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Intravenous Conscious Sedation for Dental Surgery: Bolus Alfentanil with Propofol Infusion Enabling Early Recovery after Surgery with Fast Track Patient Discharge

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Abstract

We prospectively audited 350 patients undergoing dental procedures with bolus alfentanil followed by propofol Target-Controlled Infusion (TCI) conscious sedation to evaluate patient safety, adverse effects, post-operative discharge time and patient feedback. Our anaesthetic technique was specifically adapted to facilitate early recovery after surgery (ERAS) with subsequent 'fast track' discharge within 20 minutes after completion of surgery. Bolus alfentanil was administered as an analgesic base to permit surgical infiltration of local anaesthetic (LA), with ongoing sedation provided by TCI propofol. All patients received combination nasal supplemental oxygen/capnography in addition to standard monitoring. We purposely avoided using longer acting sedation agents such as midazolam and fentanyl. The technique proved safe, with 95% of patients being discharged within 20 or less minutes of arrival in the post-operative recovery area (PACU). Adverse events, none of which proved to be serious, were experienced by 27 (7.7%) patients: 10 (2.9)% episodes of hypoxaemia, 12 (3.4%) episodes of agitation, 7 (2.0%) episodes bradycardia and a zero incidence of nausea and vomiting and of muscle rigidity. Patient feedback was unanimously positive. The technique was preferred by the surgeons in comparison with other sedation methods. We advocate this method of intravenous dental sedation with short acting anaesthetic agents as an optimal approach to enable safe, fast track discharge.

Keywords: Conscious sedation, Intravenous, Fast track discharge, Alfentanil, Propofol

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Introduction

Since the 1840s, many of the advancements in both dentistry and anaesthesia have been complimentary. The practice of administering sedation for dental procedures is well established, with a variety of techniques advocated by anaesthetists and dental sedationists in many different countries.[1,2,3]

Various combinations of agents and delivery systems are currently available.[1,4] Frequently used agents are oral benzodiazepine sedatives, ketamine, alpha 2 agonists such as dexmedetomidine, inhalational anaesthetic agents such as nitrous oxide[1,3] , propofol and longer acting intravenous agents such as midazolam and fentanyl.[5]The use of midazolam and fentanyl, either alone or in combination with bolus or TCI propofol, seems to be the cornerstone of contemporary dental sedation.[6] From discussions with the Victorian Department of Health and Human Services (DHHS), though, it is apparent that accurate data pertaining to specific types of drug utilisation and their frequency of use for dental sedation in Victoria are lacking (personal communication). Additionally, there is little information pertaining to average times spent in house between the end of surgery and discharge to home. The data from a recent audit publication examining office based dental surgery procedures in Victoria is of limited relevance as 92% of the patients described were administered general anaesthesia.[7]

In order to achieve the time and cost savings and patient convenience associated with ERAS and fast track discharge, our contention is that approaches incorporating the use of longer acting agents are now

both outdated and inferior. We acknowledge a bias, based on a pharmacokinetic background of using only "ultra-short acting "agents. With that in mind, we selected for our sedation technique propofol and alfentanil, with the avoidance of other, longer lasting agents such as benzodiazepines and longer acting narcotics. We combine the use of our primary agent, propofol, with TCI drug delivery systems and what we believe to be both appropriate, and indeed mandatory, adjunctive anaesthetic and monitoring techniques.

Only by eliminating the use of benzodiazepines and longer acting narcotics, and substituting them with alfentanil and TCI Propofol have we been able to achieve high rates of ERAS and fast track discharge. We define a fast track discharge as the patient spending 20 or less minutes in the post anaesthesia care unit (PACU).

Our sedation process is a progression on the retrospectively described technique in an Australian audit of 150 dental sedation patients published in 2015.[6] Whilst these authors likewise administered TCI Propofol, their work is fundamentally different from ours in that they used the longer acting drugs fentanyl, up to 50mcg per patient, with sedation augmentation in all of their patients by midazolam (1-3 mg per patient), coupled with an absence, in most cases, of supplemental oxygen. The authors described a 10.6% complication rate in their adult patients undergoing dental sedation, with the most common complication being hypoxaemia with a pulse oximeter reading (SPO_2) falling below 90% in 11 of 16 adverse events, providing a hypoxaemia rate of 7.3%.

