Modified Propofol-Ketamine Cosmetic Surgery: Anesthesia Technique for Surgeon-Administered Anesthesia With Particular Reference to Liposuction

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Propofol-ketamine (PK) anesthesia was originally described by Friedberg as dissociative monitored anesthesia care (MAC), which gives the patient the subjective experience of general anesthetic with few risks and virtually no postoperative nausea, vomiting, dysphoria, or hallucinations. Friedberg has a stellar 10-year record of safety with patients receiving propofol-ketamine anesthesia, with a 0.5% postoperative nausea and vomiting (PONV) rate. There were no hospitalizations in his group for either uncontrolled pain or PONV, the 2 most common reasons for admission following day surgery. For the surgeon who chooses to administer his or her own anesthesia, this paper describes a variation of Friedberg's original work. (See www.doctorfriedberg.com for other information.)

Any physician administering sedation has patient safety and comfort as his or her foremost consideration. Safety means the least possible stress on the patient: the least pain and immobility plus the easiest anesthetic and recovery experience. Surgical duration should be minimized. All anesthetic agents have potentially negative effects that can be minimized by judiciously titrating to effect, rather than administering dosages on a per body weight basis. The physician who chooses to administer his or her own sedation is supported by recommendations of the American Society of Anesthesiology's "Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists," which specifically mention proprofol and ketamine, the technique that is the subject of this paper.[1]

Liposuction may be performed with just oral medication and local anesthesia. Although this is possible, physicians working in this fashion inevitably have a reputation for causing pain. Even if only 5% of their patients become anxious and perceive discomfort during the procedure, the word gets around. The surgeon will find that doing it right 95% of the time does not prevent a negative reputation.

Many physicians have described a small series of self-administered anesthetic regimens without complications. After personally giving anesthesia for several thousand cases using intravenous opiate narcotics (fentanyl and meperidine) coupled with intravenous benzodiazepine-class drugs (midazolam, diazepam) plus a local anesthetic, we became very dissatisfied with the inconsistency of the level of anesthesia, the unpredictability of the respiratory status, bradyarrhythmias with the narcotics, and the unacceptable postoperative nausea and vomiting (PONV) rate. Even with minimal doses of opiates, some patients still experience PONV. Studies show PONV rates of 8–55% for outpatient procedures.[2–8]

Searching for a safer, more comfortable, and more predictable light sedation technique, we first began mixing small quantities of propofol, ketamine, and fentanyl and/or midazolam and administered this mixture intravenously in a dilute saline vehicle. This also gave an inconsistent result. Friedberg's propofol-ketamine (PK) technique[2] demonstrated a consistent level of anesthesia, stable respiratory status, and almost no PONV outcome. We also discovered that this method was recommended by the American Society of Anesthesiology's "Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists."[1] Patients emerged from anesthesia within minutes of discontinuing the propofol, and some reported feelings of euphoria. Patients experienced no dysphoria or hallucinations.

Friedberg's[2] propofol-ketamine technique is outlined in Table 1. Essentially, he uses a propofol drip to sedate his patients before injecting 50 mg of ketamine intravenous (IV) push. This allows enough analgesia for the physician to freely inject the local anesthetic and not worry about stinging or anxiety during this process. As the ketamine wears off, the local anesthetic begins working, and the physician continues the sur-

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Table 1. Elements of Friedberg's Propofol-Ketamine Technique

1. Glycopyrrolate (Robinul) 0.2 mg (intravenously) given at onset of anesthesia.
2. Propofol titrated to lack of lid reflex over a 2–5 minute time frame to preserve spontaneous ventilation and provide a stable level of propofol in the brain prior to administering the ketamine.
3. Ketamine 50 mg intravenous push after lid reflex and verbal responsiveness is lost.
4. Local anesthetic injection 2–3 minutes after ketamine is injected.
5. Depending on the degree of patient movement, an additional 25–50 mg of ketamine may be needed (the dissociative effect of ketamine is defined at the absence of patient movement with local anesthetic injection).

gery with local anesthetic while the patient is sleepy on propofol drip. No narcotic or benzodiazepine drugs are used.

Robinul 0.2 mg (1 mL) is given intravenously at the start of the procedure; this usually prevents excess salivation, which occurs occasionally with ketamine. A rare problem (less than 1% of the cases) is ketamine-induced laryngospasm. This features complete glottic closure and therefore no tell-tale, high-pitched crowing noise to aid with the diagnosis. The prodrome of this phenomenon is only a cough or sneeze to alert the practitioner. Immediate administration of 100 mg of IV lidocaine generally reverses this problem. Although Friedberg[2] gives the small (50 mg) dose of ketamine IV push, we have adopted a more conservative administration over 1 minute and have used less propofol prior to the ketamine, believing we have lower laryngospasm rates.

