Safety, Efficacy And Satisfaction Among Surgeons And Patients Of Propofol Only For Procedural Sedation During The Extraction Of Third Molars

by

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ABSTRACT

Propofol has been gaining increased attention as a sole agent in providing procedural sedation due to its predictable pharmacokinetics and favorable amnestic properties. Oral and maxillofacial surgical procedures are unique in duration and concomitant use of local anesthesia making it difficult to evaluate data obtained from other specialties. The purpose of our study is to evaluate the safety, efficacy and satisfaction among surgeons and patients using propofol only, for procedural sedation during the extraction of third molars. Propofol 10mg/ml was administered using an induction dose of 0.5 to 1mg/kg over 60 seconds followed by bolus doses of 10 – 20mg every minute to achieve a Ramsay sedation score of at least 3. Respiratory compromise was identified in 15% of patients. Hemodynamic compromise was identified in 15%. Patient and surgeon satisfaction was high however propofol does not represent the ideal drug as a sole agent for procedural sedation in oral surgery due to the frequent need for hand restraint (40%).

LIST OF ABBREVIATIONS USED

ASA	American Society of Anesthesiology
BMI	Body Mass Index
CUAO	Complete Upper Airway Obstruction
EKG	Electrocardiogram
HR	Heart Rate
N	No
NIBP	Noninvasive Blood Pressure Monitor
PUAO	Partial Upper Airway Obstruction
PSA	Procedural Sedation and Analgesia
RCT	Randomized Controlled Trial
RN	Registered Nurse
RSS	Ramsey Sedation Score
SxDiff	Surgical Difficulty
VAS	Visual Analog Scale
Y	Yes

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CHAPTER 1 INTRODUCTION

1.1 Background

Procedural sedation and analgesia (PSA) is a cornerstone to providing the oral and maxillofacial surgical patient with a favorable experience. Common procedures preformed under PSA include, dental extractions, implants, local bone grafts, biopsies, hardware removal and incision and drainage of infections. PSA allows many patients that could not tolerate the procedure under local anesthesia alone, to avoid a trip to the operating room. This reserves operating room time for those procedures that absolutely demand the benefits of a general anesthetic such as orthognathic or trauma surgery.

Wells (dentist) and Morton (dentist and physician) in the 1840's were the forfathers of anesthesia being the first to use nitrous and ether for analgesia during surgery.(1) Procedural sedation however was not developed until 1946 when Jorgensen and colleagues administered intravenous pentobarbital, merperidine and scopolamine resulting in sedation and analgesia persisting for over three hours. Much has changed since that time in the world of procedural sedation and it continues to evolve as new drugs and monitoring modalities are made available. Many specialties outside of anesthesiology have embraced procedural sedation including emergency medicine, gastroenterology, and oral and maxillofacial surgery. Residents in these specialties are now expected to become competent and proficient during their residency training in both the administration of sedation agents and the monitoring of the sedated patient.

The goals of procedural sedation are to achieve sedation, amnesia, analgesia, and anxiolysis.(2) The ideal procedural sedation medication would be able to provide all of the above while being easy to titrate, have minimal cardiorespiratory side effects, have antiemetic properties, be easy to handle, be cost effective and have ideal pharmacokinetic and pharmacodynamics properties. The ideal single medication does not yet exist.

In oral and maxillofacial surgery there are numerous combinations or "cocktails" of medications that are promoted to achieve the goals of a successful procedural sedation.

In 2006 Moore *et al* sampled 850 practicing oral surgeons across the United States regarding their practice patterns.(3) Five hundred sixty three practitioners (66.2%) responded and completed the questionnaire. On average, surgeons completed 52.7 cases of third molars per month. Cases were completed with PSA in 33.4%, while 46.3% were completed with general anesthetic and 12.9 % with local anesthetic only. The most frequently used medications in order of greatest to least common were: Midazolam (86.3%), Fentanyl (68.0%), Propofol (56.1%), Methohexital (36.2%), Ketamine (34.5%), and Diazepam (30.5%). Drug regimens ranged from single drug techniques (2%) up to five or more drug techniques. The most commonly reported drug regimen was a three drug technique (33%) consisting of a benzodiazepine, opioid, and propofol. The second most common drug regimen was a four drug combination of a benzodiazepine, opioid, propofol and ketamine. The authors commented that the survey suggested that propofol and ketamine are becoming important additions to outpatient anesthesia.

Propofol is an Alkyphenol, classified as a sedative hypnotic and was introduced to the market in 1985 by Zeneca Inc. under the trade name of Diprivan. Propofol is produced as an aqueous emulsion containing 10% intralipid, 10% soya bean oil, 2.25% glycerol,1.2% purified egg phosphatide, and 1% propofol. It comes in 20 ml, 50 ml, and 100 ml bottles in a 10mg/ml concentration. Propofol is structurally unrelated to any of the currently used barbiturate, benzodiazepine, and opioid anesthetic agents.(4) Propofol causes global CNS depression which is thought to be through agonist action on $GABA_A$ receptors and possibly through NMDA receptor blockade affecting glutamatergic activity.(4) Propofol is rated as a Pregnancy Category B drug by the Federal Drug Administration and contraindications include hypersensitivity to propofol or any component of the formulation, hypersensitivity to eggs, egg products, soybeans, or soy products.(4) Propofol has a rapid alpha phase (arm to brain time) with an onset of action typically seen within 40 seconds. The

duration of action is 4 – 8 minutes from a single bolus. Plasma levels decline rapidly as a result of both rapid redistribution and high metabolic clearance (30 – 60 mg/kg/min) resulting in a half life of 0.5 – 1 hours.(5)

Ketamine is classified as a phencyclindine derivative and is known to produce a dissociative anesthesia. The pharmacokinetics are similar to propofol with a onset of action of 30 seconds, duration of action of 7 to 11 minutes, clearance of 16 to 18 mg/kg/min. and a half life of 1 to 2 hours. This is in contrast to midazolam which is a benzodiazepine with an onset of action of 3 to 5 minutes, duration of action of 10 to 20 minutes, clearance of 7.5 mg/kg/min. and a half life of 2 to 4 hours.

For induction of a general anesthetia the recommended dosage of propofol is 2 to 2.5 mg/kg at a rate of 40mg/10seconds. For procedural sedation the recommended dose is 0.5 mg/kg over 3 to 5 minutes followed by either incremental 10 to 20 mg boluses or intravenous infusion of 25-75 mcg/kg/minute.(4) The most commonly used method in the literature however is 1mg/kg over 60 seconds followed by incremental boluses of 0.5mg/kg every 3 minutes to reach the desired level of sedation.(6)

Propofol causes respiratory depression consisting of changes in breathing patterns, ventilation depression and even apnea in a dose dependent fashion.(5) The incidence of respiratory adverse events is also dependent on the rate of administration (ie. dose given over 60 seconds versus pushed).(6) It has been suggested that a more conservative initial bolus given over 60 seconds followed with smaller subsequent doses will lead to less over sedation and fewer adverse respiratory events.(6) Propofol does not depress sinoatrial node activity or atrioventricular conduction at therapeutic doses. However, propofol does appear to have a dose dependent negative inotropic effect with afterload reduction that can result in hypotension.(5) The proposed mechanism for this complication is sympathetic nervous system impairment which inhibits the baroreflex regulatory mechanism.(5)

The most commonly used combination of drugs for PSA at the Capital District Health Authority's Oral and Maxillofacial Surgery Department is Midazolam and Fentanyl with Dexamethasone given for it's anti-inflammatory and antiemetic effects. Approximately 3500 PSAs are conducted annually in the department by 6 staff consultants and 6 residents. Several studies exist comparing the safety and efficacy of Midazolam and Fentanyl with that of Propofol. The best quality evidence is found in the Emergency Medicine literature in a systematic review completed by Hohl *et al* in 2008 entitled "Safety and Clinical Effectiveness of Midazolam versus propofol for Procedural Sedation in the Emergency Department".(7) The objective of this study was to compare the adverse events profile and clinical effectiveness of midazolam versus Ppropofol for procedural sedation in the emergency department. Midazolam and propofol were chosen for comparison because registry data from the United States and Canada indicated that these were the two most commonly used sedative agents. Twenty-eight articles met the inclusion criteria and of these, 4 articles were randomized controlled trials that made head to head comparisons between midazolam and propofol. All of the 28 articles were examined for major and minor adverse events however only the randomized controlled trials were used in the evaluation of clinical effectiveness.

RCT1- Sedation for Cardioversion in the Emergency Department: Analysis of Effectiveness in Four Protocols, by Coll- Vinent *et al* published in the Annals of Emergency Medicine 2003.(8)

This was a well designed study comparing the safety and efficacy of 4 different procedural sedation protocols. Thirty-two hemodynamically stable patients who required cardioversion under deep procedural sedation were enrolled. Strict inclusion criteria were exercised to avoid confounding of the outcome measures. Patients were randomized into 4 groups: Etomidate (n=9), Propofol (n=9), Midazolam (n=8), and Midazolam + flumazenil (n=6). Patients all fasted for 4 hours prior to the cardioversions. All cardioverisons were performed in a room with the emergency physician investigator, anesthesiologist, and a registered

nurse. Dosages of medications utilized were: Group 1: Etomidate 0.2 mg/kg, Group 2: Propofol 1.5 mg/kg, Group 3: Midazolam 0.2 mg/kg, and Group 4: Midazolam 0.2 mg/kg followed by flumazenil 0.5mg after the procedure was completed. All medications were given over 20 seconds with additional doses given only if adequate sedation was not achieved after 3 – 5 minutes. Induction time was defined as the time measured from injection of the test drug to loss of lid reflex. Awakening time was defined as the time to spontaneous eye opening after induction. Total recuperation time was defined as the time from induction until the patient achieved baseline scores on 4 objective psychomotor tests. Apnea was defined as absence of spontaneous respiration for $\geq$ 20 seconds while desaturation was oxygen saturation below 90%. Patients were monitored for the following adverse effects; nausea, vomiting, injection site pain, myoclonus, bronchospasm, procedural recall, and re-sedation. Patient satisfaction was evaluated prior to discharge with an ordinal scale. A single additional dose was required in one patient in the etomidate arm, one patient in the propofol arm and 5 patients who received midazolam. Eventually all patients reached Ramsay sedation scores of 6 (no response to pain) and all cardioversions were successful. There was no significant difference in induction time between groups. Awakening time was significantly different between groups with a median time of: Etomidate 9.5 min, Propofol 8 min, Midazolam 21 min, and Midazolam + flumazenil 3 min. Five sixths (5/6) of the Midazolam + flumazenil groups experienced re-sedation (Ramsay sedation score of $\geq$ 3) that delayed discharge. Total recuperation time was significantly different between groups with propofol being most favorable with a median of 10 minutes (range 5-15 min). Apnea was observed in each group: Etomidate (n=2/9), Propofol (n=2/9), Midazolam (n=3/8), and Midazolam + flumazenil (n=1/6). Desaturation was observed in most groups: Etomidate (n=1/9), Propofol (n=4/9), Midazolam (n=0/8), and Midazolam + flumazenil (n=2/6). Desaturations did not represent a clinical problem as they were quickly corrected with bag mask ventilator support. Clinically significant hypotension was not seen in any group.

Etomidate, known for its hemodynamic stability was problematic in this study with 3 cases of prolonged myoclonus and 1 possible seizure. Midazolam had considerable prolonged recovery times with a median time of 45 mins while the Midazolam + Flumazenil had a very high rate of re-sedation.
In conclusion the authors found that propofol had the best combination of short induction time, recovery and most favorable adverse event profile.

RCT2 – Nursing use between 2 methods of procedural sedation: midazolam versus propofol, by Holger *et al* published in the American Journal of Emergency Medicine 2005.(9)

This was a randomized controlled study enrolling 40 patients with 32 completing the study. This study was based out of a busy emergency department and randomly assigned patients to one of two treatment arms. One group received procedural sedation with propofol and the other group received procedural sedation with midazolam. All patients required painful procedures that were less than 15 minutes in length. The majority of procedures consisted of orthopedic reductions and abscess incision and drainage. Patients in both groups received narcotics for pain control prior to the procedural sedation and if they had not yet received a narcotic, fentanyl 0.2 mcg/kg was administered 2 minutes prior to the first dose of midazolam or propofol. The midazolam group consisted of 17 patients that were administered 1mg of midazolam every 2 minutes until a minimum Ramsay sedation score of 3 was reached. The propofol group consisted of 15 patients that were administered a 0.5 mg/kg propofol push followed by additional boluses of 0.25 mg/kg every 30 to 45 seconds until a minimum Ramsay sedation score of 3 was reached. Eight patients that were enrolled in the study failed to complete it due to failure to reach an adequate depth of sedation as determined by the treating physician. Seven of these were planned for the midazolam arm and 1 was in the propofol arm. These 8 patients were not included in the final data analysis. Patients were pre-oxygenated via non-rebreather mask for 5 minutes before the procedure. Patients were monitored by pulse oxymetry, EKG, and NIBP every

5 minutes. Recovery was defined as normal vital signs, oriented to person, place and time, no slurred speech and a return of normal balance and gait. Titration time, procedure time, and time to recovery were recorded. Physicians and RN's evaluated their satisfaction using a VAS for the above 3 phases of the procedural sedation. Patients were asked to rank their satisfaction using a VAS as well as complete a questionnaire no sooner than 24 hours regarding recall, vomiting, anxiety and sleepiness. The primary outcome measure was RN monitoring time while secondary measures included adverse event (hypoxia) and VAS satisfaction scores.

Propofol was noted to reduce the total time spent in the emergency department by 24 minutes. Satisfaction scores were similar for both drugs however physicians were more satisfied with propofol during the titration period of the study. It should be noted that the titration period of the procedural sedation was significantly longer for the midazolam group (median 12 min) compared with the propofol group (median 4 min). One patient in each group experience nausea and vomiting but no other adverse events were noted in either group including hypoxia. Twenty-four hour recall was not different between groups.
The authors concluded that when midazolam was compared with propofol for procedural sedation in the emergency room, propofol required less RN time resulting in lower costs.

RCT3 – Age effect on Efficacy and Side Effects of Two Sedation and Analgesia Protocols on Patients Going through Cardioversion: A Randomized Clinical Trial by Parlak *et al* in the Journal of Academic Emergency Medicine 2006. (10)

The objective of this study was to compare the safety and efficacy of midazolam versus propofol for procedural sedation in patients older versus those younger than 65 years requiring cardioversion. Patients were divided into 4 groups.

Group 1: (n=12) Age < 65 years receiving fentanyl 1ug/kg followed 3 minutes later by 2 mg midazolam over 30 seconds then 1 mg every 2 minutes until a RSS of 5 was reached.

Group 2: (n=111) Age < 65 years receiving fentanyl 1ug/kg followed 3 minutes later by 20 mg propofol over 30 seconds then 20 mg every 2 minutes until a RSS of 5 was reached.

Group 3: (n=25) Age ≥ 65 years receiving fentanyl 0.5 ug/kg followed 3 minutes later by 2 mg midazolam over 30 seconds then 1 mg every 2 minutes until a RSS of 5 was reached.

