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Brain Monitored Propofol Ketamine for Elective Cosmetic Surgery

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Additional information is available at the end of the chapter

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Abstract

Brain monitored level of propofol hypnosis provides a numerically reproducible paradigm to block negative ketamine side effects. 50 mg IV ketamine 3 minutes prior to local anesthetic injection blocks virtually all midbrain NMDA receptors and is the basis for nonopioid preemptive analgesia. Opioid avoidance essentially eliminates postoperative nausea and vomiting (PONV) as well as the need for antiemetic agents. Over the past 20 years, no elective cosmetic surgical cases required hospital admission for either post-operative pain control or PONV.

Keywords: brain monitoring, BIS/EMG, propofol, ketamine, nonopioid preemptive analgesia (NOPA), PONV

1. Introduction

Elective cosmetic surgery *excludes* medically indicated procedures like postmastectomy breast reconstruction, burn and tendon repair that are the more properly included in the area of plastic surgery. As such, general anesthesia (GA) risks that may be acceptable for *medically indicated*, plastic surgery patients may not be acceptable for elective cosmetic surgery patients. Cosmetic surgery is “want to” surgery. Plastic surgery is “have to” surgery.

While all cosmetic surgery can be performed under local anesthesia only, most surgical candidates desire to not hear, feel or remember their procedures. Most surgeons prefer to concentrate on their surgery and not to have to speak with their patients during surgery. As such GA is commonly requested by many surgeons. Brain monitored propofol ketamine (“Goldilocks”) anesthesia (not too much, not too little, but just right) bridges the patient care gap between surgery under local only and the more commonly performed GA. “Goldilocks” anesthesia

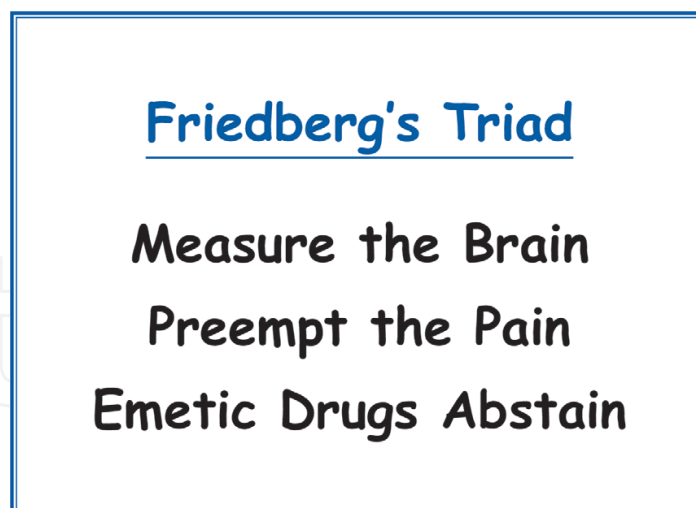


Figure 1. Friedberg's triad.

simulates GA conditions (nonverbal, predominantly immobile patients) while *trespassing the least* on patient physiology, satisfying both patient and surgeon desires. “Goldilocks” anesthesia is **numerically reproducible**. “Goldilocks” anesthesia embodies Friedberg's triad; i.e. Measure the brain, Preempt the pain, Emetic drugs abstain (**Figure 1**).

2. Direct cerebral cortical (brain) monitoring

*When you can **MEASURE** what you are speaking about, and express it in **NUMBERS**, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of **SCIENCE**.*

William Thompson, knighted Lord Kelvin Popular lectures and addresses 1891–1894.

What was true for temperature measurement more than a century ago is also true for the direct measurement of patient's cortical response to anesthetics. Without such measurement, there can be no science. Without science, there can be no reproducibility across the broad, and often unpredictable yet well-recognized, spectrum of individual patient response to medications.

Brain weight does not vary with body weight (i.e. the brain weight of a 100-kg male is **NOT** twice that of a 50-kg female). Traditional anesthetic dosing based on body weight does not account for individual sensitivities to medications and is, therefore, frequently in error.

Further adding to the possibility of dosing error is the twentieth century practice of relying on heart rate (HR) and blood pressure (BP) changes to ascertain cortical drug response. **HR and BP changes primarily reflect brain stem response but are unreliable to accurately determine cortical response.** Prior to the ability to measure cortical response, the knowledge gap between brain stem and cortical response led to routine overmedication (to avoid under medication with awareness and recall).

Pain and consciousness are processed at higher cortical levels (**Figure 2**). Fifty percent of patients experiencing awareness with recall under anesthesia had no HR or BP changes with which to alert their anesthesiologist [1]. Preventing anesthesia awareness is the *least* important value of direct brain monitoring. No deaths have yet been reported from anesthesia awareness. However, one American overmedication death occurs daily! [2]. **Preventing over medication** is the major value of direct brain monitoring (**Figure 3**).

Complex mathematical modeling, i.e. pharmacodynamics (PD) and pharmacokinetics (PK), is based on body weight that may not accurately reflect individual cortical sensitivities. While currently unavailable in the US, target controlled infusion (TCI) only infers cortical response based on blood drug concentrations, again with possible error.

