Comparison of Buffered vs. Non-Buffered Lidocaine used in Dental and Oral Surgical Procedures:

Clinical Outcomes

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RESEARCH PROTOCOL
Comparison of Buffered vs. Non-Buffered Lidocaine used in dental and oral surgical procedures: Clinical Outcomes

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

Background:
Based on discovery of the anesthetic effects and 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) 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)

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.
Perhaps more important, the local anesthetic drug is more effective both in onset and potency if the pH is closer to the drugs pKa, over 8.0. The drug injected at a neutral pH reduces the need for buffering by tissue fluid while retaining the desired qualities of the vasopressor.
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)
Mean maximum blood levels of non-buffered local anesthetic drugs occurs approximately 30min post oral injection.(4) No data exist on peak blood levels for buffered local anesthetics used in dental and oral surgical procedures

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 the peak blood level of lidocaine as compared to the non-buffered drug combination.

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 blood levels at 30min post injection mandibular block with buffered and non-buffered 2% lidocaine with 1/100k epinephrine.

Assess outcomes (pain levels during and post-injection, and onset of anesthesia symptoms) after buffered and non-buffered oral administration of 2% lidocaine with 1/100k epinephrine.

Assess possible topical anesthetic properties of buffered and non-buffered oral administration of 2% lidocaine with 1/100k epinephrine

Hypotheses:

No difference in peak blood levels exist between buffered and non-buffered intraoral injection of 2% lidocaine with 1/100k epinephrine.

Injection of buffered local anesthetic will produce less discomfort for the subject as compared to the drug with a low pH.

Buffered local anesthetic will not produce a topical anesthetic effect

Study Time Frame: 6 months

Month One

IRB approvals. Recruit dental student volunteers. Prepare case-books.

Months Two-Three

Clinical Study

Months Four-Five

Analyze Lab, QOL data

Month Six

Prepare Abstracts, Papers

Methods: Blinded, Randomized Clinical Design

Recruit subjects with IRB approved consent at UNC
Target enrollment 24 subjects
Subjects will serve as their own controls in a cross-over study design.
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, during at 30min intervals and after post-anesthetic clinical signs disappear: targeted lower lip no longer numb.
Randomized subjects to be injected alternatively with 4cc of buffered and 4cc non-buffered oral administration 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, Dr Phero, will administer the drugs in the OMS clinic.
In week One each subject would receive anesthetic to block the inferior alveolar and lingual N; Halstead or Gow-Gates techniques. No Buccal N. block.
At least a week later injections would involve the alternate local anesthetic combination.
Venous blood samples would be drawn from the antecubital fossa 30min post oral injection and assayed for blood lidocaine levels
Timed Assessment: pre, during injection, and post-anesthetic for Clinical Onset of Anesthesia Signs: subject reported molar area numbness and numb lower lip on ipsilateral injected side.
Assessment for pain level on injection; modified Likert-type scale

In addition at each clinic session an assessment of a topical anesthetic effect on contralateral lower lip with 5 drops of the injected drug placed on the clinically dry lower lip mucosa, Outcome yes/no.

Study Subjects:

Inclusion Criteria

Age 20-35 years
ASA I
Willingness to complete QOL instrument
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

Venous blood samples (10cc) will be drawn from the antecubital fossa 30min post oral injection. . Ms Marsh, RN OMS clinic
Timed assessment pre, during injection, and post-anesthetic clinical Signs: molar area anesthesia, incisor area anesthesia, and numb lower lip for topical

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 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 Primary interest is the difference between type of injection – 95% confidence intervals for the difference between injection types will be calculated. For all outcome variables, an assessment of treatment difference, calculated as 1% Buffered minus 2% Non-Buffered, will be performed using Wilcoxon rank sum tests with Proc NPAR1WAY (SAS v 9.3). Statistical significance was set as $P < 0.05$ for all outcomes. Ref: http://www2.sas.com/proceedings/sugi24/Posters/p221-24.pdf

For Lidocaine levels from venous blood, samples will be transported immediately after blood draw to the analytic lab (Macdonald, Jeffrey M-Biomedical Engineering, Medicine)

References:
1-Leonard M: Carl Koller: Mankind's gretest benefactor? The story of local anesthesia. J Dent Res77:535, 1998.
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3-Liposomal bupivacaine: A long-acting local anesthetic for postsurgical analgesia. Formulary 47:212, 2012.
4-Moore et al: Pharmacokinetics of lidocaine with epinephrine following local anesthesia reversal with phentolamine mesylate. Anesth Prog 55:40, 2007.