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Propofol-Ketamine Technique: Dissociative Anesthesia for Office Surgery (A 5-Year Review of 1264 Cases)

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Abstract. Propofol-ketamine technique is a room air, spontaneous ventilation (RASV), intravenous dissociative anesthetic technique which simulates the operating conditions of general anesthesia without the increased equipment requirements or costs. A total of 2059 procedures were performed on 1264 patients by 38 different surgeons. There were no hospital admissions for postoperative nausea and vomiting (PONV) or uncontrolled pain. All patients were pleased with their anesthetic and no hallucinations were reported. Cost:benefit analysis is presented as well as discussion of dissociative anesthesia being exempt from current California law (AB595).

Key words: Propofol—Ketamine—Dissociative anesthesia—Intravenous anesthesia—Office surgery

Propofol (Diprivan, Zeneca) and ketamine (Ketalar, Parke-Davis) technique [1] is this anesthesiologist's evolution of Vinnik's diazepam (Valium, Roche) and ketamine technique for office anesthesia [2,3]. Diazepam is an agent with a high margin of safety, which is important if it is to be given by the surgeon as Vinnik recommends. Diazepam has little appeal for the anesthesiologist because its long half-life may result in significant hangover when hypnotic doses are employed. Diazepam causes venous irritation and phlebitis, which Vinnik avoids by injecting the diazepam into an external jugular heparin lock [4]. Anesthesiologists are less than enthusiastic about this solution to venous irritation. Most anesthesiologists are unaware of Vinnik's work on the ease of prevention of ketamine-induced hallucinations. Ketamine is not a comfortable choice for many anesthesiologists. Propofol has significant anti-emetic properties [5] and euphoriogenic qualities as well. Propofol has an evanescent half-life resulting in minimal postoperative hangover when the drug is discontinued. Propofol is a more attractive agent for use in office surgery for the anesthesiologist.

Minimizing office overhead is another consideration. With propofol-ketamine technique, there is no need for an anesthesia machine, scheduled maintenance or scavenging considerations for exhaled gases and vapors. Gone also are the need for soda lime, anesthesia breathing circuits, and endotracheal tubes. No endotracheal tubes means the end of sore throat complaints. Also eliminated are chipped tooth issues as well as the stress of the unexpected difficult or impossible intubation. The expense of endotracheal tubes, muscle relaxants, and inhalational agents are eliminated. All medications (glycopyrrolate [Robinul, Robins], midazolam [Versed, Roche], propofol, & ketamine) are nontriggering agents for malignant hypothermia. There is no need to stock dantrolene (Dantrium, Procter & Gamble). The basic requirements for an oxygen source, Ambu bag, and suction apparatus (commonly found in most office surgery suites) do not impose an undue burden.

Method

All patients were interviewed by the author prior to surgery to elicit age, weight, procedure, medications taken, allergy to medications, smoking history, alcohol tolerance, history of asthma or hepatitis, history of prior surgery and anesthesia experiences (i.e., nausea, emesis, and hangover), susceptibility to motion sickness and morning caffeine usage. Smokers were strongly encouraged to stop smoking at least the day before surgery, longer if possible, with the goal of quitting altogether. Patients on antidepressants or antihypertensives were given their

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customary morning doses with enough water to swallow them comfortably. Caffeine users were encouraged to have their usual morning dose without dairy product. No patients in this series were taking Fen-Phen within two weeks prior to surgery.

Prior to anesthetizing the patient, the upper airway was examined and the heart and lungs auscultated. Laboratory results as well as chest x-ray and EKG, when appropriate, were reviewed as well. The EKG, NIABP, and pulse oximetry monitoring were explained to the patients. The agents for the anesthetic technique were discussed with all patients, with particular attention given to the expected postoperative dry mouth from the glycopyrrolate and the history and hallucinogenic potential of ketamine. All patients signed informed consents for anesthesia. All anesthetics were administered by the author. All data were collected by the author.