With the Federal Drug Administration (FDA) 1996 approval of the bispectral index™ (BIS) brain monitor, the promise of *direct measurement* of cortical hypnotic response to anesthetic drugs was made available to the anesthesia community. Competing cortical monitors have been introduced since 1996, but the BIS monitor remains the most well-validated brain monitor on the market to date.

Anesthesia may be defined as the sum of hypnosis plus analgesia (**Figure 4**). Implicit in “hypnosis” is amnesia for surgery and within “analgesia” is sufficient muscle relaxation to imbricate the rectus abdominis sheath for classical abdominoplasty. Measured hypnosis enables differentiation of cortical- versus spinal cord–originated patient movement. As opposed to cortically originating patient movement, spinal cord–originated patient movement is devoid of awareness with recall concerns. Knowledge of the origin of patient movement facilitates origin-appropriate treatment of patient movement, thus assuring adequate local anesthesia during sedation (**Table 1**).

As an index, the BIS scale is from 0 to 100. The lower the number, the deeper the level of hypnosis (**Table 2**). Although validated in over 3500 published papers, the promise of direct

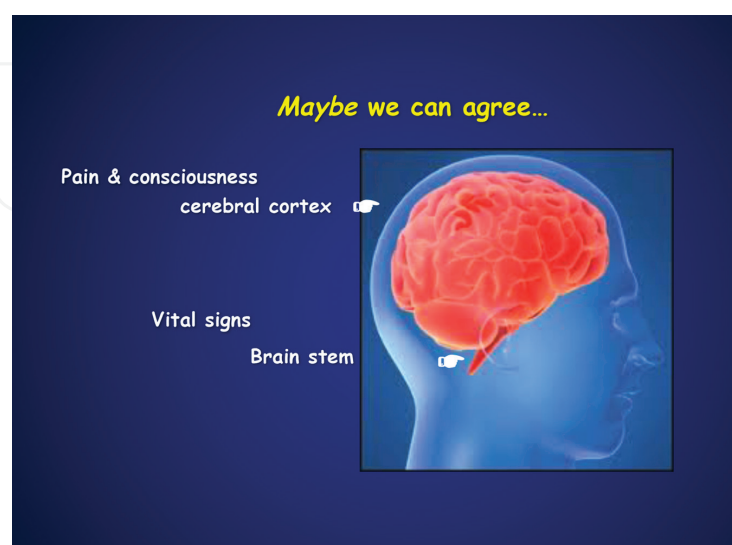


Figure 2. Cortex and brain stem.

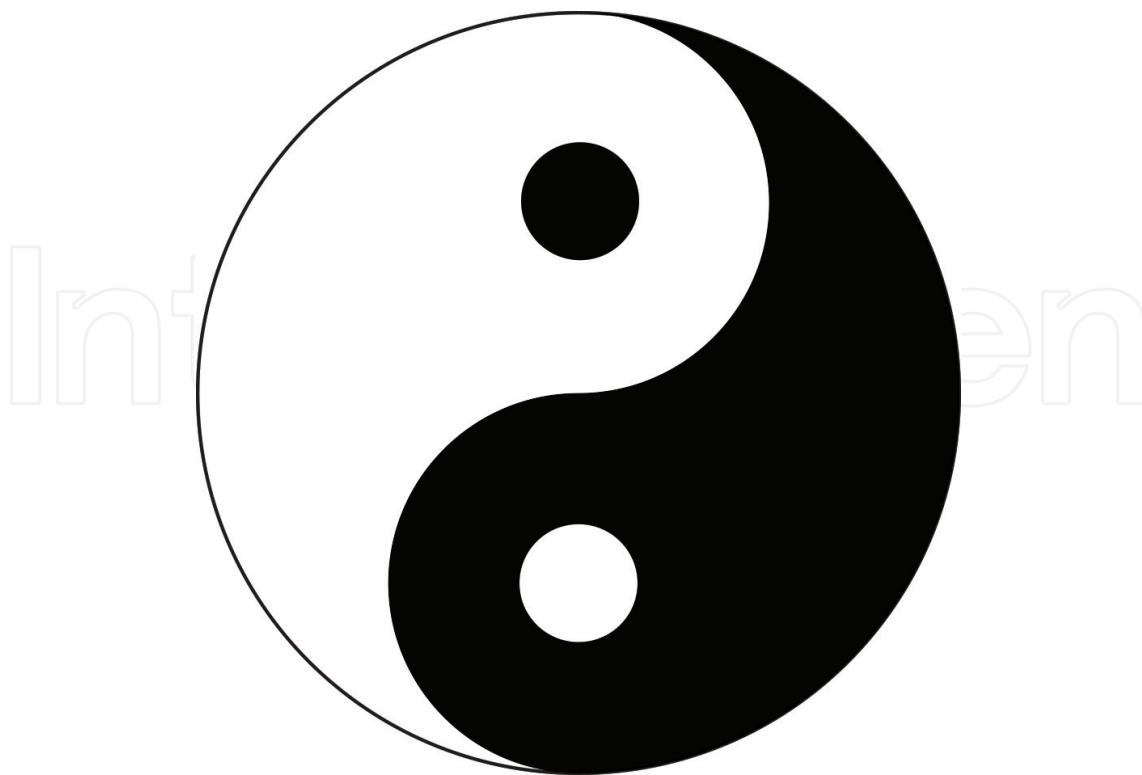


Figure 3. Hypnosis + analgesia = anesthesia.

brain monitoring has remained unrealized for several reasons. First, the BIS only measures response to hypnotic, not analgesic, drugs primarily acting of the cerebral cortex like propofol and inhalation agents like isoflurane, sevoflurane and desflurane. Drugs that act at lower brain centers are benzodiazepines (i.e. diazepam and midazolam), opioids (i.e. morphine, meperidine, hydromorphone, fentanyl, sufentanil, alfentanil, remifentanil), and N_2O . One cannot depend on reliable BIS cortical measurement from subcortically acting agents.

