

# Dental Sedation with Propofol-based Target Controlled Infusions: Changing Sedation Patterns and Our Current Approach after 2800 Office-based Procedures

Douglas G Wells<sup>1,\*</sup>, Sam Verco<sup>2</sup>, Andrew Bridgeman<sup>3</sup>, Roland Barrowman<sup>3</sup>, Jason Savage<sup>2</sup>, Brent Woods<sup>2</sup>, and Bernard Lim<sup>3</sup>

<sup>1</sup>Mobile Anaesthetist, Australia

<sup>2</sup>Victorian Oral and Facial Surgeons, Melbourne, Australia

<sup>3</sup>Facial and Oral Surgery Clinics, Melbourne, Australia

\*Corresponding author: Douglas G Wells, Mobile Anaesthetist, PO Box 540 Kew, Victoria 3101, Australia, E-mail: kdwells3238@gmail.com

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## Abstract

We describe the changing patterns of our office-based dental sedation technique over the past 5 years, based on the cumulative experience gained from treating 2800 patients. We also report the changing rate over time of minor, clinically insignificant adverse events based on a recent 652-patient audit of our office-based intravenous sedation (IVS). Our current preference, with most patients, is to administer a combination of propofol via a Target Controlled Infusion (TCI) in combination with TCI remifentanyl. The rationale and reasons for this and the progressively changing doses of intravenous (IV) agents are discussed. Our office-based TCI IVS technique affords patient safety, high satisfaction rates and much faster discharge times in comparison with discharge times from mainstream hospitals. The surgeons are provided with greater scheduling flexibility plus the ability to operate in their own office with familiar staff.

## Introduction

The rising cost of health care, coupled with an ever-increasing cost of living, favors the delivery of office-based dental sedation in order to provide both optimal patient care and financial advantage for patients. Over the past 5 years, we have safely and effectively provided maxillo-facial dental care under IVS for 2800 patients.

Whilst there is a plethora of techniques applicable for dental sedation and advocates for and against various techniques, the provision of safe, algorithmic delivered ultra-short acting IV agents has, at least on face value, considerable merit in comparison with other techniques. We have observed significant prejudice against TCI sedation not only from within the anaesthesia community but also from those non-anaesthetists who practice dental sedation. Our belief is that this stems from a lack of understanding of TCI anaesthesia on the part of many anaesthetists- frequently we hear from them "It sounds dangerous." Essentially these practitioners are voicing concerns over delivery techniques that they have either failed to comprehend or failed to master. Similar criticisms from non-anaesthetist sedationists, those typically practicing benzodiazepine/fentanyl-based techniques, presumably indicate a desire for the maintenance of their status quo.

An additional advantage of an office-based sedation program is the increased flexibility provided to the surgeons. They are afforded the opportunity to schedule surgery at a time of their choosing, perhaps using familiar staff to work with. Any change-over time between cases can be utilised to do office work or consult with other patients. With appropriate facility fees, both the practice and the patient can be economically advantaged.

## Materials and Methods

A review of our technique for IVS for office-based patients over 5 years (yrs) time period (July 2018-December 2023). Additional detailed analysis of 652 cases (July 2022-September 2023) was done (see Table 1 and Table 2 for data collected).

All patients receiving office-based TCI sedation are treated under the guidelines of Mobile Anaesthesia Services, Department of Health in the state of Victoria. We have previously described the regulatory requirements, pre-operative workup procedure, consent, monitoring of anaesthesia and the "hand holding" technique relating to the progressive step-up of propofol sedation [1,2].

## Office-based IVS: Inclusion and Exclusion Criteria

**Inclusion criteria:** American Society of Anesthesiology (ASA) 1, 2 and stable 3 patients are considered for sedation.

### Exclusion criteria:

- Age <11 years
- Weight < 40 kg, >120 kg
- Body Mass Index (BMI) greater than 35 kg/m<sup>2</sup>
- Barrett's oesophagus (see technique)

Prior to discharge, all patients are requested to complete a patient evaluation survey to rate their sedation experience. Eight categories can each attract a score of up to four points each, giving a maximum possible rating of 32 points.

## Sedation technique

We utilise Effect Target (Cet) delivery of both propofol (Schnider model) and, most frequently, remifentanyl (Minto model). A smaller number of selected patients receive a bolus dose of alfentanil in place of remifentanyl. The Paedfusor propofol program, though available, is no longer used for children under 16 years of age- the Schnider program seems to work very well in paediatric patients over 40 kg, irrespective of age. (It did seem that the Paedfusor model was delivering higher propofol infusion rates for a given age than a non-age adjusted Schnider model).

