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Pain experiences in pediatric dental patients to buffered and conventional local anesthesia

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Pain Experiences in Pediatric Dental Patients to Buffered and Conventional Local Anesthesia

by

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THESIS

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Abstract

The purpose of this study was to compare the pain experiences of pediatric dental patients with the use of a buffered local anesthetic versus customary non-buffered local anesthetic. Twenty subjects, between ages nine and twelve, were enrolled in this prospective, double-blind, randomized, crossover trial stratified by gender. The clinician screened, examined, and delivered both types of anesthetic, and patients were evaluated for pain after injection using Visual Analog Scales (VAS). Results showed pain scores for buffered anesthetic to trend lower, although the difference was not statistically significant from that of the conventionally available anesthetic. Data demonstrated safety in pediatric subjects. This study has developed a framework to further test local anesthesia at physiologic pH in pediatric dental patients.

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Introduction

Local anesthesia is an essential procedure in the comprehensive treatment of pediatric dental patients. In the treatment of patients with dental disease and infection, local anesthesia is commonly required when performing operative procedures[i]. The use of local anesthesia serves two main purposes: (i) enables the patient to remain free of pain during the procedures and (ii) permits the practitioner to complete the procedure without fear of hurting the patient which might otherwise impede the practitioner's ability to provide comprehensive care[ii].

However, patients are often fearful of local anesthesia because traditional preparations of local anesthesia are acidic and can be painful[iii]. Thus, an important advance in the areas of patient comfort and pain control during dental procedures could be a preparation of local anesthesic that significantly reduced the pain upon injection.

A 2010 Cochrane Review found that adjusting the pH of lidocaine with sodium bicarbonate reduced the pain of injection for both adults and children[iv]. Since the Cochrane review released this meta-analysis, numerous research studies have been completed looking into alkalinization of commercially available anesthetics in the outpatient setting. A February 2013 study utilized an automated buffering system with standard 1.7mL anesthetic cartridges with results demonstrating a significantly less painful injection experience[v]. Hobeich et al used pH-adjusted lidocaine to look at onset and pain on injection for maxillary infiltration injections in adult subjects. This study found that there was no difference between commercially available acidic solutions and

buffered anesthetic[vi]. Lee et al completed a randomized trial of patients with buffered and non-buffered lidocaine and reported that buffered lidocaine for local anesthesia reduced the anesthetic pain effectively[vii]. Zaiac et al conducted a study that diluted lidocaine with epinephrine with buffering agent and saline. This small study found that 28 of the 31 participants experienced less pain upon injection with the saline and lidocaine solution[viii]. Welch et al also showed that simultaneous injections of a buffered and nonbuffered anethetic resulted in a statistically significant difference of pain experience, the buffered anesthetic was found to be more comfortable[ix]. However, Beck et al found that there was no difference in pain experience for subjects receiving buffered lidocaine compared to traditional lidocaine, bupivicaine and chloroprocaine[x]. In a study comparing injected lidocaine, buffered lidocaine and saline, buffered lidocaine was found to be the most tolerable injection in 256 subjects[xi]. In a prospective study of 100 adult patients alkanized anesthetic showed a significant reduction in pain[xii]. A 2001 statement in The Journal of Paediatric Drugs listed buffered anesthetic as a strong form of pharmacologic pain and anxiety control in pediatric patients in need of emergency treatment[xiii]. While the medical literature has multiple pediatric trials with buffered anesthetic, there are currently no published dental trials.

The purpose of this study was to compare the pain experience of pediatric subjects of the two injection techniques using a buffered local anesthetic in comparison to that of conventional local anesthetic.

Materials and Methods/Clinical Procedures

The study was a randomized double-blind cross-over trial, comparing lidocaine 2% with 1:100,000 epinephrine with buffered lidocaine 2% with 1:100,000 epinephrine. Twenty (20) pediatric subjects were enrolled. A pediatric dental resident screened, examined, and delivered anesthetic using both types (buffered anesthetic and regular anesthetic). A registered dental assistant trained in the use of the Visual Analog Scale (VAS) evaluated pain of the patient after injection.

This study utilized a local anesthetic buffering system, the Onset™ system. This is an FDA Class 1 compounding device manufactured by Onpharma Inc. It is a simple and portable local anesthesia buffering system that compounds anesthetic solution and 8.4% sodium bicarbonate neutralizing additive solution in a precise manner that brings the anesthetic solution up to human physiologic pH. In contrast, commercially available local anesthetics have a low pH to allow for prolonged shelf life and to maintain the anesthetic molecules in solution. The combination of a buffering sodium bicarbonate agent and local anesthetic has been reported to result in pain-free injections for both adults and children[xiv]. The neutralizing additive solution is a sterile, nonpyrogenic, solution of sodium bicarbonate (NaHCO3) in water. It is well documented that sodium bicarbonate Inj., 8.4% USP Neutralizing Additive Solution (NDC Code 509-100-03) and Lidocaine w/ Epinephrine are compatible[xv]. Sodium bicarbonate has been used in medicine and dentistry as regularly as saline, and pre-dates the FDA. It is commercially available and currently being used by health professionals on a regular basis.

