

# **Comparison of Buffered 1% vs. Non-Buffered 2% or 1% Lidocaine used in dental and oral surgical procedures: Clinical Outcomes**

**NCT number** NCT03127943  
**Document Date** 04/14/2017

**4/14/17 version**

**Research Protocol**

**Pilot Study: Comparison of Buffered 1% vs. Non-Buffered 1% Lidocaine used in dental and oral surgical procedures: Clinical Outcomes Mandible**

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**Goal:**

Assess the clinical impact of Buffered 1% lidocaine with epinephrine as compared to the Non-buffered 1% lidocaine with epinephrine in dental and oral surgical procedures.

**Background:**

Based on the discovery of its topical and locally injected anesthetic effects at the end of the 19<sup>th</sup> century, cocaine was rapidly adopted as a means of blocking painful sensory impulses from the periphery during surgical procedures.(1) In the last decade local anesthetics have been administered more often, alone or in combination with IV or inhalation anesthetics for most surgical procedures. For clinical procedures in the head and neck the local anesthetic drugs have been combined with a vasoconstrictor, usually epinephrine, to prolong the anesthetic effect at the locally injected anatomic site. To achieve pulpal and periosteal anesthesia by nerve or field block for procedures in dentistry, lidocaine at a 2% concentration has been preferred by clinicians for its reliable outcomes. To prolong the shelf life of the vasopressor, the drug combination must be formulated with a low pH, approximately pH 3.5 for lidocaine with 1/100k epinephrine (Epi).

With a better understanding of the pharmacology, new options for improving local anesthetic effectiveness including buffering the commercially supplied drugs to a neutral pH just prior to injection, continue to emerge.(2) When injected, the low pH causes the “sting” felt by patients on injection. Buffering to a neutral pH eliminates this discomfort and makes the maximum concentration of the non-ionized form of the anesthetic drug immediately available to the targeted nerve membrane.(3-7) Until recently, buffering local anesthetics containing Epi followed with bicarbonate just prior to injection was impractical for the quantities used in intraoral procedures. However, today we do have options to efficiently accomplish this buffering technique.(Anutra Medical, RTP, NC).

Buffering local anesthetics just prior to use produces positive outcomes including less “sting” on injection, faster onset of the drug, and possibly added drug potency, ie the same positive clinical effect at lower dosage. In pilot studies with healthy adults as their own controls Phero et al and Warren et al have shown that Buffered 1% lidocaine with 1/100k Epi was as effective as Non-buffered 2% lidocaine with 1/100k Epi for pulpal anesthesia on a 1<sup>st</sup> molar or canine after nerve block in the mandible or field block in the maxilla-Phase one of this study.(8,9) These outcomes could be beneficial for performing multiple procedures in children whose lidocaine dosage is limited by body weight or others with chronic liver disease.

**Rationale:**

The recently reported results from the two clinical studies involving buffered lidocaine with Epi have led to clinicians questioning whether the Buffered 1% lidocaine with Epi might be as effective for achieving pulpal and periosteal anesthesia for dental procedures as Non-Buffered 1% lidocaine with Epi-Phase two of this study, outcomes not usually considered by most clinicians. This protocol addresses that question.

**Goal:**

Assess outcomes after mandibular nerve block anesthesia using Buffered 1% lidocaine with 1/100k epinephrine as compared to Non-buffered 1% lidocaine with 1/100k epinephrine.

**Specific Aims:**

Compare clinical depths of pulpal anesthesia for maxillary(Phase one) and mandibular(Phase two) molar and canine teeth at 30min intervals Post-injection

Assess pain levels during injection

Assess time after injection to lower lip numb

**Hypotheses:**

No differences exist in anesthetic depth for pulpal anesthesia after intraoral injection for maxillary field block(Phase one) or mandibular nerve block between Buffered 1% lidocaine with 1/100k epinephrine as compared to Non-buffered 1% lidocaine with 1/100k epinephrine.

**Study Time Frame: 6 months**Month One

IRB approvals. Prepare case-books.

Months Two-Three

Recruit 24 volunteers as subjects.

Clinical Study

Months Four-Five

Analyze data

Month Six

Prepare Abstracts, Papers

**Methods: Blinded, Randomized Clinical Design**

Recruit subjects with IRB approved consent at UNC

Obtain NIH clinical trial registration

Target enrollment of 24 subjects each phase, 48 total subjects.

Subjects will serve as their own controls in a cross-over AB/BA study design which is uniform within sequences, uniform within periods, and balanced

Sample size justification: Primary interest is estimation of effect size from pilot study. 24 subjects should be sufficient to provide data to assess whether a larger study is warranted and provide estimates for sample size calculation for larger studies.

Vital signs recorded: 10 min before, just after drug administration, and before discharge

Randomized subjects to be injected orally for Maxillary field block(Posterior superior and Palatal sensory nerves Phase one) or mandibular nerve block (Inferior alveolar, Lingual, and

Buccal sensory nerves Phase two) alternatively with 4cc of buffered 1% lidocaine (40mg.) with 1/100k Epi and 4cc non-buffered of 1% lidocaine(40mg.) with 1/100k Epi.

SAS will be used to create randomization schedules:

The randomization will be performed first to type of drug given with a balanced randomization (half subjects buffered; half to non-buffered)

An OMS faculty will administer the drugs in the OMS clinic.