Materials and Methods

All patients scheduled to undergo elective dental procedures under IV sedation at Victorian Oral and Facial Surgeons (VOFS) from July 1, 2018 until completion of 350 cases in February, 2020 were entered into the audit. All cases were anaesthetised by the same practitioner (DW), and operated on by surgeons (SV or BW).

An initial surgical consult was followed by a telephone preoperative assessment by DW, with all patients submitting a completed preoperative sedation questionnaire at least 24 hours prior to surgery. Written consent for anaesthesia and surgery was obtained from all patients, with all data being tabulated in a non-identifiable manner. The entire peri-operative sedation experience is in accordance with the requirements of the Victorian DHHS relating to accreditation of Mobile Anaesthesia.

The patient characteristics are presented in Table 2: Number of patients and gender, ASA status, age range, mean age, height, weight and BMI.

The surgical procedures were performed in a reclining dental chair, in accordance with the standards pertaining to the Australian and New Zealand College of Anaesthetists (ANZCA) Guidelines for the Perioperative Care of Patients Selected for Day Stay Procedures, ANZCA PS15[8] and the provisions required by the Victorian DHHS pertaining to the delivery of dental sedation by Mobile Anaesthesia Services.

Table 3 lists the operative procedures performed.

All patients were monitored according to ANZCA PS18 2017, Recommendations on monitoring during Anaesthesia[9] by blood pressure (BP) cuff, SPO_2, nasal capnography, ECG when required and, most importantly, by a verbal contact, positive feedback hand holding process where the patients were frequently asked to squeeze the anaesthetist's hand twice "if they wished to be more asleep". Intranasal oxygen (3L/min) was administered via a binasal oxygen delivery/capnographic monitoring system (Parker Medical Company). The intent of the sedation delivery process was to achieve a level where the patient was comfortable and relaxed but still able to respond purposely to verbal command. This was ideally at a Modified Ramsey Sedation Level 3, not beyond Level 4 (ref Table 1 Modified Ramsay Sedation Scale). A registered, anaesthesia trained nurse was present during the procedure and post-operatively in the PACU.

Modified Ramsay Sedation Scale
1. Awake and alert, minimal or no cognitive impairment
2. Awake but tranquil, purposeful responses to verbal commands at a conversational level
3. Appears asleep, purposeful response to verbal commands at a conversational level
4. Appears asleep, purposeful responses to verbal commands but at a louder than conversational level, requiring light glabella tap, or both
5. Asleep, sluggish purposeful responses only to loud verbal commands, strong glabellar tap, or both
6. Asleep, sluggish purposeful responses only to painful stimuli
7. Asleep, reflex withdrawal to painful stimuli only
8. Unresponsive to external stimuli, including pain

Table 1:

Patient Characteristics	
Sex – Male	115
Sex – Female	235
ASA Status – I	239
ASA Status – II	107
ASA Status – III	4
Age Range (years)	11 - 77
Age Mean (years)	28.4 (SD: 12.6)
Height (cm)	168 (SD: 9.9)
Weight (kg)	70.1 (SD: 15.2)
BMI (kg/m^2)	24.6 (SD: 4.5)

Table 2:

Procedures*	
Removal of third molars	306 patients
Other extractions	55 patients
Other procedures	3 patients
*Some patients underwent more than one procedure	

Table 3:

Sedation technique

The procedure is explained to the patients before intravenous (IV) cannulation and commencement of drug delivery-they are told "they will be administered a powerful, ultra-short acting narcotic which will permit the administration of a near- painless injection of LA by the surgeon, which, although they will be aware of it, will seem as if it is something occurring far away". After the injection of LA, it is explained to the patient that they will progressively be sedated to a comfortable level by way of the "feedback hand holding interaction". We explain that many patients can expect little, or even no recall of the procedure afterwards.