The control local anesthetic used in the study was 2% lidocaine, part of the amide family of local anesthetics with 1:100,000 ppm epinephrine. It has been widely used in dentistry and medicine and has long-standing proven records of safety[xvi].

Approval for this study was granted by the University of California San Francisco IRB, Committee on Human Research in November of 2011.

At a screening visit, prospective subjects were evaluated for the presence of bilateral, mandibular, dental disease of moderate severity requiring therapeutic operative procedures. A complete medical history was taken. A complete dental examination was then performed. Radiographs were taken as appropriate.

In order to participate in this study, the inclusion criteria for the subject was as follows:

1. Informed consent provided both the subject and the legal guardian
2. 9-12 years of age
3. Comprehend the visual analog scale (confirmed by principal investigator)
4. Comprehend the numeric rating scale (confirmed by principal investigator)
5. Comprehend the verbal rating scale (confirmed by principal investigator)
6. In the opinion of the investigator, be a subject who can be expected to comply with the protocol
7. Present moderate mandibular dental disease bilaterally

8. Have 4 to 7 natural teeth (with at least one posterior tooth) present in each mandibular quadrant with moderate dental disease on at least one tooth
9. Be willing to attend the clinic for 3 or more appointments

Exclusion criteria for this study was as follows:

1. Antibiotic premedication requirement
2. A history of allergy, sensitivity, or any other form of adverse reactions to local anesthetics of the amide type, or epinephrine
3. A history of specific systemic illness that would preclude administration of a local anesthetic or vasoconstrictor (epinephrine) (e.g. liver , renal, cardiovascular diseases, blood dyscrasias, psychiatric disorders, etc.)
4. A history of systemic illness that would interfere with healing response (e.g. liver disease, blood dyscrasias, uncontrolled diabetes, etc.)
5. Current systemic medication that interferes with healing response
6. Current systemic medication which contraindicates the use of local anesthetics or epinephrine
7. Pregnant or lactating females (contradicts the use of local anesthetic in non-emergency type dental procedures)
8. Current alcohol or drug abuse
9. Received an anesthetic, analgesic or sedative within 24 hours prior to the therapy appointments
10. Acute infections or conditions in the oral cavity requiring immediate treatment
11. Participation in a clinical study of an investigational drug within the previous 4 weeks

12. Previous enrollment in the present study

Internal Review Board approval was obtained and 20 healthy pediatric volunteers aged between nine to 12 years were included. Subjects in this age range have been shown to give a valid interpretation of the visual analog scale (VAS) pain score[xvii]. All participants provided assent, and legal guardians provided informed, written consent.

Based on data from medical trials of buffered anesthetic, a power calculation for sample size indicated that 20 subjects would provide a 90% chance of detecting an effect size of 0.83 (a change of 0.83 standard deviations), with a significance level of 5% and a correlation of 0.5 between responses from the same subject.
The 20 subjects provided 90% power to detect a difference of at least 5mm on VAS scores (2 sided, type I error = 5%) when the standard deviation is 6.5mm. It would still have provided 84% power if the variance happened to be 20% higher.

Of the 20 subjects, there were 10 males and 10 females. A computer-generated randomization sheet was used to assign the order of treatment procedures (conventional local anesthetic or buffered local anesthetic) and side of dentition receiving the therapy (right or left sides) for each subject in each gender. Thus, a gender-stratified crossover trial design randomly assigns the order of treatments, so each subject can be used as his or her own control. The randomization was determined using a computer-generated sequence of random numbers by Dr. Peter Loomer, one of the primary investigators who was not involved in clinical care of the patients. The randomization of the order was

administrated by the dental assistant. Both the study subject and the investigator who enrolled the volunteers and administrated the local anesthetic were blinded to the order of injection. The second injection/treatment appointment was at least 1 week after the first treatment.

Two treatment visits were required to complete bilateral, mandibular dental operative restorations. At each treatment visit, local anesthetic was delivered to the right or left side of the dentition using one of the two anesthetic types, as pre-assigned. All local anesthetic injections (1.7 ml) were given by a single operator via the inferior alveolar nerve block and long buccal nerve block using a standard dental aspirating syringe fitted with a 27-gauge needle. The injections were administered at a rate of 1.7 ml per minute. This operator had no involvement when subjects performed their pain scores. The operator stepped out of the room after each injection was completed, and the subject was asked to record a visual analog scale (VAS) pain score by the trained research assistant. The VAS was used to assess pain sensitivity. The system utilizes a 100-mm horizontal line with the left endpoint marked “no pain” and the right endpoint marked “pain as bad as it can be.”

