A Comparison of Emergence Agitation/Delirium in Pediatric Dental Patients with Sevoflurane and using Sevoflurane with a Washout Propofol Technique.

THESIS

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By

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Abstract

Background: Emergence Agitation/Delirium (EA/ED) is a frequent finding in younger children who undergo general anesthesia for surgical procedures. The objective of this double-blind controlled study was to determine if providing for the elimination of sevoflurane prior to the end of the surgery, with a washout propofol technique, is effective at reducing the incidence, severity, and probability of EA/ED.

Methods: Twenty children, aged 2-7, who were scheduled for full mouth dental rehabilitation under general anesthesia were enrolled in this study and divided into two groups. The control group received a standard general anesthetic using sevoflurane. In contrast, the test group received the same general anesthetic until the last 30 minutes of the procedure, at this time the sevoflurane was turned off and an adequate level of anesthesia maintained via the intermittent administration of propofol. Using this approach most, if not all, the administered sevoflurane could be eliminated prior to emergence. Primary outcome measures were the incidence of EA/ED using the Watcha scale during the recovery process. Secondary outcome measures were duration of recovery and the incidence of Post-Operative Nausea and Vomiting (PONV).

Results: All twenty children completed the study. EA/ED, using a Watcha score of ≥ 3, was found in 8 children (50%in the control group, 30% in the test group, $P = 0.650$). When using a Watcha score of 4, five children were found to exhibit EA/ED (40% in the

control group and 10% in the test group (p = 0.305). The probability of a child experiencing EA/ED at any time during recovery using Watcha ≥ 3 was 33.8% in the control/sevoflurane group and 9.94% in the test/Propofol group (P = 0.107). Using a Watcha score of 4, the probability of a child experiencing EA/ED at any time during recovery was 15.1% in the control/sevoflurane group and 1.43% in the test/Propofol group (P = 0.058). The average recovery time for the control group was 34.5 minutes and 41.5 minutes for the test group (P = 0.038). No patient in either group experienced an incidence of PONV.

Conclusion: Although this pilot study did not show a statistically significant difference in the incidence, severity, and probability of EA/ED in children recovering from dental surgery under general anesthesia using a standard volatile anesthesia versus the 'wash-out' technique described in this study using propofol, a trend toward a lower incidence of EA/ED in the group receiving propofol was recognizable. The data collected from this small study suggests that the magnitude of improvement may be statistically significant and warrants the extension of this project to include a larger test population.

Dedication

This document is dedicated to my fiancé Alex Linden. You are my guidance, inspiration, support, and drive. Without you none of this would be possible. I love you.

Acknowledgments

I would like to acknowledge all of my committee members.

To Dr. Smiley for allowing me the opportunity to learn and practice my sometimes outlandish ideas, while also being a positive role model both in life and anesthesiology.

To Dr. Johnston for his work with data processing and his willingness to help at a moment's notice, without his effort my project would have been lost.

To Dr. Prior for being my constant companion in my thirst for anesthesiology knowledge. You have been an inspiration to me and I am forever grateful to have had the opportunity to learn, grow, laugh, and struggle together. It has been an amazing ride.

Vita

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Publications

Comparing Potential Early Caries Assessment Methods for Teledentistry *BMC Oral Health* 2013, **13**:16

Fields of Study

Major Field: Dentistry(Anesthesiology)

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Objectives

To compare and contrast the incidence of emergence delirium/agitation (EA/ED), and time until discharge, in a pediatric population recovering from general anesthesia with either a single volatile agent (sevoflurane) alone or the same volatile agent washed out by the intravenous administration of propofol.

Background and Rationale

General anesthesia (GA) is utilized for pediatric dental patients to provide high quality, comprehensive, and humane dental care when the delivery of dental treatment using more routine methods (Local anesthesia (LA), nitrous oxide sedation, etc.) is not an option. The circumstances in which general anesthesia may be necessary include, but are not limited to, patients of a young age, complex medical/physical/mental conditions, extensive treatment needs, uncooperative or combative behavior (age appropriate or not), and severe situational anxiety [1, 2].

Unfortunately, a significant percentage of pediatric patients emerging from general anesthesia experience a variety of behavioral changes that have been described variously as excitement, delirium and agitation [3, 4]. To complicate the situation, researchers are not consistent in describing such events, where the child is irritable, uncompromising, uncooperative, incoherent, inconsolably crying, moaning, or thrashing in a dissociated state of consciousness, as emergence agitation/emergence delirium [5]. Such children, for a short time, often appear not to recognize familiar objects or people, including family members [4]. Of the changes in behavior patterns observed, combative behavior has been more frequently described than either simple restlessness and/or incoherence, all of which have often been grouped collectively under the heading emergence agitation/emergence

delirium (EA/ED) [3]. These behavioral fluctuations usually occur soon after emergence from general anesthesia, are generally self-limiting, resolving spontaneously within 30 minutes [5, 6].

The exact incidence of EA/ED after general anesthesia varies widely in the literature but is generally reported in the region of 10 - 50% [3, 6-9]. However, there have been articles published suggesting a figure as high as 80% [10, 11]. EA/ED has been associated with almost all anesthetics but the more rapid acting volatile agents, sevoflurane and desflurane, have been the most implicated [3, 6-8, 10-14]. Despite the evidence showing an increased incidence of EA/ED with rapid acting volatile agents, the slower equilibrating isoflurane has also been shown to be associated with this phenomenon [3, 8, 15].

