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The Effect of Local Anesthesia When Used in Dental Restorative Cases Under General Anesthesia on Control of Intraoperative Physiologic Parameters and Post-Operative Comfort

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The Effect of Local Anesthesia When Used in Dental Restorative Cases Under General Anesthesia on Control of Intraoperative Physiologic Parameters and Post-Operative Comfort

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Dentistry at Virginia Commonwealth University.

By

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DEPT OF PEDIATRIC DENTISTRY

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Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at Virginia Commonwealth University. REDCap is a secure, web-based software platform designed to support data capture for research studies. [1]

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Abstract

THE EFFECT OF LOCAL ANESTHESIA WHEN USED IN DENTAL RESTORATIVE CASES UNDER GENERAL ANESTHESIA ON CONTROL OF INTRAOPERATIVE PHYSIOLOGIC PARAMETERS AND POST-OPERATIVE COMFORT

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Purpose:

To determine the effect of local anesthesia on post-operative pain and physiologic parameters intraoperatively in patients undergoing dental care under general anesthesia.

Methods:

This study was modeled as a double-blinded randomized control trial. Patients included healthy children under the age of six scheduled for restorative dental treatment under general anesthesia. Patient behavior was evaluated pre and post-operatively using the FLACC score and post-operatively using the Parental Pain Score Measure. Intraoperatively, all participants followed a standardized general anesthesia protocol and were given either local anesthetic infiltration by the dental surgeon performing the surgery or no anesthesia was utilized. Intraoperatively physiologic stability was observed during points of potential stimulation noted by fluctuations in heart rate, and respiratory rate, ETCO2.

Results:

No statistically significant differences in FLACC score and PPPM score were seen between the two treatment groups. Intraoperatively, patients treated with preemptive LA had statistically significant lower heart rates and ETCO2 than those patients who did not receive local anesthesia.

Introduction

General anesthesia is defined as a drug induced loss of consciousness in which a patient is not rousable, even by painful stimulation including surgical stimuli.[2] General Anesthesia is an accepted advanced behavior management technique approved by the American Academy of Pediatric Dentistry (AAPD) used to accomplish extensive dental treatment in young and pre-cooperative children while meeting the overarching goals of providing oral health care in a comfortable, minimally restrictive, safe and effective manner.[3] The use of general anesthesia (GA) in dentistry is advantageous because it provides immobility, amnesia, sedation, and analgesia. Due to these effects children are able to undergo significant dental treatment in a single sitting with relative ease and little memory of the event.[2]

Local anesthesia is the medically induced disruption of neural conduction through the inhibition of the influx of sodium ions through channels within neuronal membranes.[4] Local anesthetics are routinely used in both medicine and dentistry for the prevention of pain during procedures as well as management of post-operative pain. The use of local anesthesia (LA) results in a temporary loss of sensation or pain in a localized region of the body without alteration of the patients level of consciousness.[5] A number of local anesthetics are available for dental use and fall into two general classifications based upon chemical structure– the amide local anesthetics and the ester local anesthetics. Ester anesthetics include procaine and benzocaine. The amide class includes commonly used drugs including lidocaine, articaine, mepivacaine, bupivacaine and prilocaine.[5] Although a number of anesthetics are used in dentistry a smaller selection is used in pediatrics. A study by Brickhouse et al. evaluated local anesthetic usage amongst providers caring for children and noted that despite an increase in articaine usage, lidocaine with epinephrine is still the preferred dental local anesthetic for use in children.[6] Local anesthesia is universally used in dentistry for treatment of non-sedated and sedated pediatric patients in the dental office yet its role for dental treatment under general anesthesia is still relatively poorly defined.

The practice of anesthesia encompasses many modalities to minimize pain and allow for surgical procedures. Historically, general anesthesia and local anesthesia evolved as separate and distant surgical anesthesia modalities. General anesthesia has served as the main approach to surgical pain for the last 150 years.[7] It was not until the 1980's, when combining the two anesthesia techniques was explored, with new evidence from animal studies. In one of these studies Woolf et al. tested central pain sensitization and hypersensitivity in decerebrated rats testing pain reflexes between those that received and those that did not receive local anesthesia. They found that peripheral injury leads to central spinal cord changes and this change could be prevented through use of a preemptive sensory neuronal block with local anesthesia. These results suggested that the clinical use of preemptive peripheral neuronal blockade with regional anesthesia is beneficial in reducing surgical pain and post injury pain hypersensitivity.[8] The preemptive use of regional anesthesia during GA has many potential benefits which overall increase the safety profile of GA. Regional blockade of nociceptive pathways under GA helps to reduce the amount of sensory information transmitted to the Central Nervous System and therefore reduces the amount of potent anesthetic agent needed to produce a favorable state of surgical anesthesia. Additionally, the concomitant use of LA with GA has shown to reduce subjective post-operative pain and the use of analgesics in the recovery period.[7]

