Buffering of Local Anaesthesia in Dentistry: A Review

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ABSTRACT

Background: Local anaesthetics (LA) constitutes one of the most important aspects of pain management in dentistry. It is currently being stored and marketed in an acidic form to maximize stability, and water solubility and prolong shelf life. However, acidic local anaesthetic solution has been associated with certain disadvantages including the slow onset of action and, pain during its administration. Buffering of the local anaesthetics has been documented to decrease the pain of injection and, shorten the onset time of the anaesthesia thereby, providing more comfortable and reliable anaesthesia.
Objective: To present a review of local anaesthetic buffering in dentistry
Data Sources: PubMed, Google Scholar, CINAHL and, MEDLINE databases were searched without a date limit. The phrases "local anaesthetic buffering" and Alkalinisation of local anaesthetics" were used to find articles related to local anaesthetic buffering.
Study Selection: A total of 24 publications were included in this review and, buffering agents, mechanisms, methods and, benefits of local anaesthetic buffering were discussed.
Finding: There was a paucity of literature on the effect of buffering on the duration of action of local anaesthetics.
Conclusion: Dental professionals are advised to adopt chair-side buffering of LA to increase patient confidence and acceptance of dental treatment.

Keywords: Buffering, Local anaesthesia, pH, Pain.

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Received: 9-Nov, 2022
Revision: 22 Jan, 2023
Accepted: 29 Jan, 2023

Citation: Mujtaba B, Braimah RO. Buffering of Local Anaesthesia in Dentistry: A Review. Nig J Dent Res 2023; 8(1):14-19. https://dx.doi.org/10.4314/njdr.v8i1.4

INTRODUCTION

Management of pain in dentistry has been achieved with the use of local anaesthetics. Many agents have been used for achieving local anaesthesia in dentistry such as bupivacaine, lignocaine, etidocaine, (more, chronologically). However, lignocaine remains the main choice for most dental practitioners.[1]

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[2] It has a sole purpose of notifying the defense system of the body to react to noxious stimulus in order to minimize tissue damage.[3] The sensation of pain is associated with the activation of receptors in the sensory nerve fibers including the myelinated Aσ-fiber and, unmyelinated C-fibers.[4] The special type of receptors called nociceptors is the specialized sensory nerves capable of detecting a painful stimuli.[5] The intensity, location, and quality of pain will vary depending on the type of stimulus as well as the type of nerve fibers activated in the process. Nociceptors are responsible for initiating signal to the central nervous system, usually in relation to a powerful noxious stimulus.[2] The signal usually comes as an action potential that is conveyed from those pain receptors through various synaptic networks in the spinal cord for processing in the cerebral cortex.[4, 5] Once this signal reaches the cerebral cortex, the sensation of pain is experienced.[4]

Local anaesthetic solutions are currently being stored and marketed in an acidic form, with a pH of between 3.5 to 5.5 in majority of the solutions.[6, 7] This is to maximize stability and water solubility. However, acidic local anaesthetic solution has been associated with pain during its administration. Pain associated with the administration of LA elicits fear and anxiety in some patients and it is one of the reasons why patients avoid early presentation for dental treatment. Buffering of local anaesthetics has been defined as the process of adding a planned amount of basic solution (typically sodium bicarbonate) to the LA solution to raise the pH of the solution before injecting it in to the target tissue.[8] The process entails the use of sodium bicarbonate solution that is incorporated into the LA cartridge just prior to its administration using the available buffering techniques such as the Onpharma and Anutra buffering systems.[9] Buffering of LA solution has been documented to increase its pH, making it closer to physiologic pH (Usually, 7.0 ± 0.23) and, thereby improving some of its properties like lesser pain of injection, lower onset of the LA.[10, 11] Furthermore, buffering of LA makes injection more comfortable and acceptable to the patients, lessens the total operative time, improves patients' confidence on the dentist and lessens patients' anxiety on dental treatment.[8]

The purpose of this article is to present a review of local anaesthetic buffering in dentistry. PubMed, Google scholar, CINAHL and, MEDLINE data bases were searched without date limit. The phrases "local anaesthetic buffering" and Alkalinisation of local anaesthetics" were used to find articles related to local anaesthetic buffering. Only articles specific to sodium bicarbonate buffering of LA in dental practice were used. Articles in languages other than English were omitted. A total of 24 publications were included in this review and, buffering agent, mechanisms, methods and, benefit of local anaesthetic buffering were discussed.