EA/ED can result in injury to the child, accidental removal of a surgical dressing, prolonged or new hemorrhage from the surgical site due to increased blood pressure seen with EA/ED, and importantly, parental dissatisfaction with the anesthetic [4]. Despite the fact that EA/ED is self-limiting, many practitioners may feel inclined to treat the behavior with medications, most of which prolong further patient recovery and often complicate the transfer of patient care from the anesthesiologist to the parent at the end of the procedure. The literature is especially aware of this in the outpatient dental environment where pediatric dentists believe parenting styles have changed [16]. More recent parenting developments seem to tolerate much less emotional or physical ‘harm’ being

associated with dental care, whether real or imagined, compared to previous generations [16].

Most of the literature has been unsuccessful in distinguishing between emergence agitation (EA) and emergence delirium (ED) [4]. Thus, for the purpose of this project, EA/ED will be treated as one entity.

The etiology for EA/ED is still not completely understood [4] and explains in part the lack of a uniform strategy for prevention or treatment being found in the literature or practice[4]. Many different medications have been proposed, and often researched, for prevention and to a lesser extent treatment. These have included narcotics, benzodiazepines, alpha-2 agonists, hypnotics, NSAIDS, to name just some of the more popular groups.

A recent literature review found no previous study that has comparatively investigated EA/ED and recovery time in total inhalational and modified inhalational/intravenous anesthetics for outpatient dental surgeries.

This study aims to match two groups having similar operative needs with two similar anesthetic techniques that differ only in the terminal portion of the anesthetic delivery. The control group was maintained, as is usual practice, on an inhalational-based anesthetic (sevoflurane) until completion of the surgery, whereupon the agent was

stopped and the patient allowed to wake up and recover. In the test group the agent (sevoflurane) was turned off 30 minutes before the anticipated end of treatment and the patient's state of anesthesia then maintained alone with the intravenous anesthetic agent propofol. In this manner a significant amount of time was provided during which the patient could eliminate most, if not all, of the inhalation agent.

In this study we hypothesize that the incidence of EA/ED can be greatly reduced by providing a short washout period for the elimination of the volatile agent (sevoflurane) and during this period maintaining the anesthetic level of the patient through the administration of a propofol until the completion of the case. In addition by titrating propofol to the patient's presentation/hemodynamic responses, we hypothesize that this technique will not increase the required postoperative patient care time from extubation until discharge of the patient from the facility.

Methods and Research Design

Inclusion criteria for this study consisted of the following parameters; ASA I or ASA II, free of any developmental delays or psychiatric conditions (including ADHD), and between 2 to 7 years of age. All patients who participated in this study met these criteria.

Study patients were selected from patients scheduled for full mouth dental rehabilitation under general anesthesia at two separate locations, the Ohio State University Pediatric Dental Clinic and the Dental Surgery Center at Nationwide Children's Hospital. The patients had to meet the above inclusion criteria. Due to a difference in protocols between the two study sites, the control group of this study was selected at the Ohio State University Pediatric Dental Clinic, and the test group from the Dental Surgery Center at Nationwide's Children's Hospital. Therefore, patients were not randomly assigned to a control or test group. Their treatment location determined which group they would belong to. IRB approval was received prior to the commencement of the study and consent was obtained from the families of all patients.

Induction of general anesthesia was the same for all patients. Patients were brought to the surgery suite with their guardian. General anesthesia was introduced through the inhalation of sevoflurane in oxygen via a simple facemask. After the patient had reached

an adequate level of anesthesia a bolus of propofol (1-2 mg/kg) was given and a nasotracheal endotracheal tube placed. The concentration of sevoflurane was started at 1.0 MAC (minimum alveolar concentration – a level required by the average member of the population) and titrated to maintain an adequate level of anesthesia. Additionally, nitrous oxide was used for all patients at a concentration of 50%. To help minimize post-operative nausea and vomiting (PONV), all patients received 0.1 mg/kg of dexamethasone at the start of the procedure. For postoperative pain, all patients received 0.05 to 0.1 mg/kg of morphine at the start of the procedure, not to exceed a maximum dose of 2 mg, and Toradol (ketorolac) given shortly before extubation, dosed at 1 mg/kg up to a total of 30 mg.

The control group had anesthesia maintained with sevoflurane (started at 1 MAC and titrated to effect) and Nitrous Oxide (50%). At the completion of surgery, sevoflurane and nitrous oxide were turned off and the patient given 100% oxygen. Following standard protocols, and after a purposeful response, the patient was extubated awake.

The experimental arm of the investigation aimed to provide an environment where the patient would eliminate the volatile agent prior to being extubated. This was accomplished by discontinuing the administration of sevoflurane and switching to Propofol boluses titrated to maintain anesthesia for approximately 30 minutes prior to the anticipated end of surgery. The propofol boluses were dosed at 0.5 to 2 mg/kg, depending on clinical presentation, to maintain an adequate level of anesthesia. The administration

of a 50% mixture of oxygen and nitrous oxide was continued until the end of the procedure. After completion of surgery the administration of both propofol and nitrous oxide was terminated and the patient was allowed to awaken from anesthesia breathing 100% oxygen. Upon termination of the procedure the patient was extubated at a similar level of anesthesia and in a similar manner as described for Group A.

During each patient's anesthetic experience the following were recorded for all patients; age, weight, gender, mask acceptance score, treatment points, morphine dose, amount of local anesthesia used, treatment time, the duration of anesthesia that was maintained using propofol boluses, incidence of post-operative nausea and vomiting, and recovery time.

The patient's acceptance of anesthesia was documented using the Mask Acceptance Score and this value was determined by the anesthesia provider [17].