Pain management is an important part of any surgical field and has evolved greatly due to the complexity of the neuronal pathways for pain modulation. In surgical settings, acute pain arises subsequent to local tissue trauma which results in an acute inflammatory response. This response activates a vast complement of receptors in neuronal terminals of nociceptive sensory neurons which, triggers depolarization of the neuronal membrane and conduction of an action potential to the spinal and medullary dorsal horns. It has been found that repeated nociceptive stimulation can alter the sensitivity level of both the peripheral neuronal terminals and centrally in the spinal and medullary dorsal horns. This alters the threshold of stimulation necessary to generate an action potential. This sensitization is defined as the reversible heightening of peripheral and central neuronal excitability which in turn increases the synaptic response and reduces synaptic inhibition. This can result in neurons firing after low- intensity stimulation or continued firing for a long duration after stimulation has been removed. It has been thought that the use of preemptive LA, by blocking nociceptive input from the site of injury to the CNS, prevents sensitization changes at the spinal cord level.[7] This effect was highlighted in the study by Mamiya et al. who found that the coadministration of LA and GA minimized intraoperative hemodynamic changes seen intraoperatively during bilateral mandibular sagittal splitting osteotomy and decreased the depth of anesthesia needed to complete surgery therefore decreasing stimulation of the autonomic-endocrine-immune system and reducing potential for spinal cord hypersensitivity.[9] As a result, consideration should be given to combining preemptive LA to allow for reduction of potential anesthetic maintenance during dental cases under GA.[5] Preemptive anesthesia has many proposed benefits, however its effectiveness can be limited if an insufficient degree of preventive blockade is achieved, if a partial preemptive effect of opioids is already in effect during the procedure, or if performed in a surgery with low intensity noxious stimuli.[10] Boric et al. evaluated a wide array of interventions for post-operative pain management in children. This systematic review showed that LA is efficacious in the reduction of post-operative pain following surgery in various areas of medicine including urological procedures, abdominal surgery, and spinal surgery. However, the benefit of local anesthesia for dental treatment under GA is still unclear and requires more research to assess true value in the prevention of central sensitization and post-operative pain management.[11]

For pain to be reliably treated it requires an appropriate diagnosis including the pain source, level, and nature.[12] It has been shown that pain is underestimated and undertreated in children because of the inability for young children to verbally convey and relay information. Children possess unique cognitive strategies including the tendencies to exaggerate or suppress pain leading to inaccurate diagnosis. Observational pain scales are widely used in pediatrics since they utilize non-verbal forms of expression such as facial expression and body movement to reduce bias and increase pain assessment reliability.[13] A number of observational pain scores have been validated for use in young children for postoperative pain evaluation including; Child Facial Coding System, Objective Pain Scale (OPS), Evaluation Enfant Douleur (EVENDOL), Children and Infants Postoperative Pain Scale (CHIPPS), and The Faces, Legs, Activity, Cry and Consolability Scale (FLACC). It is important to use validated age appropriate pain scores in children so that their pain can be appropriately assessed and managed.[12] The most widely used of these scores is the FLACC score. This behavioral pain assessment scale evaluates five categories of pain behaviors: (1) facial expression (2) leg movement (3)activity (4) crying and (5) consolability. Scores are derived by scoring each category on a scale of 0-2 , to reach an overall score of 0-10 with a score of zero representing no pain and a score of 10 representing heightened pain.[14,15] This observational scale was evaluated in a study by Chang et al. where they found, in general, the FLACC score tends to underestimate to a degree the severity of pain a child may be experiencing.[13] This is important to consider when using this scale as a sole tool for pain assessment.

Dental rehabilitation under GA has shown to cause a moderate to severe amount of pain in the post-operative period.[16] Cantekin et al. found 43% of dental rehabilitation patients have post-operative throat or mouth pain, and 51% of patients had a FLACC score greater than 0 at discharge and 27% had a FLACC score of 3 or greater at time of discharge.[15] Costa et al. found similar findings noting that 45% of children had a FLACC score greater than 0 at discharge and 29% had a FLACC score of 3 or more. They also noted significant discomfort in the immediate post-operative period associated with the number of crowns and space maintainers a patient had placed in surgery.[17] Similar results were seen by Hu et al. who noted significantly higher dental pain in patients who had greater than 14 teeth treated compared to patients who had less than 14 teeth treated. However, in their study they noted a 82% of patients suffered from post-operative dental pain which is a significantly higher number of patients than previous studies which could be attributed to the lack of pre-emptive analgesics in the protocol.[18] This higher level of reported post-operative pain was seen in a study by Keles et al. who noted that 90% of patients have post-operative pain after dental surgery. They saw an increase in pain based on procedure performed with increased pain in patients who received pulpotomies in comparison to other restorative dental procedures.[19]

Despite the extensive use of general anesthesia in pediatric dentistry, no definitive guidelines exist for the use of local anesthetic in these procedures. The AAPD guidelines merely note that local anesthesia (LA) has been reported to reduce pain in the postoperative period with marginal evidence.[2] To date, there have been very mixed results as to the use of local anesthetic in general anesthesia cases and provider usage greatly varies. Townsend, Martin et al. found 51% of dentists administer local anesthesia less than half of the time during general anesthesia cases, 76% administered LA before treatment when used, and 89% via local infiltration when used. It was also shown that dentists and pediatric dentists who completed residency training used less LA during GA cases. They also showed that 21% of dentists never use LA during GA cases and 8% always use LA during GA cases.[20] Townsend, Hagan et al. found that 90% of dental anesthesiologists prefer local anesthesia at least some of the time and 40% prefer LA use with very rare exceptions. In this study, anesthesiologists who preferred LA supplementation felt that it was important for stabilization of interoperative vital signs, allowed for decreased depth of general anesthesia, helped to avoid activation of deep pain pathways, and improved patient recovery.[21] This variability in use also exists in the profession of oral surgery where a study by De Verbizier et al. noted that 59% of oral surgeons used local anesthesia in cases under general anesthesia of which 46% administered preoperatively, 24% used intraoperatively, and 11% administer post-operatively.[22] From these studies we can see that LA usage for dental cases under general anesthesia varies greatly and rationale is based on varying limited evidence.

