducing pain on injection and resulting in quicker onset of anaesthesia.

Keywords: Alkalinisation; Lidocaine; Onset of anaesthesia; Pain; Sodium bicarbonate.

INTRODUCTION

Local anesthetics (LAs) form is the backbone of pain control techniques andmost utilized drugs in dentistry.A Canadian study suggests that the average annual usage per individual dentist is about 1,800 cartridges of dental anesthetic, or nine cartridges per day for a dentist who practices 200 days per year.[1] The injection of local anesthetic agents into the skin and mucous membrane is one of the most common minor surgical maneuvers. Although it is short-lived, the perceived pain of the injection of local anaesthetic is terrible or intolerable for some patients to decline further interventions under local anesthesia. To give additionalanalgesicsor sedatives orboth, can be impractical, time consuming and at times contraindicated too.[2]The presence of acidity in the solution is thought to be important reasons for pain at the site of injection.Dentist's primary tool for pain management islocal anesthetic but acidity presence may contribute to lengthy anesthetic waiting periods and also cause the "bee sting effect" or burning and stinging during the injection.[3] Many dentists are surprised to know that the most widely used dental anesthetic solutions are formulated at the potential of hydrogen(pH) of lemon juice.[4]

Lidocaine is a local anesthetic of amide class that is available in a variety of concentrations. It is often combined with varying concentrations of epinephrine to prolong its actions and improve hemostasis.[5] Lidocaine is manufactured at pH of 5.0-7.0 which makes more soluble and stable and extends its shelf life to three to four years.[6] The pH of commercially available local anesthetics (LAs) is purposefully low (pH 3–4). Decrease in pH extends the shelf life of solution and prevents its early oxidation.[3] However, a low pH may produce a burning sensation on the injection site,slower onset of anesthesia anddecrease in its clinical efficacy.[2] Buffering of local anesthetics (alkalinization) by adding sodium bicarbonate has been suggested to achieve

better pain control, reduce pain on site of injection and produce faster onset of local anesthetics. The study aims to assess the efficacy of alkalinised lignocaine on pain and onset of anesthesiaduring intraoralnerve block injection.

MATERIALS AND METHODS

An experimental comparative study was conducted after the approval by the Institutional ReviewCommittee of Kantipur Dental College. A total 80 healthy adult patients aged 18–55 years with written consent participated in the study. The patients who have to undergoextraction under local anaesthesia in the mandibular region presented to theDepartment of Oral and Maxillofacial Surgery at Kantipur Dental College and Hospital were included. Patient's age, sex and medical history of significant relevance were recorded andtreatment plan were explained. The inclusion criteria consisted of patients with American society of Anaesthesiology 1(ASA 1).Patients with known history of lignocaine allergy andany pre-existing systemic disease or condition were excluded from the study.

All the patients were given standard nerve blocks: inferior alveolar, lingual, and long buccal nerve.Patientswere divided into two groups, study and control; 40 in each group. Slips of paper containing numbers 1 to 80 were placed in one container. Each patient was asked to pick a slip and patient withodd numbers were allotted to control group and even numbers to study group. For control group; lignocaine hydrochloride with adrenaline 1:80,000 solution by injection was given. For study group; lignocaine hydrochloride with adrenaline 1:80,000 and sodium bicarbonate was added to the solution. A total of 8.4% sodium bicarbonate 3 ml was added to a 30 ml vial containing 2% lignocaine hydrochloride with 1:80,000 adrenaline solution, which yielded a 1/10 dilution.[7]

The procedures wereexplained to all thepatients. Both the operators and patients were unaware of which anaesthetic solution was administered to the patient. Anaesthetic solution were prepared and administered to the patient depending on the odd or evennumber picked by the patient (study and control group).The pain score was evaluated during injection and onset of anaesthesia in both the group. All injections in both groups were given using non-pyrogenic, non-toxic, sterile, single-use syringes with a luer lock and 25G (1.5 inch) needle. A maximum of 2.5 ml solution was used for all three blocks.

Pain score during injection was assessed using 4 point scale: 0 = no pain, 1 = mild pain (pain reported only in response to questioning and without any behavioural signs), 2 = moderate pain (pain reported in response to questioning and accompanied by signs, or pain reported spontaneously without questioning) and 3 = severe pain (strong vocal response or response accompanied by grimaces, withdrawal of the arm, or tears).[2] Pain during injection was defined as pain that was described by the patient on a four-point Visual Analogue Scale (VAS) during injection of the solution and not on the needle-prick.

The time of onset of anaesthesia is defined as the first sensation of numbness or tingling in the anaesthetised region. It was calculated from the point of retrieval of the needle after the injection. A straight probe was used to assess the onset of anaesthesia by inserting it in the gingival sulcus of the teeth in the area of anaesthesia. The results were quantified and analysed.