In week One, Each subject would receive either the buffered or the non-buffered anesthetic to block the Inferior alveolar, Lingual and Buccal nerves.

At least a week later, longer than the 1.5-2hr. elimination half-life of the drug lidocaine,

injections for the nerve block would involve the alternate local anesthetic combination.

**Study Subjects: 24**

Inclusion Criteria

Age 18-30 years

ASA I

Willingness to participate in two sessions

Exclusion Criteria

Allergy to lidocaine class of anesthetic drugs

Local anesthetic drug use in past week

Current symptoms in teeth or oral mucosa

**Data Collection: UNC OMS clinic: Timed assessment pre, and post-anesthetic clinical effects**

**Clinical outcomes recorded from subjects' subjective responses**

Reported pain on injection: 10pt Likert-type scale anchored No pain, Worst pain imaginable

Time to lower lip numbness after injection for nerve block

Ipsilateral Mandibular teeth to be tested: 1st molar and canine

Assessment: pre, and post-anesthetic administration for pulpal anesthesia

Pulp Test/Response to electrical stimulation: Yes or No

Testing interval: Pre-local anesthetic, and

Post-local anesthetic at 30min, 90min, 120min.

Pulp Test/ Response to Cold: Yes or No

Testing interval: Pre-local anesthetic, and

Post-local anesthetic at 30min, 90min, 120min.

**Data Collection/Analysis:**

Data will be managed by Dr Phillips and staff. Data collection forms for clinical data will be developed to use Teleform for direct scanning input into an ACCESS database. Similar forms have been used in previous studies including three with local anesthesia. All databases are stored on a password protected School of Dentistry server with specific group assignment. SAS will be used for database management and statistical analysis. Descriptive statistics are used to verify correct entry through range and logical checks.

**Statistical analysis Each Phase** .....Effect sizes are currently unknown for the difference in type of injection in time to onset of anesthesia or pain level during injection. Primary interest is the difference between type of injection. In order to check the assumption of negligible carryover effects an unpaired t-test or a Wilcoxon Rank Sum test, depending on the distribution of the outcome, will be used to compare the within subject sums of the results from sequence AB to the within subject sums from sequence BA. Under the assumption that the carryover effects are equal ( $\lambda_A = \lambda_B = \lambda$ ), the differences for every patient will be calculated and multiplied by  $\frac{1}{2}$ . The two sequences will be compared using a two-sample t test or a Wilcoxon rank sum test depending on the distribution of the outcome.

$$H_0 : \mu_{AB} - \mu_{BA} = 0$$

The expression:

$$\mu_{AB} - \mu_{BA} = 2(\mu_A - \mu_B)$$

so testing  $H_0 : \mu_{AB} - \mu_{BA} = 0$ , is equivalent to testing:

$$H_0 : \mu_A - \mu_B = 0$$

Sample Size: With a sample size in each sequence group of 12 (a total sample size of 24) a 2x2 crossover design will have 90% power to detect a difference in means of -10.00.(10)

#### References:

- 1-Leonard M: Carl Koller: Mankind's greatest benefactor? The story of local anesthesia. J Dent Res77:535, 1998.
- 2-Strichartz GR, Sanchez V, Arthur R, Chafetz R, Martin D: Fundamental properties of local anesthetics II. Measured octanol: Buffer partition coefficients and Pka values of clinically used drugs. Anesth Analg 71: 158, 1990
- 3-Christoph RA, Buchanan L, Begalia K, Schwaryz S: Pain reduction in local anesthetic administration through pH buffering. Ann Emerg Med 17:117, 1988.
- 4-Masters JE: Randomised control trial of pH buffered lignocaine with adrenalin in outpatient operations. Br J Plastic Surg 51:385, 1998.
- 5-Meechan JG, Day PF: A comparison of intraoral injection discomfort produced by plain and epinephrine-containing lidocaine local anesthetic solutions: a randomized, double-blind, split-mouth, volunteer investigation. Anesth Prog 49: 44, 2002.
- 6-Kashyap VM, Desai R, Reddy PB, Menon S: Effect of alkinisation of lignocaine for intraoral nerve block on pain during injection, and speed of onset of anaesthesia. Br J Oral Maxillofac Surg 49: e72, 2011.
- 7-Lee HJL, Cho YJ, Gong HS, Rhee SH, Park HS, Baek GH: The effect of buffered lidocaine in local anesthesia: a prospective, randomized, double-blind study. J Hand Surg 38A: 971, 2013.
- 8 Phero J, Warren V, Fisher A, Rivera E, Saha P, Reside G, Phillips C, White R: Buffered 1% Lidocaine with Epinephrine Can Be as Effective as Non-buffered 2% Lidocaine with Epinephrine for Maxillary Field Block. In Press J Oral Maxillofac Surg 2017.
- 9- Warren VT, Fisher AG, Rivera EM, Saha PT, Turner B, Reside G, Phillips C, White RP Jr: Buffered 1% Lidocaine with Epinephrine is as Effective as Non-buffered 2% Lidocaine with Epinephrine for Mandibular Nerve Block. In Press J Oral Maxillofac Surg 2017.
- 10-<http://www2.sas.com/proceedings/sugi24/Posters/p221-24.pdf> SAS Users Group International Conference, Florida 04/11-14/1999