Table 1: Mask Acceptance Scores

Very good, immediate acceptance, no struggle	1
Good, slight resistance, minimal struggle	2
Moderate, struggle against mask, passive/minimal active physical restrain	3
Difficult, refused mask, active physical restrain necessary	4

Treatment points (Tx points) were calculated by assigning points for certain procedures and then totaling all of these points together to provide a cumulative score for each patient (see table 3).

Table 2: Treatment points

Extraction	2
Stainless steel crown or veneered stainless steel crown	2
Direct restoration	1
Pulpal therapy	1

This data was then given to a statistician for analysis and specifically to determine if statically significant differences were found between the groups.

The presence of EA/ED was determined using the Watcha scale [18]. This was performed and assessed by an observer blinded to the group assignment of the patient. Assessments were made every 5 minutes during recovery until discharge. Previous literature designates EA/ED in a patient having a single Watcha score of 3 or 4 [18].

Table 3: Watcha Behavior Scale for Emergence Agitation/Delirium

Calm	1
Crying but can be consoled	2
Crying cannot be consoled	3
Agitated and thrashing around	4

Specifically, four separate patient outcomes were followed and recorded. The incidence of EA/ED determined by any patient having a single score Watcha score of 3 or 4 during any time, including recovery, was recorded. Finally, the probability of a patient experiencing EA/ED during any 5-minute moment in their recovery process was also determined. EA/ED was initially diagnosed in patients who had a Watcha score of 3 or 4 and then again using the more rigorous scoring of 4 to determine an episode of EA/ED.

All data was then analyzed and interpreted by an independent statistician.

Results

Twenty children were enrolled in this pilot study, ten in each arm of the study. The mean, standard deviation, variance and 95% confidence intervals were calculated for each listed category and data-appropriate statistical tests conducted. A probability (p) value < 0.05 was accepted as representing a statically significant result.

Table 4: Patient Characteristics and Duration of Anesthesia/Surgery (±standard deviation)

	Control Group	Propofol Group	P value
Age (yrs)	4.41 (±0.91)	4.62 (±0.61)	0.552
Weight (kgs)	18.2 (±3.05)	16.3 (±1.77)	0.105
Gender (female/male)	4/6	6/4	0.821
Mask Score	1.9 (±1.3)	1.7 (±1.1)	0.605
Tx (pts)	19.6 (±3.10)	18.1 (±6.61)	0.527
Morphine (mg/kg)	0.069 (±0.025)	0.07 (±0.028)	0.934
Local (ml)	0.66 (±0.232)	1.04 (±0.890)	0.215
Tx time	101.0 (±8.33)	73.0 (±9.55)	0.040
Propofol time	NA	26.5 (±4.12)	-
PONV	0	0	1.000
Recovery time	34.5 (±6.43)	41.5 (±7.47)	0.038

The only statistically significant differences found between the groups were treatment (Tx) time and recovery time. The control group had an average treatment and recovery time of 101.0 minutes and 34.5 minutes, where as the test group had an average treatment

and recovery time of 73.0 minutes and 41.5 minutes respectively (p = 0.040 for Tx time and p = 0.038 for recovery time). A deeper look into the statistics of the two statically significant findings (Tx time and recovery time) are listed in tables 5-7 (Tx time) and 8-10 (recovery time).

Table 5: Treatment (Tx) time

	Control Group	Propofol Group
Mean	101.0	73.00
Std Dev	26.33	30.20
Std Error	8.328	9.551
Minimum	60.00	35.00
Maximum	145.0	140.0
95% CL mean	82.16/119.8	51.39/94.61
95% CL std dev	18.11/48.07	20.77/55.14

Table 6: Treatment time variances for Tx time

Method	Variances	DF	T Value	Pr > t
Pooled	Equal	18	2.21	0.0403
Satterthwaite	Unequal	17.67	2.21	0.0406