In current literature, there are only a few studies published assessing the effectiveness of LA intraoperatively in controlling post-operative pain in GA dental cases. Atan et al. found that the number of surgical procedures performed was significantly associated with an increase in post-operative discomfort and the use of local anesthesia decreased post-operative discomfort. Additionally, they noted a tendency for children who were given LA during GA to experience post-operative dizziness.[23] This finding of increased post-operative distress with LA was also noted by Al- Bahlani et al.[24] Leong et al. noted significantly lower pain in patients that received intraligamental injection of LA the first night post operatively, and no significant difference in postoperative anxiety between the groups.[25] Sammons et al. noted a similar but less sustained decrease in post-operative pain with intraligamental LA finding an immediate decrease in pain post-operatively that was no longer significantly different 1 hr post-operatively.[26] Noble et al. noted the same improved post-operative symptoms in patients with LA with 37% of patients who received LA behavior was rated as "happy" at discharge as opposed to 16% in the no LA group.[27] Conversely, Coulthard et al. noted no significant differences in postoperative pain between groups on waking from GA, 30 mins post operatively, and 24 hours post-operatively.[28] Similar findings were seen in a study by Townsend, Ganzberg et al. noting no difference in need of postoperative pain medication between those groups that received LA with IV ketorolac and those that received ketorolac alone. Additionally, they found no significant difference in post-operative symptoms between those that received LA and those that did not. However, they noted a few post-operative negative comments in patients that received LA attributed to the sensation of numbness.[29] Moness et al. specifically looked the use of LA for management of post-operative pain in a randomized control trial and noted no statistically significant differences in post-operative pain between those that receive LA and those that did not in both restorative and extraction groups.[30] This finding was also noted by McWillams et al. however, they also noted that LA decreased the amount of post-operative bleeding and need for suctioning.[31] Additionally, Andrzejowski et al. and Gazal et al. noted this same lack of significant difference between treatment groups with the use of bupivacaine swabs in extraction cases.[32,33] A systematic review of the literature was performed by Parekh et al. however, due to the significant variability between the few studies present on the topic, the effect of LA under GA could not be determined nor the effect estimated.[34]

Lastly, the effects of LA use on control of physiologic stability intraoperatively have not been well studied in dental cases. Watts et al. noted a statistically significant difference in end tidal carbon dioxide (EtCO2) in the cases where dental extractions were performed. It was found that usage of LA in these cases showed better stability of EtCO2. No statistically significant difference was found in observed respiratory rate and heart rate.[35] Additionally, El Batawi et al. noted statistically higher heart rate and respiratory rate when cutting dentinal tissue, tooth extraction and pulpotomy, and an increase in EtCO2 during dental extraction and pulpotomy in those patients who had not received LA.[36] Very limited research is available on this subject and more research is needed to confirm the validity of the results of these studies.

Current guidelines for local anesthetic use during dental cases under general anesthesia are not specified. In the literature, there are mixed reports regarding local anesthetic use with some addressing solely intraoperative effects, or postoperative pain. Additional research is needed due to the limited numbers of studies in the area and the lack of evidence for definitive guidelines.

The purpose of this study is first; to determine the effect of local anesthesia on postoperative irritability and pain management in dental cases under general anesthesia and second, to determine the effect of local anesthetic use on control of physiologic parameters intraoperatively in patients undergoing dental care under general anesthesia. This information is important because currently no guidelines exist to define usage of local anesthetics in dental cases under GA. Current practitioner usage is due to clinical judgement and the practice varies widely across the United States.[20] The goal of this study is to provide some answers to whether local anesthesia is beneficial intraoperatively as a means to help control physiologic parameters, and provide evidence if local anesthesia usage helps control postoperative pain, as well as ease of recovery in Post Anesthesia Recovery Unit (PACU) and at home. This information will be obtained through the use of pain scores pre and post operatively in the hospital, parental behavior questionnaire for postoperative evaluation and evaluation of physiologic parameters during times of increased stimulation intraoperatively.

Methods

This study was modeled as a double-blinded randomized control trial. Patients included healthy children (ASA 1 or ASA 2) without any history of behavioral issues under the age of six who had been treatment planned to have exclusively restorative treatment including prefabricated crowns, space maintainers and the use of rubber dam clamps.

Dental treatment was performed under general anesthesia at the Children's Hospital of Richmond Brook Road and Children's Pavilion campuses. Study approval was obtained from Virginia Commonwealth University Institutional Review Board. Research candidates were recruited from patients presenting for or needing full mouth dental rehabilitation. Patients were recruited by dentists from VCU Pediatric Dental Clinic and Children's Hospital of Brook Road Pediatric Dental Clinic during GA consultation appointments. During the consultation appointment, all potential research candidates where briefed on the study and provided a copy of the research consent for personal review. On the day of surgery, patients were approached by the nursing staff to avoid potential coercion and were presented the opportunity to participate in the study after having time to evaluate the research at home. Parents were given the opportunity on day of surgery to ask any further questions to both the dental surgeon and nursing staff before consenting to be included in the study. All consents were obtained prior to surgery including research participation, anesthesia and surgical consent. Participant information was collected and enclosed in a Google Doc Sheet on a secure VCU server. All patients were assigned a participant number which was used to randomize participants and de-identify patient information for data collection. Participant numbers were used to randomize patients assigning them into local anesthesia or no local anesthesia treatment groups. Block randomization with a block size of 4 was completed to allow for relatively equal distribution of patients between treatment groups. Randomized groups were assigned to participant numbers and enclosed in confidential envelopes to be opened and reviewed by the dental surgeon and disclosed with the anesthesiologist only. All other research team members, as well as parents or guardians, were blinded to the participants treatment group.

On the day of surgery, Patients were evaluated preoperatively using the FLACC pain/behavior scale by the preoperative nurse who was blinded to the candidates group in the study. Postoperatively, patients were evaluated by the nursing staff blinded to the patients' treatment group in the Post Anesthesia Care Unit (PACU) before discharge using the same initial pain/behavior scale, the FLACC scale. This pain scale was selected for the study, since it is the pain measure currently used at the Children's Pavilion Hospital and Brook Rd Campuses, all nursing staff are familiar and routinely use this scale as part of their practice. Also, the FLACC scale has been shown to be one of the most effective and widely used pain scales in evaluating patients post-operative pain in children of the ages represented in our study.[12,14]

FLACC Behavioral Scale

Categories	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to, distractable	Difficult to console or comfort
Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between zero and ten.			