Second, the original factory default setting included only the BIS value and horizontally displayed BIS trend. BIS values are calculated by an algorithm that delays data by 15–30 s from real time. This delay puts the anesthesiologist in the unfavorable position of catching up to dynamically changing patient hypnotic requirements as opposed to having real-time information with which to formulate a response ahead of patient movement. BIS without EMG is *not useful* and is akin to trying to drive a car with only the rearview mirror information.

The electromyogram (EMG) is the electrical activity of the *frontalis* muscle between the eyebrows. This EMG is as real time and as instantaneous a signal as that of the EKG of the cardiac muscle. Unfortunately, the EMG was originally perceived as a “contaminant” of the BIS signal and not understood as a useful piece of information. *Prompt attention* to EMG spikes during sedation by increasing sedation to return the activity to baseline precludes “contamination” of the BIS value. Trending EMG spike activity enables the anesthesiologist to proactively respond to rapidly changing patient needs, providing a stable level of hypnosis throughout a case. BIS **with** EMG trending is very useful and is akin to driving a car looking through the forward-facing windshield.

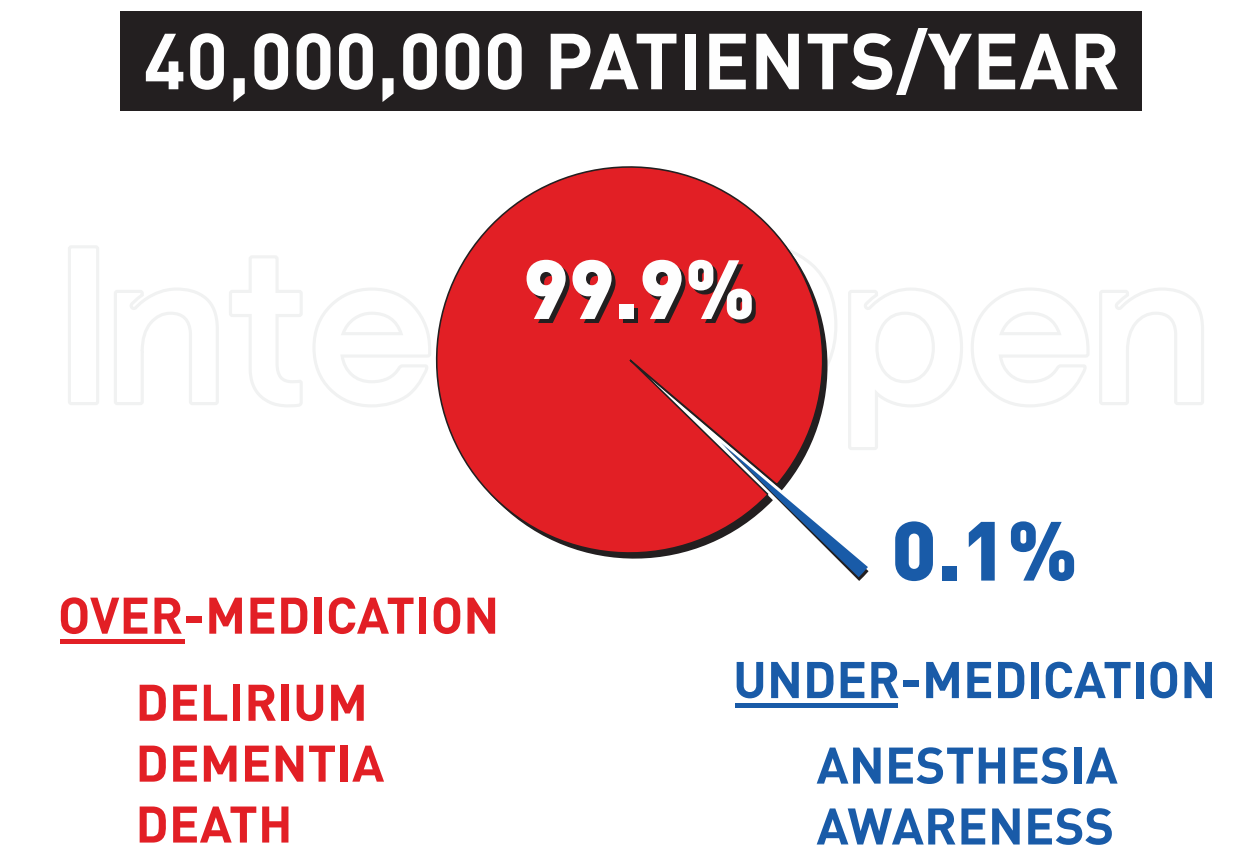


Figure 4. The value proposition of direct cortical monitoring.