The intended effect of the propofol-ketamine anesthetic technique is to provide a moderate sedation/analgesia. The sedation levels are elucidated in Table 2.

Prior to adopting an infusion pump, Friedberg[2] diluted 10 mg/mL stock propofol to 5 mg/mL by adding an equal volume of either saline or Ringer's lactate solution. Although this was satisfactory in his hands, we found that using a greater dilution resulted in less airway positioning to maintain proper oxygen saturation. By empirical means, a solution of six 20 mL vials of propofol in 1000 mL saline as a dilution worked best. We spoke to the scientists at the manufacturer, and they said that although their official recommendation was that dilution of propofol theoretically could cause some problems with the emulsion, if the mix were used within a few hours no untoward result was expected. A bolus or loading dose of propofol is not used because the object of the gradual induction is threefold: (1) accurately, rather than rapidly, medicating the patient; (2) developing a sense of the patient's individual dose requirement; and (3) creating a stable brain level of propofol to prevent hallucinations or dysphoria from the ketamine.

The dilute propofol produces patient responses that are generally very indolent—a big advantage for safety. An extra 5 minutes conversing with a patient while he or she fell asleep was well worth it to avoid the excitement of respiratory depression, however transient.

Because the level of sedation achieved may be greater than that intended, safe practice mandates that those physicians administering their own sedation be able to recognize and rescue from deeper-than-intended levels of sedation/anesthesia. The attractive aspect of this sedation technique is that in terms of responsiveness, the patient is often in the deep sedation/analgesia category with a slow, purposeful response following painful stimulation (Table 2). As for the airway and ventilation, the patients are usually in the moderate sedation/analgesia category with no intervention re-

Table 2. Continuum of Depth of Sedation: Definition of General Anesthesia and Levels of Sedation/Analgesia*

	Minimal Sedation "Anxiolysis"	Moderate Sedation/ Analgesia	Deep Sedation/ Analgesia	General Anesthesia
Responsiveness	Normal response to verbal	Purposeful† response to verbal stimulation or tactile stimulation	Purposeful† response to following painful stimulation	Unarousable, even following painful stimulation
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be imparied

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†Reflex withdrawal from a painful stimulus is *not* considered a purposeful response.

quired for the airway, and usually no oxygen required. The patients ventilate spontaneously, rarely even needing airway positioning or supplemental oxygen to maintain their saturations. They never need cardiovascular supplementation with ephedrine, such as would be the case sometimes under general anesthesia. Unfortunately, anesthetic techniques using primarily opiates have more of a tendency to be in the lighter category for level of consciousness and heavier category for airway control and respiratory drive. This is less stable and less desirable.

The amnestic qualities of propofol are as powerful as midazolam. As long as dilute propofol drip is running, the patient rarely has any memory of the procedure, and while the ideal would be to have no pain for any patient, it is our opinion that modest pain occasionally is a better trade-off for the surgeon doing his or her own sedation than giving more medication and risking respiratory consequences. Occasionally, a second dose of 25 or 50 mg of ketamine is helpful for painful periods in the surgery or during reinjection of local anesthetic when the original anesthetic placement or dose is not adequate. Note, however, that appropriate response to pain during the surgery is the administration of more local anesthetic, rather than repeat dosing with ketamine.

For small cases, the ketamine is not necessary if the surgeon is willing to cover pain responses with the purely soporific and amnestic drug propofol. It must be remembered that propofol has no analgesic effects, and pain is, of course, a stressor as well. For elderly people undergoing facelifts, or other situations where the patient might be more susceptible to medication because of factors like low body weight, 25 mg or less of ketamine might occasionally be appropriate for the local anesthetic injection. Although ketamine combined with propofol can produce respiratory depression very briefly, this condition generally responds well to airway positioning and possibly a nasal airway without mechanical ventilation. Increased salivation effects due to ketamine is usually well-controlled by Robinul per the above protocol.

Tachycardia reported when ketamine was administered as a sole anesthetic is generally minimized when ketamine is administered in the presence of a hypnotic level of propofol. Any tachycardia may be a concern in patients with undiagnosed coronary artery disease (eg, sedentary, middle-aged patients who may seek out liposuction in preference to diet and exercise). These patients are protected from an unintentional chemical stress test if they receive a prophylactic dose of 10 mg labetalol prior to injection of epinephrine-containing tumescent solution. Labetalol has a tachyarrhythmia-protective effect on cardiac function. Low-grade tachycardias may be tolerated by the treating physician if labetalol has been administered, as there is some assurance that they will not degenerate into very rapid, unstable heart rates.