Table 7: Equality of variances for Tx time

Method	Num DF	Den DF	F Value	Pr > F
Folded F	9	9	1.32	0.6894

Table 8: Distribution of Tx time

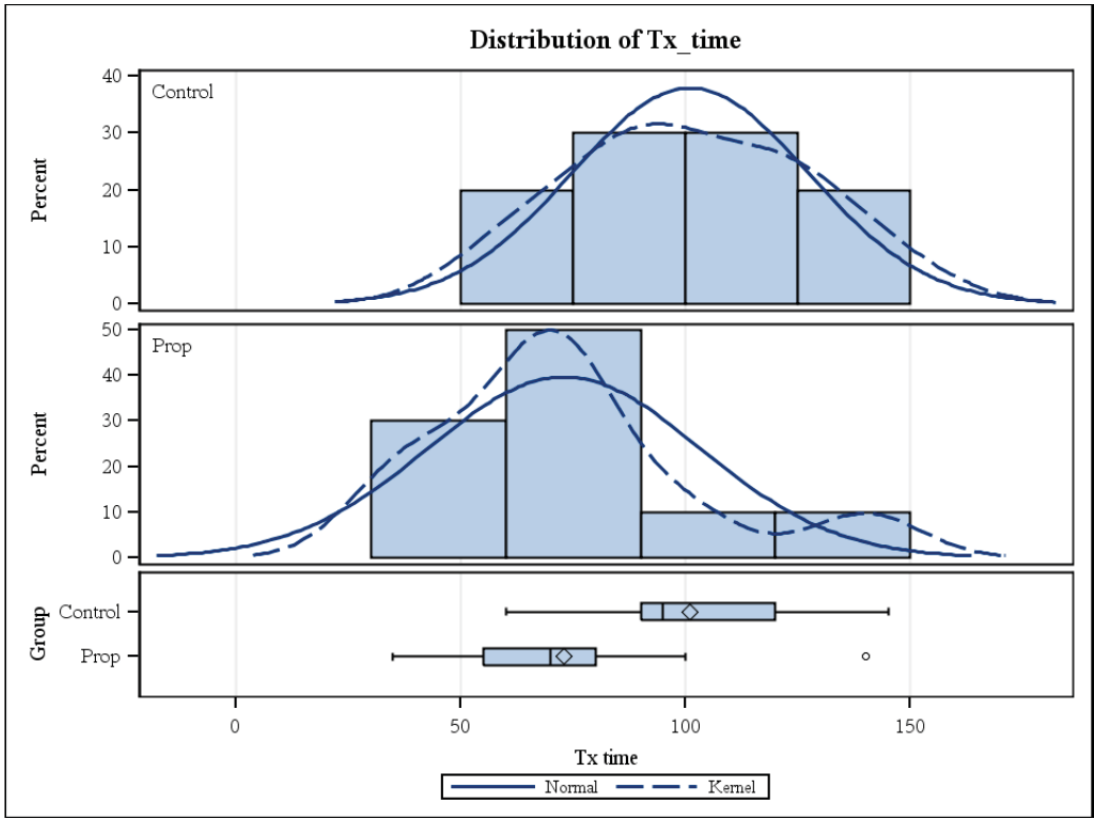


Table 9: Recovery time

	Control Group	Propofol Group
Mean	34.50	41.50
Std Dev	6.433	7.472
Std Error	2.034	2.363
Minimum	25.00	30.00
Maximum	45.00	50.00
95% CL mean	29.90/39.10	36.16/46.84
95% CL std dev	4.425/11.75	5.140/10.31

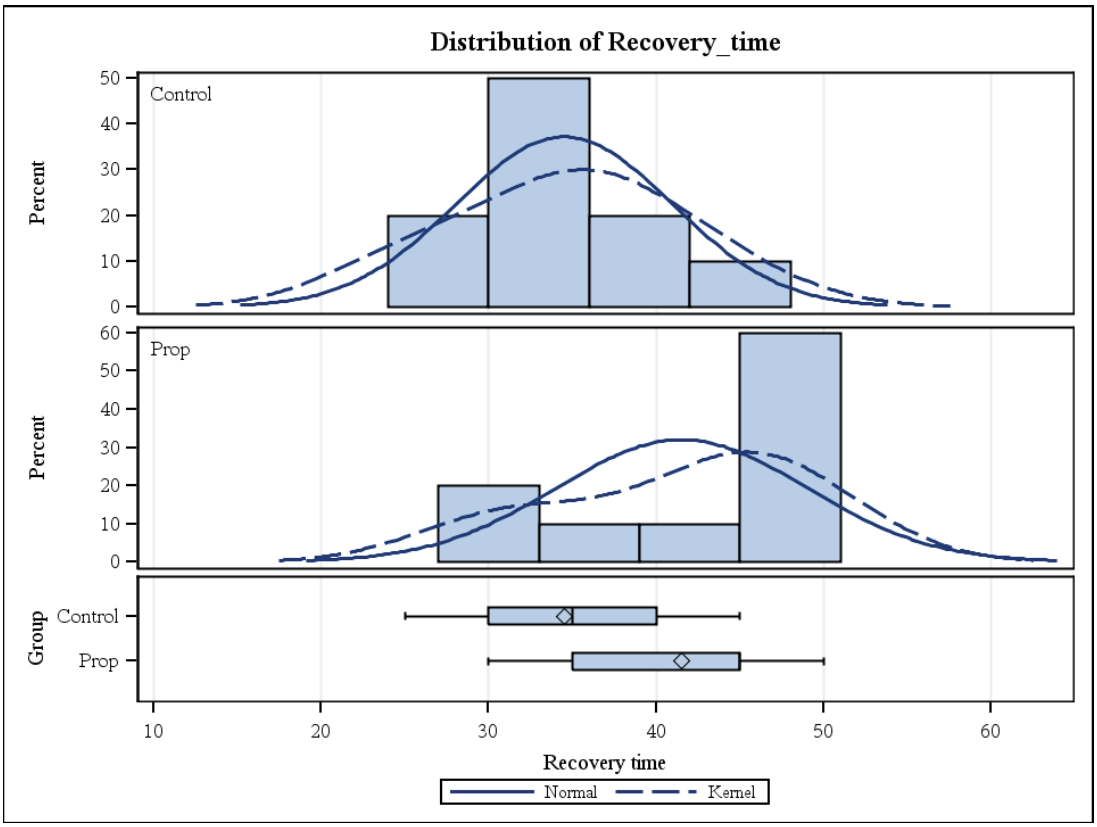
Table 10: Treatment time variances for recovery time

Method	Variances	DF	T Value	Pr > t
Pooled	Equal	18	-2.24	0.0376
Satterthwaite	Unequal	17.611	-2.24	0.0379

Table 11: Equality of variances for recovery time

Method	Num DF	Den DF	F Value	Pr > F
Folded F	9	9	1.35	0.6629

Table 12: Distribution of recovery time



No patient in either group experienced any case of PONV.