Following IV cannulation, the propofol infusion was commenced at a low level via a computerised delivery system (Alaris Medical, Alaris PK Carefusion System) with effect site targeting (Cet) in Schnider mode. This low-level infusion, typically 0.5-0.8 micrograms/millilitre (mcg/ml), was administered both with the aim of providing anti-emesis prior to the administration of alfentanil and some degree of anxiolysis during the time of surgical injection of LA. The alfentanil bolus followed, typically in the range of 10-20 mcg/kg. This dose was adjusted according to patient age, body mass and level of anxiety.

After bolus alfentanil administration, the patient was requested to express when the narcotic effect became subjectively apparent- this typically becomes noticeable around 25-30 seconds after administration, and results in an episode of sudden tranquillity accompanied by either reduced respiratory rate or, sometimes, apnoea of around 10-20 seconds duration. This apnoeic period, rather than being of concern, is taken by the surgeon to be reflective of a time of maximal analgesia and to be the optimal time to administer the LA (0.5% Bupivacaine with adrenaline 1:200,000, typically around 20 ml.) At this stage, the patients are invariably unresponsive to the painful aspect of the LA injection, yet completely co-operative and capable of inspiring, if requested.

Following the administration of LA, with return of the capnographic waveform to near pre-alfentanil baseline, the propofol infusion is incrementally increased to a level providing optimal patient comfort. At this time, feedback hand holding, in company with continuous monitoring of the capnographic wave form, is essential in determining the appropriate level of propofol sedation. Towards the end of the procedure, the propofol Cet level is set to zero, and the infusion terminated. In this manner, the decay of the Cet propofol can be observed as it falls from its sedation level (typically 1.8-2.5 mcg/ml) to an alert level of around 1.1 to 1.2 mcg/ml. The patient is then converted from supine to a sitting position in the dental chair, and, when ready, is assisted into an adjacent wheelchair and taken to a recliner chair in PACU, into which they ambulate from the wheelchair. Discharge follows shortly afterwards.

Results

Table 4 describes relevant sedation data, and adverse events. A total of 27 patients (7.7%) experienced 29 adverse events, all of which were readily corrected, with none proving to be serious.

Hypoxaemia: 10 cases- all patients responded to simple measures such as instruction to breathe, reduced propofol level or increased oxygen flow rate. No patients required positive pressure ventilation by bag and mask. Only one case was attributed to alfentanil, the remainder to excessive sedation depth with Propofol.

Sedation Data	
Time in operating room (min)	24.7 (SD: 8.4)
Time in PACU (min)	14.6 (SD: 5.5)
Fast Track Discharge Percentage	95%
Alfentanil Dose (mcg)	1088 (SD: 228)
Cet Propofol (mcg/ml)	2.0 (SD: 0.49)
Cet Range (mcg/ml)	0.5 – 3.3
Adverse Events	27 patients (7.7%)
- Hypoxaemia	10 cases
- Bradycardia	7 cases
- Agitation	12 cases
- Nausea	0 cases
- Rigidity	0 cases
Reported amnesia	92patients (26.2 %)

Table 4:

Bradycardia: 7 cases -all attributable to alfentanil-6 responded spontaneously, with only one patient requiring atropine

Agitation: 12 cases- extremely anxious patients demanding higher levels of sedation, with 8 patients having a background of heavy smoking or recreational drug abuse. All responded to reductions in propofol level.

Nausea: zero cases- antiemetics used prophylactically on one occasion only.

Rigidity: no cases.

Mean Alfentanil Dose: 1088 mcg +/- 228 mcg.

Mean Propofol Level: 2.04+/-0.49 mcg/ml.

Propofol Cet Range: 0.5-3.3ug/ml.

Amnesia: 92 patients (26.2%) voluntarily reported amnestic comments at completion of the procedure.

Mean OR Time: 24.7+/-8.4 mins.