Figure 1: The FLACC Score

The FLACC Score is an observational pain scale targeted to assess pain in young children (2-7) through assessment of the behavioural expression of pain in each of the five categories)FACE, LEGS, ACTIVITY, CRY and CONSOLABILITY). Each subset is scored with a range of 0-2, with zero representing an area displaying little distress, to two representing a significant pain/distress expression. All five categories are totaled for an overall score ranging from 0-10. [14]

Intraoperatively, participants followed a standardized general anesthesia protocol developed by a group of VCU pediatric anesthesiologists representing standard general anesthesia practice for dentistry cases at VCU Children's Pavilion Hospital and Brook Rd. Preoperatively, patients were given preemptive analgesic, acetaminophen, PO. It has been shown that increased post-operative pain management can be achieved with preemptive verses preventive usage in pediatric dental anesthesia.[37] General anesthesia was then induced with sevoflurane. A propofol bolus was administered after IV placement to facilitate nasotracheal intubation without neuromuscular blockade, followed by potent agent maintenance of sevoflurane. Phenylephrine nasal drops were given if bleeding was present from nares, and antiemetics were administered if it was specifically indicated. Intravenous fluids were maintained throughout the case at a rate of 10-20 cc/kg. No narcotics were administered. After intubation, a full series of radiographs were obtained. The throat pack was placed, and intraoperative baseline vitals were recorded by the anesthesiologist.

Intraoperatively, patients were given either local anesthetic, 2% Lidocaine with 1:100,000 epinephrine, or no anesthesia was utilized. The patient treatment group was contained in a secure envelope only to be shared with the dental surgeon and anesthesiologist and was not disclosed until the start of surgery. Patients randomized to the LA group followed a standardized LA protocol and were given 2% Lidocaine with 1:100,000 epinephrine at all quadrants of potentially stimulating treatment up to a max dose of 36mg of Lidocaine, or 1.7ml total at the start of the case. Intraoperatively, the patients' physiologic stability was observed during points of potential stimulation, i.e. crown and space maintainer seating and rubber dam clamp placement, in each quadrant in the mouth. At each of these intervals, the stimulating event was announced by the dental surgeon performing the case and the anesthesiologist recorded the specific quadrant, treatment type, and fluctuations including the time, heart rate, respiratory rate, end tidal CO_2, as well as need for anesthesiologist intervention. Observations were recorded by the anesthesiologist overseeing the case during the procedure on a standardized record log. Fluctuations were evaluated based upon standard deviation from the patients' baseline vitals at the start of surgery.

Intra-Operative Evaluation:

Stimulating Event:	**Time:**	**RR**	**BP**	**HR**	**ETCO2**	**Anesthesiologist Intervention:**
Baseline Intraoperatively						
Rubber Dam Clamp (1)						
Rubber Dam Clamp (2)						
Rubber Dam Clamp (3)						
Rubber Dam Clamp (4)						
Crown Seating (Quad 1)						
Crown Seating (Quad 2)						
Crown Seating (Quad 3)						
Crown Seating (Quad 4)						
Crown Seating (Maxillary Ant.)						
Crown Seating (Mandibular Ant.)						
Other:						
Other:						
Other:						
Other:						

(To be completed by anesthesiologist, nurse anesthetist, resident or dental assistant throughout dental case.)

Please record time corresponding to stimulating event (peak reading within 3 mins after stimulation). If a stimulating event is encountered outside of those listed (seating of band and loop or distal shoe etc.) Please add and list under "other". If any significant anesthesiology intervention is needed in response to change in vitals at any stimulating periods please denote (Y) in the anesthesiologist intervention column.

Figure 2: Intra-Operative Evaluation Anesthesia Record.

This table was used as a data collection sheet intraoperatively completed by the Anesthesiologist, Nurse Anesthetist or Anesthesia Resident throughout the dental case denting changes at potentially stimulating events as indicated by the Dental Surgeon performing the case

Upon the completion of surgery, the patients' parent or guardian was given a standard set of post-operative instructions prior to discharge encompassing the possibility of anesthetized tissues, and were presented both written and verbal. Patients were then discharged home when stable. That evening, the parent or guardian was contacted by phone by a research member, blinded to the study group, for post-operative evaluation. They were asked a series of questions from the Parental Post-Operative Pain Measure (PPPM) targeted to objectively assess the patients' post-operative discomfort. The PPPM is a 15 item questionnaire validated to access post-operative pain in children based on objective behaviors, indicative of pain, demonstrated by a child that can be readily accessed by their parent. The PPPM can range in a score from 0-15 with one point being assigned to each positively answered question on the questionnaire. Using this scale a score of 6 or greater is indicative of clinically significant pain. [38,39]

PARENTS' POSTOPERATIVE PAIN MEASURE (PPPM)

Children sometimes have changes in behavior when recovering from surgery. The following is a list of behaviors that your child may or may not have exhibited while recovering from surgery between ______ and ______ today. For each of the behaviors below, circle the appropriate response, *yes* or *no*.

When your child was recovering from surgery between ______ and ______ today, did s/he . . .

1)	Whine or complain more than usual?	Yes	No
2)	Cry more easily than usual?	Yes	No
3)	Play less than usual?	Yes	No
4)	Not do the things s/he normally does?	Yes	No
5)	Act more worried than usual?	Yes	No
6)	Act more quiet than usual?	Yes	No
7)	Have less energy than usual?	Yes	No
8)	Refuse to eat?	Yes	No
9)	Eat less than usual?	Yes	No
10)	Hold the sore part of his/her body?	Yes	No
11)	Try not to bump the sore part of his/her body?	Yes	No
12)	Groan or moan more than usual?	Yes	No
13)	Look more flushed than usual?	Yes	No
14)	Want to be close to you more than usual?	Yes	No
15)	Take medication when s/he normally refuses?	Yes	No

Figure 3: Parental Post-Operative Pain Measure.