The pH of both solutions were evaluated using a standard pH meter; 3.05 was the measured pH for 2% lignocaine with 1:80,000 adrenaline (Jasocaine – A 2% , Jayson Pharmaceuticals, Bangladesh) and 7.38 for 2% lignocaine with 1:80,000 adrenaline with a 1/10 addition of 8.4% sodium bicarbonate.

Statistical analysis was done by using SPSS version 20. Shapiro- Wilk normality test was done and showed that the samples followed a normal distribution. Data for VAS were analysed using chi square test and time of onset of anaesthesia were analysed using Student's t-test. A probability of less than 0.05 was accepted as significant.

RESULT

A total of 80 patients (33 males and 47 females), between the age 18 – 70 years old participated in the study.Based on gender, the mean time taken for the onset of local anesthesia in male patients was 2.23 minutes, whereas in female was 3.48 minutes, showing no statistically significant (p = 0.284) (Table 1).

Table 1:Distribution of study participants based on onset of Local Anaesthesia between gender

Gender	Mean±SD	p-Value
Male	2.23±1.0	0.284
Female	2.48±1.0	

t-test

Table 2 : Distribution of study population based on VAS score between gender

Gender	No pain	Mild pain	Moderate pain	Severe pain	p-Value
Male	**9(27.3)**	9(27.3)	**13(39.4)**	2(6.0)	0.09
Female	**17(37)**	3(6.5)	**22(47.8)**	4(8.7)	

Chi square

Table 3: Distribution of Study Population Based on VAS Score between groups

Gender	No pain	Mild pain	Moderate pain	Severe pain	p-Value
Case	**26(66.7)**	12(30.8)	**1(2.5)**	0	0.00*
Control	**0**	0	**34(85)**	6(15)	

Chi square

Table 4: Distribution of study participants based on onset of Local Anaesthesia between groups

Group	Mean±SD	p-Value
Case	**1.39±0.3**	0.00*
Control	**3.33±0.2**	

t test

In addition,there was no statistically significant difference between genders regarding pain perception (p = 0.09) (Table 2)

Among the patients who were given solutions without sodium bicarbonate, 34 experienced moderate pain and 6experienced severe pain during injection, from which can be deduced that all patients had pain. There was a significant difference between the control and study group as only 13 patients given local anaesthetic with sodium bicarbonate had mild pain during injection (Table 3). All patients given injections containing sodium bicarbonate had a more rapid onset of anaesthesia than the control group. The time to achieve anaesthesia was greatly reduced when buffered injections were given (Table 4).

DISCUSSION

Pain is defined as an unpleasant emotional experience usually initiated by a noxious stimulus and transmitted over a specialized neural network to the central nervous system where it is interpreted as such.[8] Pain impacts an individual's quality of life. Intraoral local anesthesia is perceived as the most painful and, in some instances, as the only painful part of the treatment leading to in extreme cases, avoidance of dental care.[2] There are several causes for local anesthetic injection pain such as; the speed of injection, pain due to increase in volume in the tissues that causes pressure and one being the acidity of the solution itself.[9] Pain can be avoided by injecting the solution slowly, acidity of the solution can be dealt with altering the pH. For nerves with intact sheaths, local anaesthetics are more potent in alkaline, than in neutral or acid, conditions.[10] This was demonstrated in our study by adding sodium bicarbonate to the solution.

Sodium bicarbonate is a systemic alkalinizing agent. It is a chemical compound made of sodium (Na^+ and bicarbonate ($H_2CO_3^-$). After administration, sodium bicarbonate dissociates to form sodium (Na^+) and bicarbonate ($H_2CO_3^-$). Bicarbonate anions can consume hydrogen ions (H^+) and subsequently convert to carbonic acid (H_2CO_3). Carbonic acid subsequently converts to water (H_2O) and carbondioxide (CO_2) for excretion from lungs.[11] The main therapeutic effect of sodium bicarbonate administration is increasing plasma bicarbonate levels, which are known to buffer excess hydrogen ion concentration, thereby raising solution pH to combat clinical manifestations of acidosis.[12] We used sodium bicarbonate to increase the pH of the local anaesthetic solution to a more physiological pH.

The pH of commercially available dental anesthetic cartridges containing 2% lidocaine with epinephrine 1:100,000 ranges from 2.8644 to 4.16,45 or on average about 3.5, which are adjusted to this pH to prolong shelf life to around 36 months, and prevents the early oxidation of adrenaline, the solution is more likely to produce a burning sensation on injection and a slower onset of anaesthesia.[2,13] In this study, the pH of the control anesthetic was 3.05.