A total of 8 patients (40%) experienced emergence delirium when using a single Watcha score of ≥3 to define EA/ED. Five of these patients were in the control group and three were in the test group (50%: 30%) (p = 0.650). The relative time a patient spent with a Watcha score of 3 or 4 at any given point during their recovery was 33.81% for the control group and 9.94% for the test group, see table 13 (p = 0.107). A total of 5 patients (25%) experienced emergence delirium when using a single Watcha score of 4 to define EA/ED. Four of these patients were in the control group and one was in the test group (40%: 10%) (p = 0.303). The chance of a patient having a Watcha score of 4 at any given point during their recovery was 15.1% for the control group and 1.43% for the test group, see table 4 (p = 0.058).

Table 13: Patient Scores for Emergence Agitation/Delirium during Recovery

	Control Group	Propofol Group	P value
EA/ED Frequency WACHA 3 or 4	5 (50%)	3 (30%)	0.650
EA/ED Frequency WACHA 4	4 (40%)	1 (10%)	0.303
Relative time of Watcha Score of 3 or 4	0.338 (±0.125)	0.0994 (±0.0581)	0.107
Relative time of Watcha Score 4	0.151 (±0.197)	0.0143 (±.0143)	0.058

Table 14 lists all patient results found in this study in regards to EA/ED. FREQ refers to the number of 5-minute recovery periods experienced for that patient. GE3 is the odds-ratio of any one recovery-score being a Watcha 3 or 4 and GE4 is odds-ratio of any one

recovery score being a Watcha 4. Finally, Ever3or4 records whether or not a patient had at least one Watcha score of 3 or 4, and Ever4, if the patient had at least one Watcha score of 4, at anytime during the study.

Table 14: Watcha results for all patients

Obs	Group	Patient	_FREQ_	GE3	GE4	Ever3or4	Ever4
1	Control	1	8	0.25000	0.00000	Yes	No
2	Control	2	7	0.71429	0.42857	Yes	Yes
3	Control	3	9	0.00000	0.00000	No	No
4	Control	4	6	0.66667	0.33333	Yes	Yes
5	Control	5	8	0.00000	0.00000	No	No
6	Control	6	10	0.00000	0.00000	No	No
7	Control	7	8	0.87500	0.37500	Yes	Yes
8	Control	8	6	0.00000	0.00000	No	No
9	Control	9	8	0.87500	0.37500	Yes	Yes
10	Control	10	6	0.00000	0.00000	No	No
11	Prop	1	7	0.42857	0.14286	Yes	Yes
12	Prop	2	10	0.00000	0.00000	No	No
13	Prop	3	7	0.00000	0.00000	No	No
14	Prop	4	10	0.00000	0.00000	No	No
15	Prop	5	10	0.00000	0.00000	No	No
16	Prop	6	11	0.00000	0.00000	No	No
17	Prop	7	8	0.00000	0.00000	No	No
18	Prop	8	10	0.00000	0.00000	No	No
19	Prop	9	11	0.45455	0.00000	Yes	No
20	Prop	10	9	0.11111	0.00000	Yes	No

Tables 15 – 17 list the data for the control and the test groups for GE3, the relative time a patient experienced a Watcha score of 3 or 4 with each group.

Table 15: GE3

Group	Control Group	Propofol Group
Number	10	10
Mean	0.3381	0.0994
Std Dev	0.3952	0.1837
Std Err	0.1250	0.0581
Minimum	0.000	0.000
Maximum	0.8750	0.4545
95% CL mean	0.0554/0.6208	-0.0320/0.2308
95% CL std dev	0.2718/0.7214	0.1264/0.3354

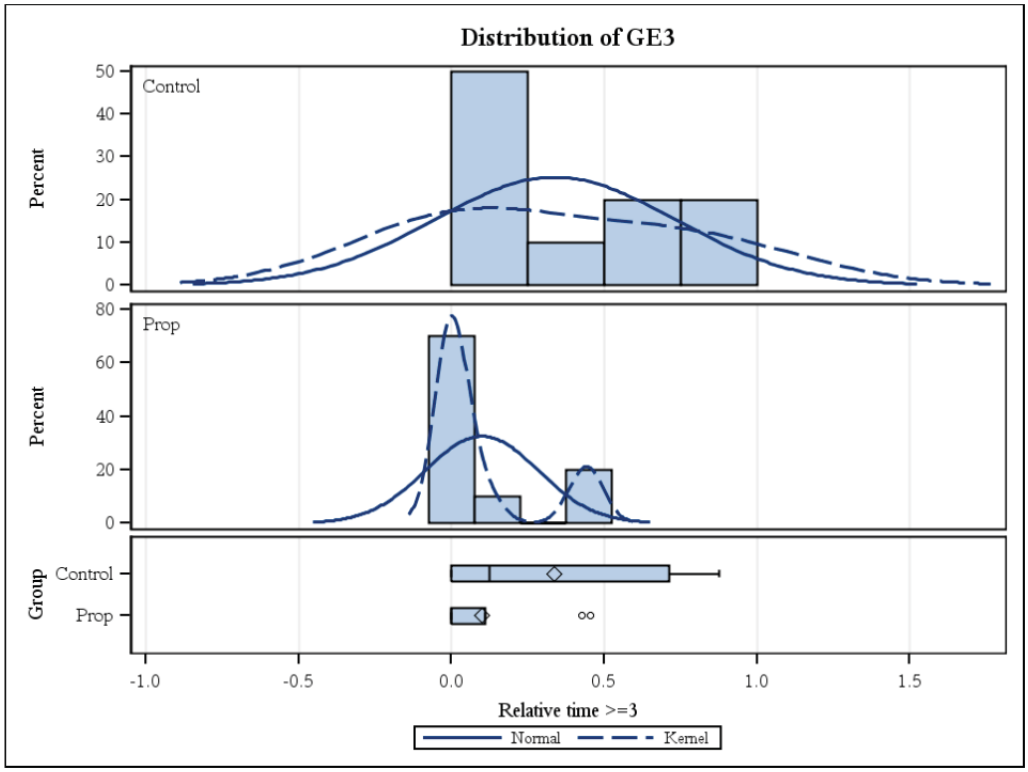
Table 16: GE3 variances

Method	Variances	DF	T Value	Pr > t
Pooled	Equal	18	1.73	0.1004
Satterthwaite	Unequal	12.717	1.73	0.1074

Table 17: Equality of variances for GE3

Method	Num DF	Den DF	F Value	Pr > F
Folded F	9	9	4.63	0.0323

Table 18: Distribution of GE3



Tables 19 – 22, list the detailed data for GE4, the relative time a patient experienced a Watcha score of 4 with each group.