This pain measure is targeted for use by parents and children have returned home after surgery. It has been validated to be an appropriate tool to accurately assess children's pain post-operatively. This tool was initially validated for use in children 7-12 but revalidated and extension has been completed to allow it to serve as an accurate pain measure in children 2-6 in addition. The PPPM can range in a score from 0-15 with one point being assigned to each positively answered question on the questionnaire. [38,39]

At the completion of the surgery all information collected as part of this study was de-identified and labeled with a participant number and stored in a secure locker until logged digitally on a secure server. Patient identifiers were stored separately on a secure google doc to maintain patient confidentiality throughout the study.

Differences between groups at baseline including the baseline FLACC, the number of teeth treated, the procedure time, and pain measures postoperative were compared using nonparametric Kruskal-Wallis tests due to a small sample size. Biometric measures at stimulating events were modeled using repeated measures ANOVA while adjusting for repeated measures on the same patients. Significance level was set at 0.05. All analyses were performed in SAS EG v.8.2 (SAS Institute, Cary, NC).

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Results

A total of 10 patients were enrolled into the study. Five patients were randomized to receive LA four patients did not receive LA, and one participant had to be excluded due to need for extractions. Baseline FLACC scores did not differ between the groups (p-value=0.6547), nor did number of teeth treated (p-value=0.2663). There was a significant difference in the procedure time between the two groups (p-value=0.0275). Procedures with local anesthesia took significantly longer than those without. The median procedure time for procedures with local was 1:38 (IQR: 85-118 minutes) compared to 1:03 (IQR: 57.5-71.5 minutes) for cases without. Postoperative FLACC scores ranged from 0 to 10 with an IQR of 0-4. When calculating the change in FLACC scores from baseline to post-operative, the median change was 0 (IQR: 0-4). By group, the median for those that received local anesthesia was 0 (IQR: 0-4) and 1.5 (IQR: 1-4) for those with no local, indicating a post-operative FLACC that was higher by 1.5 than baseline. Change in FLACC score was also not significantly associated with number of teeth treated (Spearman Correlation=-0.34, p-value=0.3720).

Post-operative phone calls could only be completed for 5 of the 9 subjects (2 from LA group, 3 from No LA group). Post-operative pain scores were not significantly different between the two groups (p-value=0.7389), nor were they significantly associated with the number of teeth treated (Spearman Correlation=0.44, p-value=0.4535).

Table 1: Comparison of Groups

	Local (n=5)	**No Local (n=4)**	**P-value**
	Median (IQR)	Median (IQR)	
Teeth Treated	7 (4-10)	4.5 (2.5-6)	0.2663
Procedure Time (minutes)	98 (85-118)	63 (57.5-71.5)	0.0275*
Baseline FLACC	0 (0-2)	0 (0-1)	0.6547
Change in FLACC	0 (0-4)	1.5 (-1, 4)	0.9004
Postoperative Pain	5 (3-7)	3 (3-7)	0.7389

Repeated measures ANOVA models were used to estimate the biometric measures (heart rate, respiratory rate, end tidal CO2, systolic blood pressure, and diastolic blood pressure) based on the biometric measure value at baseline, treatment group, and the type of stimulating events (crown seating or rubber dam placement). Results are presented in Table 2. Treatment group was significantly associated with the intraoperative heart rate values (p-value=0.0205). Those who received local anesthesia demonstrated a significantly lower average heart rate than those who did not receive local anesthesia by an average of 9.45bpm (95% CI: 2.04-16.85). Respiratory rate was significantly associated with baseline respiratory rate (p-value=0.0029). Baseline respiratory rate was the only variable significantly positively associated with respiratory rate (p-value=0.0001). For a 1 breath increase in respiratory rate at baseline, there was an average increase in RR at stimulating events of 0.58 (95% CI: 0.41-0.75). End tidal CO2 was significantly associated with treatment group (p-value=0.0197). The group that did not receive LA had a higher average ETCO2 by an average of 3.45 mmHg(95% CI: 0.77-6.12). Systolic blood pressure was significantly associated with baseline systolic BP measure (p-value=0.0019). An increase in baseline systolic BP was associated with an average increase intraoperatively of 0.60 (95% CI: 0.32-0.88). Diastolic blood pressure was not significantly associated with any of the measures. Complete results are presented in Table 2. Figures 1 demonstrates the individual patient biometric measures throughout the procedure. Figure 2 displays the boxplots for the groups by stimulating event.

Table 2: Summary of Repeated Measures ANOVA Models for Intraoperative Biometric Measures

	Heart Rate	**Respiratory Rate**	**ETCO2**	**Systolic BP**	**Diastolic BP**
Baseline Value (P-value)	**0.2327**	**0.0001 ***	**0.0663**	**0.0019***	**0.4421**
1 unit increase	0.35 (0.26)	0.58 (0.07)	0.14 (0.06)	0.60 (0.11)	0.10 (0.12)
Group (P-value)	**0.0205 ***	**0.9904**	**0.0197 ***	**0.7638**	**0.5965**
Local	113.91 (1.96)	22.13 (1.01)	42.56 (0.69)	88.96 (1.05)	39.62 (1.06)
No Local	123.36 (2.26)	22.11 (1.16)	46.01 (0.8)	88.44 (1.21)	38.68 (1.23)
Event Type (P-value)	**0.1473**	**0.5211**	**0.6997**	**0.1512**	**0.5336**
Crown Seating	116.22 (2.02)	22.64 (1.05)	44.08 (0.69)	87.45 (1.06)	38.64 (1.08)
Rubber Dam	121.05 (2.16)	21.60 (1.12)	44.49 (0.74)	89.96 (1.12)	39.67 (1.14)