Group 4: (n=2) Age ≥ 65 years receiving fentanyl 0.5 ug/kg followed 3 minutes later by 20 mg propofol over 30 seconds then 1 mg every 2 minutes until a RSS of 5 was reached.

Patients were monitored by emergency medicine or anesthesiology residents with EGK, NIBP, and pulse oximetery. Desaturation was defined as blood oxygen level lower than 95% and apnea was defined as respiratory arrest lasting longer than 20 seconds.

The midazolam dose between the age groups was significantly lower in the ≥ 65 years while the propofol groups had similar dose between groups. Group 1 (midazolam < 65y) had 1 patient with an episode of apnea and 2 patients with desaturation. Group 3 (midazolam ≥ 65y) had 6 patients with an episode of apnea and 16 patients with desaturations. The propofol groups had less adverse respiratory events with Group 2 (< 65y) having 1 patient with an episode of apnea and 1 patient with desaturation. Group 4 (≥ 65y) had 2 patients with an episode of apnea and 4 patients with desaturation. Induction time was no different between groups however both midazolam groups had over double the recovery times of the propofol groups. Patient satisfaction was high and equal between the groups however event recall was highest in ≥ 65 y midazolam group.

The authors concluded that propofol was that better choice for procedural sedation for cardioversion especially in the older population because of its short recovery time and fewer side effects.

RCT4 – Propofol versus Midazolam/Fentanyl for Reduction of Anterior Shoulder Dislocation by Taylor *et al* in Academic Emergency Medicine 2005.(11)

The objective of this study was to compare the safety and efficacy of profofol versus midazolam and fentanyl for procedural sedation when reducing dislocated shoulders in the emergency department. Eighty-six patients were randomized to one of these two study arms and the researcher was blinded as to the nature of the medications being used. Primary outcomes included muscle tone at time of shoulder reduction, ease of shoulder reduction, and time from successful reduction to first awakening. Forty-eight patients were enrolled in the propofol arm of the study while thirty-eight patients were enrolled in the midazolam/fentanyl arm. All patients received IV morphine for analgesia on admission prior to procedural sedation. The dose was titrated to a reduction in pain sale (1-10) of 2 points. Patients in the propofol arm received an IV bolus pushed over 30 seconds titrated to a sedation endpoint that was not clarified using the Ramsey sedation score. The average dose given was 1.8mg/kg. The second study arm received fentanyl 1.25 mcg/kg IV followed 2 minutes later byxz a midazolam bolus pushed over 30 seconds again titrated to a sedation endpoint. The average dose of fentanyl was 97.2 mcg and the average midazolam dose was 4.1 mg. All patients received supplemental oxygen and EKG and pulse oximeter were used throughout.

Muscle tone was not statistically different between groups however ease of reduction was found to be easier in the propofol group. Time to first awakening (eyes first open) after shoulder reduction was not significantly different between the groups but the time to full consciousness (GCS 15 and oriented to person, place and time) was significantly less in the propfol group (6.8 minutes) compared with the midazolam/fentanyl group (28.5 minutes). Respiratory depression was more common in the propofol group with desaturation less than 90% occurring in 8.3% compared with only 5.3% in the midazolam/fentanyl group. Bag mask ventilation was required in 8.3% of the propofol patients and only 2.8% of the midazolam/fentanyl patients. These finding however failed to reach statistical significance. Memory of the

procedure was more common in the midazolam group (8.3% versus 2.1%) however this was not statistically significant.

The authors concluded that propofol is as effective as midazolam/fentanyl for reduction of shoulder dislocation however the convenience associated with rapid awakening should not overshadow the trend towards increased risk for respiratory depression.

The primary endpoint in the systematic review by Hohl *et al* was the mean difference between major adverse events and the secondary endpoint was mean difference in the proportion of patients that were successfully sedated. Successful procedural sedation was defined by the ability to complete the planned intervention at a target level of sedation without deviating from the sedation protocol.(7)

Adverse events were grouped into major and minor. Minor adverse events included, bag-mask valve ventilation, use of an oral airway, transient apnea, vomiting without aspiration, transient hypotension, myoclonus, pain with injection of agent, use of a reversal agent and dizziness. Major adverse events included death, disability, hospital admission, prolonged ED stay, intubation, and vomiting with aspiration pneumonitis.

At total of 847 patients underwent procedural sedation using midazolam and 2,453 using propofol, in the 28 studies included in the systematic review by Hohl *et al*.(7) Due to heterogeneity, minor adverse events could not be pooled. Major adverse events occurred in 0/847 midazolam sedations and 1/2453 propofol sedations. This was statistically insignificant ($p = 0.56$). The single major adverse event occurred in an 18 year old patient and was described in an observational study which was not discussed above. This patient required intubation due to iatrogenic narcotic overdose. Clinical effectiveness could not be compared in the above randomized controlled trials because patient and clinician satisfactions scores, pain and recall scores were inconsistently reported between trials and therefore could not be combined to produce a valid outcome.

The secondary outcome analysis identified procedural sedation success in 89.9% of cases involving midazolam compared to 92.8% of procedural sedation involving propofol. However, once again this result was not statistically significant ($p = 0.19$).

Extensive literature also exists testing the safety and efficacy of propfol combined with ketamine for PSA. This combination has been termed ketafol by many researches.(6) The idea behind combining the 2 drugs is the theory that you will have to use less of each individual drug thereby minimizing the undesirable side effects of each agent while still achieving optimal PSA. The cardiodepressant effect and lack of analgesia of propofol is counteracted by the cardiostimulant properties and potent analgesia of ketamine.(12) In 2007 Slavik *et al* completed a systematic review looking at 8 clinical trials that compared ketafol with propofol montherapy. The ratios ranged from 10:1 up to 2:1 (propofol mg: ketamine mg). The researchers found conflicting evidence regarding hemodynamic and respiratory complications and concluded that additional research to elucidate the role for this combination.(13)

In 2012 Andolfatto *et al* completed the largest reported randomized double-blind comparison of ketamine-propofol combination versus propofol alone for ED procedural sedation and analgesia to date.(6) Two hundred eighty-four patients were randomly assigned to one of 2 groups. Group 1 ($n = 142$) received ketafol while Group 2 ($n = 142$) receive propofol alone. The primary outcome was the proportion of patients experiencing a respiratory adverse event as defined by the Quebec Criteria.(14) Secondary outcomes included sedation consistency, total medication dosage, and sedation efficacy. Group 1 received 1:1 ratio ketamine and propofol at an induction dose of 0.375mg/kg ketamine and 0.375 mg/kg propofol over 15 – 30 seconds followed by incremental bolus every minute until a deep sedation was achieved to allow for completion of the emergency room procedure. Group 2 received propofol only at an induction dose of 0.75 mg/kg over 15 – 30 seconds followed by incremental bolus every minute until a deep sedation was achieved.

The proportion of patients experiencing adverse respiratory events was similar between the two groups.

Oxygen desaturation incidence was 27% in the ketafol group and 25% in the propofol group. Induction time, hemodynamic stability, and sedation efficacy were also very similar between groups. Sedation consistency was better in the ketafol group compared with the propofol group with only 46% of patients requiring additional doses of ketafol to maintain a Ramsay sedation score of ≥ 5 compared with 65% of the propofol patients ($p < 0.001$). Propofol patients also experienced much more procedural agitation (10% vs. 4%). Thus it was concluded by the authors that deep sedation can be reliably achieved with either ketafol or propofol. However the addition of ketamine to propafol appears to blunt some of the peaks and valleys seen in the propofol only group which is likely responsible for some of the increased agitation seen in this group.

The safety and efficacy of ketafol has also been described in the oral and maxillofacial literature. Cillo *et al* conducted a prospective randomized controlled clinical trial involving 64 adult patients undergoing total intravenous general anesthesia.(12) The patients were randomized into 4 groups. All groups received 2 mg of midazolam and 8 mg of decadron. Group A received propofol and saline. Group B received propofol-ketamine in a ratio of 10:1. Group C received propofol-ketamine in a ratio of 5:1. Group D received propofol-ketamine in a ratio of 3:1. Compared with Group A (propofol only), Group D (3:1) patients required a significantly lower propofol dose but had significant increases in systolic blood pressure intraoperatively and took a significantly longer time to recover. Otherwise, time to injection, movement on injection and time of surgery was not different. Compared with Group A (propofol only), Group B (10:1) showed no significant differences with respect to total propofol dose, intraoperative blood pressures, time to injection, movement on injection and time of surgery. Group B patient did have the fastest time to recovery of all groups (18.2 minutes) and this was found to be statistically significant $p < 0.05$. The authors concluded that an admixture of 10:1 propofol-ketamine produced the best intraoperative hemodynamics matched with the fastest recovery times for outpatient dentoalveolar surgery.

The safety and efficacy of remifentanil compared to fentanyl has also been investigated in the oral

and maxillofacial setting. Lacombe *et al* designed a randomized, prospective, single-blinded controlled study comparing midazolam, fentanyl, and propofol, versus midazolam, remifentanil and propofol infusion.(15) The authors found that the patients in the remifentanil group showed a significant lowering of the respiratory rate compared with the fentanyl group (16 ± 4.7 versus 23 ± 4.3 $P < 0.001$) but otherwise both groups showed stable hemodynamics within 20% of baseline. The remifentanil group required 33% less propofol for induction, had a lower maintenance rate and had more rapid awakening from deep sedation without increased adverse effects.

Several other excellent sedation studies comparing various combinations of drugs like etomidate, methohexital, midazolam, and propofol are available in both the Oral and Maxillofacial surgery journals as well as in the emergency medicine and gastroenterology literature.(16–23) However the common denominator among the majority of these studies is the use of some type of opioid. Opioids such as fentanyl are often used for their analgesic properties however their side effect profile includes nausea, vomiting, bradypneic hypoventilation, apnea and hypoxia and have been associated with several deaths.(24) An increasing body of research from the emergency medicine literature suggests that procedural sedation can be carried out in a safe and effective manner in the ED without the use of an opioid thus avoiding the adverse effects associated with this class of medications.

Zed *et al* published his experience with 113 patients undergoing procedural sedation in the emergency department for various procedures, the most common being orthopedic manipulation and cardioversion.(2) In 94 patients, propofol alone was used for sedation by using an induction bolus of 0.25 – 0.5mg/kg over 60 seconds followed by 10 – 20 mg every minute until adequate sedation was achieved. No patients experienced apnea and only 1 had an episode of oxygen desaturation. Nine patients had an episode of clinically insignificant hypotension and 94% of the patients had no recall of the procedure. Overall 90% of the procedures were completed successfully with patient and physician satisfaction being high. Recovery to

baseline psychomotor activity was 7.6 minutes.

Black *et al* concluded in her qualitative systematic review of "Propofol for Procedural Sedation in the Emergency Department" that no significant difference was found in terms of pain, recall and satisfaction when opioids were added to propofol compared with propofol alone.(25) Furthermore, the addition of an opioid may have resulted in a higher incidence of adverse respiratory events.(25) Included within this systematic review was a study by Miner *et al* comparing propofol procedural sedation with and without alfentanil.(26) Miner concluded that the addition of supplemental opioid did not appear beneficial and increased the need for clinical interventions associated with respiratory depression.

In the maxillofacial literature, only a single study could be found that contained a true propofol only sedation arm.(27) This was published by Valtonen *et al* in 1989 and had a relatively small sample size of 12 patients. Patients served as their own control having third molars on one side extracted under propofol only infusion and then, two weeks later, having the other side extracted using bolus diazepam. Valtonen found no difference between groups with respect to respiratory depression. However, mean arterial pressure and heart rate were lower in the propofol group. Recovery times and amnesia were superior in the propofol only data. Eight of 12 patients subjectively preferred the propofol sedation. The authors concluded that propofol infusion appears to be a safe and effective alternative in minor oral surgery.

Oral and Maxillofacial surgical procedures are unique in duration of procedure and use of local anesthesia making it difficult to generalize data obtained from other specialties. There is an absolute lack of quality studies exploring propofol only in the oral and maxillofacial surgery literature. There appears to be a trend in other specialties toward using propofol only and it needs to be further evaluated in the OMF setting.

The purpose of our study was to evaluate the safety, efficacy and satisfaction among surgeons and patients of propofol only for procedural sedation during the extraction of third molars.

CHAPTER 2 METHODS

2.1 Patients

A prospective, observational study was designed using a convenience sample of patients who required extraction of their third molars at the Victoria General Hospital (VGH), Halifax, Nova Scotia, Canada, using propofol intravenous sedation. All patients were presenting for the removal of at least 3 third molar teeth and were classified ASA I according to the American Society of Anesthesiologists physical status classification system. Prior to surgery the patients were requested to fast for a minimum of 8 hours prior to surgery. The patients were required to bring a driver to the clinic who was to be present during patient education prior to the surgery and after the completion of surgery. The RN assessed all patients preoperatively and reviewed medical history, medications, allergies, record baseline vitals, height, weight (BMI) and verified NPO status. The RN completed the Corah anxiety scale for each patient (Appendix A).(28) The surgeon then reviewed the medical history and discussed the risks, benefits, and alternatives to the surgery. Consent for both the surgical procedure and the research study was obtained. A preoperative dose of 600mg Ibuprofen was given by mouth preoperatively when indicated. An 18 or 22 gauge intravenous catheter was placed in the antecubital fossa whenever possible, or the next largest accessible vein. Intravenous fluids consisted of ringers lactate. Local anesthetic consisted of Lidocaine 2% with 1:100,000 epinephrine.

2.2 Sedation and Monitoring

Propofol 10mg/ml was then administered using an induction dose of 0.5 to 1mg/kg over 60 seconds followed by bolus doses of 10 – 20mg every minute to achieve a Ramsay sedation score of at least 3 (Appendix B).(9,29) The patient was monitored for the following physiologic parameters: non-invasive blood pressure monitoring at time 0 and then every 5 minutes; 3 lead electrocardiogram (EKG); pulse oximetry; and capnography. Furthermore, a Ramsay sedation score was assessed and recorded every 5

minutes. Patients received oxygen at a rate of 2 liters per minute via nasal cannula for the duration of the procedure. Supplemental oxygen and capnography with continuous quantitative capnometry were made possible via the Omniline® nasal cannula manufactured by Oridion connect to the GE Healthcare Datex-Ohmeda S/5™ Anesthesia Monitor.

2.3 Data Collection

Data was collected using a custom made procedural sedation physiologic monitoring form (Appendix C). Dosage and time to the nearest minute were documented along with start and stop times for the surgery. Start time was defined as time at first incision and stop time was defined as time of last stitch (or extraction when no final stitch was required). A minimum of 3 people were present in the operating room at all times during the procedures. This was in keeping with current CDHA requirements and included:

1. The staff surgeon who was responsible for completing the required surgery and monitoring of the patient.
2. An oral and maxillofacial surgery resident who established intravenous access, monitored the patient, administered medications, and maintained the airway when necessary.
3. A RN or Dental Assistant who assisted the surgeon with the procedure.