We have used this general method for liposuction successfully for over 1000 cases using a pediatric microdropper on the IV bag in order to control the flow most accurately. The patients have very little problem with respiratory sedation, even when the flow is wide open for a period of several minutes. Even at a wide-open rate, the microdropper can only deliver the full contents of the liter bag in 40 minutes. Earlier use of a propofol pump convinced us that the dilutional method was more accurate and more easily titratable to the patient's level of arousal. Additionally, the full-strength propofol (10 mg/mL) frequently obstructed veins, and the experience for the surgeon was of attempting to force a highly viscous fluid through a small opening. Intravenous dexamethasone (8 mg) both for antinausea effects and for postoperative swelling is also administered.

Anesthesiologists' principal objection to ketamine has been the unpredictable outcome of hallucinations or dysphoria. In response, Vinnik developed diazepam-ketamine anesthesia.[9] He conceptualized the principle of hypnosis first, then dissociative analgesia as the method to prevent the hallucinations reported with ketamine. Friedberg[2] enlarged on Vinnik's work by demonstrating that this principle applied to propofol as well as diazepam hypnosis.[10] Late dysphoric reactions are generally not a feature of the small 50–100 mg ketamine doses, however, and these hallucinogenic effects of ketamine are successfully prevented by the amnestic qualities of propofol.

A few notes on lidocaine are appropriate here, because the local anesthetic is the most central and critical part of the propofol-ketamine technique. Lidocaine, although the safest of the medications used in this protocol, still merits care, particularly with dosing limits. First, for liposuction: although it is probably safe in higher doses than the established[11] 55 mg/kg for most patients (B. Hildreth, MD, unpublished study, February 1998, and P. Lillis, MD, unpublished study, January 2001),[12] 55 mg/kg may easily be a problem in older people. Prolongation of lidocaine metabolism and potential toxicity really does occur with some drug combinations, and if possible the surgeon should discontinue every other drug the patient is taking for 24 to 48 hours before the procedure and for at least 24 hours afterward while the lidocaine is still being metabolized and released from fat storage.

Table 3 lists lidocaine interactions that have been suggested in the literature[13–15]; there are newer drugs in these classes that might also possibly cause problems, and the surgeon is advised to consult references in regard to any drug the patient takes. Any medication metabolized by the cytochrome P450 system (CYP3A4) can theoretically prolong lidocaine's presence in the body. The real implications of Table 3 in reference to tumescent anesthesia are not clear at present, and prohibitions against these medications used with lidocaine should not be taken as scientifically proven. For example, in regard to propofol-lidocaine interactions, there is considerable clinical experience suggesting that listing propofol as an inhibitor of the

Table 3. Drugs That Inhibit Cytochrome P450*

Acebutolol	Methylprednisolone (Medrol)
Amiodarone (Cordarone)	Metoprolol (Lopressor)
Atenolol	Metronidazole (Flagyl)
Carbamazepine (Tegretol, Atretol)	Miconazole (Monistat)
Chloramphenicol (Chloromycetin)	Midazolam (Versed)
Clarithromycin (Biaxin)	Nadolol (Corgard, Corzide)
Cyclosporin (Neoral, Sandimmune)	Nicardipine (Cardene)
Danazol (Danocrine)	Nifedipine (Procardia, Adalat)
Dexamethasone (Decadron)	Pentoxifylline (Trental)
Diltiazem (Cardizem)	Pindolol (Visken)
Erythromycin	Propranolol (Inderal)
Esmolol (Brevibloc)	Propofol (Diprivan)
Fluconazole (Diflucan)	Quinidine
Fluoxetine (Prozac)	Sertraline (Zoloft)
Flurazepam (Dalmane)	Selective serotonin reuptake inhibitor antidepressants
Isoniazid (Nydrazid, Rifantate, Rifater)	Tetracycline
Itraconazole (Sporanox)	Terfenadine (Seldane)
Ketoconazole (Nizoral)	Thyroxine
Labetalol (Normodyne, Trandate)	Timolol (Timolide, Timoptic)
Methadone (Dolophine)	Triazolam (Halcion)
Methylprednisolone (Medrol)	Valproic acid (Depakene)
Metoprolol (Lopressor)	Verapamil (Calan, Isoptin, Verelan)

*Adapted from Klein and Kassardjian,[13] *Physician's Drug Reference*,[14] and Shiffman.[15]

cytochrome P450 system (CYP3A4) is an error. To wit:

- Friedberg[2] has a decade of safe, clinical experience in over 3000 patients treated with lidocaine and propofol. We have over 1000.
- Intraoperatively, there were no seizures, severe hypotension, or electrocardiogram atrial-ventricular dissociation.
- Postoperatively, there were no patient complaints of tinnitus or metal taste on the tongue.