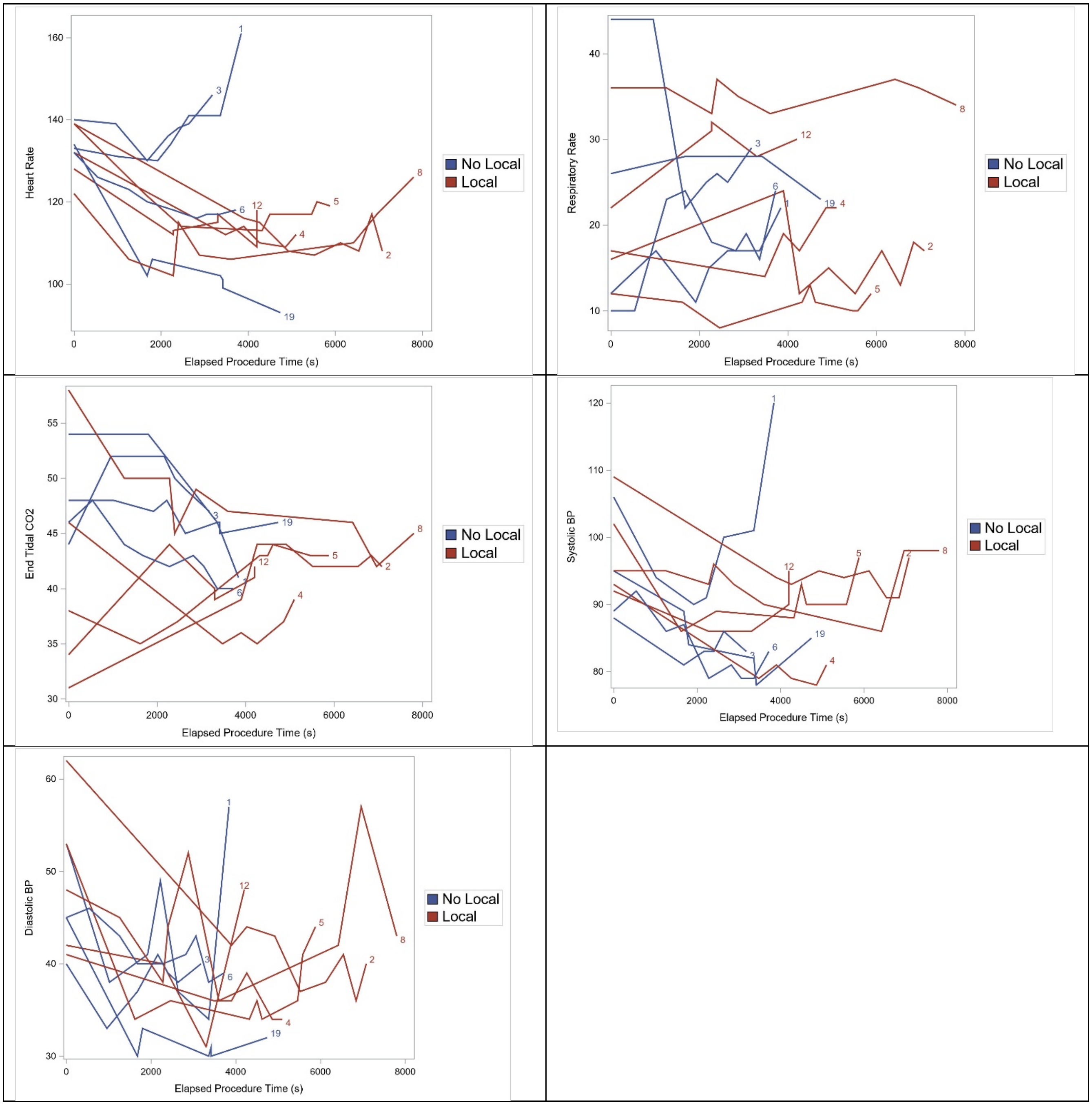

Figure 4: Individual Patient Biometric Trends

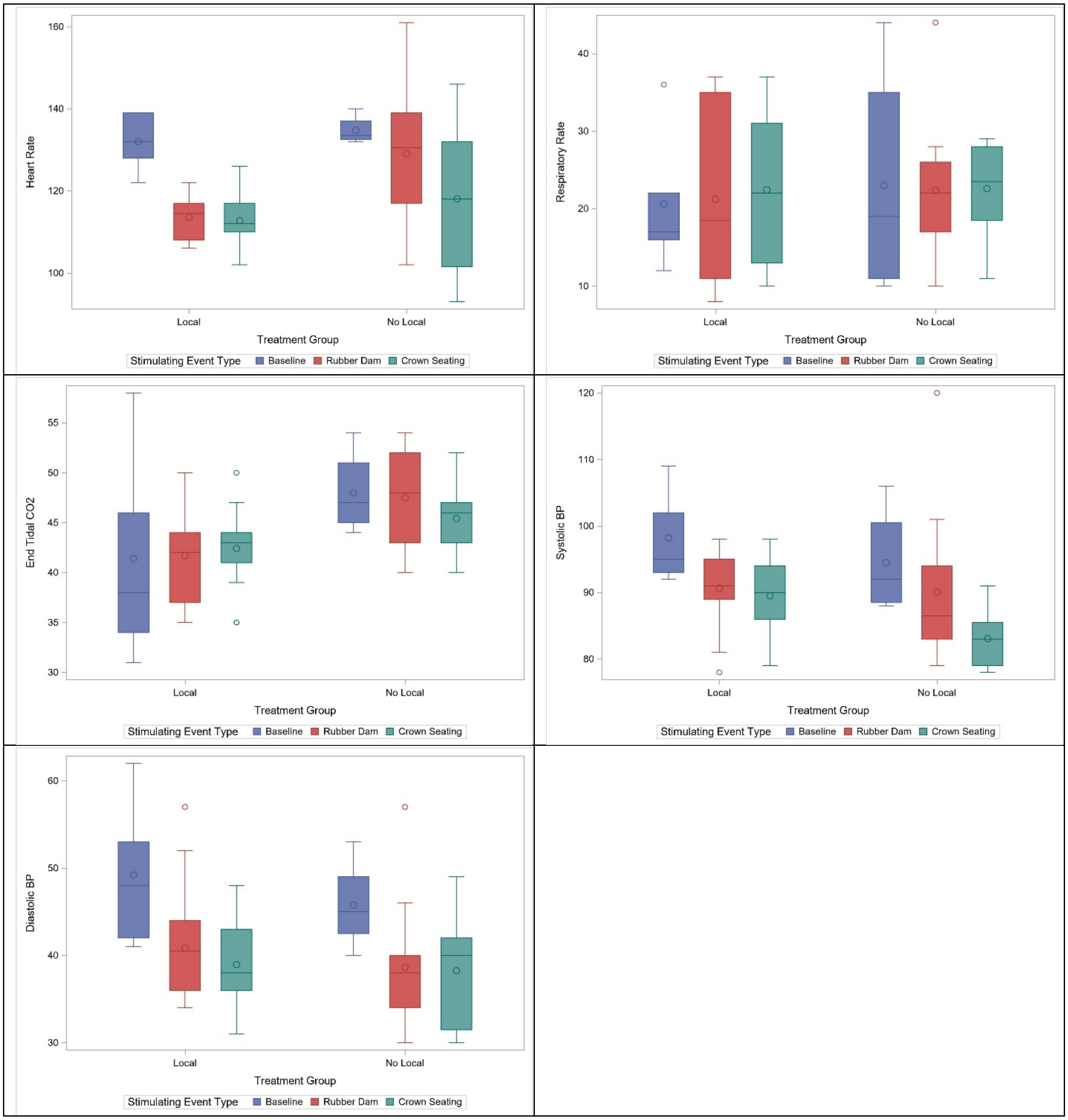

Figure 5: Biometric Values by Treatment Group and Stimulating Events

Discussion

In this study, we noted longer average treatment times and more treatment rendered for the patients randomized to the local anesthesia treatment group. Participants randomized to the local anesthesia group had cases that lasted 100 mins on average compared to an average case length of 64.5 mins in the no local anesthesia group. This range in times is consistent with that seen in the literature for typical dental cases completed under general anesthesia.[40] Additionally, participants randomized to the local anesthesia group had treatment consisting of a median of 7 teeth treated, as opposed to a median of 4.25 teeth treated in the no local anesthesia group. Although not significant, this difference can relate to clinically significant differences in treatment time. This trend occurred due to random assignment and is believed to be unrelated to the experimental variable tested in this study. Additionally, 4 of the 5 cases randomized to the local anesthesia group had treatment involving more complex anterior crown treatments as opposed to only 2 of 4 in the no local anesthesia group. This assignment happened by chance due to random assignment, but can account for the discrepancy in treatment times between the local anesthesia and the no local anesthesia group. On average, an increase in time for dental general anesthesia procedures is related to the number of teeth treated and type of treatment rendered. This finding directly correlates with the results we have found in this study. [40]

In this study, no statistically significant difference in the increase in immediate post-operative discomfort/distress, as denoted by the post-operative FLACC score, between the two treatment groups was noted. However, accounting for each patients' individual baseline FLACC score, a median change from baseline to post-operatively of 0 was seen in the LA group versus 1.5 in the no LA group. This change indicates that on average, patients in the local anesthesia group had less immediate post-operative distress or discomfort than those that did not have local anesthesia, although not significant. The findings of this study are supported by other findings in the literature by Coulthard et al., Townsend et al., Moness et al. and McWillams et al. which noted no significant differences in post-operative discomfort or distress between the those that received local anesthesia and those that did not receive local anesthesia. [28–31]