Respiratory compromise was defined as apnea for more than 30 seconds or an oxygen saturation of less than 90%. Hemodynamic compromise was defined as a systolic blood pressure of less than 90 mm Hg or a decrease from baseline of > 20%. Major complications were defined as the need to perform bag-valve-mask ventilation, intubation, or blood pressure or heart rate interventions. Other major complications included aspiration, unplanned hospital admission, and death. All complications were documented.

Furthermore, the "Quebec Criteria" for reporting adverse events was also used (Appendix D) to facilitate future efforts in combining procedural sedation outcomes.(14) Patient recovery was assessed using a standard CDHA Aldrete recovery room assessment (Appendix E). Once the patient has returned to preoperative mental status, patient satisfaction and recall were assessed (Appendix F).(19) Surgeon satisfaction and surgical difficulty were also evaluated (Appendix G). The level of difficulty for each tooth extracted was quantified using the scale found in Appendix G. The score for each tooth ranged from 1 to 4 and there were always 3 or 4 teeth to be extracted. Thus the surgical difficulty (SxDiff) was tabulated by adding up all the individual tooth difficulty scores. Consequently, the range was between 3 and 16 for each case. Between 24 and 48 hours after discharge, a follow up telephone survey was conducted with each patient to reassess the aforementioned parameters (Appendix F).

2.4 Statistics

Data was analyzed with SPSS 17.0. Descriptive statics will be presented. For each measure there will be a mean or median if the variable is not normally distributed. When a mean is presented the standard deviation will be given. When a median is presented, the "IQR" (interquartile range) will be presented. Some of the measures are categorical i.e. Yes/No or present/absent. For these the proportion of the outcomes will be presented. Although the study is largely descriptive in nature, the relationship among the variables will be looked at. For example the correlations among the variables; such as comparing preoperative anxiety and surgeon level of satisfaction or BMI and frequency of desaturation will be explored. When comparing groups on a continuous measure that is normally distributed, t-test will be used while Mann-Whitney tests will be used on skewed data. Pearson's and Spearman's correlations will be used when comparing normal and skewed proportions respectively.

T-tests were used to analyze the relationship of propofol total dose (dependent variable) with several different grouping variables (incidence of desaturation, partial upper airway obstruction, and complete upper airway obstruction). The t-test, also known as student's t-test or an unpaired t-test, is a parametric test used to assess if there is significant difference between the mean values of two study groups.(30) This test assumes that each participant is represented in the data only once, that the outcome measurement is normally distributed, that the outcome variance in each group is approximately equal, and that the sample size is large enough ($n \geq 30$) (30). Our data set was tested for normality earlier and variance was tested using Leven's test. The non-parametric equivalent to an independent samples t-test is the Mann – Whittney U test.(30) The Corah Anxiety Scale data was previously shown to be skewed (non-parametric) so the Mann – Whitney test was chosen to explore if there was any difference in mean anxiety scores in those patients that experienced oxygen desaturation, PUAO and CUAO. ANCOVA was utilized to rule out the effect that BMI may be having on the above results.

CHAPTER 3 RESULTS

Forty patients were enrolled in this prospective study between May 2011 and August 2013. 23 (57.5%) were female and 17 (42.5%) were males. The average patient age was 21.65 years and the average BMI was 24.56 as seen in below Table 1.0. Average Corah Anxiety score preoperative was 14.63/42. The average interval anxiety score preoperative was 9.35/20 (Table 1.0).

Table 1.0 - Descriptive Statistics of preoperative patient evaluation.

	N	Minimum	Maximum	Mean	Std. Deviation
Age	40	15	32	21.65	4.191
BMI	40	19.62	34.71	24.5628	3.46993
Corah Anxiety Score	40	2	42	14.63	13.664
Interval Anxiety	40	4	20	9.35	4.470

The sedation protocol was considered efficacious by the surgeon in 95% of the cases. Patients #26 and #33 required the addition of 5mg of midazolam in order to complete the procedure due to excessive arm movement that was compromising the surgical field for the surgeon (Table 2.0).

Table 2.0 - Sedation was efficacious? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	38	95.0	95.0	95.0
	No	2	5.0	5.0	100.0
	Total	40	100.0	100.0	

Desaturation (SpO_2 Less than 90%) occurred in 5 of the 40 patients enrolled in the study 12.5%. (Table 3.0)

Table 3.0 - Oxygen desaturation? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	5	**12.5**	12.5	12.5
	No	35	87.5	87.5	100.0
	Total	40	100.0	100.0	

A single additional patient experienced central apnea after the induction bolus of propofol that lasted longer than 30 seconds but less than 1 minute. This patient maintained oxygen saturation of 98% throughout (Table 4.0).

Table 4.0 - Central apnea? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	1	**2.5**	2.5	2.5
	No	39	97.5	97.5	100.0
	Total	40	100.0	100.0	

Table 3.0 and 4.0 together capture all of those patients meeting the traditional definition of Respiratory Compromise. A further breakdown of those patients is presented below (Table 5.0).

Table 5.0 – Summary of those patients meeting traditional criteria for Respiratory Compromise.

Patient Number	Respiratory event	Lowest SpO_2	Intervention
#4	PUAO	87%	Suctioning
#18	PUAO	88%	Airway repositioning
#20	PUAO	87%	Airway repositioning
#26	PUAO	79%	Airway repositioning
#29	PUAO	89%	Airway repositioning
#30*	Central apnea	98%	Airway repositioning

*Note: Patient #30 was given jaw thrust and found to be making no respiratory effort so Bag mask was set up but prior to bagging patient regained respiratory effort never dropping SpO2.

Seven other patients were diagnosed as having a PUAO without it causing a desaturation. (Table 6.0).

Table 6.0 - Partial upper airway obstruction PUAO? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	12	30.0	30.0	30.0
	No	28	70.0	70.0	100.0
	Total	40	100.0	100.0	

A total of 7 patients experienced complete upper airway obstruction none of which caused an oxygen desaturation (Table 7.0).

Table 7.0 - Complete upper airway obstruction? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	7	17.5	17.5	17.5
	No	33	82.5	82.5	100.0
	Total	40	100.0	100.0	

No cases of Laryngospasm were observed at any point in the procedures. Asymptomatic bradycardia was observed in 4 patients (10%) and hypotension in 2 patients however no intervention was required in any of the cases as the patients were stable and their vitals normalized by the end of the procedure (Table 8.0 and Table 9.0)

Table 8.0 - Bradycardia? (HR < 60) Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	4	**10.0**	10.0	10.0
	No	36	90.0	90.0	100.0
	Total	40	100.0	100.0	

Table 9.0 - Hypotension (systolic < 90 mmHg) ? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	2	**5.0**	5.0	5.0
	No	38	95.0	95.0	100.0
	Total	40	100.0	100.0	

A Paradoxical response was considered to have occurred when the patient required hand holding by a third party in order to complete the procedure. This occurred in 40% of the cases (Table 10.0).

Table 10.0 - Paradoxical response to sedation? Y or N

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	16	**40.0**	40.0	40.0
	No	24	60.0	60.0	100.0
	Total	40	100.0	100.0	

The surgical difficulty was found to be distributed normally, seen by the closely related mean and median values (Table 11.0, Figure 1.0)

Table 11.0 – Descriptive data regarding surgical difficulty showing normally distributed data set.

Surgical Difficulty		Statistic	Std. Error
	Mean	**9.6000**	.52721
95% Confidence Interval for Mean	Lower Bound	8.5336	
	Upper Bound	10.6664	
	5% Trimmed Mean	9.5833	
	Median	**9.0000**	
	Variance	11.118	
	Std. Deviation	3.33436	
	Minimum	3.00	
	Maximum	16.00	
	Interquartile Range	4.00	
	Skewness	.024	.374

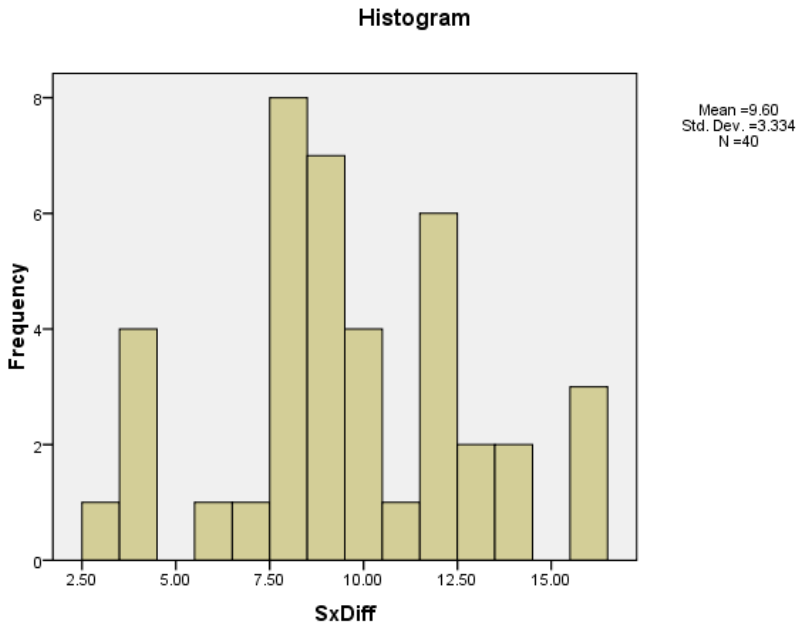

Figure 1.0 – Bar graph showing normally distributed surgical difficulty data.

The total milligrams of propofol used for each case was tabulated and also displayed a normal distribution (Table 12.0, Figure 2.0).

Table 12.0 – Descriptive data regarding total dose of propofol showing normally distributed data set.

			Statistic	Std. Error
Total dose of propofol		Mean	**304.7500**	18.17997
	95% Confidence Interval for Mean	Lower Bound	267.9775	
		Upper Bound	341.5225	
		5% Trimmed Mean	298.0556	
		Median	**302.5000**	
		Variance	13220.449	
		Std. Deviation	114.98021	
		Minimum	110.00	
		Maximum	680.00	
		Interquartile Range	158.75	
		Skewness	.946	.374

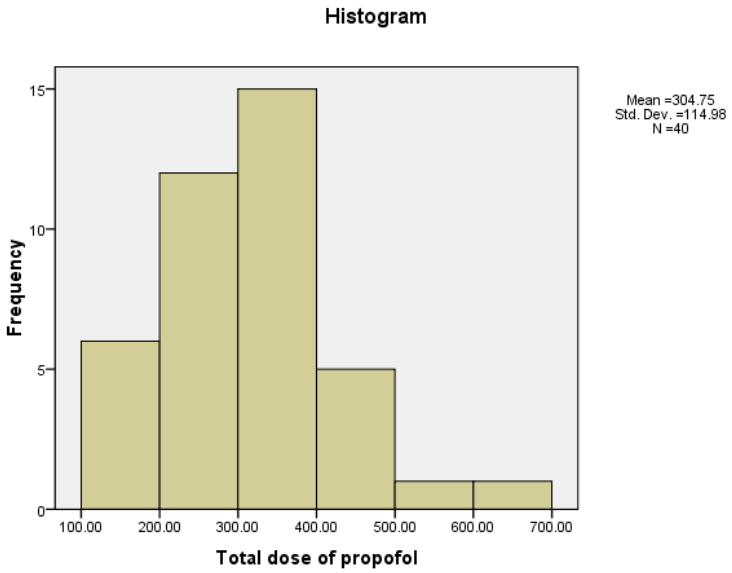

Figure 2.0 – Bar graph showing normally distributed propofol dose range.

Total surgical time ranged from 4 minutes to 39 minutes with a mean of 16.7 minutes. This data displayed a normal distribution (Table 13.0, Figure 3.0).

Table 13.0 – Descriptive data regarding total surgery time showing normally distributed data.

Total Surgical Time		Statistic (minutes)	Std. Error
	Mean	**16.7000**	1.27812
95% Confidence Interval for Mean	Lower Bound	14.1148	
	Upper Bound	19.2852	
	5% Trimmed Mean	16.3056	
	Median	**15.0000**	
	Variance	65.344	
	Std. Deviation	8.08354	
	Minimum	4.00	
	Maximum	39.00	
	Interquartile Range	10.00	
	Skewness	.686	.374

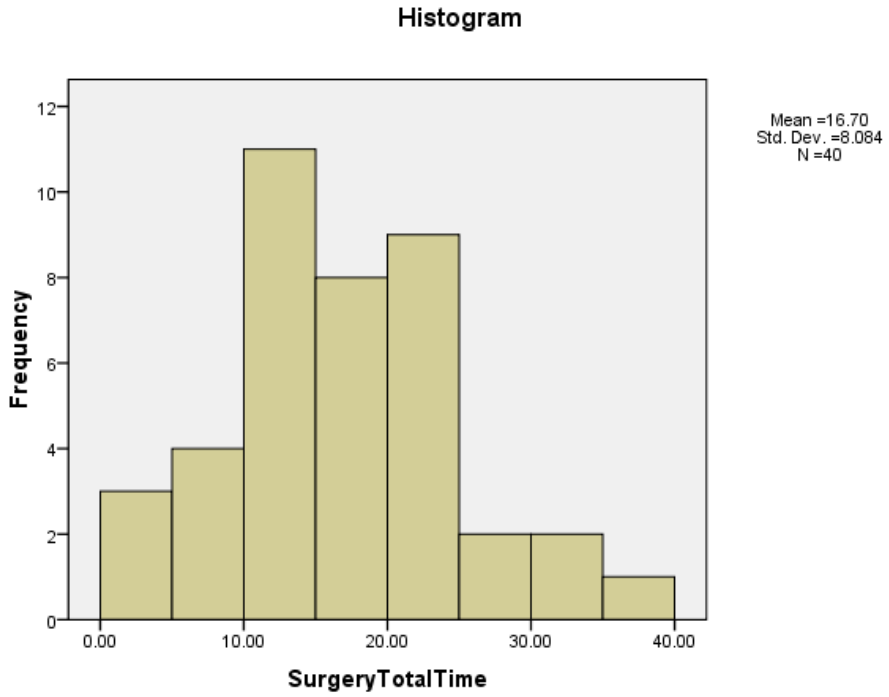

Figure 3.0 – Bar graph showing normally distributed surgical time range.

Given that the above 3 data sets (surgical difficulty, total surgery time and total dose of propofol) were all normally distributed, Pearson's correlations could be used to test the relationship between these variables for significance. As can be seen in Table 14.0, as surgical difficulty increased, total surgery time and total dose of propofol also increased ($p < 0.001$ and $p < 0.05$ respectively).