Meantime in PACU: 14.6+/- 5.5 mins.

Fast Track Discharge Rate: 95%. Our definition of delayed discharge was more than 20 mins spent in the PACU- 18 pts failed to be discharged within this time frame.

Surgeon acceptance: The technique was rated by both surgeons as superior to other forms of sedation with which they were familiar.

Immediately prior to discharge, all patients were requested to complete a patient assessment form of their sedation experience. This included rating their sedation experience on a linear analogue scale ranging from "poor" to "fair" to "good". 347 patients (99%) rated their experience as "good". A subset of 100 patients were also requested to mail in an identical assessment several days after the procedure, in order to eliminate any bias from propofol induced euphoria- the satisfactions levels remained identical.

Discussion

The cornerstone of the fast track discharge technique described is the use of alfentanil to permit profound, short term analgesia at the time of local anaesthetic administration, followed only by a propofol TCI, Cet (Schnider, not Marsh) conscious sedation strategy. The avoidance of benzodiazepines and longer acting narcotics is essential. In order to reduce drug related complications, we minimise the number of agents to which the patients are exposed. It is extremely rare to administer intravenous antibiotics or anti-emetics. All patients do receive dexamethasone 4milligrams (mg) and parecoxib 20-40 mg. We are not aware of other dental sedation publications describing the use of bolus alfentanil in combination with Propofol TCI.

Alfentanil

Alfentanil is a short acting, synthetic opioid mu receptor narcotic agonist often compared with fentanyl. It is about one-eighth as potent as fentanyl. Alfentanil's short duration of action makes it attractive as an analgesic supplement for short ambulatory surgical procedures.[10,11] The duration of action is often cited as 10-15 mins[10] but, based on our examination of capnographic waveforms, the observable respiratory depressant effect following a single bolus seems clearly less than this. In comparison with fentanyl, alfentanil has a three-four times faster onset with earlier peak analgesic effect and only one third the duration of action.[12] Very simply, at pH 7.4 alfentanil with a pKa of 6.5 is around 90% unionised whilst fentanyl, with a pKa of 8.4, is only about 10% unionised. Thus, alfentanil crosses lipid membranes (ie, the brain) much more readily, explaining its faster onset in comparison with fentanyl. The rapid dissipation of alfentanil's effect occurs due to both redistribution from the brain to other tissues and rapid elimination from the body, secondary to the short elimination half-life.[13,14]

From a clinical perspective, it is important to note that the dose requirements of both alfentanil and fentanyl decrease significantly with increasing age-namely a 50% decrease from age 20-89.[15] This factor alone has clear implications in the conscious sedation use of bolus alfentanil in older patients- we reduce the dose in patients around 60 years age and over. In addition, alfentanil should not be utilised with repeated bolus doses due to this approach creating significant increases in half-life, and hence duration of action.[10]

A study by Kwak et al did compare alfentanil and fentanyl for third molar extraction during TCI propofol infusion, but fentanyl 100mcg as a bolus dose was given against a comparative alfentanil infusion prior to LA infiltration. There was no difference in patient satisfaction between the two groups, but just prior to the injection of LA, the authors cite a total alfentanil dose of only 120 mcg having been infused. In our experience with alfentanil this dose is completely inadequate in eliminating the pain of injection of LA. Not surprisingly, there was more respiratory depression in the fentanyl group than the alfentanil group.[16]

An appealing aspect of our technique is that bolus dose alfentanil, with or without a concurrent low dose propofol infusion, permits the injection of painless LA, without the need for accompanying benzodiazepine sedation. After administration of LA, the sedation level can be increased to the desired level by progressively increasing the propofol TCI level. With a duration of effect of only 4-8 mins, a more rapid awak-

ening at procedure end with propofol is to be anticipated than with midazolam, considering midazolam's duration of effect is as long as 15-80 mins.[17]