Both the patient and the operator were blinded to the anesthetic type being used. Pulp sensitivity was determined with dry ice cold sensitivity testing on the buccal surface of the posterior teeth in the anesthetized quadrant. To confirm the validity of the reading, a control, unanesthetized tooth on the contralateral side of the mandible was tested at the same times. The criterion for successful anesthesia was no patient response to the cold

stimulus.

In addition to objective assessments of pulp anesthesia patients were asked to inform the investigator who was testing pulp sensitivity when subjective feelings of anesthesia in the lip and lingual mucosa appeared.

The subject subsequently received comprehensive dental care in the quadrant anesthetized. The subjects were free to interrupt the procedure at any time to request better pain control. In some cases this required the administration of additional anesthetic. The practitioner did record these injections. The subjects were given verbal and written post-treatment instructions.

Each subject was contacted by telephone within 48 hours after treatment and asked standardized follow-up questions: [1] "Have you had any health problems since you left the dental clinic?" and [2] "Have you had any soreness in your mouth since you left the dental clinic?" If yes, "Is the soreness at the injection sites?". These questions were asked to determine if there were any adverse reactions to the treatment.

Please see the appendix for copies of the assent and informed consent.

Statistical Analysis

The primary efficacy variable, the VAS pain score, was compared between the two treatment groups (conventional vs. buffered anesthetic), side of dentition (right vs. left) and gender (male vs. female) by Mann-Whitney if the data was not normally distributed and Student's paired t test if the data was normally distributed. The corresponding 95% confidence interval was determined and statistical significance was assigned for an outcome with a p value ≤ 0.05.

Statistical analysis was undertaken in Stata version 12 for Windows (StataCorp. 2011. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP. StataCorp, College Station, TX).

Results

Subject Demographics were 20 patients, 10 boys and 10 girls. The age range was 9-12 years old, with a mean age of 10.00 and a standard deviation of 1.06. Safety data collected indicated that there were no adverse reactions reported by any patients during or after treatment. Please add how many patients needed additional anesthesia for treatment procedure.

The results of the painful reaction based for the anesthesia procedures using VAS scores were presented in Table 1-3. Although the buffered anesthetics had lower VAS scores,

there were no statistical significant differences in VAS scored between the buffered and non-buffered treatment group for inferior alveolar nerve block (P=0.23, paired t-test) and long buccal nerve block (P=0.57, paired t-test). IA injections were reported to be more painful (higher VAS) than LB injections (P<0.05, paired t-test).

Table 1: Inferior Alveolar Nerve Block: VAS scores for buffered versus non-buffered injections (make sure you standardize the decimals for numbers in your tables.)

Group	Observed (n)	Mean	Standard Error	Standard Deviation	95% Confidence Interval
Non-Buffered	20	43.00	6.04	27.01	30.36-55.64
Buffered	20	33.05	5.54	24.80	21.44-44.66
Combined	40	38.03	4.13	26.09	29.68-46.37
Difference between two groups	20 pairs	9.95	8.20		-6.65-26.55

Table 2: Long Buccal Nerve Block: VAS scores for buffered versus non-buffered injections

Group	Observed	Mean	Standard Error	Standard Deviation	95% Confidence Interval	95% Confidence Interval
Non-Buffered	20	7.25	1.89	8.47	3.29	11.21
Buffered	20	9.75	3.97	17.76	1.44	18.06
Combined	40	8.5	2.18	13.79	4.09	12.91
Difference		-2.5	4.40		-11.41	6.41

Table 3: Mean VAS for buffered versus non-buffered anesthetic injections

Anesthetic Injection	Buffered (n=20) Mean (SD)	Non-Buffered (n=20) Mean (SD)	*P (paired t-test)*
Inferior Alveolar	33.1 (5.5)	43.0 (6.0)	0.23
Long Buccal	9.8 (3.9)	7.3 (1.9)	0.57

Figure 1 illustrated the VAS scores between male and females. For both the IA (Inferior Alveolar) or LB (Long Buccal) injections, the median Pain VAS for females was higher than those for males. There was no statistical significance ($p>0.05$, paired t-test) in VAS for injections using buffered anesthetic, in comparison to non-buffered within or between genders, with exception of the LB between gender using buffered anesthetic? ($p=0.01$, paired t-test).