BIS values	Hypnotic sedation/anesthesia levels
98–100	Awake
78–82	Minimal sedation
70–80	Moderate sedation
60–70	Deep sedation
45–60 + systemic analgesia	General anesthesia
<45	OVERMEDICATED

Table 1. BIS values and hypnotic sedation/anesthesia levels.

Anesthesiologists process information most consistently on the horizontal sweep as displayed in the EKG and SpO₂ trends. EMG is displayed on the original factory default, but only as a vertical column. Contained in the software of every free-standing BIS unit is the option to select EMG and save it to trend below the BIS trend on a horizontal sweep display. As of 2017, the factory default setting now displays both BIS and EMG trends. However, the lower EMG trend as pictured by the recent company literature is without important EMG spikes.

There are two vertical numerical scales on either side of the BIS monitor display (**Figure 5**). The left side scale (yellow) for the BIS is from 0 to 100. The right side scale (red) is from 30 to

Propofol titrated to $60 < \text{BIS} < 75$ with baseline EMG indicated an asleep, amnestic patient.

A blanchd surgical field does not equal adequate local analgesia.

Surgery below the clavicles with patient movement without EMG activity indicates more local analgesia in the immediate area of stimulation.

Table 2. The surgeon’s golden rules for success with brain monitored propofol ketamine.

100 for the EMG. Spikes in EMG signify incipient patient arousal demanding an increase in propofol (or inhalational agent) sufficient to return the EMG to baseline (i.e. 0 on the top BIS scale and 30 on the bottom EMG scale). (**Figure 6**).

In the pre-BIS era, anesthesiologists considered the absence of HR and BP changes with skin incision to define adequate depth of anesthesia. Nondissociative attempts at preemptive anesthesia have met with variable successes. Postoperative pain management continues to be an issue. HR and BP primarily reflect brain stem changes, while pain and consciousness are processed at higher cortical levels. Twenty-first century standard of care anesthesia monitoring demands cortical monitoring as a standard of care. It is an untenable assertion that 16 million of the 40 million (40%) American patients every year emerge from anesthesia with “brain fog” caused by a previously undiagnosed, underlying condition. Without numerically measuring the depth of sedation/anesthesia, discovering the role of routine overmedication in postoperative “brain fog” will be problematic [3].



Figure 5. BIS VISTA monitor.

Once sedated, the brain cannot differentiate the signal from a well-intentioned surgeon's scalpel (or trocar) and the malevolent intentions of a mugger's knife. Success with preemptive analgesia makes it imperative to prevent the brain from receiving the noxious input from the violation of the integument's barrier to the outside world of danger. Although other pain receptors exist within the body, the most significant information to prevent the wind-up phenomenon and postoperative pain is that of skin incision.

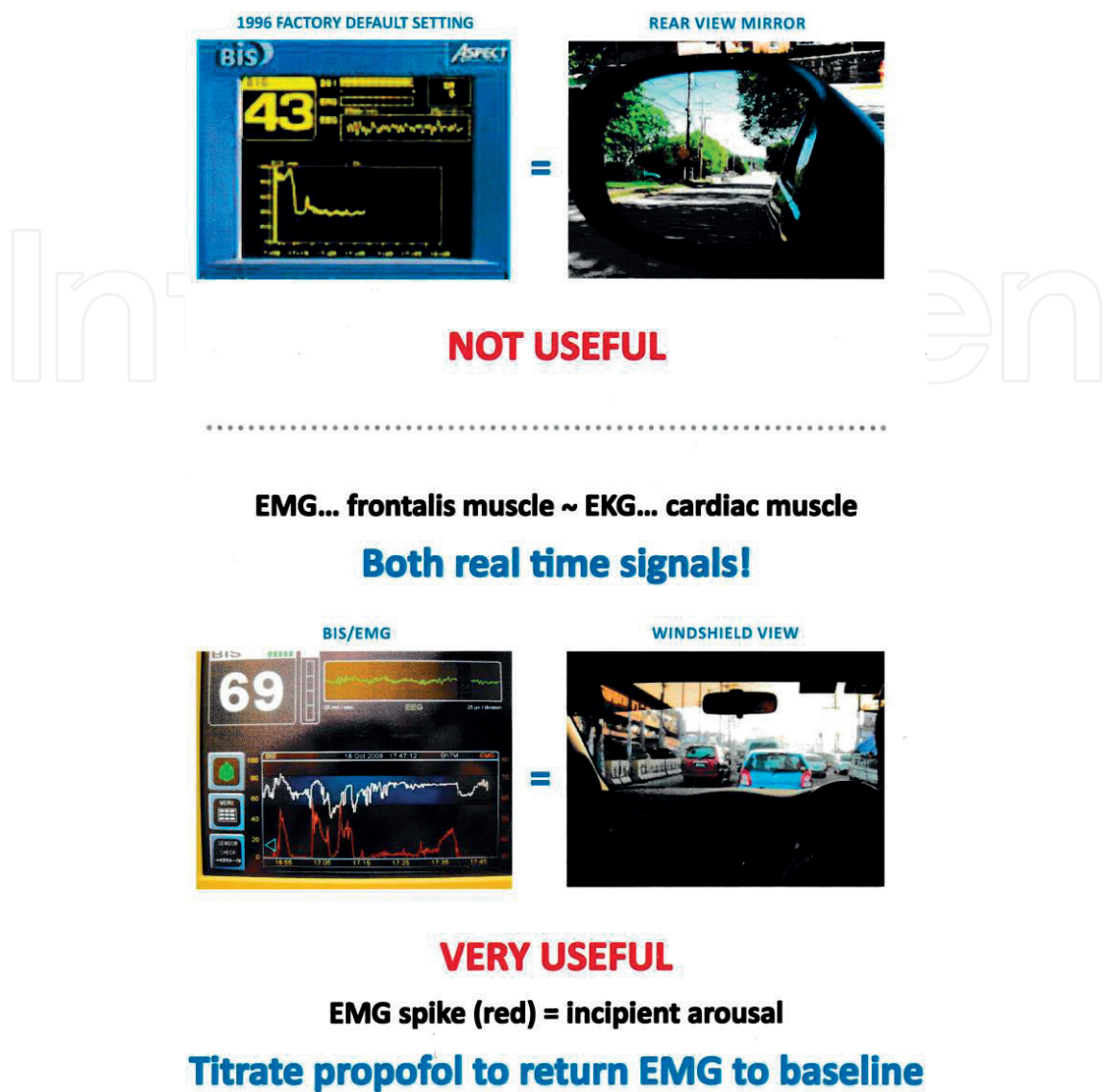
The N-methyl, D-aspartate (NMDA) receptors in the midbrain are the final gatekeepers of noxious input to the cortex. Ketamine is a major NMDA antagonist (propofol has substantially less NMDA antagonism than ketamine). When the initial local anesthetic injection is performed (common to virtually all elective cosmetic surgeries), the **absence of an EMG spike** with multiple local anesthetic injections defines midbrain NMDA receptor saturation and creates nonopioid, preemptive analgesia.