Alkalinizing the local anaesthetic solution with sodium bicarbonate will increase its pH, which increases the speed of onset of its action, making the injection more comfortable and effective. Molecules in the local anesthetic solutions mostly exist in a water-soluble state and are acidic (RNH^+). Conversely, for the anaesthetic to penetrate the nerve

sheath, it must be in its unionized free base form; then, H^+ ion needs to dissociate from the ionized molecule.[14] As the physiological pH is about 7.4, an increase in H^+ in the tissues could cause pain by activating nociceptors such as the acid-sensing ion channels (ASICs).[15] Buffering the local anaesthetic solution could produce less pain because fewer acid-sensing nociceptors would be activated. In addition, it is believed that using alkalinized agents, the body takes less time to change the solution from the ionized to the unionized form, increasing nerve penetration and producing rapid onset of the anaesthetic effect.[15,16]

In our study, we added 8.4% sodium bicarbonate to local anaesthetic solution in a dilution of 1/10 (3 ml of sodium bicarbonate to 30 ml of local anaesthetic solution). This reduced the pH from 3.05 to 7.38, which caused the availability of the lipophilic uncharged lidocaine molecules (RN), also called the base, to be more available for diffusion into the membrane of the nerve as the solution was close to the physiological tissue pH of 7.4. This reduced the pain caused by the injection itself.[2,7]

The efficacy and onset time of anaesthetics could be affected in inflamed tissues, such as in cases of pulpitis and abscess.[13] The Henderson-Hasselbalch equation demonstrates that if a local anaesthetic solution is buffered to a pH closer to its pKa, more of the free base form will be available.[17] Infected tissues have a pH as low as 5.0, which favours the ionized configuration of local anaesthetics and reduces anaesthetic penetration into the nerve.[15]

The increase in the effect of the local anaesthetic block attributes to the ion-trapping, which is also sometimes referred to as "diffusion trapping," or the "cation-trap effect."[13] The ion-trapping theory postulates that CO_2 rapidly penetrates the nerve membrane and enters the axoplasm, where it reacts with water to create carbonic acid. This process acidifies the axoplasm, which makes hydrogen ions (H^+) available to convert into ionized anesthetic the de-ionized anesthetic molecules (made more abundant via alkalinization) that have crossed the membrane and entered the axoplasm.[17] The converted ionized anesthetic molecules are not lipid-soluble; hence, they cannot easily leave the axon once converted and are effectively "trapped" in the axon of the nerve. The trapped ionized form of lidocaine blocks sodium channels from within the axon, eventually resulting in analgesia.[2,15] By acidifying the axoplasm, the free CO_2 created in the alkalinization process may also establish a pH gradient across the nerve membrane, promoting diffusion of the more basic deionized anesthetic molecules across the membrane and into the axon. Alternatively, the acidification process sets up a concentration gradient, causing the more abundant deionized anesthetic outside the nerve sheath to diffuse into the axon.[18]

All patients given local anaesthetic solution without sodium bicarbonate had pain during injection whereas patients whom alkalinized local anesthetic solution was given had obvious benefits in reducing the pain during injection which was confirmed by our results.

The deionized, free-base, or "active" form of the local anesthetic readily penetrates the lipid-rich nerve sheath.[19] Alkalinizing the anesthetic solution before injection immediately increases the active form of the drug. Neutralizing anesthetic solutions would increase their uncharged basic form; thus, the diffusion of the anesthetic solution through interstitial tissues is increased.[2] This would result in a higher concentration of the drug in the nerve axoplasm and a more rapid block of the sensory fibers. As a more rapid block develops, the pain on skin infiltration is believed to be blocked before it has even been sensed.[20] The process of combining sodium bicarbonate with lidocaine HCl creates water, salt, and free carbon dioxide. The free CO_2 in lidocaine solution has an independent anesthetic effect and that CO_2 and local anesthetics have similar effects on peripheral nerves.[21] Sodium bicarbonate ions also non-specifically reduce the margin of safety for nerve conduction, and may have a direct action on the binding of the local anaesthetic to the sodium channel.[2]The only limitation of adding sodium bicarbonate to the local anesthetic solution is the shelf life of the preparation,its only 1 week and should be used within the week.[22] Our study also concluded that the addition of sodium bicarbonate to solutions of lignocaine reduced the duration of onset of anaesthesia.

CONCLUSION

In conclusion, the present study showed, buffered local anesthetics is more effective than non-buffered solutions. Buffering local anesthetics has greater likelihood of achieving faster onset of anesthesia and reducing pain during intra-oral injection. It is simple, inexpensive and can easily be performed by surgeons shortly before local anesthetic injection.

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