Table 14.0 - Pearson's Correlations

		Surgical Difficulty	Surgery Total Time	Total dose of propofol
Surgical Difficulty	Pearson Correlation	1	.596**	.380*
	Sig. (2-tailed)		.000	.015
	N	40	40	40
Surgery Total Time	Pearson Correlation	.596**	1	.568**
	Sig. (2-tailed)	**.000**		.000
	N	40	40	40
Total dose of propofol	Pearson Correlation	.380*	.568**	1
	Sig. (2-tailed)	**.015**	.000	
	N	40	40	40

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Corah Anxiety and Interval anxiety scores were tested for normality and both were positively skewed (Table 15.0, Figure 4.0 and 5.0). These two anxiety scores correlated well with one another (Table 16.0 - $p < 0.01$) so, for the sake of simplicity, the decision was made to use the Corah Anxiety score solely in all future statistical analysis.

Table 15.0 – Descriptives of Corah Anxiety and Interval Anxiety Score showing that both data sets are positively (right) skewed.

			Statistic	Std. Error
Corah Anxiety Score		Mean	**14.63**	2.160
	95% Confidence Interval for Mean	Lower Bound	10.26	
		Upper Bound	18.99	
		5% Trimmed Mean	13.81	
		Median	**8.00**	
		Variance	186.702	
		Std. Deviation	13.664	
		Minimum	2	
		Maximum	42	
		Interquartile Range	10	
		Skewness	**1.242**	**.374**
Interval Anxiety Scale Score		Mean	**9.35**	.707
	95% Confidence Interval for Mean	Lower Bound	7.92	
		Upper Bound	10.78	
		5% Trimmed Mean	9.08	
		Median	**7.50**	
		Variance	19.977	
		Std. Deviation	4.470	
		Minimum	4	
		Maximum	20	
		Interquartile Range	8	
		Skewness	**.846**	**.374**

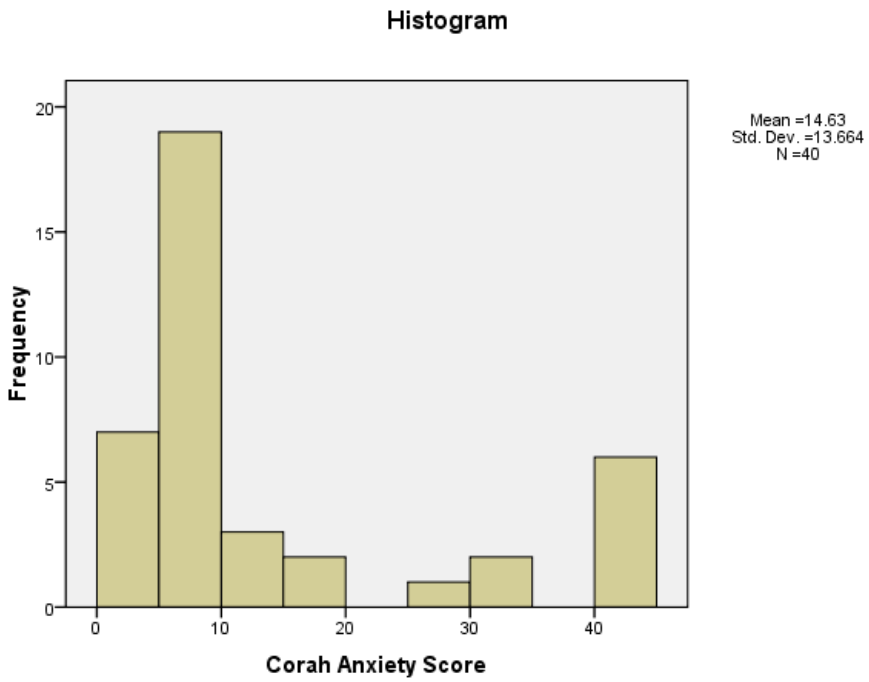

Figure 4.0 – Bar graph showing positively skewed distribution of Corah Anxiety scores.

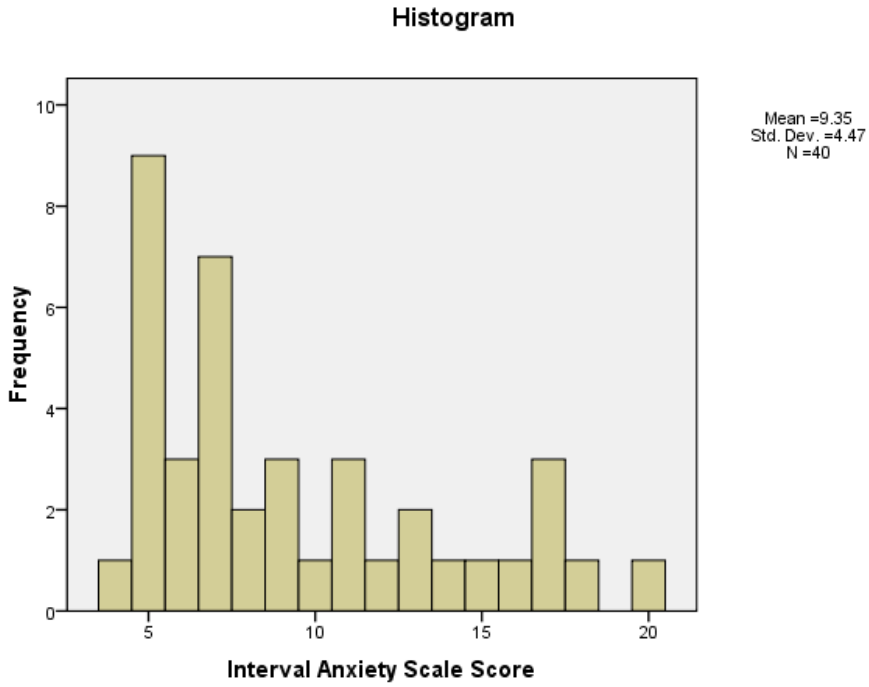

Figure 5.0 – Bar graph showing positively skewed distribution of Interval Anxiety Scale scores.

Table 16.0 - Spearman's Correlations for two anxiety scores.

			Corah Anxiety Score	Interval Anxiety Scale Score
Spearman's rho	Corah Anxiety Score	Correlation Coefficient	1.000	.732**
		Sig. (2-tailed)	.	**.000**
		N	40	40
	Interval Anxiety Scale Score	Correlation Coefficient	.732**	1.000
		Sig. (2-tailed)	.000	.
		N	40	40

**. Correlation is significant at the 0.01 level (2-tailed).

Spearman's test for correlation was then used to assess for a relationship between pre operative anxiety level and the total propofol dose used. No correlation between pre operative anxiety and total propofol dose used during the case was found (Table 17.0, p= 0.663).

Table 17.0- No significant Correlations between Corah anxiety and total propofol dose.

			Corah Anxiety Score	Total dose of propofol
Spearman's rho	Corah Anxiety Score	Correlation Coefficient	1.000	-.071
		Sig. (2-tailed)	.	**.663**
		N	40	40
	Total dose of propofol	Correlation Coefficient	-.071	1.000
		Sig. (2-tailed)	**.663**	.
		N	40	40

The average propofol dose of the 5 patients who experienced an oxygen desaturation was 488.00 mg (SD +/- 123.17) versus an average dose of 278.57 mg (SD +/- 87.96) in those with no desaturation. Table 18.0 shows the results of a t-test showing a statistically significant difference between mean total propofol dose and incidence oxygen desaturation ($p < 0.01$).

Table 18.0 - Independent Samples t-Test showing significant difference of the mean propofol dose and presence or absence oxygen desaturation.

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
Total dose of propofol	Equal variances assumed	38	**.000**	209.42857
	Equal variances not assumed	4.601	.017	209.42857

ANCOVA was then utilized to rule out that BMI may have had an effect on the above results. Table 19.0 shows that BMI did not have a significant effect on the above results ($p = 0.787$) and that after removing this variable, "total dose of propofol" was still significantly related to oxygen desaturation.

Table 19.0 – ANCOVA Tests of Between-Subjects Effects

Dependent Variable:Total dose of propofol

Source	Sig.
Corrected Model	.000
Intercept	.003
BMI	**.787**
O2Desat	**.000**

Twelve patients were documented as having experienced PUAO. The mean dose of propofol in those having PUAO was 403.75mg (SD +/- 110.31) and the mean dose of propofol in those not having PUAO was 262.32mg (SD +/- 88.97). Table 20.0 shows the results of a t-test showing a significant relationship between total propofol dose and occurrence of PUAO ($p < 0.001$).

Table 20.0 - Independent Samples t-Test showing significant relationship between total propofol and PUAO.

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
Total dose of propofol	Equal variances assumed	38	**.000**	141.42857
	Equal variances not assumed	17.436	.001	141.42857

ANCOVA was again utilized to rule out the effect that BMI may be having on the above results. Table 21.0 shows that BMI did have a significant effect on the above result (p = 0.041) however after removing the effect that BMI was having, "total dose of propofol" was still significantly related to PUAO.

Table 21.0 - ANCOVA Tests of Between-Subjects Effects

Dependent Variable:Total dose of propofol

Source	Sig.
Corrected Model	.000
Intercept	.308
BMI	**.041**
PUAO	**.000**

Finally Table 22.0 shows a t-test indicating that there was no significant mean difference in total propofol dose between those subjects experiencing CUAO (n = 7 mean dose 375.71mg SD +/- 155.68) and those subjects who did not (n = 33 mean dose 289.70mg SD +/- 101.16) (p = 0.072) .

Table 22.0 - Independent Samples t-Test showing insignificant relationship between total propofol CUAO.

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
Total dose of propofol	Equal variances assumed	38	**.072**	86.01732
	Equal variances not assumed	7.112	.203	86.01732

ANCOVA was again utilized to rule out the effect that BMI may be having on the above results. Table 23.0 shows that BMI did not have a significant effect on the above result (p = 0.222). However, after removing the effect that BMI was having, mean "total dose of propofol" was now noted to be significantly different between groups.

Table 23.0 – ANCOVA Tests of Between-Subjects Effects

Dependent Variable:Total dose of propofol

Source	Sig.
Corrected Model	.095
Intercept	.172
BMI	**.222**
CUAO	**.044**

Tables 24.0 to 29.0 shows that the mean difference between ranks of preoperative anxiety scores were all statistically insignificant.

Table 24.0 - Mann-Whitney mean ranks of preoperative anxiety scores between groups that did, or did not desaturate.

	Oxygen desaturation? Y or N	N	Mean Rank	Sum of Ranks
Corah Anxiety Score	Yes	5	**14.40**	72.00
	No	35	**21.37**	748.00
	Total	40		

Table 25.0 – Test Statistics showing insignificant anxiety mean rank scores between oxygen desaturation groups.

	Corah Anxiety Score
Mann-Whitney U	57.000
Wilcoxon W	72.000
Z	-1.327
Asymp. Sig. (2-tailed)	**.185**

Table 26.0 - Mann-Whitney mean ranks of preoperative anxiety scores between groups that did, or did not have a PUAO.

	Partial upper airway obstruction PUAO? Y or N	N	Mean Rank	Sum of Ranks
Corah Anxiety Score	Yes	12	**19.92**	239.00
	No	28	**20.75**	581.00
	Total	40		

Table 27.0 – Test Statistics showing insignificant anxiety mean rank scores between oxygen PUAO groups.

	Corah Anxiety Score
Mann-Whitney U	161.000
Wilcoxon W	239.000
Z	-.220
Asymp. Sig. (2-tailed)	**.826**

Table 28.0 - Mann-Whitney mean ranks of preoperative anxiety scores between groups that did, or did not have a CUAO.

	Complete upper airway obstruction? Y or N	N	Mean Rank	Sum of Ranks
Corah Anxiety Score	Yes	7	**20.00**	140.00
	No	33	**20.61**	680.00
	Total	40		

Table 29.0 – Test Statistics showing insignificant anxiety mean rank scores between oxygen CUAO groups.

	Corah Anxiety Score
Mann-Whitney U	112.000
Wilcoxon W	140.000
Z	-.133
Asymp. Sig. (2-tailed)	**.895**

Upon completion of the procedure, patients went to the post recovery area where an RN documented the patient's Aldrete score (Appendix E) at time 0 and every 5 minutes.The average time to obtain an Aldrete score of 10/10, which is when a patient is considered sufficiently recovered to be discharged, was 3.50 minutes (Table 30.0).

Table 30.0 - Descriptive Statistics of Aldrete recovery score.

	N	Minimum	Maximum	Mean	Std. Deviation
Time reached Aldrete score of 10 (minutes)	40	0	30	**3.50**	5.905

Between 24 and 48 hours after discharge home, patients were contacted by telephone and questioned about their surgical and procedural sedation experience using a brief questionnaire. (Appendix F) Summaries of the patient responses are found below in Tables 31.0 – Table 36.0. Overall patients were very happy with how their procedural sedation went with low levels of pain and anxiety with very low anxiety and pain.

Table 31.0 – Summary of replies to 24 hours post operative questionnaire; Questions 1 - 7

Question #		% Yes	% No	Missing
1	Do you remember entering the operating room?	92.5	2.5	5
2	Do you remember events of the operation?	12.5	82.5	5
3	Do you remember unpleasant experiences during the operation?	5	90	5
4	Do you remember having pain during the operation?	5	90	5
5	Do you remember having nausea during the operation?	0	95	5
6	Do you remember vomiting during the operation?	0	95	5
7	Were you anxious during the operation?	0	95	5

Table 32.0 – Question #8 - Estimated anxiety (0-10) 24 hour post op

		Frequency	Percent	Valid Percent	Cumulative Percent
Score	0	35	87.5	92.1	92.1
	1	1	2.5	2.6	94.7
	2	1	2.5	2.6	97.4
	5	1	2.5	2.6	100.0
	Total	38	95.0	100.0	
Missing	System	2	5.0		
	Total	40	100.0		

Table 33.0 – Question #9 - Estimated severity of nausea (0-10) 24 hour post op

		Frequency	Percent	Valid Percent	Cumulative Percent
Score	0	34	85.0	89.5	89.5
	1	1	2.5	2.6	92.1
	2	3	7.5	7.9	100.0
	Total	38	95.0	100.0	
Missing	System	2	5.0		
	Total	40	100.0		

Table 34.0 – Question #10 - Estimated severity of pain (0-10) 24 hour post op

		Frequency	Percent	Valid Percent	Cumulative Percent
Score	0	29	72.5	76.3	76.3
	1	2	5.0	5.3	81.6
	2	4	10.0	10.5	92.1
	3	1	2.5	2.6	94.7
	5	1	2.5	2.6	97.4
	6	1	2.5	2.6	100.0
	Total	38	95.0	100.0	
Missing	System	2	5.0		
	Total	40	100.0		

Table 35.0 – Summary Statistics of Questions 8,9, and 10

		Estimated anxiety (0-10) 24 hour post op	Estimated severity of nausea (0-10) 24 hour post op	Estimated severity of pain (0-10) 24 hour post op
N	Valid	38	38	38
	Missing	2	2	2
	Mean	**.21**	**.18**	**.63**
	Median	.00	.00	.00
	Mode	0	0	0
	Std. Deviation	.875	.563	1.403
	Minimum	0	0	0
	Maximum	5	2	6

Table 36.0 – Summary of replies to 24 hours post operative questionnaire; Questions 11-12

Question #		**Mean response**
11	Number of episodes of vomiting prior to going home?	0
12	Number of episodes of dry heaves/retching prior to going home?	0

At the end of the procedure, the surgeon was asked to rank their level of satisfaction using a 5 point Likert scale (Appendix G). The surgeon's responsed neutral or greater 82.5% and the results are summarized below in Table 37.0.