Absent the ability to differentiate cortical- from spinal cord-originating movement during sedation forced anesthesiologists to treat every patient movement "as if" the patient might be awake and recall his or her surgery. All patient movement does not have the same significance. Like GA, "Goldilocks" anesthesia requires patients to be retrained on the operating table. Patient movement per se can be generated without cortical input, i.e. from spinal cord reflexes. A headless chicken still generates movement.

No spinal cord pathways exist to activate the facial *frontalis* muscle. During the case, patient movement without an EMG spike is an indication for additional local anesthesia in the immediate area of surgical stimulation. Only after two attempts of reinjection after the initial injection (three total injections) fails to eliminate patient movement should additional ketamine be given. Conversely, if patient movement is accompanied by an EMG spike, both additional local anesthesia **and** additional propofol should be administered. Additional local anesthetics should cause the patient movement to cease in the overwhelming majority of cases. Additional propofol must be administered in sufficient amounts to **return the EMG to baseline** to maintain the patient unconscious and amnesic.

It is not the absolute value (or spike) of any individual BIS reading that may determine recall. Rather, it is the area under the trend curve. Three to five minutes of a BIS >80 will more likely produce recall than less area under the curve. Restraint from the surgeon or operating room staff making loud, negative comments with patient movement deprives the unconscious patient subliminal input with which to process memories. One cannot control the emotional maturity of the personnel in the operating room. Many times, demonstrating to both the surgeon and his staff of an objective numerical measure of the patient's level of consciousness (i.e. BIS < 75 with baseline EMG) can calm otherwise overanxious personalities and preserve a peaceful operating room.

The use of EMG spike activity enables the differentiation between cortically generated patient movement and that originating from the spinal cord. Conducting a cosmetic surgery case in this fashion assures the patient receives critical adequate local anesthesia for the case and sets the stage for minimal postoperative pain management.



(over)

Figure 6. Why BIS is not commonly utilized.

Over the past two decades of experience in >4000 patients, the infrequent postoperative discomfort was readily managed with intravenous (IV) ketorolac 30–60 mg and/or oral acetaminophen 1000 mg. Rapid propofol emergence allowed patients who did request additional analgesia to safely swallow oral acetaminophen without aspiration risk. Higher acetaminophen blood levels are unquestionably achieved with the IV versus the oral preparation. However, since adequate pain relief was observed with the oral form, cost considerations precluded the use of IV acetaminophen. Very few patients required IV fentanyl (25–100 mcg) for pain management. The author's experience was entirely in the office-based setting. There were no postoperative hospitalizations for postoperative pain management during the period 1992–2017 in >6000 patients.

Prior to BIS/EMG monitoring, treating all movement left many patients overmedicated and unable to quickly emerge from anesthesia to go home or to a recovery center. Patient movement during sedation was generally regarded by the surgeon that the patient was “too light” and needed more sedation. Anesthesiologists often responded to the surgeon’s demand with “needs more local.” A circular argument ensued, physicians’ feelings got bruised, but more importantly, the patient was ill-served, overmedicated, and often, with postoperative pain management issues.

The net effect of pre-BIS/EMG sedation attempts resulted in many surgeons encouraging (or even demanding) the abandonment of sedation in preference to GA with neuromuscular blocking agents. GA exposes the elective cosmetic surgery patient to the unnecessary risks of difficult intubation, failed intubation, misplaced endotracheal tube (ET), esophageal or endobronchial intubation, kinked or occluded ET, teeth damage, anesthesia machine mishaps (i.e. empty vaporizer, vaporizer filling error, reversed oxygen and nitrous oxide gases) and, very rarely, malignant hyperthermia (MH). No endotracheal intubations were required in the author’s 25-year experience.