Figure 1: Pain VAS for IA and LB Injections by Gender

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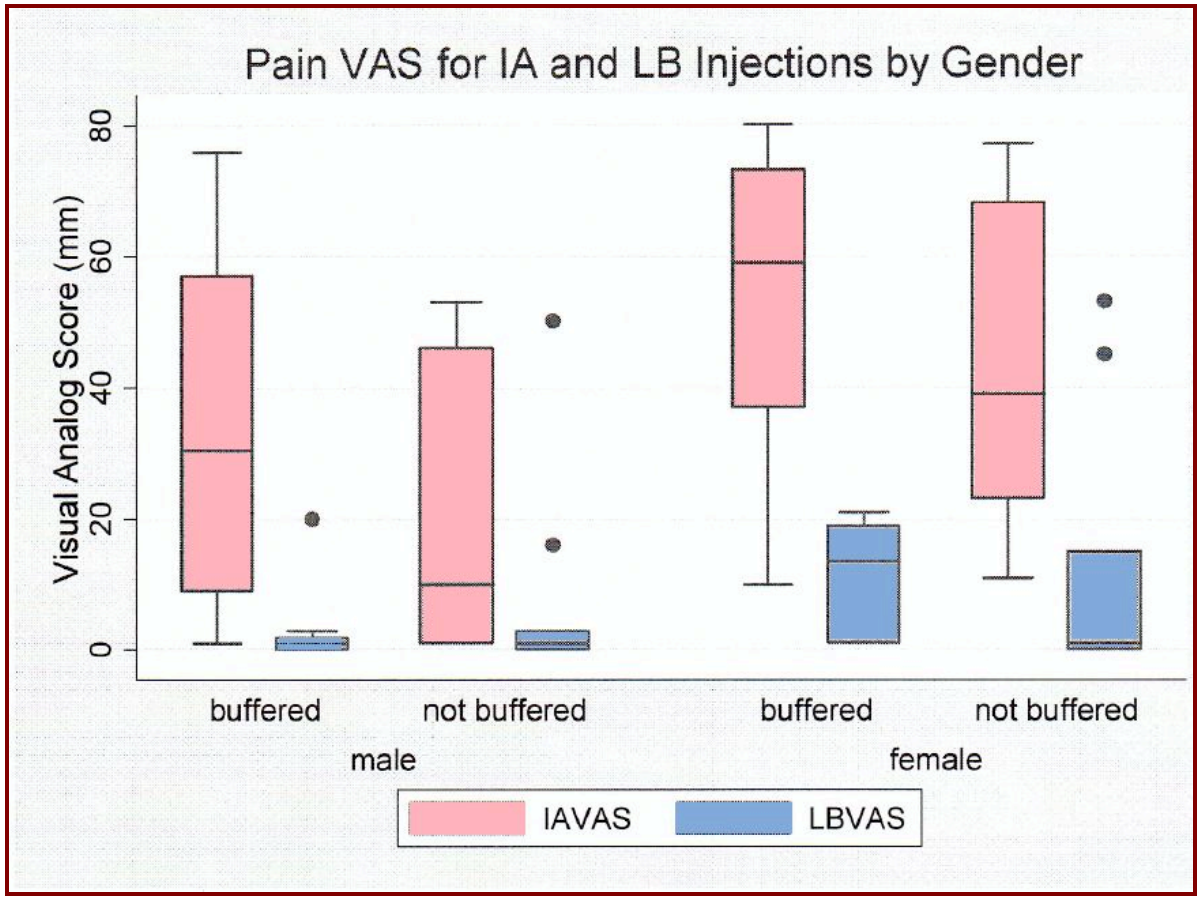

Discussion

In the last 20 years, there have been quite a few studies looking into alternative techniques for increased patient comfort during injection. This includes cooling the skin[xviii], infusing anesthetic at a controlled rate/pressure[xix] and warming the anesthetic cartridge[xx]. Strazer et al completed a review with the following clinical tips for practitioners: smaller needle diameter, perpendicular angle of the needle as inserting, a pause while injecting, and keeping a palpable amount of anesthetic in front of the needle tip while inserting[xxi]. These studies find trends that are important as practitioners work towards finding ways to reduce discomfort and anxiety in patients. The over-all goal is to increase patient satisfaction.

Although previous studies have shown significant reduction in pain during local anesthestic procedures by using buffered anethestic reagents in adults or pediatric patients (literature citation), new did not find statistically significant differences between buffered and non-buffered injections but only a trend to less pain (i.e. lower pain scores) in the buffered injections. The following factors may contribute to these finding.

This study had several limitations that may have affected the results. First, it is important to note that in pediatric populations, there is difficulty in assessing pain scores[xxii]. Wong-Baker Faces scale, numeric rating scale, verbal rating scale, and VAS all have a proven record in pediatric populations. We chose VAS as our pain scoring system

because it has strong literature support in this particular patient population and age group[xxiii]. We did not notice our children having difficulty in using the scoring system.

