Pilot Study: Comparison of Buffered 1% vs. Non-Buffered 2% Lidocaine Used in Dental and Oral Surgical Procedures: Clinical Outcomes Maxilla

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Research Protocol
Pilot Study: Comparison of Buffered 1% vs. Non-Buffered 2% Lidocaine used in dental and oral surgical procedures: Clinical Outcomes Maxilla

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Goal:
Assess the clinical impact of buffered 1% lidocaine with epinephrine as compared to the non-buffered 2% lidocaine with epinephrine used in dental and oral surgical procedures.

Background:
Based on discovery of the anesthetic effects followed by the invention of the hypodermic syringe at the end of the 19th century, cocaine was rapidly adopted as a means of blocking painful sensory impulses during surgical procedures.(1) The discovery of procaine early in the 20th century led to this newer drug replacing cocaine avoiding the potential addictive properties of the latter. Lidocaine and its derivatives, products of the late 20th century, mepivicaine, bupivacaine, and articaine, are widely used today with invasive procedures.(2) Innovation continues allowing clinicians wider use of local anesthetics in the head and neck region. Recently local anesthetics have been administered in vehicles such as liposomes to produce longer term sensory nerve blockade, reducing the need for analgesic drugs, chiefly opioids, to reduce pain.(3) New options for improving local anesthetic effectiveness continue to emerge with a better understanding of the pharmacology.(4) 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.

The addition of a vasopressor, usually epinephrine, to lidocaine and other injected local anesthetics serves to prolong the anesthetic effect by reducing blood flow to the anatomic area and the diffusion of the drug away from the anatomic site of injection. 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. When injected, the low pH causes the “sting” felt by patients on injection. Buffering to a neutral pH eliminates the discomfort. (5-9)

Perhaps more important, the local anesthetic drug is more effective if the pH is closer to the local anesthetic drugs pKa,, approximately 8.0 for the most commonly used, since more of the unionized form of the drug is available to affect the nerve membrane. The drug injected at a neutral pH reduces the need for buffering by tissue fluid while retaining the desired qualities of the vasopressor. The clinical outcome is a rapid onset of the local anesthetic.(8,9)

Anecdotal data suggest that the buffered form of the local anesthetic is more potent at equal dosages, and a lower dosage of the buffered drug might be used with an effect equal to higher dosage not buffered. Clinical data are needed to confirm these anecdotal

data. No published data exist comparing buffered local anesthetics at lower drug concentrations to current dosages commonly used in dental and oral surgical procedures

Until recently, buffering the drug combination with bicarbonate just prior to injection was impractical for the small quantities used in intraoral procedures. However, today we do have a kit capable of efficiently accomplishing this end.(Anutra Medical, NC) This option greatly facilitates clinical studies of dosages common for intraoral injections.

Rationale:
Anecdotal reports suggest buffering lidocaine with epinephrine just before intraoral injection reduces time of onset, results in a deeper anesthetic effect, without the "sting" with injection from a low pH. Additional data are needed to establish clinical important outcomes such as depth of local anesthesia with lower drug dosages of buffered lidocaine with epinephrine as compared to the non-buffered drug combinations currently in wide use.

Clinical pilot studies are proposed as the start of a series of investigations to support or modify the use of the buffered anesthetic for intraoral procedures.
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Specific Aims:
Compare clinical depths of pulpal anesthesia for maxillary molar and canine teeth at 30min intervals post injection after maxillary field block anesthesia with buffered 1% lidocaine with 1/100k epinephrine as compared to non-buffered 2% lidocaine with 1/100k epinephrine.

Hypotheses:
No differences exist in anesthetic depth for pulpal anesthesia after intraoral injection for maxillary field block anesthesia between buffered 1% lidocaine with 1/100k epinephrine as compared to non-buffered 2% lidocaine with 1/100k epinephrine.

Study Time Frame: 6 months
Month One
IRB approvals. Recruit 24 volunteers as subjects. Prepare case-books.
Months Two-Three
Clinical Study
Months Four-Five
Analyze Lab 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 24 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 30min later after
Randomized subjects to be injected orally for maxillary field block (Posterior alveolar, Anterior alveolar, Palatal sensory nerves) alternatively with 4cc of buffered 1% lidocaine with 1/100k epinephrine and 4cc non-buffered of 2% lidocaine with 1/100k epinephrine.
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 resident or clinical OMS faculty will administer the drugs in the OMS clinic.

<u>In week One</u> each subject would receive anesthetic to block the Posterior alveolar, Anterior alveolar, Palatal nerves.
<u>At least a week later</u>, longer than the elimination half-life of the drug lidocaine= 1.5-2hr, injections for the maxillary field block would involve the alternate local anesthetic combination.

Ipsilateral Maxillary teeth to be tested
Pulpal anesthesia first molar
Pulpal anesthesia canine

Timed Assessment: pre, and post-anesthetic administration for Clinical Signs
Onset of Anesthesia Signs: subject reported numb face on injected side.

Assessment: pre, and post-anesthetic administration for pulpal anesthesia
Pulp Tester/electrical stimulation: Record level of first response
Testing interval: Pre-local anesthetic,
Post-local anesthestic at 30min. 90min, 120min.
Response to Cold/ice cone Yes or No
Testing interval: Pre-local anesthetic,
Post-local anesthestic at 30min. 90min, 120min.

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 teeth or oral mucosa

Data Collection: UNC OMS clinic
Timed assessment pre, and post-anesthetic clinical effects
Signs: molar area anesthesia, canine area anesthesia
Pulpal anesthesia first molar: quantitative (pulp tester), qualitative (cold)
Pulpal anesthesia canine: quantitative (pulp tester), qualitative (cold)

Data Collection/Analysis:
Data will be managed by Dr Phillip's staff. Data collection forms and questionnaires 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. 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 …..Effect sizes are currently unknown for the difference in type of injection in blood level or time to onset of anesthesia or pain level post-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 ($\lambda_A = \lambda_A = \lambda$), the differences for every patient will be calculated and multiplied by ½. The two sequences will be compared using a two-sample t test or a Wilcoxon rank sumtest 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

assuming that the Sq(MSE) is 10 using a two group t-test with a 0.05 two sided significance level

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