The advent of the use of the laryngeal mask airway (LMA) has greatly reduced or eliminated many ET issues. This author routinely places an armored (or flexible) LMA for rhinoplasty cases both to cover the glottic chink and using the inflatable cuff to prevent blood from entering the esophagus. For nonrhinoplasty cases, airway management is dependent upon patient response (**Table 3**).

The very small MH risk necessitates any GA facility stocking dantrolene, an expensive agent with a 3-year shelf life. Delays in treating MH are prompt recognition due to its rare occurrence and partly due to the difficulty of dissolving the treatment into solution to administer. A newer formulation of dantrolene (i.e. Ryanodex®) is easier to dissolve into solution for administration but may not be widely found.

Neither propofol nor ketamine is a triggering agent for MH. The early diagnosis of MH is most often made by unexplained tachycardia. Tachycardia is frequently observed following the injection of epinephrine containing local anesthesia at the beginning of the case. When the injection is temporally associated with the dissociative ketamine dose, some are more apt to believe the ketamine, not the epinephrine, was the source of the tachycardia. Often, in the performance of “Goldilocks” anesthesia, incremental propofol induction followed the ketamine, but the surgeon did not inject the local analgesia by as long as 10 minutes after the

Chin extended, head rotated to the side (initially to the right but sometimes better airway results turning to the left).

IV bag (not heated) under the shoulders (not the neck), increasing the force of extension on the genioglossus muscle.

#28 Fr latex (or latex free) lubricated nasal airway, often better tolerated than oral airways.

#4 LMA.

N.B. 50–60% of brain monitored PK cases/25 years have been performed without airway instrumentation. No endotracheal intubations required in 25 years, >6000 patients.

Table 3. Airway management flow chart (assumes incremental propofol induction).

ketamine administration. No tachycardia or hypertension was observed when ketamine was administered well prior to the lidocaine with epinephrine solution injection. Nontriggering “Goldilocks” anesthesia also means surgical facilities need not stock dantrolene.

3. Propofol

Propofol is a 1,4-diisopropyl quinol with sedative-hypnotic properties. Because of its slight solubility in water, the drug is formulated as an emulsion for clinical use. It is highly lipophilic and distributes extensively in the body. The drug was introduced to the North American market in 1989 and has largely displaced both thiopental and methohexital for induction of general anesthesia and maintenance of sedation.

Propofol’s rapid metabolism accounts for its short activity. It is also a potent antiemetic, especially in the absence of concomitant opioid administration. Only after much experience with the drug for sedation was the patients’ clear head and happy affect after emergence was this quality appreciated by the author. Unfortunately, these qualities have also made propofol a drug of abuse within small numbers of the profession (“white rabbit”) as well as by celebrities like Michael Jackson.

Propofol also results in inhibition of the N-methyl, D-aspartate (NMDA) subtype of glutamate receptor [4]. Lack of recall was observed in 95% of patients at BIS of 77 [5]. Propofol at 25–50 mcg/kg/min was sufficient to produce sedation to $60 < \text{BIS} < 75$ with baseline EMG for many patients. However, as little as 2.5 mcg/kg/min and as much as 200 mcg/kg/min have been required to achieve the same numerically defined level of sedation at $60 < \text{BIS} < 75$ with baseline EMG. This 20-year experience represents nearly a hundred-fold variation in propofol requirements. Incrementally inducing patients starting with 50 mcg/kg propofol miniboluses (*Watch YouTube Propofol induction with BIS monitor without instrumenting airway*) allows the anesthesiologist to identify outliers early in the case and enables all patients to receive “not too much, too little, but just the right amount” and not to hear, feel or remember their surgery. The expression “not too much, too little, but just the right amount” is the basis for using the shorthand expression “Goldilocks” anesthesia. Those unfamiliar with the Goldilocks story should watch YouTube Goldilocks and the Three Bears—Fairy Tales.

Textbook doses for propofol sedation do not discuss the value of incremental induction not only to identify outliers but also to dramatically minimize airway management and eliminate precipitous blood pressure drops. Incremental propofol induction more often maintains the airway patency by preserving muscle tone of the *temporalis*, *masseter*, *genioglossus* and *orbicularis oris*.

Propofol was introduced to North America in 1989 and quickly replaced both thiopental and methohexital as the preferred induction agent. As a proprietary agent, a 20 cc propofol bottle retailed around \$12–15 USD, making a continuous infusion for surgery apparently prohibitive for multihour surgeries in a cost-conscious office-based cosmetic surgery suite.

After five years of performing propofol ketamine (PK) intravenous sedation using an average three 20 cc bottles of propofol per hour, the author’s surgeons kept clamoring for a less expensive

way to administer it, especially for 4–6 hours rhytidectomies with or without browlifts, platysmal plications or blepharoplasties. Five years of data on 1264 patients demonstrated no reduction in propofol requirements with either 2 or 4 mg preoperative midazolam as administered [6].