As will be described, one of our adaptive changes has been to lower the initial propofol infusion rate prior to administration of the narcotic, in company with the subsequent delivery of higher remifentanyl doses, should remifentanyl be selected.

A primary concern of ours has always been the exposure of all patients to as few drugs as possible. We routinely use a four-drug technique: propofol, a narcotic, dexamethasone and a non-steroidal analgesic. In terms of drug utilisation, our adage remains: "Less is better".

Patients are now sedated as far as a Modified Ramsay sedation scale of 4 (formerly 3), described as "appears asleep, purposeful responses to verbal commands but at a louder than conversational level, requiring light glabellar tap, or both".

Any patient with Barrett's oesophagus is excluded, although admittedly the reported aspiration rates for sedation procedures, excluding those for gastroenterology, are extremely low [3]. Of greater concern, in terms of delayed gastric emptying, is the increasing use of semiglutamide (Ozempic) not only in Type 2 Diabetes but also as a weight loss agent. Fortunately, our basal metabolic index (BMI) limit of 35 Kg/m<sup>2</sup> excludes many of these patients. Those patients taking Ozempic should discontinue this drug for two weeks pre-surgery.

## Results

Table 1 provides cursory details of a recent subset of 652 office-based patients we sedated over 15 months. Table 2 describes the breakdown of 27 adverse events from within this 652-patient cohort. Table 3 details the frequency of adverse events from previously reported TCI dental sedation and other sedation papers and, where noted, the Cet or plasma target (Cpt) propofol and Cet remifentanyl levels administered.

Formerly, we found hypoxaemia to be a prominent adverse event. We now rarely encounter it. The most common adverse events at present are paradoxical reactions (agitation/anxiety or myoclonus) and bradycardia in patients with low commencement heart rates. We

**Table 1:** Breakdown of 652 cases: July 2022-September 2023.

Age Range:	11-82 years
ASA 1 and 2:	637
ASA 3:	15
Average maximum propofol Cet:	2.3 mcg/ml
Remifentanyl:	528
Alfentanil:	119
Alfentanil + Remifentanyl:	4 (agitation- remifentanyl added to alfentanil)
No narcotic	1 ( patient preference)
Average time on OR	28 mins. (range15-135 mins.)
Average time in PACU	12 mins. (range 8-35 mins.)
Average patient satisfaction	31.6/32

document any fall in SpO<sub>2</sub> below 90% and note any propofol-induced myoclonic-type features as an adverse event, no matter how minor, and are surprised when these seem not to be reported in other studies.

Patients universally provide positive assessments for their TCI propofol-based sedation procedures upon completion of the multi-category assessment form.

## Discussion

The focus of this paper is the current way we sedate our patients, the manner in which our technique has evolved, the comparative different adverse event rates of different studies and the change in our adverse event rates over time. Our intent is not to describe in great detail patient demographics and surgical details relating to the 2800 dental patients we have sedated in-office to date. Data of this type has been well reported by others [4,5].

Propofol-based TCI sedation for dental surgical procedures is widely used in many parts of the world, with the exception of North America. From personal communication, it is apparent that TCI sedation techniques are now gaining regulatory approval in Canada, but are yet to be widely applied (D Lobb, Edmonton Canada). The USA remains a holdout: author DW spent almost 15 years practising there and encountered no exposure to intravenous anaesthesia.

Many centers still practice what might be called "hybrid sedation", using a potpourri of various sedation agents, often in combination. It does seem that some believe a sedation technique garners superiority *via* the administration of multiple, different drugs. Seeking a fast-track patient discharge coupled with high patient satisfaction, to us, it is illogical to mix the ultra-short-acting agents we use with any longer-acting agents, such as benzodiazepines, alpha 2 agonists or fentanyl.

Dexmedetomidine might well be the next "buzz" drug to be adopted in the sedation gamut-with an onset of 5 minutes (mins) and a peak action at 15 mins it is at least superior to clonidine [6]. Whilst a rhinoplasty comparison between dexmedetomidine and remifentanyl showed greater surgeon satisfaction and superior surgical field visualisation with dexmedetomidine, patient satisfaction and analgesia were better with remifentanyl [7].