Second, the study had a small sample size for the variation of VAS scores that was found to be larger than we anticipated in the sample size calculation. Therefore, we did not have enough power to reach statistic significance. However, the study has now laid a foundation for future studies evaluating pain during injection for pediatric dental patients in a larger sample size and helped to identify areas for future study. A larger sample size will be needed to demonstrate statistical differences between the two study groups. In addition, using an adjunctive measure of pain that is more objective than VAS such as heart rate monitoring, may have yielded different results. In the future taking a heart rate reading while the patient is supine before injection, during injection, and after injection, and taking a mean of these three readings may provide interesting data. It also may be possible to look at the statistical results using mixed effects regression models with random person effects.

The study demonstrated that buffering cartridges of anesthetic in an outpatient dental setting is safe, with no adverse reactions reported by the study participants. Additionally, no patient reported negative feedback regarding any experiences during the study. This is important for practitioners who are interested in trying in-office buffering with their patients.

In summary, this study, while limited in scope, demonstrated that buffering anesthetic is a safe way to adjust pH of commercially available 2% lidocaine with 1:100,000 epinephrine in the dental office. The trend suggests a less painful Inferior Alveolar injection, which is in agreement with the literature available[xxiv], however, a larger study is needed to conform these findings.

References

[i] Becker DE, Reed KL. Local anesthetics: review of pharmacological considerations. Anesth Prog. 2012 Summer;59(2):90-101; quiz 102-3. doi: 10.2344/0003-3006-59.2.90.

[ii] Reed KL, Malamed SF, Fonner AM. Local anesthesia part 2: technical considerations. Anesth Prog. 2012 Fall;59(3):127-36; quiz 137. doi: 10.2344/0003-3006-59.3.127.

[iii] P. Milgrom, S. Caldwell, T. Getz, P. Weinstein and D. Ramsay. Four dimensions of fear of dental injections. 1997; *JADA* 128(6): 756-66.

[iv] M. Cepeda, A. Tzortzopoulou, M. Thackrey, J. Hudcova, P. Arora Gandhi, and R. Schumann. Adjusting the pH of lidocaine for reducing pain on injection. 2010; *Cochrane Database Syst Rev.* (12):CD006581

[v] Malamed SF, Tavana S, Falkel M. Faster onset and more comfortable injection with alkalinized 2% lidocaine with epinephrine 1:100,000. 2013; *Compend Contin Educ Dent*. Feb;34 Spec No 1:10-20.

[vi] Hobeich P, Simon S, Schneiderman E, He J. A prospective, randomized, double-blind comparison of the injection pain and anesthetic onset of 2% lidocaine with 1:100,000 epinephrine buffered with 5% and 10% sodium bicarbonate in maxillary infiltrations. 2013; J Endod. 2013 May;39(5):597-9. doi: 10.1016/j.joen.2013.01.008.

[vii] Lee HJ, Cho YJ, Gong HS, Rhee SH, Park HS, Baek GH. The effect of buffered lidocaine in local anesthesia: a prospective, randomized, double-blind study. 2013; J Hand Surg Am. 2013 May;38(5):971-5. doi: 10.1016/j.jhsa.2013.02.016.

[viii] Zaiac M, Aguilera SB, Zaulyanov-Scanlan L, Caperton C, Chimento S. Virtually painless local anesthesia: diluted lidocaine proves to be superior to buffered lidocaine for subcutaneous infiltration. 2012; J Drugs Dermatol. 2012 Oct;11(10):e39-42.

[ix] Welch MN, Czyz CN, Kalwerisky K, Holck DE, Mihora LD. Double-blind, bilateral pain comparison with simultaneous injection of 2% lidocaine versus buffered 2% lidocaine for periocular anesthesia. 2012; Ophthalmology. 2012 Oct;119(10):2048-52. doi: 10.1016/j.ophtha.2012.05.029.

[x] Beck RM, Zbierajewski FJ, Barber MK, Engoren M, Thomas R. A comparison of the pain perceived during intravenous catheter insertion after injection with various local anesthetics. 2011; AANA J. 2011 Aug;79(4 Suppl):S58-61.

[xi] Ganter-Ritz V, Speroni KG, Atherton M. A randomized double-blind study comparing intradermal anesthetic tolerability, efficacy, and cost-effectiveness of lidocaine, buffered lidocaine, and bacteriostatic normal saline for peripheral intravenous insertion. 2012; J Infus Nurs. 2012 Mar-Apr;35(2):93-9. doi: 10.1097/NAN.0b013e31824241cc.

[xii] Kashyap VM, Desai R, Reddy PB, Menon S. Effect of alkalinisation of lignocaine for intraoral nerve block on pain during injection, and speed of onset of anaesthesia. 2011; Br J Oral Maxillofac Surg. 2011 Dec;49(8):e72-5. doi: 10.1016/j.bjoms.2011.04.068.