Table 19: GE4

Group	Control Group	Propofol Group
Number	10	10
Mean	0.1512	0.0143
Std Dev	0.1965	0.0452
Std Err	0.0621	0.0143
Minimum	0.000	0.000
Maximum	0.4286	0.1429
95% CL mean	0.0106/0.2917	-0.0180/0.0466
95% CL std dev	0.1351/0.3587	0.0311/0.0825

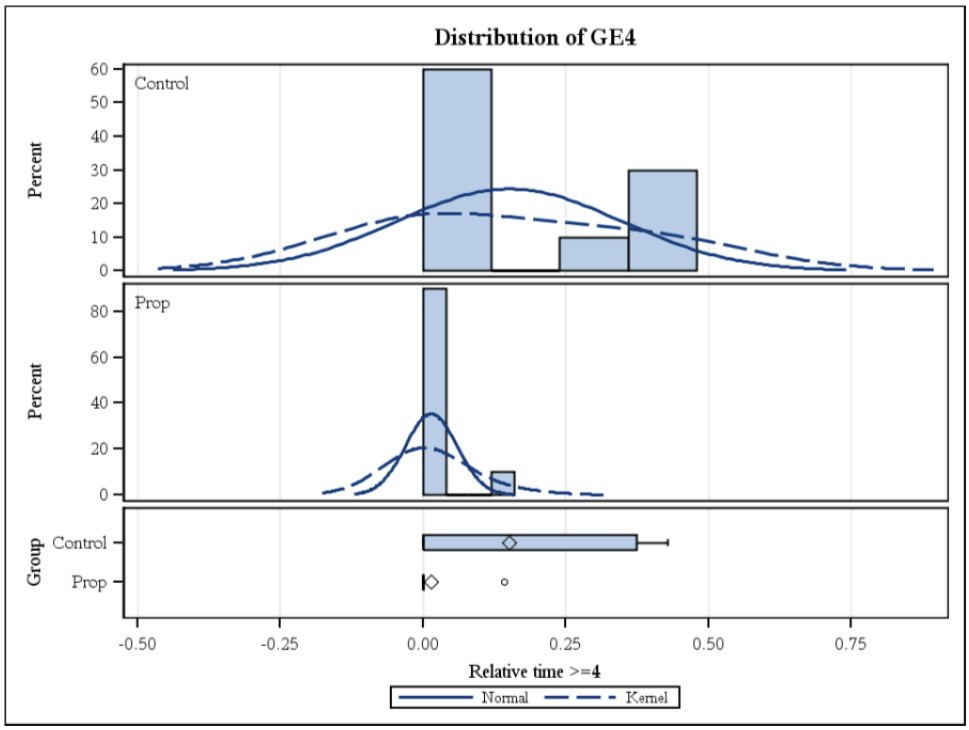
Table 20: GE4 variances

Method	Variances	DF	T Value	Pr > t
Pooled	Equal	18	2.15	0.0456
Satterthwaite	Unequal	9.9489	2.15	0.0575

Table 21: Equality of variances for GE4

Method	Num DF	Den DF	F Value	Pr > F
Folded F	9	9	18.92	0.0002

Table 22: Distribution of GE4



Tables 23 – 24, show the frequency of each group's incidence of EA/ED, when EA/ED is defined as at least a single Watcha score of 3 or 4 during recovery.

Table 23: Frequency of EA/ED Watcha 3 or 4

Table of Group by Ever3or4			
Group	**Ever3or4**		
	No	**Yes**	**Total**
Control	5 50.00	5 50.00	10
Prop	7 70.00	3 30.00	10
Total	12	8	20

Table 24: Fischer's Exact Test. Frequency of EA/ED - Watcha 3 or 4

Fisher's Exact Test	
Cell(1,1)Frequency(F)	5
Left-sided Pr<=F	0.3250
Right-sided Pr>=F	0.9151
Table Probability (P)	0.2401
Two-sided Pr<=P	0.6499

Tables 25 – 26, show the frequency of each group's incidence of EA/ED, when EA/ED is defined as at least a single Watcha score of 3 or 4 during recovery.