Even remimazolam, widely used in South Korea and China, fails our selection criteria for routine use, short of the possibility of assisting in the treatment of propofol-induced paradoxical reactions. With a slow onset time of 1-3 mins or even longer and duration of action of around 10 mins, it falls far short of that of propofol's 15-30 seconds onset and 3.5-4 mins duration [8].

**Table 2:** Breakdown of adverse events from 652 patient cohort.

Total Adverse Events:	27-all minor, transient and none of clinical significance Rate 4.1%
Pre-induction vasovagal episodes:	2
Pre-induction hyperventilation:	1 (successful treatment with remifentanyl)
Hypoxaemia- SpO <sub>2</sub> <90%:	5 (lowest SpO <sub>2</sub> 85%-all encouraged to breathe)
Bradycardia- <40 bpm:	6 (3 requiring anticholinergics)
Paradoxical/agitation/myoclonic reactions:	13 (1 requiring midazolam, remainder treated with substitution or increased remifentanyl)

**Table 3:** Published adverse events/Sedation levels.

Author	Year	Study size (patients)	% Adverse event rate	Propofol level (mcg/ml)	Remifentanyl Cet (ng/ml)
Cashion G, et al. [13]	2015	155	10.6	Cpt 1.55	
Wells DG, et al. [1]	2020	350	7.7	Cet 2	
Barends CRM, et al. [10]	2020	2315	1.1- severe	Cet 2.6	Cet 0.84
			10.5- significant		
			6-moderate		
Wells DG, et al. [2]	2021	150	9.3	Cet 1.72	Cet 4.4
Lobb D, et al. [5]	2023	101	0	Cet 1.63	Cet 1.52

Agents such as alpha 2 agonists and the new benzodiazepines just do not fit into our framework of providing both a fast-track discharge of 15 mins or less and also exposing our patients to the least possible number of different drugs.

For reasons previously alluded to, just as the majority of anaesthetists prefer to use volatile agents for general anaesthesia (GA), many sedationists utilise benzodiazepine/fentanyl-based techniques. Certainly, both of these approaches are safe and reliable yet, because they impose far less of a mental workload on the practitioner than TCI sedation or TCI total intravenous anaesthesia (TIVA), are in many ways easier to administer and therefore more commonly utilised.

This discussion is aimed at a target audience of those sedationists who are either hesitant to adopt TCI techniques or are currently using TCI with the intention of further developing their prowess. Change can certainly be daunting and difficult, but a well-known adage is relevant: “The stationary condition is the beginning of the end”.

The drugs we use, described from mostly a practical angle, will be discussed, as will the manner in which our techniques have evolved. Essentially we will examine 3 drugs- alfentanil, remifentanyl and propofol, two of which are delivered *via* a four-stage process:

- 1) A low-level infusion of propofol is commenced to act primarily as an anti-emetic, but also as an anxiolytic.
- 2) The selected narcotic is administered as a bolus to provide analgesia for the injection of local anaesthetic. We generally prefer to bolus with remifentanyl.
- 3) A short waiting period as the narcotic effect diminishes following the injection of LA by the surgeon.
- 4) The propofol infusion is progressively stepped up to provide sedation and amnesia, with remifentanyl being re-introduced if required.

### Alfentanil

Alfentanil was the narcotic we commenced our sedation with, and is still utilised in some circumstances. Short-acting because of its high lipid solubility, alfentanil is easy to use and produces profound analgesia. Its use does not require any TCI algorithmic knowledge.

Alfentanil should be considered to be a “workhorse” narcotic when used in combination with propofol TCI. Even though considered to be short-acting, its duration of action is far longer than that of remifentanyl.

The main advantage is its simplicity of use- alfentanil is a one-shot treatment. The main disadvantage is, should the use of additional narcotic analgesia be required, the cumulative respiratory depressant effect of repeat alfentanil doses precludes this approach for short-duration procedures. Using a dose of 6 mcg/kg, far less than what we usually administer, respiratory depression is still present 15 mins later [9].

By virtue of its extended duration of action as compared with remifentanyl, alfentanil does have a place in those situations where extensive surgery requires a widespread injection of LA taking longer administration times.

Additionally, alfentanil seems easier to use in the very elderly compared with remifentanyl. We routinely use alfentanil, and not remifentanyl, in those patients aged 75 years or older, in an age-adjusted dosage pattern. Remifentanyl, we find, is just difficult to accurately administer in a bolus dose fashion in elderly patients.