Table 37.0 – Descriptive data of Surgeon level of satisfaction

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Very Satisfied	20	50.0	50.0	50.0
	Satisfied	8	20.0	20.0	70.0
	Neutral	5	12.5	12.5	82.5
	Unsatisfied	6	15.0	15.0	97.5
	Very unsatisfied	1	2.5	2.5	100.0
	Total	40	100.0	100.0	

Surgeon level of satisfaction was tested for normality to aid in choosing parametric versus non-parametric means of testing correlations with surgical difficulty. Table 38.0 shows that the data is slightly skewed.

Table 38.0 – Descriptives showing slightly skewed data set.

			Statistic	Std. Error
Surgeon level of satisfaction		Mean	**2.00**	.193
	95% Confidence Interval for Mean	Lower Bound	1.61	
		Upper Bound	2.39	
		5% Trimmed Mean	1.92	
		Median	**1.50**	
		Variance	1.487	
		Std. Deviation	1.219	
		Minimum	1	
		Maximum	5	
		Range	4	
		Interquartile Range	2	
		Skewness	.893	.374
		Kurtosis	-.514	.733

Surgical difficulty had been previously shown to be normally distributed data and the Shapiro-Wilk test verified that the surgeon level of satisfaction data was slightly skewed. (Table 39.0)

Table 39.0 - Tests of Normality for surgical difficulty and surgeon level of satisfaction.

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Surgical difficulty	.141	40	.045	.956	40	**.126**
Surgeon level of satisfaction	.294	40	.000	.782	40	**.000**

a. Lilliefors Significance Correction

Table 40.0 - Pearson's Correlations showing no correlation between surgical difficulty and surgeon level of satisfaction.

		Surgeon level of satisfaction	Surgical Difficulty
Surgeon level of satisfaction	Pearson Correlation	1	.050
	Sig. (2-tailed)		.757
	N	40	40
Surgical difficulty	Pearson Correlation	.050	1
	Sig. (2-tailed)	**.757**	
	N	40	40

Given that the surgical difficulty data was normally distributed and the surgeon level of satisfaction data was only slightly skewed both Pearson's and Spearman's correlations tests were used to see if the surgical difficulty could be blamed for the varying levels of surgeon satisfaction.

Table 41.0 - Spearman's Correlations showing no correlation between surgical difficulty and surgeon level of satisfaction.

			Surgeon level of satisfaction	Surgical Difficulty
Spearman's rho	Surgeon level of satisfaction	Correlation Coefficient	1.000	.085
		Sig. (2-tailed)	.	.602
		N	40	40
	Surgical difficulty	Correlation Coefficient	.085	1.000
		Sig. (2-tailed)	**.602**	.
		N	40	40

Both Pearson's and Spearman's tests showed no relationship between surgical difficulty and the surgeon level of satisfaction (Table 40.0 and 41.0). This lack of relationship is once again displayed in a dot plot format below in Figure 5.0

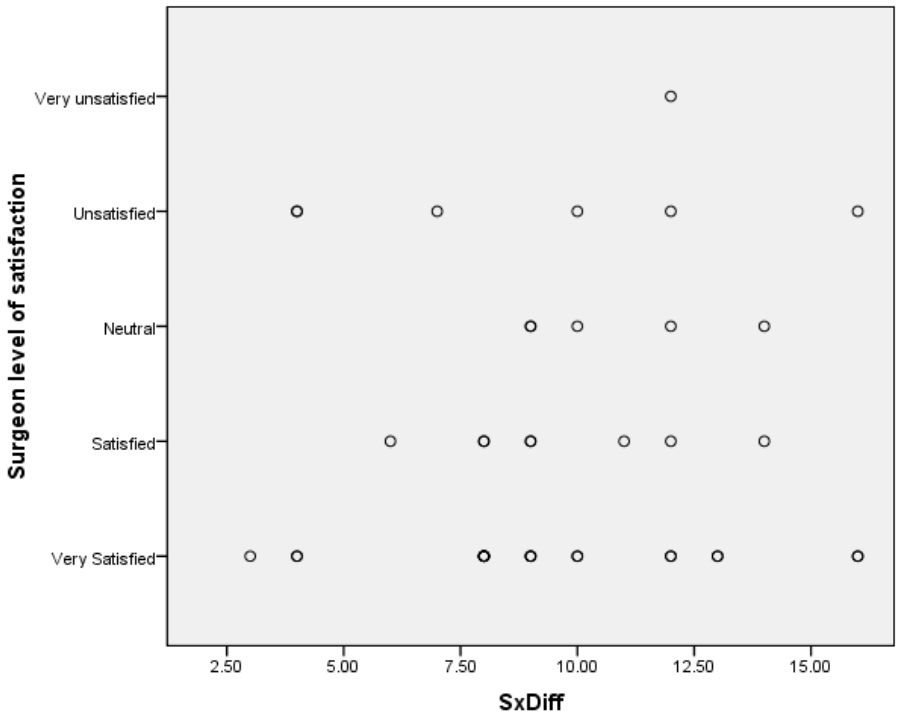

Figure 6.0 – Dot plot showing no relationship between surgical difficulty and surgeon level of satisfaction.

Pre-operative measures such as BMI and Corah Anxiety score were also tested for any possible correlation with the surgeon's level of satisfaction. These were chosen to help determine if we could predict who would do well with propofol only sedation before it was initiated. Pre-operative measures such as BMI and Corah Anxiety score also showed no correlation with surgeon level of satisfaction (Table 42.0).

Table 42.0 – Spearman's correlations showing no relationship between surgeon level of satisfaction and BMI or pre-operative anxiety.

			Surgeon level of satisfaction	BMI
Spearman's rho	Surgeon level of satisfaction	Correlation Coefficient	1.000	-.051
		Sig. (2-tailed)	.	.756
		N	40	40
	BMI	Correlation Coefficient	-.051	1.000
		Sig. (2-tailed)	**.756**	.
		N	40	40
	Corah Anxiety Score	Correlation Coefficient	-.026	.009
		Sig. (2-tailed)	**.872**	.955
		N	40	40

Tables 43.0 and 44.0 show no significant correlation between surgeon level of satisfaction and paradoxical response (Tables 43.0 and 44.0)

Table 43.0 - Surgeon level of satisfaction Crosstabulation with Paradoxical response.

		Paradoxical response to sedation?		Total
		Yes	No	
Surgeon level of satisfaction	Very Satisfied	6	14	20
	Satisfied	1	7	8
	Neutral	3	2	5
	Unsatisfied	5	1	6
	Very unsatisfied	1	0	1
Total		16	24	40

Table 44.0 – Test for correlation between Surgeon level of satisfaction and Paradoxical movements.

		Value	Asymp. Std. Error	Approx. T	Approx. Sig.
Interval by Interval	Pearson's R	-.424	.139	-2.884	.006
Ordinal by Ordinal	Spearman Correlation	**-.357**	.154	-2.357	.024

CHAPTER 4 DISCUSSION

Today, the sedation options available for oral and maxillofacial surgeons are vast. A large range of medications and routes such as oral, intramuscular, inhalational, and intravenous, exist. The most commonly utilized route is intravenous sedation as it allows one to safely titrate the medication(s) and it provides venous access in case the administration of reversal or emergency medications is necessary. There are several methods by which intravenous sedation can be administered and these include patient controlled, continuous infusion or manual bolus infusion. Patient controlled sedation was reported in the oral and maxillofacial surgery literature by Rodrigo *et al* in 2004. (31) Many practitioners prefer to have better control over the depth of sedation and thus this method is not popular. Continuous intravenous infusion is commonly used and minimizes the large variations in the plasma concentrations of the medications that can be seen with other IV sedation methods. Manual bolus infusion provides satisfactory sedation for short oral and maxillofacial surgery procedures and is preferred by many practitioners. Some researchers feel that the infusion pumps are impractical and cumbersome for short procedures. Futhermore, the safety and simplicity of manual bolus dosing has been demonstrated(13,32).

Titration allows for a specific level or depth of sedation to be achieved and this is procedure and surgeon specific. Moderate to deep sedation is typically desired for the removal of third molars. The 2012 American Association of Oral and Maxillofacial Surgeon's Parameters of Care is now in its 5th edition.(33) This document is supported by the International Association of Oral and Maxillofacial Surgeons (IAOMS) and the Canadian Association of Oral and Maxillofacial Surgeon (CAOMS).

4.1 Defining levels of sedation

Having a clear definition and understanding regarding the different levels of sedation is important. The Parameters of Care agree with the distinction between the different levels put forth by the ASA in 2009

and are as follows:(33)

"Minimal Sedation (Anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes and ventilatory and cardiovascular functions are unaffected.

Moderate Sedation/Analgesia is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.

Deep Sedation/Analgesia is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully** following repeated or painful stimulation. The ability to independently maintain ventilatory function may be impaired. Patients may require assistance in maintaining a patent airway, and spontaneous ventilation may be inadequate. Cardiovascular function is usually maintained.

General Anesthesia is a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation. The ability to maintain ventilatory function is often impaired. Patients often require assistance in maintaining a patent airway, and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function. Cardiovascular function may be impaired.

The original wording was maintained in the above definitions because it is important that the subtle differences between levels of sedation and anesthesia are appreciated. The key component to "minimal sedation" is the fact that cardiovascular and ventilatory reflexes are unaffected. Single intravenous drug or

oral sedation would typically be used to achieve minimal sedation. Albeit a continuum, moderate sedation is distinct from minimal sedation in that cardiopulmonary function begins to be affected yet the patient still responds purposefully. As soon as the ventilatory status of the patient is impaired the practitioner must be competent in airway management. With deep sedation and analgesia the patient's ventilatory function is further impaired and the practitioner will need to be prepared to assist the patient in ventilation if required. However, patients should still respond to a painful stimulus. This is one of the defining points that differentiate deep sedation from general anesthesia in which patients are not arousable even to painful stimuli. Ventilatory function is often impaired at this level of anesthesia and practitioners often use supraglotic devices, such as a laryngeal mask, or perform endotracheal intubation to facilitate ventilatory support. Moderate to deep levels of sedation are often what are being sought for outpatient oral and maxillofacial surgical procedures carried out in the office using multidrug intravenous sedation.

What is crucial to understand is that these levels of sedation represent a continuum from the normal awake patient to full general anesthesia. This can result in a deeper level of sedation being obtained than initially desired. Consequently, any practitioner providing sedation must be prepared to manage a patient that inadvertently becomes more deeply sedated than originally planned.

4.2 Defining sedation related adverse events

Serious adverse events during procedural sedation are fortunately rare. This makes designing studies comparing the safety of different sedation protocols difficult as the rarity of such events necessitates impossibly large sample sizes. A possible solution lies in combining the outcomes of multiple sedation research studies. Theoretically, meta-analysis can pool massive numbers of outcomes and capture rare or uncommon events. Unfortunately, the terminology used to describe sedation outcomes and adverse events has historically been broad, with there being significant variation on the definition and method of capturing

adverse sedation events. This complicates one's ability to perform systematic reviews and meta-analysis which would allow for the development of evidence based procedural sedation guidelines. This problem was identified by Bhatt *et al* (14) . Bhatt organized a group of pediatric sedation researchers and experts to develop consensus-based recommendations for standardizing procedural sedation terminology and reporting of adverse events (14). The Panel consisted of 6 pediatric emergency physicians and 2 pediatric anesthesiologists. Their recommendations for sedation research were published in 2009 and have been referred to as the "Quebec Criteria" as the group was based out of Montreal (14). (Appendix D)

The panel identified that the traditional way of measuring adverse events was using a pre-specified "threshold and duration" to describe adverse events. For instance, if a patient had a desaturation of <90% (threshold) for > 30 seconds (duration) this would be captured and recorded in the traditional manner as a "respiratory compromise episode". Bhatt *et al* felt that this was sub-optimal as this mode of documentation misses several clinically important situations that may speak more accurately to the depth of sedation and the true frequency of adverse events. They instead promoted an "intervention-based definition".

The "intervention based definition" requires specific clinical criteria to be present as well as one or more interventions to be performed to treat the event. For instance, if a patient were clinically noted to be experiencing a partial upper airway obstruction, the operator may preemptively perform a chin lift jaw thrust maneuver. This patient may then only desaturate to 91% and then return to 99 or 100% shortly there after. Using the traditional criteria, this episode would not have been recorded while the proposed "intervention-based definition" would have captured the event.

The Quebec Criteria expand greatly on respiratory compromise, appropriately breaking it down into oxygenation and ventilatory adverse events. Ventilation is further broken down into central apnea, complete upper airway obstruction (CUAO), partial upper airway obstruction (PUAO), laryngospasm, and pulmonary

aspiration. Once again, in order for an adverse event to be recorded there would need to be both a clinical finding as well as an intervention to correct it. Thus if a patient was snoring during sedation they would be clinically diagnosed as having a PUAO but if no intervention was made to correct it, then the Quebec Criteria would deem this clinically insignificant and the event would not be captured.

The committee also agreed that standardized reporting on events such as bradycardia, hypotension, retching/vomiting, excitatory movements, paradoxical response and permanent complications was necessary.

Traditionally respiratory compromise was defined as apnea for more than 30 seconds or an oxygen saturation of less than 90%. Hemodynamic compromise was defined as a systolic blood pressure of less than 90 mm Hg or a decrease from baseline of > 20%.

This study used both the Quebec Criteria for adverse event reporting in addition to the traditional definition of respiratory and hemodynamic compromise. This allows the collected data to contribute to future systematic reviews while still allowing it to be compared with previous studies that utilized traditional definitions of adverse events.

4.3 Safety of Propofol only sedation during extraction of third molars

Using the traditional criteria the incidence of respiratory compromise was found to be 15% (Table 5.0). This included the 5 patients who experienced oxygen desaturation below 90% in association with a PUAO and 1 additional patient who experienced a central apnea which was not associated with an oxygen desaturation. When using the Quebec criteria a respiratory compromise incidence of 50% was found. This included the 12 patients (30%) who experienced PUAO (Table 6.0), the 8 patients (17.5%) who experienced CUAO (Table 7.0), and the one patient (2.5%) who experienced central apnea (Table 8.0).

Using the traditional criteria, the incidence of bradycardia (HR < 60) was 10% and hypotension was

5%. When using the Quebec Criteria, the incidence of both of these hemodynamic parameters was zero as there was no intervention done to correct any of the above hemodynamic events thus rendering the events insignificant according to the Quebec Criteria.

The Quebec Criteria were discussed by Green *et al* in a pediatric editorial in 2008.(34) Green mentions that despite the pediatric intent of the guidelines, each element applies readily to adults and represent an advance in sedation research and deserve use. Green speculates that by using the new criteria the frequency of most "adverse events" will decrease substantially. When comparing the traditional and the Quebec Criteria in our own study this was exactly what was observed when it came to hemodynamic adverse events. However, when looking at respiratory adverse events the opposite trend was observed. Traditional criteria identified adverse respiratory events in 15% of the cases while the Quebec criteria identified events in 50% of the cases.