All operating rooms had oxygen, Ambu bags, and suction apparatus in good working order, in addition to "crash" carts with functioning defibrillators. Although not required, an anesthesia machine was present in approximately 50% of the cases. A continuous intravenous line was established with a 20 or 22 gauge intravenous catheter connected to a 15 drop $\cdot$ cc^{-1} intravenous set. The EKG, NIABP, and pulse oximeter were applied and baseline values were determined before any medications were administered.

Glycopyrrolate 0.2 mg (1 cc) was given at the outset. If the case duration was expected to be about 90 min or less, or if the patients were older than 65–70 years of age, midazolam was not used. Most commonly, midazolam was given in 2 mg increments times one. If the patient did not report feeling any differently after the first 2 mg had circulated for a few minutes, a second 2 mg bolus of midazolam was given.

The propofol infusion was started and titrated prn. The patient was engaged in conversation until loss of verbal contact occurred. At that point, the lid reflex was elicited. If no blink occurred, the patient was asked if she was asleep yet. A nonresponse was sought. Total propofol dosage was determined by subtracting what remained in the bag from the total amount injected into the bag during the course of the case.

Once unconsciousness or hypnosis was achieved, a bolus dose of 50 mg ketamine was administered. The surgeon was notified that in 2 min it was expected that the patient would be in a dissociative state and should not respond to the injection of local anesthetic. If the patient made purposeful movements (i.e., wincing or reaching of the hand to the area being injected) in response to the injection of local anesthetic, the local anesthetic injection was terminated until a second dose of ketamine (25–50 mg) was administered and the dissociative state was obtained. The patients had hypnosis maintained for a minimum of 20 min after the attainment of the dissociative state to allow the ketamine to redistribute out of the brain [6]. The patients were maintained on the infusion of propofol until the termination of the procedure.

For procedures where the head was expected to be in a neutral position (i.e., blepharoplasty), a #28 nasopharyngeal airway was used to maintain a patent airway. For rhinoplasty with osteotomies, a #4 laryngeal mask airway was used to prevent blood from spilling onto the larynx as well as keeping the majority from draining into the stomach.

No opioids, H_2 antagonists, antihistamines, or antiemetics were administered preoperatively. When the procedure undertaken seemed to have a high risk of postoperative pain, prophylactic analgesia was administered in the last intraoperative hour. Most commonly, this was meperidine (Demerol, Winthrop) in 20 mg increments. Other agents were used as noted in Results. Rescue analgesia and/or anti-emetic therapy was used as needed in recovery. All patients were asked by the author postoperatively and prior to discharge from the office as to whether or not they had experienced dreaming. If an affirmative response was given, the patient was then asked if the dreams were pleasant or unpleasant.

Results

A total of 1264 patients were tabulated for 38 different surgeons in this 5-year series, which ran from March 26, 1992 to March 25, 1997. A grand total of 2059 procedures were performed owing to the number of patients having had multiple procedures for the same anesthetic. Ninety-nine percent of patients maintained a SpO_2 > 90% breathing room air spontaneously. In two cases, surgery was interrupted briefly for positive pressure ventilation to restore an adequate SpO_2 while the propofol infusion was decreased to allow resumption of spontaneous ventilation. In three elderly patients, oxygen (1–2 L $\cdot$ min^{-1}) was administered by nasal cannula to maintain SpO_2 > 90%.

Procedure distribution was scalp/hair 39, browlift 75, blepharoplasty 239, rhytidectomy 159, rhinoplasty 87, otoplasty 10, facial resurfacing (chemical peel, dermabrasion, and/or laser) 532, fat transfer 219, breast (augmentation, pexy, or reduction) 229, liposuction 407, abdominoplasty 23, oral, dental and miscellaneous 40.

By gender there were 1027 female (81%) and 237 male patients (19%). Only 88 patients (7%) were over 65 years of age and 31 patients (3%) were less than 20 years of age. Average[1] surgery time was 153 min. 194 patients (15%) had procedures exceeding 240 min. The shortest procedure was 20 min. The longest procedure was 540 minutes.