The LA Buffering Agent: Sodium Bicarbonate (*$NaHCO_3$*)

Sodium bicarbonate is the most commonly used buffering agent.[12, 13, 14] It has been used by physicians as a systemic alkalinizing agent in cases of acidosis.[15, 16] When used with local anaesthetics, it was found to buffer LA to a pH that is near physiological value (7.0 ± 0.23).[10] Sodium bicarbonate is available in 10mls vial and 50mls bottle at a concentration of 8.4%. For buffering of LA solution, varying concentrations of the LA solution to sodium bicarbonate has been used with 10:1 being the commonest ratio.[16] Goodchild et al.[17] compared the change in pH of three different concentration of LA and sodium bicarbonate mixtures (9:1, 19:1, and, 18:1) and, found out that, all the three different concentrations raised the pH close to physiologic pH with no statistically significant difference among the solutions. However, care should be taken not to add too much alkali that can cause precipitation of uncharged basic ions in the solution that can be seen as a white clouding of the LA solution. Moreso, sodium bicarbonate buffered LA loose stability within 3 to 7 days.[17] Therefore, for maximal effect, it is advisable to prepare fresh solution each time at the point care.

Mechanisms and Basis of LA Buffering with Sodium Bicarbonate

Local anaesthetic solution exists in equilibrium in two forms[18]:

1. Uncharged, deionized, free based form which is lipid soluble (R): This molecule form

of the LA can cross the lipid barrier of the nerve membrane.

2. Charged, cationic form which is only water-soluble (RH^+): This molecule form can pass only through tissue fluid barriers.

$$R + H^+ \leftrightarrow RH^+$$

(Uncharged) (Proton from HCL) (Cationic)

The balance in both charged and uncharged form of the LA molecules above is notably affected by the acidity of the local anaesthetic solution.[19] The lower the pH, the more the concentration of the charged cationic form due to supply of hydrogen ion from the hydrochloric acid used in acidifying the local anaesthetic solution and contrarily the higher the pH, the more the concentration of the uncharged form as the hydrogen ion lowers down. Practically, both forms of the LA molecules are required in the tissues for it to work. The LA molecules act by diffusing into the nerve membrane (in the uncharged form) then re-equilibrate to form both charged cationic and uncharged based forms adjacent to the outside of the nerve cell membrane and then subsequently the charged molecule will bind to the sodium receptor in the sodium channel and block its permeability.[20]

Commercially, LA is stored and marketed in acidic form with a pH of 3.5 to 5.5 and even more acidic with the addition of a vasoconstrictor commonly adrenaline, just to maintain stability, water solubility as well as prolonged its shelf life.[12, 13]

When buffer (commonly 8.4% sodium bicarbonate) is added to the LA solution, this raises the pH of the solution to a certain pH. Malamed et al.[15] in their study comparing buffered with nonbuffered lignocaine with adrenaline during inferior alveolar nerve block demonstrated a pH of 7.31 with 8.4% sodium bicarbonate buffering. Similarly, Kashap et al.[21] demonstrated a pH of 7.38. This pH range will favour the uncharged base form of the local anaesthetic molecules to predominate, being a lipid-soluble molecule, thereby making the LA act more quickly.

Sodium bicarbonate buffering results in carbon dioxide and water production as shown in the following equation [22]:

$$NaHCO_3\,(aq) + HCl\,(aq) \rightarrow NaCl\,(aq) + CO_2\,(g) + H_2O\,(l)$$

Several authors have reported the role of carbon dioxide in local anaesthetics. Bromage et al.[23] suggested that carbon dioxide acts by enhancing the flow of local anesthetic into the nerve and established that the addition of carbon dioxide to lignocaine shortened the time to onset of local anaesthesia. The effects of carbon dioxide in LA have also been studied by Bokesch et al.[24] and establish its role in enhancing local anesthesia and related it to either a direct effect on the nerve membrane or by indirect action on intracellular pH. Condouris et al, [25] in their study reported that carbon dioxide potentiates the action of local anesthetics by enhancing nerve conduction blockade. Catchlove et al, [26] concluded that carbon dioxide potentiates local anesthesia by three mechanisms: a direct depressant effect of carbon dioxide on the nerve axon, hence concentrating the LA inside the nerve trunk; concentrating the local anesthetic inside the nerve trunk through ion trapping; and converting the local anesthetics to the active cationic form within the nerve axoplasm through its effect on pH.

