Effect of Buffered Anesthetic on Physiological Reactions during Dental Injection in Young Children under Deep Sedation: A Prospective, Single Visit, Randomized, Double–Blind Split Mouth Study

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Objectives

The aim of this study is to compare physiological responses in children during the administration of buffered (with sodium bicarbonate) versus non-buffered local anesthetic (LA) control by recording and comparing changes in vital signs and physical movements in pediatric patients undergoing a dental procedure under deep sedation.

Background

The ability to manage pain for the pediatric patient during routine dental procedures can have a profound effect on the child's behavior during current and future appointments. Many adults with dental fears and anxiety recall experiencing negative dental experiences during childhood. However, it is difficult to determine whether successful pain management is achieved in children due to their emotional or cognitive developmental levels. Younger children are often unable to provide reliable feedback on a self-reported pain scale when asked to rate their pain perception. The body's response to stress and anxiety during administration of LA can be detected by changes in physiological responses, such as blood pressure (BP), heart rate (HR) and respiratory rate (RR). The anesthesiology team routinely responds to the child's vitals and movements, that if triggered by pain during the injection of a local anesthetic, may lead to administration of additional sedative medications during treatment. Therefore, by monitoring changes in vital signs during the administration of local anesthetic agents may be more reliable to represent the level of pain that a child receives.

Local anesthetics (LAs) are the safest and the most effective medicine to prevent and manage pain. It has been routinely used for all the dental procedures. LA exists in two forms after injections: unionized form which is lipid soluble and ionized form which is not lipid soluble. Only the unionized form can cross the nerve membrane to block nerve conduction and prevent pain. The equilibrium between the two forms is dependent on the PH of the solution. LA used in dentistry is packaged in acidic solution (PH=3.85) to prevent oxidation of the vasoconstrictor, epinephrine. For anesthesia to take effect, the body must buffer the anesthesia near physiological PH (3.85 to 7.35-7.45). Therefore, the acidity of the anesthesia may delay the onset, contribute to injection burning sensation into soft tissues. Adding bicarbonate (8.4% sodium bicarbonate; approximately 1: 9 ratio) is a simple and affordable way to decrease pain of injections. Empirical evidence including a systematic review has concluded buffered LAs with sodium bicarbonate are more effective than non-buffered LAs in adult patients. However, limited studies have evaluated the effects of buffered LAs in children during procedures in the chair or under sedation and the results are conflicting. One of the reasons could be that children are not able to report pain on a reliable quantifiable scale.

Measuring physiological responses (vital sign changes or physical movements due to pain reflex) upon LA administration could be a more reliable alternative. It has been showed that buffered or unbuffered local anesthetic may signify differences in pain perception that can be noted by measuring physiological responses in children. Pediatric Sedation Unit (PSU) at Rainbow Babies and Children's Hospitals uses propofol to deep-sedate pediatric patients that have extensive dental restorative needs. Because

propofol is a sedative agent without potent and long-lasting analgesic effect, intra-oral LA injections are necessary to control for pain caused during invasive dental procedures in PSU. In addition, children's vital signs are monitored throughout the sedation procedure. In this study, we are going to evaluate and compare the changes in vital signs and physical movements in children during the administration of buffered anesthetic versus nonbuffered LA.

	Inclusion Criteria
1.	Age range: 2-6 year old
2.	Healthy children or children with mild controlled systemic illness
3.	Treatment planned to receive restorative work on both sides of mouth (left vs right) under deep sedation, requiring local anesthetic administration

	Exclusion Criteria
1.	Children present with any illness or symptoms that can alter pain perception such as pain in head and neck area due to TMJ disorders, arthritis, autoimmune diseases.
2.	Antibiotic premedication requirement
3.	History of taking medications (NSAIDs, narcotics, sedatives, and antianxiety or antidepressant medications) that may affect anesthetic assessment.
4.	Has signs of dental pain, odontogenic abscess or facial cellulitis
5.	Allergy to local anesthetics or sulfites

Number of Research Participants

We will enroll 20 children who were patients of the Rainbow Babies and Children's Hospital's (RBC) Tapper Dental Clinic or Dental Clinic of Rainbow Center for Women and Children.

Recruitment Methods

Potential subjects will originate from the clinical practice of the study investigators in Tapper Dental Clinic at Rainbow Babies and Children's Hospital (RBC) or in Dental Clinic at Rainbow Center for Women and Children (RCWC). Research subjects are those patients who are recommended to receive dental surgery under deep sedation by the dentists and this treatment plan is accepted by their legal guardians. The legal guardian(s) of research subjects will be approached by research members right after the consultation appointment at the dental chair side. There are no planned recruitment materials aside from consent forms.

Setting

Research activities will be conducted at UHCMC and outpatient facilities of the study investigators. Recruitment and consent will occur in the clinic of study investigators. Study measurement will occur at RBC in the Pediatric Sedation Unit. Data collection from the EMR will occur at UHCMC.

Study Design

This is a prospective, single visit, randomized, double–blind split mouth study.

Study Procedures

I. All standard of care dental procedures will be followed for enrolled patients except as noted below:

1. IDS will dispense two types of local anesthetic solutionsto dental providers blindly: control solution (non-buffered LA, 2% lidocaine with epinephrine 1:100,000)) and test solution (buffered LA). Both types of solution will be administered to each subject. The types of solutions are labelled with numbers and the research team will remain blind to the type until the study is over.