The number of respiratory events seen in our study was in keeping with published reports of respiratory depression which have been reported to occur with a frequency of between 0.9% up to 49%.(2,25) Black *et al* reported in her systematic review that when propofol was compared to methohexital, etomidate, propofol/ketamine, and midazolam/fentanyl in randomized trials, no significant difference in rates of respiratory depression were observed.(25) Black *et al* summarized the following additional outcomes from 13 randomized controlled clinical trials that evaluated propofol for procedural sedation in adults in the emergency department. (Table 45.0)

Table 45.0 – Summary of propofol procedural sedation clinical outcomes as reported by Black *et al*.

Clinical finding	Result
Time to onset of sedation	2.0 – 6.7 minutes
Recovery	5 – 10 minutes
Procedural success	90 – 100%
Hypotension	0 – 17.1%
Patient satisfaction	94%
Apnea	17.7%

4.4 Preoperative anxiety score

Green *et al* in his editorial regarding the Quebec Criteria commended Bhatt et al on the inclusion of a preoperative anxiety score stating that this is often ignored or overlooked in the emergency department sedation literature. For the present study, the "Corah Dental Anxiety Score" was administered preoperatively as this has been most commonly reported in the oral surgery literature. (35) (Appendix A) Mean Corah Dental Anxiety score was 14.63 and was not found to be statistically significantly correlated with incidence of oxygen desaturation, PUAO, CUAO or surgeon satisfaction.

4.5 Quantifying the depth of sedation

Green et al did not think that the Quebec Criteria were without their shortcomings. Firstly, the Criteria did not propose a mechanism to quantify the depth of sedation. Secondly, the Criteria made no mention of the fasting time prior to procedural sedation. Finally, the Criteria only briefly mentioned capnography and the role it can play in detecting ventilator depression. The above topics and how our study overcame these shortcomings are discussed below.

To quantify the depth of sedation the Ramsay Sedation Scale (RSS) was used. This was first published in 1974 as a means of quantifying the level of sedation in 30 ICU patients sedated with alphaxalone-alphadolone. This easy to use 6 point scale is intended to be employed bedside. A level 1 on the Ramsay Sedation score indicates that the patient is anxious and agitated or restless or both. A level 2 indicates that the patient is cooperative, oriented, tranquil and accepts mechanical ventilation. A level 3 indicates that patient responds to commands only. A level 4 indicates a brisk response to light glabellar tap, whereas a level 5 indicates a sluggish response to light glabellar tap. A level 6 corresponds to a patient that is deeply sedated showing no response to a glabellar tap.(29) Since its development it has been widely used in the sedation literature in all specialties and has been validated and deemed to be reliable.(9,36,37) A level of 3 or 4 has been considered moderate sedation while levels 5 and 6 are considered deep.(38)

Our patients were on average sedated to a RSSS of 3 – 4. No absolute level of RSS was required prior to proceeding with local anesthesia and then the procedure. This was intentionally done to avoid prolonging the procedure unnecessarily in those patients who, despite the usual dosing of propofol were at a lighter level of sedation but nevertheless were happy to proceed with surgery.

4.6 Fasting guidelines

Due to the rare nature of peri-operative aspiration, fasting guidelines are based on expert consensus instead of published evidence.(39) There is insufficient evidence to associate fasting time, gastric pH or volume, with the probability of aspiration. There is no evidence that fasting has an impact on the incidence or outcome of this complication. The American College of Emergency Physicians Sedation Guidelines state: Recent food intake is not a contraindication for administering procedural sedation and analgesia but should be considered in choosing the timing and target level of sedation.(39) In a separate guideline for procedural

sedation and analgesia, the ASA states "The literature does not provide sufficient evidence to test the hypothesis that pre-procedure fasting results in a decreased incidence of adverse outcomes in patients undergoing either moderate or deep sedation."(39) Due to the lack of evidence the ASA used a task force that concluded that "In urgent, emergent, or other situations in which gastric emptying is impaired, the potential for pulmonary aspiration of gastric contents must be considered in determining the target level of sedation, whether the procedure should be delayed, or whether the trachea should be protected by intubation." Green *et al* recommended a 3-hour fasting period prior to procedural sedation and analgesia for elective procedures instead of the traditional fasting scale used by the ASA for patients undergoing general anesthesia (ranges from waiting 8 hours after a heavy meal to only 2 hours after having had clear liquids prior to induction for a general anesthetic). Green's guideline is based on the intuitive recognition that vomiting and aspiration requires something to be in the stomach. The authors clearly state that this is simply a guideline. In the current study, patients were requested to fast for 8 hours preoperatively as this mirrored similar fasting periods in comparable studies in the oral and maxillofacial surgery literature. (35) There were no cases of vomiting, retching or aspiration in our study.

4.7 Appropriate Monitoring

The appropriate monitoring for a patient is clearly discussed in both the provincial dental board guideline (2010) as well as the AAOMS' Parameters of Care (2012)(33)(40). The Parameters of Care 2012 recommend the following:

Moderate sedation

1. Continuous monitoring of heart rate, blood pressure, ventilation, SpO_2 (arterial oxygen saturation), and

temperature (when indicated) at least every 5-minutes

2. Continuous electrocardiograph (ECG) monitoring

3. Consider end-tidal carbon dioxide ($ETCO_2$) measurement and provide continuous $ETCO_2$ monitoring recommended as of January 2014

Deep sedation

1. Documentation of continuous monitoring, including heart rate, blood pressure, oxygen saturation, and ventilation (and temperature, if monitored)

2. Ventilatory monitoring should include all of the following:

- Auscultation of breath sounds when appropriate.
- Observations of chest wall excursions
- Use of a precordial or pretracheal stethoscope when appropriate
- Observation of the reservoir bag when appropriate
- Monitoring colour of skin, mucosa, nail beds, and surgical site
- Monitoring of expiratory gases including $ETCO_2$ (capnometry or capnography) required as of January 2014

The most significant difference between the provincial and the Parameter of Care guidelines is the recommendation for $ETCO_2$ monitoring as provincial guidelines only necessitate its use if endotracheal intubation is used to during general anesthesia. However, this is expected to be updated soon.

The effective date for mandating the use of capnography is January 2014. Practitioners were given

approximate 24 months' notice of the impeding change to allow them adequate time to outfit their office with this technology. This recommendation stems from a wealth of research from other specialties, including anesthesiology, gastroenterology and emergency medicine, that have conclusively demonstrated an improved outcome when capnography is used for PSA.

The 2012 Parameters of Care also state "Unless there are procedural contraindications, supplemental oxygen must be administered while the patient is sedated. The ability and equipment to provide positive pressure oxygen must also be available." (33)

4.8 The role of supplemental oxygen

The American Society of Anesthesiology also recommends the use of supplemental oxygen for patients undergoing deep sedation and recommend that it be considered for those undergoing moderate sedation.(41) Pre-oxygenation of the patient about to undergo general anesthesia is standard practice. Pre-oxygenation can allow the patient to maintain normal oxygen saturation for up to 5 minutes, depending on the patient's residual volume, in the setting of pharmacologically induced apnea while a definitive airway is being established. Thus it is a logical recommendation for patients undergoing procedural sedation to have supplemental oxygen as it may potentially prevent hypoxic events. Unfortunately, until recently there has been little research to support this assumption and some authors have previously made arguments against the use of supplemental oxygen suggesting that it may delay the identification of respiratory distress by maintaining oxygen saturation even in the presence of hypoventilation.(42) The research of Deitch *et al* demonstrated both the utility of supplemental oxygen as well as $ETCO_2$ during PSA.(37)

In 2007 Deitch *et al* conducted a Randomized Controlled Trial on the Utility of Supplemental Oxygen During Emergency Department Procedural Sedation and Analgesia With Midazolam and Fentanyl.(37) This study enrolled 80 patients who were randomized into one of two study arms. Forty-four

patients received supplemental oxygen at a rate of 2 L via nasal cannula and 36 patients received compressed air as a placebo during PSA in the emergency department. The goal of this investigation was to determine if supplemental oxygen could reduce the incidence of hypoxia by 20%. Patients in both arms received midazolam and fentanyl to achieve a moderate depth of sedation with the median RSS of 4 (range 2-5). Patients were monitored with the usual monitors including EKG, oxygen saturation, pulse rate, respiratory rate, and noninvasive blood pressure.

$ETCO_2$ was also monitored by the study investigator to aid in the diagnosis of respiratory depression; however the treatment team was kept blinded to the $ETCO_2$ levels. Respiratory depression was defined as an oxygen saturation of less than 90% (hypoxia), an $ETCO_2$ greater than 50 mm Hg, an absolute $ETCO_2$ change from baseline of greater than 10 mm Hg or a loss of the $ETCO_2$ waveform. Respiratory depression was considered a secondary outcome and will be discussed later.

Overall only 13.9 % of subjects in the study developed hypoxia. Six of forty-four patients in the oxygen group and 5/36 patients in the compressed air group developed hypoxia. There were no adverse events in any of the patients who became hypoxic. The difference between groups was not statistically significant. The incidence of hypoxia was lower than anticipated and made the goal of a 20% reduction impossible.

The same authors published another Randomized controlled trial in the same journal one year later entitled "The Utility of Supplemental Oxygen During Emergency Department Procedural Sedation With Propofol".(38) This was essentially a repeat of the 2007 study with some important modifications. One hundred and ten patients were randomized into one of two study arms. Fifty-six patients received supplemental oxygen at a rate of 3 L via nasal cannula and 54 received compressed air. The goal of this investigation was the same but patients in both arms were sedated using propofol (1-1.5mg/kg push) to a deep level of sedation with the median RSS of 5 (range 2-6). Patients were monitored with the same monitors

including $ETCO_2$. Once again $ETCO_2$ was also monitored by the study investigator to aid in the diagnosis of respiratory depression; however the treatment team was kept blinded to the $ETCO_2$ levels. Respiratory depression was defined as an oxygen saturation of less than 93% (hypoxia), an $ETCO_2$ greater than 50 mm Hg, an absolute $ETCO_2$ change from baseline of greater than 10 mm Hg or a loss of the $ETCO_2$ waveform. As per the 2007 study, respiratory depression was considered a secondary outcome and will be discussed later.

Overall 22.7% of subjects in the study developed hypoxia: ten out of fifty-six patients (18%) in the oxygen group and 15/54 patients (28%) in the compressed air group (p=0.3). There were no adverse events in any of the patients who became hypoxic. A 10% reduction in hypoxia was found in the supplemental oxygen group. While this was statistically insignificant, a trend toward reduction of hypoxia was appreciated. Overall the incidence of hypoxia was likely higher in this study for several reasons. First of all, the drug(s) used changed from a midazolam/fentanyl combination to solely propofol and the depth of sedation changed from moderate to deep. Patient were given 3 L instead of only 2 L of oxygen via nasal cannula and the definition of hypoxia was changed from $SPO_2 < 90\%$ to 93%. The increased incidence was still within reported normal ranges of hypoxia. Given the trend toward a reduction of hypoxia the authors set forth to conduct a study using 100% FiO_2.

In 2011 Deitch *et al* produced a randomized controlled trial entitled "The Utility of High-Flow Oxygen During Emergency Department Procedural Sedation and Analgesia With Propofol".(43) One hundred and seventeen patients were randomized to receive 100% oxygen (n=59) or compressed air at 15 L/minute (n=58) via non-rebreather mask for 5 minutes prior to initiation of procedural sedation. Sedation was achieved using propofol (1mg/kg push followed by 0.5mg/kg bolus) to moderate depth of sedation with the median RSS of 4 (range 2-5). Hypoxia was defined as an oxygen saturation of less than 93% for 15 seconds

or greater. Respiratory depression was defined as an $ETCO_2$ greater than 50 mm Hg, an absolute $ETCO_2$ change from baseline of greater than 10 % or loss of the $ETCO_2$ waveform. $ETCO_2$ information was not blinded in this study. A significant reduction in hypoxia 11/59 (19%) versus 24/58 (41%) was observed in this study (p=0.007).

These were some of the first randomized controlled trials addressing the issue of supplemental oxygen. It was concluded by the authors that supplemental oxygen should be routinely administered as it clearly has the potential to reduce hypoxia and presented no harm to any of the patients.

4.9 The role of capnography

As eluded to in the aforementioned studies by Deitch *et al* (37,38) respiratory depression, with and without hypoxia, as defined utilizing $ETCO_2$ was a secondary outcome. In the 2007 study, (37) Deitch *et al* found that above and beyond those patients that became hypoxic, 14 patients in both the supplemental oxygen arm as well as the placebo arm met the $ETCO_2$ definition for respiratory depression. None (0/28) of these respiratory depression episodes were clinically detected by the treating physician.

In the 2008 study, (38) Deitch *et al* found that physicians identified only 1/27 patients who experienced respiratory depression as defined by $ETCO_2$ criteria . The majority of these were diagnosed via a depression in $ETCO_2$ 10mm Hg below baseline. This type of hypoventilation is appropriately termed "hypopneic hypoventilation" and should be distinguished from bradypneic hypoventilation. Hypopneic hypoventilation occurs most often is association with sedative hypnotics and describes the decrease in tidal volume in a patient developing upper airway obstruction with preservation of respiratory rate. This decrease in tidal volume decreases the minute ventilation and increases the dead space resulting in a preservation or decrease in $ETCO_2$ in the setting of hypoventilation.(38,44) These events are captured in studies that define respiratory depression as either $ETCO_2$ < 30mm Hg, or an $ETCO_2$ decrease of 10mm Hg or a decrease of

$ETCO_2$ of 10% below baseline. All of these definitions appeal to the same physiologic response to the sedative hypnotics. Some studies have failed to include this in their definition of respiratory depression and thus produce results that are invalid.(45)

Bradypneic hypoventilation on the other hand is more commonly caused by opioids and describes a type of hypoventilation characterized by a decrease in respiratory rate with preservation of the tidal volume. This results in an increase in $ETCO_2$ to above 50 mmHg. Alternatively an increase in $ETCO_2$ of 10mmHg or more or an increase of 10% or more above baseline can be seen. Regardless, the above 2 studies prompted the authors to conduct a separate study to specifically determine the utility of $ETCO_2$ for PSA.