As seen in Table 1, female patients on average were 43 years of age, weighed 60 kg, were premedicated with an average 2.9 mg of midazolam, required an average 1437 mg of propofol and an average 96 mg of ketamine for procedures of an average 151 min duration. Female patients consumed 9.8 mg $\cdot$ min^{-1} of propofol independent of body weight. The weight adjusted rate was 165

[1]Averages were computed on a Macintosh Performa 575 with a ClarisWorks 4.0 program.

Table 1. Summary

Gender	*N*	Age	Wt	Midaz	Prop	Ket	Time	mg · min^{-1}	μg · kg^{-1} · min^{-1}
F	1027	43	60	2.9	1,437	96	151	9.8	165
M	237	46	84	3.2	1,523	115	160	9.7	118

μg · kg^{-1} · min^{-1}. Male patients on average were 46 years of age, weighed 84 kg, were premedicated with an average 3.2 mg of midazolam, required an average 1523 mg of propofol and an average 115 mg of ketamine for procedures of an average 160 min duration. Male patients consumed an average 9.7 mg · min^{-1} and 118 μg · kg^{-1} · min^{-1} of propofol.

As seen in Table 2, with increasing doses of midazolam premedication, an *apparent* propofol saving effect is demonstrated. All patients were queried for the occurrence of intraoperative dreams on emergence. No hallucinations were reported either in the immediate recovery, discharge, or on postoperative office visits. Less than 1% of patients reported pleasant colorful dreams.

Seven hundred fifty-one (751) patients (60%) received neither prophylactic analgesia or rescue analgesia. The majority of patients (77%) did not receive prophylactic analgesia in the hour prior to emergence. The same number (970) did not require rescue analgesia in recovery. Two hundred ninety-four (294) patients (23%) did receive prophylactic analgesia in the hour prior to emergence. Meperidine in 20 mg increments was used in 153 patients (52%) receiving prophylaxis. Meperidine was titrated to maintain the SpO_2 > 90%. Of those receiving meperidine, 20 (13%) required rescue analgesia in recovery, usually in the form of more meperidine. Ketorolac (Toradol, Roche) 60 mg was used in 78 patients (26.5%). Of those receiving ketorolac, two (3%) required rescue analgesia. Nabumetone (Relafan, Smith Kline Beecham) 1 gm was given as a loading dose orally preoperatively in 52 patients (17.7%). Of those receiving nabumetone, 17 (33%) required rescue analgesia. Butorphanol (Stadol, Bristol-MyersSquibb) was used in five patients, only one of whom required rescue analgesia. Fentanyl (Sublimaze, Janssen) was used in six patients. There were *no* hospital admissions for intractable postoperative pain.

Five patients experienced nausea, and seven (0.6%) experienced emesis times one. Two episodes were intraoperative and without aspiration. Three other emesis patients received prophylactic meperidine, and one vomited after rescue butorphanol. One emesis occurred in recovery after the patient (#51; 8/24/92) had endured over 2 hours of postoperative nystagmus secondary to an unusually large dose of ketamine (650 mg). Twenty-one (21) patients (2%) received rescue antinausea medication: 16 were given prochlorperazine (Compazine, Smith Kline Beecham), 3 odansetron (Zofran, Cerenex/GlaxoWellcome), 2 hydroxyzine (Vistaril, Pfizer). No patient required airway support or supplemental O_2 in recovery. The majority of patients regained consciousness in 10–15 min after discontinuation of the propofol infusion. The majority of patients were discharged to home alert by the end of the first postoperative hour. No professional "after care" providers were required. Patients returned home to the care of their friends or family. Flumazenil (Romazicon, Roche) was used nine times: four with good effect, five with minimal effect. There were *no* hospital admissions for postoperative nausea or vomiting (PONV).