Propofol, like diazepam, elevates the seizure threshold for lidocaine. Another objection to the above list is that it ignores the fact that the cytochrome P450 system (CYP3A4) is an inducible system. This means that the system expands to meet an increased load (level 1 pharmacokinetics), as opposed to zero-level kinetics wherein only a fixed number of milligrams per unit of time can be metabolized. Also, it is illogical to list midazolam and not diazepam, which is commonly recommended by many of the same dermatologists who are concerned about midazolam.

A literature review only revealed one case of lidocaine toxicity after cosmetic surgery,[7] although there are many anecdotes. Notably, only 0.65 mg/L of epinephrine was used in the tumescent solution in this report. The patient had a lidocaine level of 6.3 mg/L, and she received 58 mg/kg lidocaine. The conclusion drawn from the data was that sertraline or flurazepam, the medications she was taking, were responsible for slowing the lidocaine metabolism through the above mechanisms, causing toxicity. We would draw a much more obvious conclusion: the patient did not have enough epinephrine in her solution to delay the absorption of the lidocaine properly.

Our conclusion in view of the above, however equivocal the data are, is that in the absence of contraindications it is judicious to take patients off any medications they can safely discontinue prior to tumescent surgery using lidocaine. The medication "holiday" should be long enough to metabolize other medication prior to the time of the surgery. And conservative lidocaine dosing limits for individuals who are elderly, thin, or on multiple medications are mandatory. However, blanket prohibitions of the above list are unproven and speculative.

Note that 0.1% lidocaine is quite analgesic for about 85% of people; carefully selected individuals can be anesthetized with this concentration using oral medications or a pure local anesthetic technique. A dose of 0.075% lidocaine controls pain well in roughly one third of the patients. A 15-minute wait after administering the lidocaine (or its administration over a prolonged period, such as a half hour) before starting the surgery improves analgesia and probably limits blood loss to some degree. For very small cases, of course, 0.15% can be used for more analgesia if lidocaine limits are not approached. And generally, a super-wet technique, with the tissues maximally distended with the solution, is best to prevent bleeding as well as to improve analgesia. We will sometimes add fentanyl 0.05 mg/mL, 2 to 4 mL/L, to the propofol mix if the patient is having pain due to low lidocaine concentra-

tions in the tumescent fluid. This sometimes is necessary for small individuals with consequently lower total lidocaine dosing limits who are having extensive surgery. Although this produces PONV for an evitable number, we feel that it is a reasonable trade-off for some cases. The opiate makes the respiratory status less predictable, bradyarrhythmias more likely, and the patients must be watched more carefully, particularly in recovery. Friedberg[2] does not use opiate analgesics, but his practice consists primarily of facelifts and liposuction cases of 5000 mL or less, where conventional lidocaine limits and higher concentrations usually produce excellent analgesia with more concentrated lidocaine solutions.

Adding bicarbonate 8.4%, 12 mL/L of local anesthetic solution, is well known to make the solution pH closer to the body's and produce less pain at the time of local anesthetic administration. This is not necessary when ketamine is used if the local anesthetic is pumped in during the peak of ketamine analgesia, which is the first 10 minutes after administration. However, we have continued the use of bicarbonate because we believe that in terms of patient stress reduction, every little bit helps.

Cold stress during surgery is also a well-known problem and should be minimized. IV and tumescent fluids warmed to body temperature are advisable. Preheated blankets and—better yet—surgical devices that circulate warmed fluid under the patient during the procedure in the cold operating room are additionally advisable; however, with the necessarily messy nature of super-wet tumescent liposuction, we have never instituted the latter.