In 2010 Deitch *et al* reported on a similar study as those reported above entitled "Does End Tidal CO_2 Monitoring During Emergency Department Procedural Sedation and Analgesia With Propofol Decrease the Incidence of Hypoxic Events?"(46) This study randomized 132 patients into one of two arms; $ETCO_2$ data available and $ETCO_2$ data not available to the treating physician. $ETCO_2$ data was available to the study investigator for both groups. Hypoxia was defined similar to the above studies and was observed in 17/68 (25%) in the $ETCO_2$ arm and 27/64 (42%) with blinded capnography (p=0.35). Overall there was a 32.5% rate of hypoxia. In the subjects where capnography data was available to the treating physician there was 17% less desaturations compared with those subjects with blinded capnography. In keeping with the above finding, there were 18% more interventions such as verbal/physical stimulus or airway reposition, in the group in which the treating physician was aware of the capnography data. In both arms of the study, capnography identified all cases of trending hypoxia anywhere from 5 to 240 seconds (median 60 seconds) before the actual hypoxic threshold was met.(46)

In 2011 Waugh *et al* included Deitch's 2008 study, along with four other well designed randomized controlled trials, in a meta-analysis intended to evaluate the utility of capnography during procedural

sedation.(38,47–50)

One of the studies included in this meta-analysis deserves separate attention. Burton *et al* conducted a prospective blinded study entitled "Does End-tidal Carbon Dioxide Monitoring Detect Respiratory Events Prior to Current Sedation Monitoring Practices?"(41) Sixty patients undergoing procedural sedation in the emergency department were enrolled in a single arm designed study. The medication used for procedural sedation was not controlled for, however the majority of sedations were carried out with propofol (68%) or ketamine (20%). The dosage or depth of sedation was not disclosed. All patients were monitored with the standard procedural sedation monitors including combined oral/nasal cannula for $ETCO_2$ monitoring. Supplemental oxygen was delivered at 2L/min. Acute respiratory events were defined as apnea, an SpO_2 of less than 92% or the need to perform any one of the following actions; increase the amount of supplemental oxygen from 2L to 4L/min; the use of a bag-valve mask; the insertion of an oral/nasal airway; an airway repositioning maneuver; physical/verbal stimulation; or the administration of reversal agents. $ETCO_2$ levels $\geq$ 50 mm Hg or $\leq$ 30 mm Hg or a change of $\geq$ 10 mm Hg from baseline were considered investigational measures of acute respiratory distress. The clinical team was blinded to study monitoring data, including $ETCO_2$ data, throughout the procedural sedation period. Investigators documented 36 cases (60%) of acute respiratory distress based on $ETCO_2$ data. However, the clinical team detected only 20 cases (33%) of acute respiratory distress using clinical observation alone. Seventeen of these 20 patients (85%) also showed $ETCO_2$ evidence of respiratory distress with 70% of these showing $ETCO_2$ changes prior to the clinical changes.

This study demonstrated that subjective clinical ventilatory assessment will miss or be delayed in diagnosing respiratory depression during PSA. The study concluded that objective ventilatory assessment via $ETCO_2$ detects respiratory depression earlier than conventional monitoring.

Waugh *et al* concluded in their meta-analysis that during procedural sedation, cases of respiratory depression were 17.6 times more likely to be detected if patients were monitored by $ETCO_2$ (95% CI 2.5 - 122.1; P<0.004).(47) Waugh states that if there is an easy, safe, and inexpensive way to enhance their detection, that it is logical to take advantage of that method.

It is now generally agreed upon in the literature that $ETCO_2$ is required for optimal monitoring of ventilation of the sedated patient.(51) However, $ETCO_2$ monitoring is not without its opponents. Some authors have specifically addressed these controversies in the literature. (48,52,53)

One of the arguments targets the clinical significance of subclinical $ETCO_2$ changes on patient outcomes. There were no adverse events in any of the patients in the above mentioned studies regardless of whether or not $ETCO_2$ was utilized.

There is also an increased costs associated with monitoring $ETCO_2$ including the upfront cost of the monitors as well as the ongoing costs of the required single use specialized nasal cannulas. At the CDHA OMFS department approximately 3500 procedural sedations are performed annually by the 6 attending surgeons and 6 residents. The standard nasal cannulas costs $0.34/per while those used in this study that allow $ETCO_2$ monitoring costs $7/per. If the study tubing was used for all sedations through out the year this would equate to a cost increase of $23,310.

Fortunately adverse events are rare; however they do occur and are most commonly respiratory in nature. The cost associated with harming even a single patient due to a potentially preventable respiratory compromise far outweighs the annual disposable costs of CO_2 monitoring equipment. Furthermore, less costly nasal cannulas are likely to come to market.

There is a paucity of research in the oral and maxillofacial literature regarding the utility of $ETCO_2$

during procedural sedation.(54) $ETCO_2$ was monitored in our study primarily for the continuous capnogram which allowed us to accurately monitor breath to breath ventilatory status which aided in the diagnosis of apnea as well as complete or partial airway obstruction. While continuous capnometry was available in our study, respiratory compromise was still defined using the traditional definitions as well as those found in the Quebec Criteria. Future research efforts would benefit from utilizing the data provided by continuous capnometry data.

4.10 Effects of dose in Propofol only sedation during extraction of third molars

The propofol induction (1 mg/kg) and maintenance protocol (10 – 20 mg every minute) chosen for this study was based on existing studies available at the time and expert opinion.(2) This induction dose is in keeping with the most commonly reported protocols.(25) The average total propofol dose used was 304 mg (Table 12.0). The propofol dose was positively correlated with surgical difficulty and surgical time and was statistically significant (Table 14.0). The mean dose of propofol was found to be statistically significantly different between groups that experienced oxygen desaturation, PUAO, and CUAO and those that did not (Table 18.0 – 23.0). Oxygen desaturation and PUAO were statistically significant and shown to be independent of the effect of BMI. No effort was made to evaluate differences in propofol dose and central apnea because this was such a rare event (N=1). Interestingly, the average dose of and the incidence of CUAO only reached statistical significance after controlling for the effect of BMI (Table 23.0).

Patient recovered quickly reaching an Aldrete score of 10/10 on average at 3.5 minutes. This was faster than that reported by Black *et al* as noted in Table 45.0. This may have been secondary to the nature of the titration by the physician administering the propofol. For instance, once the last third molar was extracted suturing was often required. At this point, the physician would usually elect to no longer administer additional boluses of propofol as the stimulating part of the procedure was completed. This allowed the

patient to begin recovering prior to termination of the procedure (last suture placed).

4.11 Satisfaction of Propofol only sedation during extraction of third molars

Surgeon satisfaction is noted in Table 37.0. Surgeon experiences were rated at neutral, satisfied, or very satisfied in 82.5%. In an effort to help predict those patients who would do well with only receiving propofol while still maintaining a high level of surgeon satisfaction, several parameters were examined. The parameters chosen could all be assessed prior to the start of sedation. Surgical difficulty can generally be determined from appropriate diagnostic imaging and careful patient assessment preoperatively. BMI and the Corah anxiety score are also obtained prior to initiating the procedure and these two parameters may also predict the appropriateness of using propofol alone for PSA in oral and maxillofacial surgery. Interestingly no correlation could be found between these preoperative measures and surgeon satisfaction (Table 40.0 – 42.0). Thus it is impossible to tell who will do well until after the procedural sedation and the surgery are underway.

The only outcome measure that showed a mild to moderate correlation with surgeon satisfaction was whether or not the patient required hand holding or not which was recorded under paradoxical reaction (Table 10.0 and Table 43.0).

Regardless of surgeon satisfaction patients were extremely satisfied with very few patients having recall of the procedure or any unpleasant experiences (Table 31.0 – 36.0).

4.12 Study Limitations

This study was limited by the fact that there was no control group to compare the outcomes with. Future studies would benefit from randomizing patients to one of multiple treatment arms comparing the most commonly used sedative combinations. Furthermore while capnography was used in this study, the

capnometry component could be further utilized as it is in other studies for the detection of subclinical respiratory depression.

CHAPTER 5 CONCLUSIONS

Propofol alone for procedural sedation is safe from a cardiorespiratory perspective and effective with a high level of patient and surgeon satisfaction. However, patients will frequently and unpredictably require hand holding throughout the procedure requiring a extra assistant in the operatory. Propofol alone may be better reserved for very short procedures on patients that demand sedation yet would benefit from a faster recovery.

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Appendix A

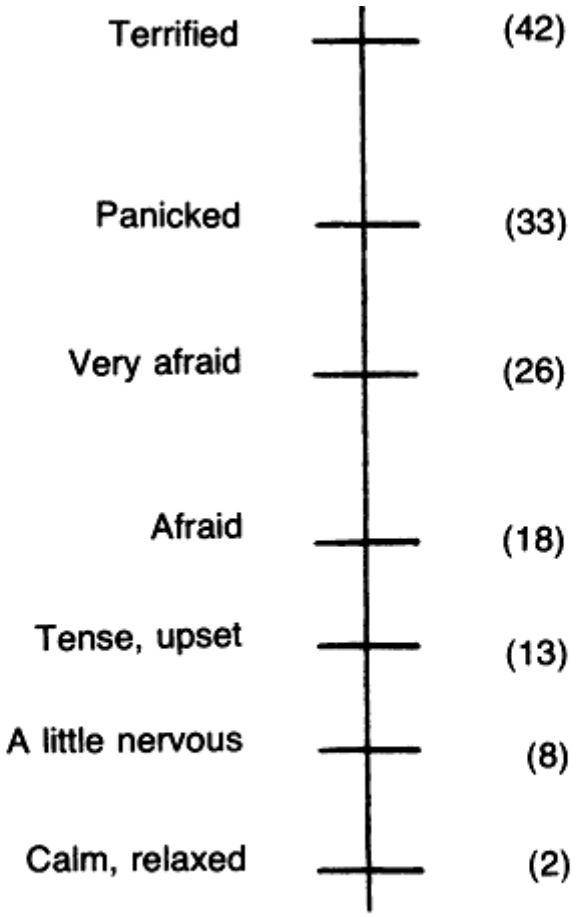

Fig. 1 — The seven-descriptor anxiety scale in graphic form. The numbers in parentheses indicate the scale values of the descriptors but were *not* shown on the scale as presented to subjects.

Appendix B

Table 1 Modified RSS score

Light
- 1 = Anxious and agitated or restless or both
- 2 = Cooperative, orientated, and tranquil
- 3 = Responds to commands only

Deep
- 4 = Brisk response to a light glabellar or loud auditory stimulus
- 5 = Sluggish response to a light glabellar tap or loud auditory stimulus
- 6 = No response to a light glabellar tap or loud auditory stimulus

Appendix C

Queen Elizabeth II Health Sciences Centre

EMERGENCY DEPARTMENT CARE MAP — PROCEDURAL SEDATION

GUIDELINES:

__ Consent obtained by physician
__ Baseline vital signs and O_2 sat
__ Allergies / Medical history reviewed
__ Patient's weight _____
__ Last po intake _____ __ Liquids __Solids
__ Suction present
__ Sedation cart present
__ VS during & post procedure:
q 5 minutes for 15 minutes
q 15 minutes X3 or until D/C criteria met
__ Discharge criteria met/report to area RN

PROCEDURE: _____

Time start: _____ **Time finish:** _____

PRE-SEDATION ASSESSMENT ASA Score is < 2 __

AIRWAY:
Assess potential for difficult mask ventilation
__Beard __Obese __No teeth __Elderly __Snores

Assess potential for difficult intubation
__Mallampati __Evaluate 3-3-2 __Anatomy
__Pathology

BREATHING: __Easy __Shallow __Wheezy
__Cough __Accessory muscles __Laboured
__Congested __Retractions __Stridor

CIRCULATION: __Pink __Warm __Dry __Pale
__Cool __Diaphoretic __Cyanosed __Hot
__Mottled __Pedal edema

IV ACCESS: __IV NS 1000 cc (document on pt record)

OXYGEN: Face Mask __40% __100%

Comments:
_____
_____

Signature: _____ **Initials:** ___

Signature: _____ **Initials:** ___

Physician signature: _____
(For medications verbally ordered)

Written discharge instructions explained to:

__Patient __Family **Initials:** _____

Vital Signs: During and Post Procedure

Time	Baseline				
BP					
Pulse					
RR					
O_2 Sat					
Discharge criteria					
Activity					
Breathing					
Circulation					
LOC					
Total scores					

Time	Medication	Dose	Route	Initials

Discharge Criteria Key

1. Activity
   0 = Unable to lift head or move extremities voluntarily or on command
   1 = Lifts head spontaneously and moves extremities voluntarily or on command
   2 = Able to ambulate as prior to sedation

2. Breathing
   0 = Apneic
   1 = Dyspnea or shallow, irregular breathing
   2 = Able to breathe deeply & cough on command

3. Circulation
   0 = Systolic BP below 100 mm Hg
   1 = Systolic BP above 100 mm Hg
   2 = Systolic BP within normal limits for pt.

4. Consciousness
   0 = Not responding, or responding only to painful stimuli
   1 = Responds to verbal stimuli but falls asleep readily
   2 = Awake, alert and oriented to baseline

TOTAL SCORE PRIOR TO D/C MUST BE 7

White copy: CHART Canary copy: MEDICAL CONTROL

Appendix D

Appendix E1. Recommended documentation for sedation research.

A. SEDATION DOCUMENTATION

1. Pre-Sedation Behavioral State

Definition: The patient's behavioral state immediately prior to sedation.

1. Indicate the state that best describes the child's behavior immediately prior to the administration of the sedation drugs:
   ☐ Calm (eg, not crying)
   ☐ Agitated but responds to comforting (eg, briefly stops crying)
   ☐ Agitated and does not respond to comforting (eg, continuous crying)

2. Efficacy of Sedation

Definition: A successful sedation creates conditions necessary to safely facilitate completion of a procedure through attenuation of pain, anxiety and movement with amnesia or decreased awareness. Patient must fulfill all criteria for a sedation to be considered successful.

1. Sedation was efficacious ☐ YES ☐ NO
   If YES, indicate which of the following criteria were met during the sedation
   ☐ The patient does not have unpleasant recall of the procedure
   ☐ The patient did not experience a sedation-related adverse event, resulting in the abandonment of the procedure
   ☐ The patient did not experience a permanent complication
   ☐ The patient did not have an unplanned admission to hospital or prolonged ED observation
   ☐ The patient did not actively resist or require physical restraint for completion of the procedure

B. ADVERSE OUTCOME DOCUMENTATION

1. Oxygenation

1.1 Oxygen Desaturation ☐ YES ☐ NO

Definition: Oxygen desaturation AND one or more intervention(s) are performed with the intention of improving the saturation

1. Baseline oxygen saturation on room air prior to PSA _____%
2. Oxygen delivered at start of Sedation phase ☐ NO ☐ YES
   If YES, Method of oxygen delivery: ☐ nasal canula ☐ blow-by ☐ face mask ☐ face mask + non-rebreather
   Flow rate delivered: _____litres/minute
3. Indicate the interventions performed in response to the oxygen desaturation *(indicate ALL that apply)*
   ☐ Vigorous tactile stimulation ☐ Oral or nasal airway placement
   ☐ Airway repositioning ☐ Application of positive pressure +/- ventilation with bag mask
   ☐ Suctioning ☐ Tracheal Intubation
   ☐ Supplementing/increasing oxygen ☐ Other _____
4. Lowest reliable oxygen saturation measured during the sedation _____%

2. Ventilation

2.1 Apnea: central ☐ YES ☐ NO

Definition: Cessation or pause of ventilatory effort AND one or more intervention(s) are performed with the intention of stimulating or assisting ventilation.