This same paper [6] also published the lowest postoperative nausea and vomiting (PONV) rate (0.6%) in the literature without antiemetic use in an Apfel-defined high-risk patient population, i.e. nonsmoking females with positive PONV and/or motion sickness histories, having emetogenic (cosmetic) surgery. Scrupulous opioid avoidance both during and after surgery has allowed this astounding PONV rate to go unchallenged to date.

Aspect Medical Systems (Aspect Medical Systems, a venture capital company, was purchased by Medtronic that has subsequently been acquired by Covidien) exhibited their bispectral index monitor™ (BIS) for measuring cortical effect at the 1997 International Anesthesia Research Society (IARS) annual meeting in San Francisco. The author was exhibiting his Society for Office Anesthesiologists (SOFA) at the same meeting and was initially exposed to the BIS monitor there. The BIS monitor appeared to offer more promise reducing propofol requirements than previous efforts with midazolam premedication [6]. Later work validated that promise [7, 8]. Entropy™ is another depth of anesthesia monitor but has not been validated in nearly as many clinical papers as BIS [9].

4. Ketamine

In the 1950s, postoperative pain was treated with morphine or meperidine, often undertreated for two reasons: (a) fear of producing opioid addiction and (b) problems of overtreatment, respiratory insufficiency or apnea and death. Naloxone was not introduced until 1971 and pulse oximetry became commercially available in 1983.

The researchers of the day postulated that, if another class of drugs could be developed that would ameliorate pain without respiratory depression, patients could be better treated for postoperative pain with neither under- nor overtreatment.

The first class of drugs explored was the phencyclidines. The parent compound, phencyclidine phosphate, was marketed as Serenyl® by Parke-Davis in 1958 but was quickly withdrawn from the market because of the high percentage of undesirable side effects, i.e. hallucinations, mania, delirium and disorientation. Later, phencyclidine phosphate, as a drug of abuse, became better known by the initials, PCP or “angel dust.”

The researchers did not give up quickly on the phencyclidine class. They began experimenting with a modified PCP molecule, ketamine, which received FDA approval in humans in 1971. The drug, like its predecessor, was introduced as the “silver bullet,” a complete, total intravenous agent, meaning no other agents were needed. Because it supported both respiration and blood pressure, ketamine quickly gained a reputation as a safe drug but one not good for adult patients. It did become popular in children’s burn units, especially for the extremely painful dressing changes.

During the author's anesthesia residency at Stanford 1975–1977, he was introduced to administering ketamine in small doses (10–20 mg IV) prior to positioning elderly patients about to receive spinal anesthesia for surgery on femoral head or shaft fractures. Elderly patients were not particularly susceptible to ketamine-associated hallucinations or dysphorias. Veterinarians also adopted ketamine, quickly realizing that it was nearly impossible to kill an animal, even if the per body weight dose was more than twice the recommended amount. Also, the animals did not complain about hallucinations. While ketamine was a safe drug, two generations of human anesthesiologists have avoided its use in adult day surgery. Sometime during the mid-1970s, a Las Vegas plastic surgeon, Charles Vinnik, wearied listening to his patients cry out when he injected local anesthesia under his self-directed diazepam and meperidine IV sedation. Even though the patients had amnesia for the experience, the patients' cries were distressing to the OR staff. Vinnik asked his anesthesiologist if there was anything else he could use that would eliminate the distressing reactivity of the patients. Ketamine was suggested. Ketamine was first synthesized by Stevens in 1962 and first used in humans by Domino and Corssen in 1965. The drug was used in clinical practice barely 5 years when its use was suggested to Vinnik.

Through trial and error, Vinnik came upon his initial ketamine dose of 75 mg independent of body weight to prevent the patients from either moving or crying out after they were rendered sleepy from incremental doses of intravenous diazepam. Vinnik began with his test dose of 10 mg diazepam administered through an external jugular (to avoid venous thrombosis), followed by 5–10 mg increments to a total of 25–50 mg. Vinnik had his patients engage a 24-hour nurse to observe them after discharge to home. His cost-effective concept meant the cost of the recovery nurse did not come from him.

Although Vinnik published his diazepam-ketamine technique (i.e. **hypnosis first, then dissociation**) without the reported hallucinations or dysphorias, the 1981 paper appeared in the plastic surgery literature [10]. Vinnik's approach lay largely unnoticed in the anesthesia community until the author heard him speak in Newport Beach, CA, in December 1991, later visiting his office operating room in March 1992.

The author considered Vinnik's use of ketamine useful but doubted diazepam would be an optimal drug for day cases expected to return to home. Propofol was then considered as an alternative to diazepam for hallucination-blocking purpose. Searching the anesthesia literature to support this use of propofol turned up no useful information. March 26, 1992 was the beginning of this author's clinical trial of propofol followed by ketamine [11]. In the 1990s, ketamine became a drug of abuse, a "rave" drug and later lumped together with flunitrazepam and gamma hydroxybutyrate (GHB) as "date rape" drugs. Ketamine is also a drug of abuse. Heavy users can develop long-term bladder or urinary tract damage and incontinence.