[xiii] Kennedy RM, Luhmann JD. Pharmacological management of pain and anxiety during emergency procedures in children. 2001; *Paediatr Drugs*. 3(5):337-54.

[xiv] M. Cepeda, A. Tzortzopoulou, M. Thackrey, J. Hudcova, P. Arora Gandhi, and R. Schumann. Adjusting the pH of lidocaine for reducing pain on injection. 2010; *Cochrane Database Syst Rev.* (12):CD006581

[xv] Compatibility section under Sodium Bicarbonate in *The Handbook on Injectable Drugs* by Lawrence A.Trissel, 14th ed. 2007 (American Society of Health-System Pharmacists, Bethesda, MD)

[xvi] Moore PA, Hersh EV. Local anesthetics: pharmacology and toxicity. 2010; *Dent Clin North Am*. Oct;54(4):587-99. doi: 10.1016/j.cden.2010.06.015.

[xvii] Von Baeyer C. Children's self-report of pain intensity: what we know, where we are headed. 2009; *Pain Res. Manag*. (1): 39-45

[xviii] Al Shahwan MA. Prospective comparison between buffered 1% lidocaine-epinephrine and skin cooling in reducing the pain of local anesthetic infiltration. 2012; Dermatol Surg. 2012 Oct;38(10):1654-9. doi: 10.1111/j.1524-4725.2012.02522.x.

[xix] Yag-Howard C. Commentary: A prospective comparison between neutralizing the pH of 1% lidocaine with epinephrine (buffering) and pre-operative skin cooling in reducing the pain of infiltration of local anesthetic. 2012; Dermatol Surg. 2012 Oct;38(10):1660-1. doi: 10.1111/j.1524-4725.2012.02485.x.

[xx] Hogan ME, vanderVaart S, Perampaladas K, Machado M, Einarson TR, Taddio A. Systematic review and meta-analysis of the effect of warming local anesthetics on injection pain. Ann Emerg Med. 2011 Jul;58(1):86-98.e1. doi: 10.1016/j.annemergmed.2010.12.001.

[xxi] Strazar R, Lalonde D. Minimizing injection pain in local anesthesia. CMAJ. 2012 Dec 11;184(18):2016. doi: 10.1503/cmaj.111780.

[xxii] Garra G, Singer AJ, Domingo A, Thode HC Jr. The Wong-Baker pain FACES scale measures pain, not fear. Pediatr Emerg Care. 2013 Jan;29(1):17-20. doi: 10.1097/PEC.0b013e31827b2299.

[xxiii] Castarlenas E, Miró J, Sánchez-Rodríguez E. J Pain. Is the verbal numerical rating scale a valid tool for assessing pain intensity in children below 8 years of age? 2013 Mar;14(3):297-304. doi: 10.1016/j.jpain.2012.12.004.

[xxiv] M. Cepeda, A. Tzortzopoulou, M. Thackrey, J. Hudcova, P. Arora Gandhi, and R. Schumann. Adjusting the pH of lidocaine for reducing pain on injection. 2010; *Cochrane Database Syst Rev.* (12):CD006581

Appendices

Guardian Consent:

University of California
San Francisco
Consent to participate in a Research Study

Study Title:
COMPARISON OF PAIN OF CONVENTIONAL TO BUFFERED LOCAL ANESTHESIA DURING INJECTION IN PEDIATRIC PATIENTS. A PROSPECTIVE, DOUBLE-BLIND, RANDOMIZED, CROSSOVER STUDY.

Why is this study being done?

The purpose of this study is to determine the effectiveness of buffered local anesthesia injections to numb the gums and teeth during dental treatment. The study is being conducted by Peter Loomer, DDS, PhD in the Department of Orofacial Sciences and Susan Poorsattar, DDS in the Department of Orofacial Sciences. Operative procedures (often including sealants, fillings, and extractions) are an accepted treatment for dental disease, which is characterized by deep pits/grooves and cavities on the teeth. If the disease is not treated, it can continue and may result in infection and tooth loss. Your child has been asked to participate in this study because he/she has moderate dental disease and cavities. Your child needs to have the operative procedures in order to treat the disease.

The usual method of numbing the teeth and gums is by a shot. The type of local anesthetic being tested in this study uses a buffering solution that raises the pH of anesthetic, making the anesthetic less acidic and closer to the pH of human tissues. The local anesthetic is lidocaine, which is the most commonly used local anesthetic in dentistry. If you and your child choose to participate in the study, he/she will receive treatment two times on different teeth, one time given regular local anesthetic and the other time using the buffered anesthetic.