### Remifentanyl

Remifentanyl is the definitive example of a purposely designed drug. It was intentionally synthesised so as to be rapidly metabolised

by circulating non-specific plasma esterases. This feature creates remifentanyl's brevity of action. The combination of propofol and remifentanyl is synergistic, with propofol providing sedation and hypnosis, and remifentanyl sedation and analgesia. Both agents can be either simultaneously titrated up or down, synchronously or asynchronously [10].

Remifentanyl has a rapid analgesic onset, with a maximal intensity of around 60 seconds (sec) after administration [11]. As with propofol, it has a context-sensitive half-life of around 3.5-4mins.

Remifentanyl's extremely fast onset and short duration of action renders it ideally suitable for TCI use. It offers profound analgesia with the ability to rapidly adjust the dose. These characteristics offer far more sedation flexibility than other narcotics, which includes the short-acting alfentanil. Its synergistic action with propofol reduces the amount of propofol required to achieve a given effect. To put it simply, the concurrent TCI use of remifentanyl, in either initial TCI bolus form or in TCI bolus form followed by an ongoing lower-level TCI infusion, provides the opportunity to tailor the sedation needs of both patients and sedationist more effectively.

All published reports of TCI remifentanyl we can source describe its use in an ongoing fixed-rate infusion method, with changes in the fixed rate being made as required. This is not the manner in which we use remifentanyl. Our method is to initiate a bolus dose of remifentanyl, according to the patient's age and weight. Typical Cet's employed are between 3 and 5 ng/ml, with a high of up to 6 ng/ml. The remifentanyl infusion is then allowed to simply decline, with the need to re-introduce it again in around 15% of patients. At the completion of surgery, the remifentanyl Cet is usually around 0.3-0.6 ng/ml.

## Propofol

Propofol is a near-perfect sedation agent, with only one serious drawback- in around 20% or more of patients it can feel painful on injection. With a context-sensitive half-life of around 4 mins, no matter how long an infusion runs the drug elimination half-life remains fixed and the patient will awaken shortly after cessation of the infusion. Propofol is arguably THE most effective anti-emetic agent and can be the agent of last choice when all other pharmacologic treatments for post-operative nausea and vomiting (PONV) have failed. There seems no need to routinely administer an additional anti-emetic agent in the presence of a propofol infusion, especially when combined with dexamethasone. All drugs have side effects, no matter how infrequent. We have never routinely added an additional anti-emetic agent such as a serotonin antagonist (ondansetron has only ever been used once in our series of 2800 patients).

Propofol is an extremely effective amnestic agent, with increasing amnestic levels reported above Cet's of 1.8mcg/ml. Formerly, we worked under the impression that "all patients wanted to be asleep". More targeted questioning of many patients revealed that what patients desire is first to be "pain-free", and then subsequently to be "asleep".

This patient input resulted in a change to our technique. Whereas we had formerly been progressively increasing our initial antiemetic/ anxiolytic propofol Cet's to levels of 1.2-1.4 mcg/ml, a deliberate decision was then made to REDUCE the initial propofol back towards our originally described level of 0.8mcg/ml, or even less. These lower propofol Cet's still afford a propofol infusion rate of around 2 mg/kg/hr, sufficient for anti-emesis and anxiolysis, but at a level which affords for an increased initial remifentanyl Cet-typically around 3.5 ng/ml up to 5.5 ng/ml or even more.

These higher initial remifentanyl Cet's provide for more effective analgesia at the time of injection of local anaesthetic (LA) by the surgeon but could become problematic with the increased initial propofol levels described. Respiratory depression and potentially hypoxaemia can be more frequent with the higher, combined levels of both agents. At lower levels of propofol, the patients remain, in spite of their higher remifentanyl levels, responsive to commands to breathe, should this be required.

Myoclonic-type reactions have been reported with propofol for many years [12]. We see it, in minor degrees, fairly frequently. Myoclonus usually manifests as low-level tremulous movements of the feet or legs. These can become more prominent and can spread to all limbs. It usually occurs at higher propofol Cet's, commencing around 1.6 mcg/ml or more, but we have seen it at a Cet of only 1.0 mcg/ml. Myoclonus usually subsides by decreasing the propofol Cet. To maintain sedation an increased Cet remifentanyl is added. Very occasionally a low dose of benzodiazepine might be required. If myoclonic movements do not resolve in the OR, they usually do so in the post anaesthesia care unit (PACU). Occasionally a patient will be discharged with persistent tremors and advised to expect them to resolve within the next day or so.