METHODS OF BUFFERING

The Onpharma Buffering System

This was the first chair side LA cartridge buffering system invented in the United States and approved by the US Food and Drug Administration (FDA). This system consisted of three parts including: the onset mixing pen, 8.4% Sodium bicarbonate injection solution and, cartridge connector.[27] The system is compatible with the usually commercially available local anaesthetic cartridge and the two solutions that is, 8.4% sodium bicarbonate of the Onpharma onset system and the local anaesthetic cartridge to be buffered are mixed with the onset mixing pen (a high precision mixing device) via the cartridge connector.[27] The process of mixing begins by assembling the device and dialling a specific number on the mixing pen and further depressing the button. This transfers bicarbonate into the anaesthetic cartridge through the connector. At the same time, the same amount of the LA solution is removed to maintain the standard volume.[27]

The Anutra buffering system: The system came in to use in 2015, following approval by the FDI in the United States. The Anutra system has three parts namely: the Anutra dispenser, the Anutra syringe and, the Anutra cassette.[28]

The Anutra cassette is designed to house 50mls local anaesthetic bottle as well as 10mls of sodium bicarbonate and when loaded can be fitted into the close design Anutra dispenser that permit the precise mixing of the two solutions in a closed filtered environment. The side of the dispenser has a slot where the Anutra disposable aspirating dental syringe can be fitted to collect up to 5mls of the solution at a time.[28] The dispenser also has a switch on top of it that is used to push 1ml of the buffered solution into the Anutra syringe with each turn as shown in Figure 1. This system has an advantage of buffering larger volume of the LA solution at a time thereby easing situations where multiple dental anaesthesia is required such as in multiple dental restoration.[28]

Figure 1: Diagram Showing the Anutra buffering device consisting of the Anutra syringe, opened Anutra dispenser with the Anutra cassette.

Hand Mixing

This is also called the remove and replace technique and it was the commonly used technique before the invention of Onpharma onset and Anutra system in 2010 and 2015 respectively.[17] This may continue to be the most widely used before the buffering systems become widely available. The following descriptions have been developed and proposed for hand mixing technique: under aseptic technique, the sterile glove is worn, and the rubber bung of the 2mls dental cartridge containing 2% lignocaine with adrenaline is cleaned with gauze soaked in methylated spirit. Using a brand-new sterile insulin disposable graduated syringe with an ultrafine needle, 0.18mls of the local anaesthetic solution is withdrawn from the dental cartridge. The needle of the insulin syringe which is used to withdraw the 0.18mls of the local anaesthetic solution is left intact on the cartridge. Thereafter, another insulin syringe is used to withdraw 0.18mls of 8.4% sodium bicarbonate from its 10mls ampoule. The 0.18mls of the buffer withdrawn can then be injected into the LA cartridge to replace the 0.18mls of the local anaesthetic that was withdrawn previously. Goodchild et al.[17] described similar hand mixing technique and compared it with the buffering device. Their study showed no statistically significant difference in the outcome of buffering using the hand mixing technique and the buffered local anesthetic mixing device. The disadvantage of this method is that extra effort has to be made to maintain sterility.

Benefits of LA Buffering

Rapid Onset of the Local Anaesthesia

It is believed that by 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. Faster onset with buffered LA was demonstrated by Kashyap et al.[21] in India and Malamed *et al*.[20]in the US. The advantage of faster onset can be utilized in body sites with low tissue buffering capability due to a delay in pH rise after injection such as in periapical or dentoalveolar alveolar abscess

Reduced Pain at Injection Site

Pain is the most common presenting symptom in dentistry and a great concern to the dentist.[29]Acidity of the commercially available LA solution has been clearly demonstrated to be a cause of injection pain. Extensive literature search revealed several studies comparing buffered and nonbuffered LA and, the majority of the findings in the literature demonstrated lesser pain of injection with buffered.[15, 12, 20, 21] Malamed et al.[15] on the other hand suggest that the lower pain of injection with buffered LA may be due to activation of fewer acid-sensing nociceptors when compared to non-buffered LA solutions. A less painful anaesthetic would help more patients to overcome their dental fears, improve attendance and bring a significant marketing advantage to typical dental practices.

Possible Longer Duration of Anaesthesia

There are mixed reactions in the literature as regards the effect of sodium bicarbonate LA on duration of anaesthesia with some studies reporting longer duration [30, 31, 32] and others reporting that there is no difference between buffered and non-buffered LA solution. [14, 33] It is difficult to conclude on the benefits of buffering on duration of action with the paucity of literature on this topic. More studies are needed in this area.

CONCLUSION

This review has explored the science of buffering, techniques and its role in achieving faster onset anaesthesia and reduced pain at injection sites. However, there was a paucity of literature on the effect of buffering on duration of action of local anaesthetics. Dental professionals are advised to adopt chair-side buffering of LA to increase patient confidence and acceptance of dental treatment.

Source of support
Nil
Conflict of Interest
None declared

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