Table 25: Frequency of EA/ED Watcha 4

Table of Group by Ever4			
Group	**Ever4**		
	No	**Yes**	**Total**
Control	6 60.00	4 40.00	10
Prop	9 90.00	1 10.00	10
Total	15	5	20

Table 26: Fischer's Exact Test. Frequency of EA/ED Watcha 4

Fisher's Exact Test	
Cell(1,1)Frequency(F)	6
Left-sided Pr<=F	0.1517
Right-sided Pr>=F	0.9837
Table Probability (P)	0.1354
Two-sided Pr<=P	0.3034

Discussion

Numerous scientific studies have investigated propofol's effect on EA/ED [19-23]. These studies have varied from using propofol as a single bolus administration at the end of the surgical procedure [19-20] to comparing a total intravenous anesthetic with propofol to a volatile anesthetic, such as sevoflurane [21-23]. In general these studies have found a positive correlation between the use of propofol and a lower incidence of EA/ED [19, 22-23]. However, not all of these studies have found this to be a statically significant finding [19-20]. A focused literature search also revealed that no study had yet investigated the combined use of a volatile anesthetic with a propofol TIVA (total intravenous anesthetic). Thus, it was the author's aim to discover if propofol's tendency to reduce EA/ED could be detected if it were used alone as a terminal component of a standard volatile anesthetic using sevoflurane.

The exact mechanism by which propofol works in reducing EA/ED is not completely understood [19-23]. The rapid emergence after both a single dose and moderately long infusion (<4 hrs) can be attributed to propofol's extremely large volume of distribution [24]; in these situations its quick on and off clinical action is similar to sevoflurane's. The most recent literature in EA/ED has investigated different anesthetics and their roles in increasing or decreasing the availability of excitatory neurotransmitters, such as

glutamate [25]. This preliminary scientific research seems to point to an increase in the production of glutamate from volatile anesthetics when compared to the intravenous anesthetic propofol [25]. This ground breaking research is still in its infancy, and largely from animal studies, making it difficult to extrapolate to the humans situation. However, this is an exciting and different approach to the recognized problem of EA/ED and the author of this paper believes that this is an important area of future research in EA/ED.

The only patient demographics or characteristics that demonstrated a clinically significant difference between test and control groups in our study were treatment and recovery time. The fact that each group of the study was completed at two different locations (Test Group at Nationwide Children's Hospital Dental Surgery Center, and the control at Ohio State University Pediatric Dental Clinic) is quite possibly a major contributing factor to these two findings. At OSU the dental treatment was provided by a pediatric dental resident, who, as a result of the necessary training environment, could not provide the same speed of treatment as an experienced pediatric dentist. Furthermore, at OSU the patient is recovered within the surgical suite where the parents enter the room and reconnect with the patient much earlier in the recovery process. It is common practice to bring the parents back earlier to assist with recovery and to help minimize any time the patient may spend with EA/ED. At NCH, a dedicated PACU nurse recovers each child and generally the child is close to being fully recovered prior to bringing a parent into the recovery area. A primary reason for delaying the reunion of parent and child at NCH is to shield the parent from witnessing an episode of EA/ED. Thus, the author does not put

much weight into the practical significance of the statistically significant differences calculated in treatment time or recovery length in this study.

Previous scientific literature has classified a patient as having EA/ED when the patient had one or more single ratings of a previously defined criterion for EA/ED. In many cases the Post Anesthesia Emergence Delirium Scale was used (PAED >10, severe PAED>12) [3, 6-9]. However, this scale is complex and has been shown to vary greatly when used by different examiners [18]. Since different practitioners were to be responsible for recording each patient's EA/ED score the easier to use Watcha scale was implemented for this study.

In this pilot study, the incidence of ED/EA (Watcha Score 3 or 4) in the group of children who had a washout of sevoflurane, by receiving the IV anesthetic propofol during the terminal portion of their anesthetic, was substantially lower (30%) than that of the control group (50%). In addition, the difference in incidence of severe ED/EA (Watcha Score 4) was even greater between the control group (40%) and test group (10%). The control group findings seen here are similar to results seen elsewhere in the literature [3, 6-9]. However, with p values of 0.650 (Watcha>3) and 0.303 (Watcha>4), neither of these findings reached a level of statistical significance. The rather large p values associated with these observations are almost certainly the result of the low number of participants in each group. Similar studies have used group sizes of 50 to 100 patients in each arm of the study [3, 6-9].

In addition, the percentage of time a child had EA/ED was also calculated for each arm of the study. The author believes this is a much more valuable finding as it represents the amount of time a child spent with EA/ED and the associated recovery team spent caring for a child with this profile. Using a Watcha >3 as defining emergence delirium, the control group had a 33.8% chance of having EA/ED at any given moment during recovery, whereas the test group had a 9.94% chance of having EA/ED during recovery ($p=0.107$). When changing the criteria required to make the diagnosis of EA/ED to Watcha >4, the control group had a 15.1% of having EA/ED and the test group experienced the much lower incidence of 1.43% ($p=0.058$) at any point during recovery. Although neither result is statistically significant, the results are approaching such significance. Considering the small size of the study population, these findings are truly remarkable. It is the author's opinion that these results warrant further study and that these results may become statistically significant once more participants are enrolled in each group.

Without a doubt, the biggest weakness of this study is the number of participants in each group. Two other limitations of this study are a) that different providers treated and recovered each child and b) that two different institutions were involved. To strengthen this study it would be ideal to have one pediatric dentist provide all treatment for each child, one nurse to recover each child, one nurse to score each child's recovery, and a single treatment location offering a uniform approach to treatment and recovery. Another

critique of this study is that each child was only scored at five-minute intervals in their recovery. As a consequence, the possibility exists that shorter episodes of EA/ED were missed during the recovery process. A better and more detailed representation of recovery may be obtained were a dedicated nurse to score all changes in Watcha score and to document the time these changes occur. This approach could give a more accurate representation of each child's recovery process. Unfortunately, due to the limited resources available for this trial study, it was not possible to have an independent nurse for both recovery and scoring.