Propofol

Propofol represents a near ideal sedation agent. It's characteristics are well known- a fast onset, rapid awakening regardless of the length of infusion, absence of nausea and vomiting and the capacity of providing dose dependent depth of sedation. At sub-hypnotic doses, propofol provides potent anxiolysis and amnesia.[18,19,20,21] Most of the research involving propofol is now centred on its methods of delivery. TCI is a technique that uses a computerised drug delivery system ("pump") to deliver propofol at varying rates in order to achieve a constant, pre-set level of both propofol and resultant sedation. TCI aims to eliminate the fluctuating drug and sedation levels that occur with bolus drug administration. The concept involves infusing a bolus dose of propofol, followed by a varying continued dose, in order to achieve either a constant brain (Cet) or plasma (Cpt) propofol level. A microprocessor recomputes and adjusts the infusion level at pre-set intervals (around every 10 seconds (sec)), taking into account the distribution of propofol into a central and peripheral compartment, plus allowing for propofol metabolic breakdown. TCI therefore provides a smoother sedation course than does the repeated administration of bolus propofol, or any other intermittently administered sedative drug. It also provides greater haemodynamic stability with a lower total amount of propofol administered compared with bolus dosing, faster recovery and, in endoscopy, improved operator satisfaction with the more stable sedation level afforded.[22]

The Alaris PK system provides different propofol delivery modes with some sedationists preferring either Marsh or Schnider models. We prefer the Schnider model. Schnider is superior when ERAS is required. When programmed in Cet mode Schnider delivers a more rapid, yet lower total overall propofol drug delivery in comparison with Marsh. Clearly the Schnider programme, with it's programmability involving BMI, age and gender is more capable of patient individualisation than the Marsh programme, which requires entry of age and weight only, without in fact making any age adjustments in dose delivered.[23] The Schnider model reflects also the significant reduction in clearance of Propofol from the blood that occurs with age.[24]In addition, the Schnider model permits both Effect Target (Cet) and Plasma Target (Cpt) programmability, rather than the plasma target (Cpt) only offered by the Marsh programme. Most studies have found the Schnider model to be more accurate than the Marsh model in clinical practice.[25] We found typical propofol levels in Schnider Cet mode for conscious dental sedation to be around 1.5-2.5 mcg/ml.

We have noticed a great lack of understanding amongst Australian sedationists as to the superior amnestic properties of propofol, with many seemingly adopting a prevailing view that midazolam is the optimal, and perhaps only, drug for sedation and the providence of amnesia. It seems that midazolam is thought of as being an essential component in rendering patient's unaware. A comparison of sedation between propofol alone versus midazolam, with or without narcotics, showed that in endoscopy procedures there was less memory of the procedure in the propofol group than those patients receiving midazolam. Midazolam based regimes ensue longer sedation and recovery times than propofol.[26] The propofol level at which 50% of volunteers fail to respond to verbal command is 2.35 mcg/ml .[27] Generally, at propofol infusion rates of 30mcg/kg/min, patients are amnesic (ie 12.6 ml propofol/hour) .[28] This is in a range towards the upper end of our propofol infusion levels.

Fentanyl/midazolam

A fentanyl/midazolam combination for dental sedation is frequently thought of as "a preferred approach".[5] Advocates of the use of midazolam, usually in combination with fentanyl, cite the simplicity of the method, its reproducibility and low complication rates. This ignores the unpredictable duration of midazolam, the disadvantages of its bolus dosing and the superiority of propofols' readily titratable sedation depth. The clinical half-life of propofol, 4-8 mins, is significantly shorter than midazolam, 15-80 mins, with more rapid awakening.[17,29,30] The recovery time after propofol in dental treatment has been reported as 11-22 mins compared with 30-60 mins for midazolam.[31]

A further disadvantage of the addition of midazolam as a contributing sedative, should an alfentanil-propofol combination be chosen, is that both alfentanil and midazolam, along with many other drugs, are metabolised by the same hepatic conjugative enzymes (CYP3A3/4). If both alfentanil and midazolam are administered concurrently there can be competition for the same enzymes, prolonging the actions of both drugs.[32]