1. Indicate the criteria used for recognition *(indicate ALL that apply)*
   ☐ Visual confirmation of cessation/pause of ventilation ☐ Loss of CO_2 waveform
   ☐ Cyanosis ☐ Other _____
   ☐ Oxygen desaturation
2. Indicate the interventions performed in response to the apnea (*indicate ALL that apply)*
   ☐ Vigorous tactile stimulation ☐ Application of bag mask *with* assisted ventilation
   ☐ Administration of reversal agents ☐ Tracheal intubation
   ☐ Other _____

2.2 Apnea: Obstructive

2.2.1 Partial Upper Airway Obstruction ☐ YES ☐ NO

Definition: Manifested by stridor, snoring OR chest wall and suprasternal retractions AND one or more intervention(s) are performed with the intention of relieving the partial airway obstruction.

1. Indicate the criteria used for recognition *(indicate ALL that apply)*
   ☐ Stridor ☐ Oxygen desaturation
   ☐ Snoring ☐ Other _____
   ☐ Chest wall or suprasternal retractions

2. Indicate the interventions performed in response to the partial obstruction (*indicate ALL that apply)*
   - ☐ Airway repositioning
   - ☐ Suctioning
   - ☐ Oral or nasal airway placement
   - ☐ Application of positive pressure with bag mask but *without* assisted ventilation
   - ☐ Other _____

2.2.2 Apnea: Complete Upper Airway Obstruction ☐ YES ☐ NO

Definition (general terms): Ventilatory effort with NO air exchange manifested by absence of upper airway (e.g. stridor or snoring) and breath sounds on auscultation *and* a loss of CO_2 waveform if capnography is used AND the obstruction is relieved by one or more intervention(s) performed with the intention of relieving the complete airway obstruction.

1. Indicate the criteria used for recognition *(indicate ALL that apply)*
   - ☐ Ventilatory effort with NO air exchange
   - ☐ Loss of CO_2 waveform (if capnography used)
   - ☐ Oxygen desaturation
   - ☐ Other _____
2. Indicate the interventions performed in response to the complete obstruction (*indicate ALL that apply)*
   - ☐ Airway repositioning
   - ☐ Suctioning
   - ☐ Oral or nasal airway placement
   - ☐ Administration of additional sedation agents
   - ☐ Application of positive pressure +/- ventilation with bag mask
   - ☐ Tracheal intubation
   - ☐ Administration of neuromuscular blockade agents
   - ☐ Other _____

2.3 Apnea: Laryngospasm ☐ YES ☐ NO

Definition: Partial or complete upper airway obstruction, *with* oxygen desaturation due to involuntary and sustained closure of the vocal cords AND is NOT relieved by routine airway repositioning maneuvers, suctioning or insertion of a nasal or oral airway

1. Indicate the criteria used for recognition *(indicate ALL that apply)*
   - ☐ Ventilatory effort with NO air exchange
   - ☐ Loss of CO_2 waveform (if capnography used)
   - ☐ Oxygen desaturation
   - ☐ Partial airway obstruction not relieved with airway maneuvers
   - ☐ Other _____
2. Indicate the interventions performed in response to the laryngospasm (*indicate ALL that apply)*
   - ☐ Administration of additional sedation agents
   - ☐ Application of positive pressure +/- ventilation with bag mask
   - ☐ Tracheal intubation
   - ☐ Administration of neuromuscular blockade agents
   - ☐ Other _____

3. Clinically Apparent Pulmonary Aspiration ☐ YES ☐ NO

Definition: Suspicion OR confirmation of oropharyngeal or gastric contents in the trachea during the Sedation or Physiologic Recovery phase AND the appearance of respiratory signs and symptoms that were not present prior to the sedation. The new signs and symptoms must present before the end of the ED Recovery phase.
The patient must develop one or more sign or symptom in any of the following three categories:
(i) Physical Signs: cough, crackles/rales, decreased breath sounds, tachypnea, wheezing, rhonchi OR respiratory distress
(ii) Oxygen Requirement: decrease in oxygen saturation from baseline requiring supplemental oxygen
(iii) Chest X-Ray Findings: focal infiltrate, consolidation or atelectasis

1. Indicate if there was physical evidence of regurgitation ☐ NO ☐ YES
   If YES, was this confirmed by direct visualization of gastric contents in the trachea by laryngoscopy? ☐ NO ☐ YES
2. Indicate ALL signs and symptoms present (*these MUST NOT have been present prior to the sedation)*
   - ☐ Cough
   - ☐ Crackles/rales
   - ☐ Decreased breath sounds
   - ☐ Tachypnea
   - ☐ Wheeze
   - ☐ Rhonchi
   - ☐ Respiratory distress
   - ☐ Need for supplemental oxygen
   - ☐ CXR changes
   - ☐ Other _____
3. Indicate the response to the signs and symptoms of aspiration *(indicate ALL that apply):*
   - ☐ No active intervention
   - ☐ Supplemental oxygen
   - ☐ Other _____
   - ☐ Administration of medications
   - ☐ Application of positive pressure +/- ventilation with bag mask
   - ☐ Extended observation or admission to hospital
4. Indicate the medications, if any, that were administered: *(indicate ALL that apply)*
   - ☐ No medications administered
   - ☐ Albuterol or salbutamol
   - ☐ Antibiotics
   - ☐ Steroids
   - ☐ Other _____

4. Retching/Vomiting

Definition: The motor reflex response characteristic of retching with or without the expulsion of gastric contents through the mouth or nose that occurs during Sedation, ED Recovery or Post-Discharge phases of sedation

1. Indicate whether the patient retched during sedation
   ☐ YES ☐ NO
   If YES, indicate when the retching occurred *(indicate ALL periods of occurrence)*
   ☐ Sedation – Induction ☐ ED Recovery
   ☐ Sedation – Maintenance ☐ Post-Discharge
2. Indicated whether the patient vomited during sedation
   ☐ YES ☐ NO
   If YES, indicate when the vomiting occurred *(indicate ALL periods of occurrence)*
   ☐ Sedation – Induction ☐ ED Recovery
   ☐ Sedation – Maintenance ☐ Post-Discharge
   a. If YES, indicate the number of times the patient vomited (Consider as a *single* episode if there is <2min between vomits) _____
3. Indicate whether the patient received an anti-emetic ☐ NO ☐ YES
   If YES, indicate the reason for administration ☐ as prophylaxis ☐ in response to vomiting
   Indicate which anti-emetic was administered _____

5. Cardiovascular Events
5.1. Bradycardia ☐ YES ☐ NO

Definition: Heart rate less than 2 standard deviations below normal for age as described by the AHA in the PALS provider manual during the Sedation or Physiologic Recovery phase AND one or more intervention(s) are performed with the intention of improving the heart rate and cardiac output.

1. Indicate when the bradycardia occurred: ☐ Sedation – Induction ☐ Sedation – Maintenance ☐ ED Recovery – Physiologic
2. Indicate the interventions performed in response to the bradycardia (*indicate ALL that apply)*
   ☐ Suctioning ☐ Application of bag mask *with* assisted ventilation
   ☐ Vigorous tactile stimulation ☐ Tracheal intubation
   ☐ Airway repositioning ☐ Chest compressions
   ☐ Supplemental oxygen ☐ Administration of medications
   ☐ Other _____
3. Indicate if medications were administered: ☐ NO ☐ YES
   If YES, indicate what was administered ☐ Atropine ☐ Epinephrine ☐ Reversal agents ☐ Other_____
4. Indicate if the bradycardia was isolated or associated with other events:
   ☐ Isolated ☐ With oxygen desaturation ☐ With hypotension ☐ Other _____
5. Indicate the lowest heart rate attained: _____ beats/min

5.2. Hypotension ☐ YES ☐ NO

Definition: Systolic blood pressure less than the 5th percentile for age as defined by the AHA in PALS during the Sedation or Physiologic Recovery phase AND one or more intervention(s) are performed with the intention of improving the blood pressure.

1. Indicate when the hypotension occurred: ☐ Sedation (Induction) ☐ Sedation (Maintenance) ☐ ED Recovery (Physiologic)
2. Indicate the interventions performed in response to the hypotension (*indicate ALL that apply)*
   ☐ IV fluid administration ☐ Administration of medications
   ☐ Chest compressions ☐ Other _____
3. Indicate if medications were administered: ☐ NO ☐ YES
   If YES, indicate what was administered ☐ Epinephrine ☐ Dopamine ☐ Reversal agents ☐ Other _____
4. Indicate the cause that best fits with the cause of the hypotension:
   ☐ Drug effect ☐ Unknown
   ☐ Co-morbid condition (blood loss, sepsis) ☐ Other _____
5. Indicate the lowest blood pressure attained: _____ / ____ mmHg

6. Excitatory Movements ☐ **YES** ☐ **NO**

6.1 Myoclonus, Definition: Involuntary, brief contraction of some muscle fibers, of a whole muscle, or of different muscles of one group, leading to movements of the corresponding body parts, usually not longer than $1/10^{th}$ of a second (100 milliseconds) AND interferes with the procedure, requiring an intervention or administration of medications. Hiccupping is a form of myoclonus.

6.2 Muscle rigidity, Definition: Involuntary muscle stiffening in extension that can be associated with shaking AND interferes with the procedure, requiring an intervention or administration of medications.

6.3 Generalized motor seizure, Definition: Temporary abnormal neural electro-physiologic phenomenon that manifests as involuntary contractions or series of contractions of the voluntary muscles. The contractions can be sustained (tonic) or repeated (tonic-clonic).

1. Indicate which excitatory movement occurred: ☐ Myoclonus ☐ Muscle rigidity ☐ Generalized motor seizure
2. Indicate if the excitatory movement interfered with the completion of the procedure or required treatment
   ☐ Procedure was delayed, interrupted or not completed
   ☐ Administration of medications
   ☐ Benzodiazepine
   ☐ Other _____

7.1. Paradoxical Response to Sedation ☐ **YES** ☐ **NO**

Definition: Unanticipated restlessness or agitation in response to the administration of sedation drugs occurring during the Sedation phase AND results in the unplanned administration of reversal agents or alternative sedation drugs, a delay in the completion of the procedure or discontinuation of the procedure.

1. Indicate the impact of the paradoxical reaction:
   ☐ Administration of reversal agents
   ☐ Administration of sedation drug(s) (*please specify)* _____
   ☐ Procedure performed but with physical restraint
   ☐ Delay in completion of the procedure
   ☐ Discontinuation of the procedure

7.2. Unpleasant Recovery Reactions ☐ **YES** ☐ **NO**

Definition: Abnormal patient affect or behaviors during the ED Recovery phase that requires additional treatment and a change or delay in patient discharge from the ED. The behaviors include one or more of the following

1. Indicate criteria used for recognition of the unpleasant recovery reaction:
   ☐ Crying – inconsolable ☐ Dysphoria – mood of restlessness, depression, and anxiety
   ☐ Agitation – restless, continuous activity ☐ Nightmares – unpleasant dreams
   ☐ Delirium – state of severe confusion, altered mental status
   ☐ Hallucinations – responds to sensory (i.e. seeing, hearing or feeling) phenomena that are not physically present
2. Indicate whether the patient had an unpleasant recall of the procedure
   ☐ NO ☐ YES ☐ Not questioned ☐ Too young to ascertain
3. Indicate the interventions performed in response to the unpleasant recovery reaction (*indicate ALL that apply)*
   ☐ Physical restraint ☐ Allocation of additional personnel to care for patient
   ☐ Administration of medications ☐ Delayed discharge from the ED
   ☐ Other _____

8. Permanent Complications ☐ **YES** ☐ **NO**

8.1 Permanent Neurological Injury Definition: A neurologic deficit that was not present prior to sedation and does not resolve.

8.2 Death Definition: The irreversible cessation of cerebral function and spontaneous function of the respiratory and circulatory systems.

1. Indicate which permanent complication occurred:
   ☐ Permanent neurological injury ☐ Death

9. Other

Any effect of sedation not specifically mentioned that results in an unexpected intervention should be described and documented

Appendix E

Recovery criteria.

Activity: Able to move voluntary or on command
- 2 = Four extremities
- 1 = Two extremities
- 0 = None

Respiration:
- 2 = Able to deep breathe and cough freely
- 1 = Dyspnea, shallow or limiting breathing
- 0 = Apnea

Circulation:
- 2 = BP ± 20 mm Hg of preanesthetic level
- 1 = BP ± 20-50 mm Hg of preanesthetic level
- 0 = BP ± 50 mm Hg of preanesthetic level

Consciousness:
- 2 = Fully awake
- 1 = Rousable on calling
- 0 = Not responding

O_2 saturation:
- 2 = Able to maintain O_2 saturation >92% on room air
- 1 = Needs O_2 inhalation to maintain O_2 saturation >90%
- 0 = O_2 saturation <90% even with O_2 supplementation

NOTE. A score of ≥9 is required for discharge.
Abbreviation: BP, blood pressure.

Iacombe et al. Remifentanil vs Fentanyl for Deep Sedation. J Oral Maxillofac Surg 2006.

Appendix F

Patient Questionnaire (adapted from Hasen *et al* [8])

Questions Regarding the Operation:

Do you remember entering the operating room?	Yes	No
Do you remember events of the operation?	Yes	No
Do you remember unpleasant experiences during the operation?	Yes	No
Do you remember having pain during the operation?	Yes	No
Do you remember having any nausea during the operation?	Yes	No
Do you remember vomiting during the operation?	Yes	No
Were you anxious during the operation?	Yes	No

Please estimate your anxiety during the operation on a scale of 0 to 10
(0 being no anxiety at all and 10 being extremely anxious)
0 1 2 3 4 5 6 7 8 9 10

Questions regarding the ***immediate*** post-operative period:

Please estimate the severity of **NAUSEA** on a scale of zero to ten
(with zero being "no nausea at all" and ten "worst nausea imaginable")
0 1 2 3 4 5 6 7 8 9 10
none worst

Please estimate the severity of **PAIN** on a scale of zero to ten
(with zero being "no pain at all" and ten "worst pain imaginable")
0 1 2 3 4 5 6 7 8 9 10
None worst

Number of episodes of vomiting prior to going home:_____

Number of episodes of dry heaves/retching prior to going home:_____

Appendix G

PAIN MANAGEMENT STUDY- SURGEON'S SCALE

Date of surgery: _____ Patient #: _____
Age: _____ Weight: _____ kg/lbs
Sex: M/F

Extent of Surgery Scale:

Simple (no incision) = 1
Simple (with incision) = 2
Minimal Bone Removal = 3
Full Bone Removal = 4

Please rate the extent of surgery per tooth:
(Consider also difficultly of removal, duration of surgery, and patient cooperation)

1-8: _____
2-8: _____
3-8: _____
4:8: _____

Surgery start time: _____
Surgery finish time: _____

Remarks:
_____
_____

Surgeon Level of satisfaction.

1. Very satisfied
2. Satisfied
3. Neutral
4. Unsatisfied
5. Very unsatisfied