Despite these limitations, this study provides quite a strong indication that the incidence, severity, and length of EA/ED experienced by a child during recovery can be greatly reduced by simply maintaining anesthesia during the terminal portion of a procedure using propofol, and in doing so, permitting a wash out of sevoflurane before emergence from general anesthesia commences. This may be especially important with the continuing growth of office based general anesthesia in the pediatric dental field. A smooth emergence limits the disruption to the office, provides a more pleasant experience for the patient and patient's family, does not necessitate the use of additional sedation or analgesic medications, and in surgical cases, helps reduce the incidence of post-operative hemorrhage frequently seen when patients become agitated and associated post-operative nausea and vomiting.

References

1. *Guideline on use of anesthesia personnel in the administration of office-based sedation/general anesthesia to the pediatric dental patient.* Pediatr Dent, 2008. **30**(7 Suppl): p. 160-2.

2. Ba'akdah, R., et al., *The use of general anesthesia in pediatric dental care of children at multi-dental centers in Saudi Arabia.* J ClinPediatr Dent, 2008. **33**(2): p. 147-53.

3. Voepel-Lewis, T., S. Malviya, and A.R. Tait, *A prospective cohort study of emergence agitation in the pediatric postanesthesia care unit.* AnesthAnalg, 2003. **96**(6): p. 1625-30, table of contents.

4. Vlajkovic, G.P. and R.P. Sindjelic, *Emergence delirium in children: many questions, few answers.*AnesthAnalg, 2007. **104**(1): p. 84-91.

5. Olympio, M.A., *Postanesthetic delirium: historical perspectives.* J ClinAnesth, 1991. **3**(1): p. 60-3.

6. Lake, A.P. and M. Khater, *Propofol and halothane versus sevoflurane in paediatric day-case surgery.*Br J Anaesth, 2003.**91**(3): p. 447; author reply 447-8.

7. Aono, J., et al., *Greater incidence of delirium during recovery from sevoflurane anesthesia in preschool boys.* Anesthesiology, 1997.**87**(6): p. 1298-300.

8. Cole, J.W., et al., *Emergence behaviour in children: defining the incidence of excitement and agitation following anaesthesia.* PaediatrAnaesth, 2002. **12**(5): p. 442-7.

9. Eckenhoff, J.E., D.H. Kneale, and R.D. Dripps, *The incidence and etiology of postanestheticexcitment. A clinical survey*.Anesthesiology, 1961.**22**: p. 667-73.

10. Cravero, J., S. Surgenor, and K. Whalen, *Emergence agitation in paediatric patients after sevofluraneanaesthesia and no surgery: a comparison with halothane*.PaediatrAnaesth, 2000. **10**(4): p. 419-24.

11. Kulka, P.J., M. Bressem, and M. Tryba, *Clonidine prevents sevoflurane-induced agitation in children*.AnesthAnalg, 2001. **93**(2): p. 335-8, 2nd contents page.

12. Lerman, J., *Inhalation agents in pediatric anaesthesia - an update.* CurrOpinAnaesthesiol, 2007.**20**(3): p. 221-6.

13. Shibata, S., et al., *Nitrous oxide administration during washout of sevoflurane improves postanesthetic agitation in children.* J Anesth, 2005.**19**(2): p. 160-3.

14. Welborn, L.G., et al., *Comparison of emergence and recovery characteristics of sevoflurane, desflurane, and halothane in pediatric ambulatory patients.* AnesthAnalg, 1996. **83**(5): p. 917-20.

15. Valley, R.D., et al., *Tracheal extubation of deeply anesthetized pediatric patients: a comparison of isoflurane and sevoflurane.* AnesthAnalg, 1999. **88**(4): p. 742-5.

16. Adair, S.M., et al., *A survey of members of the American Academy of Pediatric Dentistry on their use of behavior management techniques.* Pediatr Dent, 2004. **26**(2): p. 159-66.

17. Aydin, T., et al., *Do not mask the mask: use it as a premedicant.* PaediatrAnaesth, 2008. **18**(2): p. 107-12.

18. Bajwa, S.A., D. Costi, and A.M. Cyna, *A comparison of emergence delirium scales following general anesthesia in children.* Paediatr Anaesth, 2010. **20**(8): p. 704-11.

19. Kim, M.S., et al., *Comparison of propofol and fentanyl administered at the end of anaesthesia for prevention of emergence agitation after sevoflurane anaesthesia in children.* Br J Anaesth, 2013. **110**(2): p. 274-80.

20. Lee, C.J., et al., *The effect of propofol on emergence agitation in children receiving sevoflurane for adenotonsillectomy.* Korean J Anesthesiol, 2010. **59**(2): p. 75-81.

21. Konig, M.W., et al., *Quality of recovery from two types of general anesthesia for ambulatory dental surgery in children: a double-blind, randomized trial.* Paediatr Anaesth, 2009. **19**(8): p. 748-55.

22. Pieters, B.J., et al., *Emergence delirium and postoperative pain in children undergoing adenotonsillectomy: a comparison of propofol vs sevoflurane anesthesia.* Paediatr Anaesth, 2010. **20**(10): p. 944-50.

23. Chandler, J.R., et al., *Emergence delirium in children: a randomized trial to compare total intravenous anesthesia with propofol and remifentanil to inhalational sevoflurane anesthesia.* Paediatr Anaesth, 2013. **23**(4): p. 309-15.

24. Dahmani, S, et al., *Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies.* Br J Anaesth. 2010 Feb; **104**(2):216-23

25. Jacob, Z et al., *Metabolomic profiling of children's brains undergoing general anesthesia with sevoflurane and propofol.* Anesthesiology. 2012 Nov; **117**(5):1062-71