2. The test solution will be made by a mixing pen called “Onset” (Onpharma Inc., Lost Gatos, CA., USA), which is an FDA- approved device (see attachments). IDS will use a cartridge of 2% lidocaine with epinephrine 1:100,000 alkalinized at 9:1 ratio with a resulting pH of 7.21 using 8.4% sodium bicarbonate solution per manufacturer. This mixing pen Onset will deliver 0.18 mL of sodium bicarbonate solution into the anesthetic cartridge.

3. A dental provider will use a randomized coin flip to choose between the blindly labeled anesthetic agents to anesthetize one side of the mouth (left vs right). In addition, the sides of mouth will also be randomly selected by the toss of a coin. After the appropriate blind anesthetic solution has been selected, the same solution will be used to anesthetize each side of the mouth. In general, one cartridge of local anesthetic is sufficient to provide adequate anesthesia for 2 quadrants, however IDS will provide 2 cartridges of each solution in the event that a second cartridge of the same solution is needed. Maximum recommended dosage for local anesthetic will be calculated and followed for each patient. The provider will subsequently anesthetize the opposite side of the mouth with the opposite solution. The sequence used to administer the anesthetic will be inconsequential as the evaluation of pain will remain consistent due to the separation of nerve innervations in the posterior jaw.

4. Two researchers are required to present for each study. One researcher will be the provider who administrates LA and the other will be recording vital signs and physical movements during the injection (see point IV below).

II. In PSU, patients will be monitored per standard of care. This study does not cause potential interference with sedation monitoring.

III. The only additional device used in this study is Onset mixing system. The Onset device is already FDA-approved for pH buffering dental local anesthetic agents with sodium bicarbonate (see attachments).

IV. Data for this study will come from the EMR, the SDM, and intra-operative data collection sheets.

1. Vital signs, which are already recorded per standard of care at baseline and every 5 minutes, will be recorded manually for significant operative events by researchers on an intra-operative data collection sheet. Significant operative events includes: topical anesthesia, injection (needle puncturing the oral mucosal tissues), delivery of both buffered and conventional local anesthesia, surgical procedures (including tooth preparation, pulpal treatment, and tooth extractions). The necessity of additional local anesthesia delivery will also be noted.

2. Modified Behavioral Pain Scale (BPS) and Pediatric Sedation State Scale (PSSS) are valid and reliable tools in the assessment of pain in the unconscious sedated patient and monitor patient's comfort level during sedation15 , will be recorded on intra-operative data collection sheet by study personnel during the significant operative events as listed above. We removed the ventilation compliance in BPS form since this is not applicable in our study.

Study Timeline

The study timeline for research procedures with a subject is the length of their surgical case in PSU. The only additional time needed on top of their standard of care visits is the time needed to complete an informed consent discussion at the initial examination appointment.

Data to be Collected for your study (AFTER consent and HIPAA Authorization have been obtained)

Age, medical history, diagnosis, vital signs, behavioral pain scale.

Data Analysis Plan

To assess compare the changes of vital signs, pain scores between buffered and conventional local anesthesia, we will use independent t-tests (SPSS v25). We considered a P-value of 0.05 or less significant.

The variability in measurements in this dental surgical population is currently unknown, therefore a power analysis is not appropriate. The data from this study will provide the necessary information to perform a power analysis for a future, larger trial.

Risks to Research Participants

There is minimum risk in alkalizing local anesthetic solution. Sodium bicarbonate will be used as the exact FDA-approved purpose: to alkalize acid solution. There may be additional risks of alkalizing local anesthetic solution that are not known. However, numerous studies have published and no adverse effects have been reported. There is a risk of breach of confidentiality, which we plan to minimize this by de-identifying study data. There is a risk of less pain relief on one side of the mouth than the other due to one solution being less effective than the other.

Provisions to Protect the Privacy Interests of Research Participants

Study recruitment and consent discussion will take place in private as is standard for a clinical appointment with a dentist. Study activities will take place in the privacy of the chairside of Tapper Dental Clinic or dental Clinic or Rainbow Center for Women and Children.

Potential Benefit to Research Participants

There is a possibility of benefit with improved pain control on one side of the mouth, although this cannot be guaranteed. The findings of this study may benefit society in that they may help to demonstrate whether alkalizing local anesthetics can anesthetize pediatric dental patients more effectively.

Withdrawal of Research Participants

Participants could be withdrawn from study without their consent in the event of an error which renders the data yielded inaccurate (for example, monitor malfunction, recording not applied at correct time).

Should participants be withdrawn, their data will be kept but not utilized for the study. All information will be kept in a HIPPA protected file as if they had continued, all privacy maintained in regards to study data.

Alternatives to Participation

The alternative to participation is to not participate in the study and to continue with standard care.

Costs to Research Participants

There are no costs to research participants.

Research Participant Compensation

The research subject who completes the research participation will be awarded with one $25 gift card after the end of the dental sedation appointment.

Provisions to Monitor the Data to Ensure the Safety of Research Participants

As this is a pilot study and we are looking to enroll only 20 patients we will evaluate each patient after data has been collected to assure compliance with the protocol, and that the data set is complete and accurate. A bi-weekly team meeting will be held to discuss any safety events or issues.

Drugs or Devices

Onset (Onpharma) device is FDA- approved for mixing sodium bicarbonate with dental local anesthetic cartridges and it fits the purpose of the study. There is no age restriction for the application of the device.

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