Post-operative pain scores for patients enrolled in our study ranged from a FLACC score of 0-7. This correlates to post-operative pain ranging from little to none to severe post-operative pain.[41] This finding is supported by Wong et al. who noted that patients receiving dental treatment under general anesthesia have a moderate to severe level of post-operative pain.[16] This finding is also supported by Cantekin et al who noted that 51% percent of dental patients have a post-operative pain score greater than 0 at discharge and 27% have a pain score greater 3 at discharge.[15] This finding is also corroborated by Costa et al. who found that 45% of children who have undergone dental rehabilitation had a FLACC score greater than 0 at discharge and 29% had a FLACC score of 3 or greater at time of discharge.[17] In this study, immediate post-operative pain denoted by FLACC score was not associated with the number of teeth treated. Generally, literature has shown increased levels of pain with an increased number of teeth treated. However, these findings were only noted to be significant when over 14 teeth were treated.[18] In our study, we noted the median IQR of teeth treated in the local anesthesia group was 4-10, and in the no local anesthesia group was 2.5-6 which is much less than the number needed to be statistically significant in previous studies, which is likely why this finding was not observed in this study.[18]

As an additional pain measure in this study, the PPPM was used to evaluate long term post-operative pain. These measures were recorded during the post-operative phone call after the patient had returned home after surger,y therefore representing a long term post-operative pain measure evaluation. In this study, relatively low number of post-operative pain data was obtained due to the low response rate of parents for post-operative calls. We found that approximately 50% of parents answered the call for the post-operative pain evaluation. Despite the low response rate, we found that this number is similar to the typical response rate seen with our general anesthesia cases for our patient demographic. In this study, no statistically significant differences were noted between the two groups in PPPM scores after surgery. This study noted the post-operative pain measure scores with an IQR of 3-7, indicating post-operative pain ranging from slight to slightly significant.[38,39] This is important to note in order to be able to provide patients' parents which reasonable expectations in regards to post-operative pain level for children under going dental surgery.

Additionally, as a part of this study, we evaluated interoperative physiologic parameters. It was noted that patients treated with preemptive local anesthesia had heart rates approximately 10 BPM less at times of stimulating events that those who did not receive local anesthesia (113.91BPM vs 123.36BPM). This finding was also noted by El Batawi et al. who noted statistically higher heart rate in patients when cutting dentinal tissue, tooth extraction and pulpotomy in those patients that had not received LA.[36] This finding of increased heart rate at times of potentially stimulating events can be noted as a potential indicator of intraoperative patient pain. However, at the levels noted in our study no additional anesthesiologist intervention was needed at any the points of stimulation.