## Current sedation technique

Our current preferred sedation technique in most teenage or adult, ASA1 or ASA2 patients can be described as:

- 1) A low-level propofol Cet infusion is commenced at 0.6-0.8 mcg/ml.
- 2) Remifentanyl is administered as a bolus dose in a specific age and weight-adjusted Cet of approximately 3.0-6.0 ng/ml. Following LA injection, in most cases we discontinue the remifentanyl infusion.
- 3) After administration of the LA, the propofol infusion is stepped up progressively according to patient demands and in response to respiratory adequacy as evidenced by nasal capnography. Typical Cet propofol endpoints are 2.2-2.5mcg/ml.
- 4) If required, remifentanyl can be reintroduced to counter inadequate analgesia or any of the forms of paradoxical reactions (anxiety, agitation, hyperventilation, or myoclonus). Our data indicates the re-introduction of remifentanyl in around 15% of patients.

## Monitoring and Bispectral Index

Standard monitoring is utilised for all patients, with discretionary electrocardiograph (ECG) use. The capnograph is considered our most valuable monitor.

We do not employ Bispectral Index (BIS) monitoring, recognising that this is a controversial area. Published studies advocating BIS use sedate patients both more [10] or less [5] than our sedation parameters. We believe that utilising our interactive, patient hand-holding technique obviates any need for BIS analysis. Additionally, extracting data from a recent cost analysis revealed that the use of two adhesive BIS electrodes per hour would increase the hourly cost basis of our sedation program by more than 7%.

**Program:** Our preferred propofol model is Cet Schnider, which factors in patients' age, height, weight and gender. The Marsh model, although requiring entry of patient weight, makes no allowance for patient age.

The Eleved model is increasingly utilised for TCI TIVA. The recognised benefits are an automatic propofol dose adjustment in the presence of remifentanyl and a far wider programmable range of

age and weight. The bolus phase of Eleveld is slower than Schnider. Taken with our preference not to sedate patients with a BMI over 35 Kg/m<sup>2</sup>, or to sedate those less than 11 years of age, we see no added benefit of changing to the Eleveld model-although we acknowledge the considerable benefits of Eleveld for GA *via* TCI TIVA.

**Adverse events:** The rates of adverse events in several published studies are listed in table 3. There is a wide variation of reported events, in part because various authors adopt different reportable levels to describe adverse events and also because some TCI sedation publications relate to procedures other than dental sedation.

Studies are also published based on data pertaining to sedationists with widely different educational backgrounds: specialist medical practitioners (anaesthesiologists), dentists with extensive sedation training, dentists with less training and also nurses trained in sedation administration. For these reasons, it is difficult to comparably rate the frequency of adverse events.

A good example of this is the paper by Barents CRM, et al. [10]. This group retrospectively examined the records of 2315 patients who underwent 2937 procedures- mostly gastroesophageal or cardiac procedures. The rate of severe adverse events was 1.1%, but further examination shows a significant adverse event rate of 10.5% and a moderate adverse event rate of 6%. As a caveat, these patients were of higher ASA status (65% ASA2 or 3) than other reported sedation series and underwent, presumably, more complex procedures. Nevertheless, their high mean propofol Cet of 2.6 mcg/ml, administered to a cohort of relatively high ASA patients might have been of contributory significance to their adverse event rates.

The adverse event rate in our audit of 652 patients was 4.1%, lower than the adverse event rates in our previous publications of 10.6% with remifentanyl [2] and 7.7% with alfentanil [1]. We ascribe this difference to a better selection of patients by our surgeons, and an increasing familiarity with our sedation techniques, in particular when using remifentanyl. Remifentanyl is more difficult to work with than alfentanil, and we consider that our initial TCI bolus method of delivery should only be entertained by practitioners very familiar with both TCI sedation and TCI GA. An understanding of both Cet's AND age-adjusted remifentanyl bolus doses is essential, and this knowledge is difficult to gain if sedation alone is practiced.

## Conclusion

Propofol TCI sedation with ultra-short-acting narcotics, and in particular remifentanyl, affords the ability to rapidly modulate sedation levels and allows for a fast-track patient discharge of around 12 mins in most cases. It is amenable to office-based dental procedures and has proven to be safe and reliable. Patient satisfaction rates are high and the procedure conveys cost benefits to both patients and practice owners.

## Declaration of Interest

The authors have no conflicts of interest to declare.

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