How many people will take part in this study?

About twenty children will take part in this study.

What will happen if my child takes part in this research study?

If you and your child choose to participate in the study he/she will come to the dental clinic for 3 visits and be called twice on the phone.

Before the child begins the main part of the study…

The patient will be provided with a thorough dental examination by Dr. Poorsattar, with careful extra-oral and intra-oral exams to determine how much dental disease he/she has. Appropriate x-rays will be taken. This will take approximately 2 hours.

During the main part of the study…

If the screening exams and procedures show that he/she can continue to be in the study, and he/she chooses to take part, then he/she will have the following procedures done:

The patient will be "randomized" into one of the study groups. Study Group One will be receiving the standard anesthetic at the first treatment visit, and the buffered anesthetic at the second treatment visit. Study Group Two will receive the buffered anesthetic at the first treatment visit and the standard anesthetic at the second treatment visit. Randomization means that they are put into a group by chance. A computer program will place them in one of the groups. Neither the patient nor the doctor can choose the group the patient will be in. He/she will have an equal chance of being placed in any group.

Treatment Visit 1: The patient will return to the dental clinic for Visit 2, following a 1 day to 2 week waiting period. At this appointment he/she will have the teeth on one side of his/her mouth (on the bottom) treated for dental disease with operative procedures. He/she will receive local anesthetic, either by a regular pH or buffered pH, prior to starting the procedures. Your child will be asked questions about the injections and the procedures during and after the appointment, to describe the pain. If it hurts too much to have operative procedures after the local anesthetic has been given, your child may ask for further anesthetic. The appointment will take approximately 2 hours. He/she will be telephoned at home by one of the investigators within 48 hours after the appointment and answer a few questions regarding how he/she feels.

Treatment Visit 2: Between one and two weeks later, the patient will have operative procedures on the teeth on the other side of the mouth. He/she will be given local anesthesia with either regular pH or buffered pH (whichever method the patient did not have at the last appointment). The patient will answer questions about the pain. If it hurts too much to have operative procedures after the local anesthetic has been given, he/she may ask for further anesthetic. The appointment will take approximately 2 hours. He/she will be telephoned at home by one of the investigators within 48 hours after the appointment and answer a few questions.

You must inform the dentist of any changes in his/her health status during the study.

How long will my child of be in the study?

Participation in the study will take a total of about 7 hours over a period of 8 weeks.

Can my child stop being in the study?

Yes. They can decide to stop at any time. Tell the study doctor if he/she is thinking about stopping or decides to stop. The doctor will tell you how to stop participation safely.

What side effects or risks can I expect from being in this study?

Your child may have side effects while in the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give your child medicines to help lessen side effects. Many side effects go away soon after anesthesia is given. In some cases, side effects can be serious, long lasting, or may never go away. There is also risk of death.

You should talk to the study doctor about any side effects your child experiences while taking part in the study.

Likely

- He/she may experience an unpleasant taste from the local anesthetic.

Less Likely

- During two treatment visits he/she will receive local anesthetic injections. He/she may feel pain during any of the injections or the treatments thereafter. If the injections are not sufficient to control pain, he/she may be provided additional shots to help stop the pain.
- During the examination of his/her mouth, as with any dental examination visit, he/she may experience some discomfort.
- There may be some bleeding or soreness in his/her mouth or where he/she got the shots after the operative procedures. We will be provided with post-operative instructions and may call the investigators, Dr. Poorsattar at (805) 704-7516 or Dr. Loomer at (415) 502-7896 at any time.

Rare but serious

- As with any drug, the possibility of allergic reaction or side effects exists. Adverse reactions after local anesthetic injections of lidocaine with epinephrine are very rare. They include: light-headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, blurred vision, vomiting, sensations of

heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, nerve injury, trouble breathing and heart problems. With the doses used in this study, bad effects are extremely rare.

Are there benefits to taking part in the study?

There are no direct benefits to taking part in this study. While doctors hope this alteration in pH will be less painful than the standard usual treatment, there is no proof of this yet.

Information gained from this study may make it possible for future patients to have their teeth fixed with injections that are equally effective but less painful.

What other choices does my child have if they do not take part in this study?

The alternatives to participating in this study are to have his/her operative procedures with standard (unbuffered) local anesthetic.

Will medical information be kept private?

We will do our best to make sure that the personal information in the medical record is kept private. However, we cannot guarantee total privacy. Your child's personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, his/her name and other personal information will not be used.

Participation in research may involve a loss of privacy, but information about your child will be handled as confidentially as possible. A medical and dental record will be created because of his/her participation in this study. The consent forms and some of the research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

Your child's records will be handled as confidentially as is possible. They will be kept in locked cabinets by the investigators. In addition, records will be coded rather than showing my name. Access to records will be limited to study personnel. However, no individual identities will be used in any reports or publications resulting from this study.