Cost analysis is based on 1264 cases and 1997 prices, National Surgical Supply catalog, glycopyrrolate $1.43 per 20 ml multidose vial, midazolam $70.50 per 50 mg multidose vial, propofol $298.18 per 25 box of ampule 20 ml single dose vials, and ketamine $19.00 per 10 ml multidose vial. In an average case, 1 ml glycopyrrolate @$0.07, 3 ml midazolam @4.23, 8–20 ml ampules propofol @$95.42, and 2 ml ketamine @$3.80 were used. The total average cost per case was $103.52.

Discussion

Frizzelle et al. [7] published a five-level scale for sedation (Table 3) in a recent paper comparing propofol-ketamine combination for sedation of patients undergoing spinal anesthesia. Following premedication with 100 mg hydroxyzine, they were using *subhypnotic* levels of propofol and subdissociative levels of ketamine to achieve level 3 sedation. Since it is known that subhypnotic levels of propofol will not block hallucinations from ketamine [8], predictably some of their patients hallucinated. The lack of hallucinations in this series confirmed the author's earlier work that showed *hypnotic* doses of propofol prevent ketamine-induced hallucinations [9].

The endpoint of level 5 sedation, while maintaining the SpO_2 > 90% on room air, was the goal achieved in the overwhelming majority of patients in this series. A few elderly patients were not able to achieve this goal without the addition of 1–2 L · min^{-1} of nasal oxygen. No patients became medically unstable in this series. There were no cardiopulmonary arrests or 911 calls.

From Table 2, women and men consumed a surprising average 9.8 and 9.7 mg · min^{-1}, respectively, of propofol despite substantial differences in their average body weights (60 vs. 84 kg). When body weight was factored into the propofol consumption rate, women and men consumed an average 165 and 118 μg · kg^{-1} · min^{-1}, respectively. A possible explanation is that the part of the brain most sensitive to the effect of propofol is very small and doesn't vary significantly with body weight in adults.

Propofol-ketamine technique was originally conceptualized without midazolam premedication. Adding midazolam premedication was intended to reduce propofol

Table 2. Effect of midazolam premedication on propofol consumption

Midazolam	Gender	*N*	Age	Wt	Prop	Ket	Time	mg · min^{-1}	μg · kg^{-1} · min^{-1}
0 mg		354							
	F	293	42	58	1037	70	96	10.8	190
	M	61	46	85	1243	88	110	11.3	135
2 mg		316							
	F	286	42	60	1545	92	150	10.3	175
	M	60	45	83	1597	112	163	9.8	121
4 mg		303							
	F	249	43	63	1718	109	179	9.6	155
	M	54	48	86	1683	108	181	9.3	109

Table 3. Frizzelle Sedation score

Score	Degrees of sedation
1	Fully awake and oriented
2	Drowsy
3	Eyes closed but arousable to command
4	Eyes closed but arousable to mild physical stimulation (earlobe tug)
5	Eyes closed but unarousable to mild physical stimulation

requirements and thereby save on the cost of the technique. In a clinical setting, it is very difficult to determine what savings may occur in a given individual patient. From Table 4 it appears that $2.82 worth of midazolam might save either $12.00 worth of propofol in women or $24.00 in men. Similarly, $5.64 worth of midazolam might also save $24.00 worth of propofol in both men and women. Because this anecdotal series is *not* a double-blinded study, one cannot claim a statistically significant ($p < 0.05$) reduction in propofol consumption by the addition of midazolam premedication.

Oxorn et al. [10] recently published a very elegant double-blinded study of the midazolam premedication issue. "Our results indicate that although the time to loss of lid reflex was significantly shorter in patients receiving midazolam (30 μg · kg^{-1}), there was no significant difference in the dose of propofol required to induce hypnosis or maintain anesthesia. There were no group differences in postoperative sedation and orientation scores, perioperative mood profiles, incidence of dreams, and patient satisfaction scores. More patients who received midazolam requested analgesics in the PACU (11 vs. 4, $p < 0.05$). In conclusion, midazolam did not reduce the anesthetic dose requirement of propofol in patients undergoing anesthesia with nitrous oxide, nor did it accelerate patient recovery. Our results call into question the benefit of co-inducing anesthesia with propofol and midazolam." The Oxorn study results confirm the author's tendency toward eliminating the midazolam premedication from the technique.