Technique and monitoring

An additional benefit of propofol is its antiemetic properties. Our technique deliberately omits the use of standard anti-emetics, in order to minimise drug side effects. None of our patients suffered nausea or vomiting with bolus alfentanil, in spite of the known emetic properties of narcotics. We believe our low dose commencement propofol infusion was of benefit in this regard. Antiemetic effects have been shown with propofol concentrations of around 340ng/ml (0.34 mcg/ml). The initial Cet propofol level we selected, at 0.5-0.8 mcg/ml, probably contributed to our zero level of nausea and vomiting following bolus alfentanil administration.[33]

Our aim was to tailor a technique which provided for patient safety and comfort, amnesia if possible and to meet our requirements of ensuring a rapid recovery and subsequent fast track discharge. Propofol TCI sedation, in concert with bolus alfentanil analgesia, does demand fastidious attention to detail-the capnographic trace and the feedback hand holding system need to be repeatedly assessed in order that the propofol sedation depth does not become too deep. We consider the capnograph to be a more valuable monitor in the area of intravenous sedation than the pulse oximeter, with capnography acting as an "early warning sign" for the impending problem of respiratory obstruction, before any changes in pulse oximetry occur.

Pulse oximetry is a poor monitor of ventilation. It accurately detects arterial oxygen saturation, but does not reflect alveolar ventilation. A meta-analysis of sedation data concluded that respiratory depression episodes were almost 18 times more likely to be detected by capnography than other monitoring techniques.[34] The American Society of Anesthesiology closed claims database shows respiratory depression because of an overdose of sedating agents to be responsible for 21% of sedation related claims.[35] As a result, capnographic monitoring for sedation is now mandatory in the USA and UK, but, as of now, not in Australia. Once again, we emphasise the importance of close capnographic monitoring in avoiding over sedation, which we see as the most serious potential problem with this technique.

Unfortunately, propofol TCI sedation is not the type of technique suitable for application to the typical case mix in training hospitals, and therefore practitioners are likely to be underexposed to learning the process. Likewise for alfentanil sedation/analgesia. This perhaps explains the continued administration of the longer acting, more familiar sedative drugs, midazolam and fentanyl, in mainstream sedation practice today.

The technique described is likely best suited to those practitioners who have some familiarity with Total Intravenous Anaesthesia (TIVA). The experience gained from a familiarity with TIVA translates readily to the changes in drug dosage required in dental sedation for older, more obese or more medically complicated patients. There is controversy as to the level of expertise required to perform safe TCI sedation, with Blayney et al[36] holding opposing views from Cashion et al.[6] Blayney cites possible over-sedation as a risk requiring the presence of a specialist anaesthetist, whereas Cashion cites a lack of airway problems in his paper and does not see the need for solely an anaesthetist to provide TCI sedation. Obviously, those practitioners involved with TCI sedation must have received training in the technique. However, decisions about which providers should administer propofol remain controversial. The American Society of Anesthesiology (ASA) advocates propofol medicating "only by persons trained in the administration of general anesthesia". However, the American Society for Gastrointestinal Endoscopy considers propofol use safe by anyone "proficient in the management of upper and lower airway complications….and holding at least basic life support certification".[37]

It does seem ironic that, in the USA today, the FDA still has not fully approved drug delivery systems enabling the delivery of TCI propofol. For this reason, publications emanating from the USA pertaining to the methodology of conscious sedation would seem to us to have less relevance here in Australia. Put bluntly, we consider any recommendations for the sedation of older children or adults which do not encompass a TCI element to be, in most cases, less than ideal.

Conclusion

We found that a technique of bolus alfentanil analgesia, in the presence of TCI propofol sedation, proved to be safe and effective and allowed for a constant, predictable sedation level with fast track patient discharge. There was a low incidence of readily manageable complications and ready acceptance by the operators. Our belief is that this technique is superior to the more traditional sedation techniques utilising longer lasting agents such as midazolam and fentanyl.

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