The investigators will have the name, address and phone number of your child on file.

What are costs of taking part in this study?

You will not be charged for any of the study activities.

You will be charged for any of the treatments or procedures (x-rays, examinations, and deep cleaning). You will incur the cost of transportation and parking to and from the dental clinic. You will not be reimbursed for these travel costs. If your child needs other dental work, these will not be paid for by the study.

Will my child be paid for taking part in this study?

There will be no compensation for participating in this study.

What happens if my child is injured because he/she took part in this study?

If your child is injured as a result of being in this study, treatment will be available. The costs of such treatment may be covered by the University of California. The University does not normally provide any other form of compensation for injury. For further information about this, we may call the office of the Committee on Human Research at (415) 476-1814.

It is important that you tell your study doctors, Dr. Poorsattar or Dr. Loomer, if you feel that your child has been injured because of taking part in this study. You can tell the doctor in person or call him/her at (805) 704-7516 or (415) 502-7896.

What are my child's rights if they take part in this study?

Taking part in this study is your and your child's choice. He/she may choose either to take part or not to take part in the study. If your child decides to take part in this study, he/she may leave the study at any time. No matter what decision is made, there will be no penalty to your child and your child will not lose any of his/her regular benefits. Leaving the study will not affect his/her medical care. Your child can still get his/her medical care from our institution.

We will tell you and your child about new information or changes in the study that may affect his/her health or your child's willingness to continue in the study.

In the case of injury resulting from this study, your child does not lose any legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctors Dr. Poorsattar at (805) 704-7516 or Dr. Loomer at (415) 502-7896.

The study has been explained to both my child and I by either Dr. Poorsattar or Dr. Loomer and our questions were answered. If we have any further questions about this study or participation, we can call Dr. Poorsattar at (805) 704-7516 or Dr. Loomer at (415) 502-7896.

Consent

We have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

The child I am guardian of may be withdrawn from the study by the investigator if it is thought to be in his/her best medical interest, or if we fail to keep appointments.

PARTICIPATION IS VOLUNTARY. We have the right to decline to participate or withdraw at any point from the study. His/her decision to participate, decline, or withdraw will not jeopardize his/her status at UCSF.

If the child I am guardian of wishes to participate, I should sign below.

The person being considered for this study is unable to consent for himself/herself because he/she is a minor. By signing below, you are giving your permission for your child to be included in this study.

_____ _____

Date Parent or Legal Guardian's Signature

_____

Parent or Legal Guardian's Name (Print)

_____

Person Obtaining Consent

Patient Assent:

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO (UCSF)

ASSENT TO BE IN A RESEARCH STUDY
ABOUT NUMBING MEDICINE

For children 9-12 years old

Why are we meeting with you?

We want to tell you about something we are doing called a research study. A research study is when doctors collect a lot of information to learn more about something. Dr. Peter Loomer and Dr. Susan Poorsattar are doing a study to learn more about numbing the mouth to fix dental cavities. After we tell you about it, we will ask if you'd like to be in this study or not.

Why are we doing this study?

We want to find out how to numb the mouth in a way that does not sting your gums. So we are getting information from lots of boys and girls like you.

In the whole study, there will be about 20 children who have dental cavities.

What will happen to you if you are in this study?

Only if you agree, two things will happen:

1. You will get a special numbing medicine similar to what is always given.

2. You will see the dentist and get you teeth fixed just like everyone else. You will just answer a couple extra questions about how your mouth feels so the doctors can learn more about the medicine.

A. Will this study hurt?

The stick from the needle to give the medicine may hurt, but the gums and teeth will get numb fast so you will not feel any pain. It will not hurt while the doctors are fixing your teeth as long as you are numb.

Will you get better if you are in this study?

This study will not help your teeth get better. Your doctor will fix your teeth whether or not you say yes to being in this study.

B. Do you have any questions?

You can ask questions any time. You can ask now. You can ask later. You can talk to me or you can talk to someone else.

Do you have to be in this study?

No, you don't. No one will be mad at you if you don't want to do this. If you don't want to be in this study, just tell us. Or if you do want to be in the study, tell us that. And, remember, you can say yes now and change your mind later. It's up to you.

If you don't want to be in this study, just tell us.

If you want to be in this study, just tell us.
The doctor will give you a copy of this form to keep.

SIGNATURE OF PERSON CONDUCTING ASSENT DISCUSSION
I have explained the study to _____(*print name of child here*) in language he/she can understand, and the child has agreed to be in the study.

_____ _____
Signature of Person Conducting Assent Discussion Date

_____
Name of Person Conducting Assent Discussion (*print*)

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Author Signature

6/25/2013

Date