Propofol-ketamine technique allows the patient to tolerate the local anesthetic injection (interim analgesia) and remain oblivious to the course of the surgical procedure (hypnosis). Interim analgesia for the local anesthetic injection is provided by the dissociative dose of ketamine. An extremely smooth level of hypnosis is provided by a carefully titrated qualitative infusion of propofol. The steady level of hypnosis cannot be reproduced using intermittent boluses propofol. The tranquility of the surgical field approximates that of general anesthesia in over 98% of the cases. The rapid metabolic degradation of propofol obviates the need for infusion devices that permit more precise knowledge of the ongoing rate of propofol administration. By eliminating a device requiring servicing and calibration, performing the technique requires only an intravenous bag and a 60 gtts · cc^{-1} intravenous set.

Propofol has no analgesic activity. Patients will move in response to inadequate analgesia. The technique obliges the surgical team not to hurt the patient, sometimes called "prophylactic analgesia." The operative field must be injected with adequate local anesthesia via tumescence, field block, nerve block, or combination thereof. Trying to "cover" inadequate local anesthesia with more ketamine will result in unnecessarily high total ketamine doses with prolonged emergence as a consequence. Ninety-five percent of cases in this series were performed with 200 mg or less total ketamine. This is usually accomplished by doing as much of the injection as possible during the initial dissociative dose of ketamine. Re-injection does not require additional ketamine.

Surgeon satisfaction with this technique grows substantially if the first response to patient movement is to inject more local anesthetic rather than ask for the endotracheal tube. Patient movement does not mean patient awareness! Physicians trained in the 1970s (between the exit of halothane and the introduction of ethrane) are especially vulnerable to this interpretation. Propofol-ketamine technique provides good to excellent conditions for subpectoral breast implants as well as rectus muscle imbrication for classical abdominoplasties. In none of the 1264 cases, including the 23 abdominoplasties or 80 subpectoral breast augmentations, was it necessary to abandon the technique to provide good operating conditions for the surgeon.

The local analgesia having been given, there is little rationale for administering intravenous opioids. Opioids reduce the sensitivity of the pulse oximeter as they

Table 4. Theoretical propofol savings

Midaz	Gender	mg · min^{-1}[a]	Time	TPC[b]	Prop[c]	Delta	Amp (20 ml) saving
2 mg	F	10.8	150	1620	1545	75	1
	M	11.3	163	1842	1597	245	2
4 mg	F	10.8	179	1933	1718	215	2
	M	11.3	181	2045	1683	362	2

[a] Propofol consumption rates for unpremedicated (midazolam = 0 mg) patients from Table 2.
[b] Theoretical propofol consumption.
[c] Actual propofol consumption from Table 2.

depress the respiratory drive. Opioids are associated with a 15–40% incidence of PONV. This obliges one to add oxygen, a fire hazard with lasers, and supplemental antiemetic agents. These additions increase the costs and complexity of the technique. Nausea and vomiting are not associated with the use of ketamine. Opioid use makes it impractical to maintain the patient's SpO_2 > 90% with room air, spontaneous ventilation (RASV).

Ketamine intensifies the upper airway or laryngeal reflexes. Intensification of these reflexes in dissociative anesthesia provides excellent protection against aspiration. The laryngeal reflexes are the "life preserving reflexes" referred to in the exemption to the California Assembly Bill (AB) 595, which regulates office surgical suites. By *intensifying* rather than depressing these reflexes, propofol-ketamine technique qualifies for this exemption [11].