Also, we noted that patients who did not recieve local anesthesia had statistically significantly higher EtCO2 than those patients who received local anesthesia. This trend suggests increased level of comfort in these patients as the lower EtCO2 likely indicates the patient is taking smaller relaxed breaths. Additionally, this trend can highlight the direct association between EtCO2 and cardiac output which is largely heart rate dependent in children. This similar finding was noted by Watts et al. which noted a statistically significant difference in end tidal carbon dioxide (EtCO2) in the cases where dental extractions were performed with an increased level of EtCO2 seen in those patients which did not receive preemptive analgesia.[35] This similar finding was seen by El Batawi et al. which noted an increase in EtCO2 during dental extraction and pulpotomy in those patients who had not received LA.[36] Additionally, in this study we noted no statistically significant differences in respiratory rate, systolic blood pressure or diastolic blood pressure. These findings correlate with those seen by Watts et al. which noted no significant interoperative vital sign changes aside from EtCO2 intraoperatively.[35] In this study, differences were present between the local anesthesia and the no local anesthesia groups, however the values observed do not present perceived clinical significance at this time. However, with greater sample size with the trends observed may have clinical implications in future research.

This finding of increased heart rate and CO2 at times of potentially stimulating treatment can be noted as a potential indicator of intraoperative patient pain. However, at the levels noted in our study, no additional anesthesiologist intervention was needed at any the points of stimulation. As a result, the benefit of local anesthesia for dental treatment under GA is still unclear and requires more research to assess true value in the prevention of central sensitization and post-operative pain management in dental cases. [10]

The last item evaluated in this study was interoperative stimulation incited by crown seating and rubber dam clamp placement. No significant differences were noted in all physiologic parameters for crown seating and rubber dam clamp placement. However, rubber dam clamp placement on average did result in a heart rate increase 5 BPM greater than crown seating (121.05 vs. 116.22). This finding is unexpected as rubber dam placement is generally viewed as a benign treatment protocol. This is important to note in a clinical setting for both sedated and non-sedated patients as this treatment could be potentially very stimulating and good local anesthesia should be obtained for the comfort of the patient.

Due to the statistically significant beneficial effects of local anesthesia on vital sign stability intraoperatively, benefit can be seen with the administration LA at the start of treatment in cases under general anesthesia when used. This timing can achieve both intraoperative physiologic stability effects in coalition with the desired post-operative pain effects in invasive treatments such as extractions. This finding is important as discrepancy still exists in the timing of LA usage for dental treatment under general anesthesia in multiple areas of dentistry. Townsend et al. found that 76% of pediatric dentists administer LA start of dental cases under GA and De Verbizer et al. noted that only 46% of oral surgeons administer LA preoperatively during dental surgery under GA.[20,22] Further research is needed in this area to be able to provide standardized guidelines for local anesthesia usage in dental surgery treatment under general anesthesia.

One of the weaknesses of this study is the exclusion of patients requiring dental extractions. This decision was made as currently it is standard protocol at VCU School of

Dentistry to utilize local anesthesia in cases requiring extractions. One of the problems with this stipulation is that it is often unknown if dental extractions will be necessary until after radiographs the day of surgery once the patient is already under general anesthesia. In this study, one patient was excluded after enrollment due non-restorable teeth that were unable to be diagnosed on clinical exam pre-operatively. Additionally, we found patient recruitment difficult and slow for the study. We found many parents were not receptive to participation in the study and suspected that due to the Covid- 19 pandemic had apprehension in regards to participation in any additional medical procedures or protocols at this time. Due to the preliminary results of this pilot study further research is warranted and it is expected that it will have greater recruitment in future after stabilization of the Covid-19 pandemic.

Future areas of research include studies on post-operative pain management for dental cases based on extent and type of dental treatment rendered, and pain scale reliability for post-operative dental pain in children. Additionally, further studies on intraoperative vital sign stability with preemptive local anesthesia in dental cases under general anesthesia would help to support some of the trends noted in this study and increase the breadth of knowledge on the subject to facilitate the formulation of future dental guidelines. Lastly, little is known regarding the effects of deep pain pathway activation in minor surgeries including dental procedures. Further animal studies are recommended to achieve better information on this topic.

Conclusion

In conclusion, no statistically significant differences in the increase of immediate post-operative discomfort as denoted by the FLACC score or longer term discomfort as denoted by the PPPM score were seen between the two treatment groups was noted in this study. However, patients in the local anesthesia group had marginally less immediate post-operative distress or discomfort than those that did not have local anesthesia, although not significant. Additionally, we found local anesthesia provides better intraoperative vital sign stability particularly in regards to heart rate and ETCO2. It was noted patients treated with preemptive local anesthesia had heart rates approximately 10 BPM less at times of stimulating events that those who did not receive local anesthesia (113.91BPM vs 123.36BPM).) Also, patients who did not receive local had statistically significant higher ETCO2 than those patients who received local anesthesia. We noted no statistically significant differences in respiratory rate, systolic blood pressure or diastolic blood pressure however, in other studies in the literature statistically significant differences in RR have been seen.[36]. These vitals can be associated with pain intraoperatively however, though significant, these values provide marginal clinical relevance at this time. With greater sample size, the trends we are seeing may have clinical implications in future research. Therefore we believe that due to the findings seen in this pilot study further research is warranted to increase the breadth of knowledge on the subject to facilitate the formulation of future dental guidelines

This study is important as clinical guidelines do not exist at this time for the use of local anesthesia in dental cases under general anesthesia cases. Further information is needed to improve provider rationale for local anesthesia use and ultimately to gather enough evidence to develop clinical guidelines. This study provides better evidence as to local anesthesia and patients level of irritability post operatively and the effect local anesthesia has on patients vital stability intra operatively.

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