There is always a trade-off between the scope of the cosmetic correction and safety issues. We believe that 5–10 L can be suctioned safely for many people given a rapid, skillful surgery, generally using 2 operators and usually terminating the case within 1 hour (or at maximum 2), followed immediately by application of a tight garment specially manufactured for liposuction. Attention is paid to adequate and accurate tumescent anesthetic within these parameters, appropriate but not overly aggressive IV hydration after the case, and carefully determining the volume status with postural vital signs and observing urination in recovery. Although careful monitoring of the clinical status of each patient in recovery is the key to safety, an approximate IV hydration guide is 1 L given after surgery for every 2 L of suctioned aspirate. This must be modified by body weight, the age and health of the patient, the amount of tumescent solution used, and the response of the patient in surgery, but primarily by the close observation of the patient in recovery with regard to clinical status, vital signs and urinary output, which should be brisk. The dogma that 5 L is an acceptable limit[16,17] is not supported by the literature. In particular, the largest study of liposuction mortality in history, with over 500 000 patients and over 100 documented fatalities,[18(p443)] showed "no clear association in our survey between fat volume removal and fatal outcome." In addition, a complete review of the literature and prevailing opinion by the California Medical Board over the past few years did not support arbitrary volume limits for procedures performed in either hospitals or in accredited surgical centers, and it left the volume suctioned to the discretion of the individual surgeon.

A critical feature of tumescent solution is the use of adrenaline concentrations of 1:1 000 000. Klein[13,19] has reported several times the use of epinephrine solutions of 0.5–0.65 mg/L (0.5 mg or 0.5 mL of 1:1000/L is 1:2 000 000, half of the above recommendation), and this has been carried through the literature. Several deaths have occurred using this epinephrine concentration. In one paper, 4 deaths were reported, and 3 out of the 4 had 1:2 000 000 epinephrine dosing, but the adrenaline concentration was not even noted.[20] Additionally, there are anecdotal reports in Los Angeles of fatalities and several near-fatalities requiring blood transfusion in cases in which 1:2 000 000 epinephrine was used (P. Chavis, written communication, 1999). Certainly low epinephrine concentrations would seem to the experienced clinician to contribute to lack of vasoconstriction and increased bleeding, although the causal relationship has not been proven, however suggestive the evidence may be.

Using a combination of clonidine premedication with bispectral index monitoring, Friedberg[2] demonstrated a significant reduction in propofol requirements.[21] Others have also shown improvement in blood pressure and anesthetic control with clonidine premedication prior to facelift.[22,23] The FDA approved the bispectral index as a monitor of the level of hypnosis in 1996. It records the tension in the frontalis muscle and is a more subtle measure of consciousness than simply watching the pulse oximeter. This device works better during rhytidectomy than liposuction because the bispectral index readings are disturbed by cannula movement. Also, because bispectral index is an index rather than a directly measured parameter, there is a learning curve of 20–100 cases for clinician effectiveness. Because our practice includes 1- to 2-hour postoperative observation and hydration of patients, the decreased emergence time using the bispectral index is not useful enough to offset the cost of the device and the time required for the learning curve.

After roughly 500 liposuction cases using clonidine, we observed 2 episodes of bradycardia at a rate of about 40 bmp, with systolic blood pressures dropping into the 80s (mmHg). Although these patients maintained mean blood pressures greater than 55 and they responded to fluid challenges, there are other reports of clonidine causing bradycardia, which has been reported in the *Physician's Drug Reference*.[15] Although this relationship is not clearly causal, we have abandoned clonidine for this reason.

Our experience has been that our variant of Friedberg's[2] propofol-ketamine technique is reliable, safe, and most comfortable for my patients. We feel that we need to take charge of every aspect of our patients' care to produce the best result. With an anesthesia pro-

vider administering heavier drug combinations, particularly opiate analgesics, inevitably there is a PONV rate—a very unpleasant consequence for the patient. Unfortunately, these medications may sometimes be used purely for the anesthetist's convenience at the patient's expense. More drugs equals more risk, and deeper levels of anesthesia entail more physician responsibility as well as more stress and risk for the patient. No sedation technique is easy, however. Our respect for anesthesiologists has risen greatly along with our own experience in this limited area of their specialty. Patients are all different and their varying responses make anesthesia a difficult art form. Because our patients occasionally have abnormal vital signs, intensive care knowledge and airway skills are a prerequisite for administering sedation. We recommend that physicians, other than anesthesiologists or nurse anesthetists, who decide to do this compulsively acquire comprehensive skills. As anesthesiologists are so fond of telling the rest of us, proper management of events that happen in perhaps only every 500 or 1000 cases is the reason they have years of training and experience. If the reader chooses to use these techniques, be careful, and always have another person with basic cardiac life support training, at a minimum, in the room to help you monitor the patient, as recommended by the American Society of Anesthesiology's "Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists."[1] A better standard is a registered nurse or physician's assistant with ACLS training. Contemporaneous recording of the vital signs by written record, or at least by mechanical means, is also recommended. All this aside, we feel that this extradilute propofol combination with ketamine plus judicious local anesthetic is a superior alternative for many surgeries and should be given consideration by any anesthesia provider.

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