There were remarkably few side-effects experienced by patients in this series. The most common was dry mouth related to the anti-sialogogic effect of the glycopyrrolate. This caused few complaints once the author informed the patients in the preoperative interview. Less than 1% of patients reported dreams when questioned on emergence from anesthesia and before discharge from the office. Dreaming was attributed to the ketamine. However, the few dreams that were reported were always pleasant and typically colorful. None of the few dreaming patients said they were bothered by the dreams.

Ketorolac appeared to be the most effective prophylactic analgesic, based on the few who received it requiring rescue analgesia (3%). NSAIDs decrease platelet adhesiveness. Reports of postoperative hematoma [12] sharply circumscribed the use of NSAIDs. Ketorolac is contraindicated before and during surgery and whenever even slight bleeding could be a problem (e.g., after plastic surgery) [13]. Emesis was associated with only three patients (2%) of the 153 who received prophylactic analgesia with meperidine. Meperidine continued to be the most commonly used analgesic for both prophylactic and rescue analgesia.

The average cost of propofol-ketamine technique at $103.52 for 153 min of anesthesia time ($1.48 · min^{-1}) be balanced against the benefits received. Those benefits are a near zero PONV rate along with universal patient satisfaction. Surveying an affluent population, Tang et. al. [14] found that "patients were willing to pay a mean of $117 ± $82 to prevent PONV if they underwent a similar operation in the future." The $103.52 cost is trivial compared to the benefit of not losing surgical cases because patients are reluctant to have additional surgery for fear of repeating earlier unsatisfactory anesthetic experiences. One of every three patients in this series had had prior unhappy anesthetic experiences. These patients report their negative anesthesia experience to the *next* surgeon from whom they seek care. The uniform level of hypnosis the propofol infusion provides simulates the operating conditions of general inhalational anesthesia without the increased equipment demands or costs. These conditions allow the surgeon to operate without the distraction of verbal contact with the patient. All patients, including those who experienced PONV (7 of 1264), expressed satisfaction with their anesthetic experience. Patients reported they would be very pleased to have the same anesthetic for subsequent procedures.

Conclusion

Propofol-ketamine technique is this anesthesiologist's evolution of Vinnik's diazepam-ketamine technique. Vinnik's approach has the surgeon as drug administrator as well as operator. The margin of safety using diazepam is high. The same is not true for propofol. This technique is only recommended for circumstances where an individual other than the surgeon has primary responsibility for managing the propofol infusion. The author prefers that this other individual be an anesthesiologist with expertise in office anesthesia.

In elective plastic surgery, a satisfactory result does not equate with a happy patient and a less than satisfactory result does not automatically mean an unhappy patient. Patients having unhappy anesthetic experiences tend not to return for secondary surgery or additional procedures. Unhappy patients are not enthusiastic proponents of plastic surgery to their friends and family. The converse is equally true. Patients who have had a positive anesthesia experience are far more willing to have revisions or subsequent procedures and recommend plastic surgery to friends and family. The mild euphoria patients experience is not to be underestimated as a source of patient satisfaction with the technique. This phenomenon is largely unrecognized in the anesthesia literature.

Propofol-ketamine technique intensifies the life-preserving reflexes and still gives the surgeon tranquil operating conditions with minimum physiologic trespass

to the patient. Proof of that minimum physiologic trespass is that fewer than 1% of patients required supplemental O_2. An alert patient ready for discharge within the first postoperative hour is the norm nearly independent of the length of the surgical procedure. A 0.6% PONV rate as well as a universal patient satisfaction rate are overwhelming benefits in the plastic surgery patient population. It is not possible in this series to demonstrate a statistically significant ($p < 0.05$) propofol savings by the addition of midazolam premedication. The two most common objections to propofol and ketamine are the cost of the propofol and the fear of ketamine. By demonstrating a lack of hallucinations in a large series and a positive cost:benefit ratio, propofol-ketamine technique answers those objections.

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