Anesthesia trainees continue to be taught ketamine causes tachycardia, hypertension and hallucinations despite the knowledge that benzodiazepines [12] or propofol hypnosis blocks ketamine hallucinations [13]. In the pre-BIS era, loss of lid reflex and loss of verbal response defined adequate hallucination-blocking depth of propofol hypnosis. With real-time BIS/EMG monitoring, the level of hallucination-blocking propofol hypnosis is more numerically defined as $60 < \text{BIS} < 75$ with baseline EMG. Some believe the use of ketamine defeats the

ability of the BIS monitor to accurately measure propofol. This study compared ketamine doses of 0.2–0.5 mcg/kg and concluded 0.5 mcg/kg would defeat the BIS [14]. An earlier publication using **50 mg ketamine, independent of body weight**, confirmed BIS' utility [15].

More controversial is the author's use of **50 mg ketamine independent of body weight**. Brain weight does not vary with body weight (i.e. the brain weight of a 100-kg male is not twice that of a 50-kg female). The midbrain is a very small portion of the total brain weight. The NMDA receptors are a small part of the very small midbrain. After observing the same immobility (or dissociative effect) in 100-kg males as in 50-kg females, body weight was not deemed a consideration for effective ketamine dose. With the addition of BIS/EMG monitoring, absence of EMG spike is considered numerically reproducible evidence of NMDA saturation and nonopioid, preemptive analgesia.

In many third world countries, ketamine infusions are still to be found as the drug was originally marketed. However, as propofol has become generic and very inexpensive, more anesthesia providers from third world countries have accessed the author's web site to obtain information with which to execute the PK paradigm.

Ketamine, ironically, is the perfect adjuvant drug (or the 'olive' in the propofol 'martini') not the complete and total intravenous agent its makers originally intended it to be, at least in the western world.

Brain monitored PK IV sedation is less expensive, safer and simpler and gives better outcomes (i.e. virtually no PONV [16] and minimal postoperative pain). With ability to stratify anesthesia outcomes by depth of anesthesia and the negative effects of routine anesthesia overmedication (i.e. BIS <45), studies have demonstrated more apparent negative effects from this practice [17–20]. Postoperative cognitive dysfunction (POCD) is the name for the pseudo-Alzheimer's type of confusion seen more often in elderly, rhytidectomy patients. Sometimes this lasts hours, days, weeks or months. Sometimes the effects are not transitory. Rapid emergence does not preclude intraoperative overmedication. Patients are left with the long-term consequences of their anesthesiologist's short-term care.

The brain monitored PK IV sedation technique also gives providers the ability to refrain from the nefarious practice of routinely overmedicating patients for fear of undermedicating them.

5. Putting brain monitored propofol ketamine ("Goldilocks") anesthesia into practice

Teaching the technique is simple. Teaching cooperation is not.

Daniel HS Lin, DO, Cosmetic surgeon

Along with the patient, many egos enter the operating room, not the least of which is that of the surgeon's. The surgeon's cooperation with local anesthesia is essential for success. The surgeon must also understand the need for *adequate* local anesthesia. **Surgeon perfection injecting local analgesia is not a requirement, only persistence.** Surgeons typically

equate a blanched surgical field with adequate analgesia. Only with brain monitoring can the anesthesiologist hope to convince the surgeon that a blanched field only equals adequate vasoconstriction.

Prompt essentially PONV free and minimal pain recovery are the hallmarks of “Goldilocks” anesthesia. Once the surgeon observes how much better his patients do postoperatively, the need for his/her cooperation should become apparent. The office-based setting has a higher incentive for surgeon cooperation. Recovery space is limited and personnel are often multi-tasked compared with free-standing or hospital-attached day surgery center facilities. As superior and **numerically reproducible** as the “Goldilocks” anesthesia outcomes are, there are still surgeons reluctant to cooperate. Just as disappointing is the numbers of anesthesiologists who remain shackled to the outdated teachings that ketamine causes hallucinations, hypertension and tachycardia or are unwilling to reconsider using real-time BIS/EMG to titrate propofol.

The clinical pathway for brain monitored propofol ketamine (“Goldilocks”) anesthesia is a simple straightforward three-drug technique: glycopyrrolate, propofol and ketamine. Induce hypnosis first, next dissociate, then inject local analgesia (**Table 4**). (Atropine may be substituted when glycopyrrolate is unavailable. Tachycardia will more commonly result than administering glycopyrrolate). Unexplained tachycardia, not temperature elevation, is the cardinal recognition sign for MH. Once the brain is protected with propofol incrementally titrated to loss of lid reflex/loss of verbal response or $60 < \text{BIS} < 75$ with baseline EMG, the 50mg ketaamine by itself does not cause tachycardia or hypertension!

Prior to placing the BIS sensor on the forehead, the patient is advised **the number from their forehead allows them to “control” their anesthetic dose**. This control means that neither too much nor too little can be given. Then the patient is encouraged to touch the sensor pad to assure them their skin cannot be scarred even though the sensor application will be a little uncomfortable. A small discomfort for a great relief about anesthetic dosing is greatly appreciated by patients. Patients are additionally advised that 5% or one in 20 may have pleasant, colorful dreams.

The preoperative consultation includes disclosure of the dry mouth and the need to maintain eye lubrication with ointment. Patients are told to expect blurry vision upon awakening and

Glycopyrrolate 0.2 mg with 30 mg lidocaine IV
Propofol 50–100 mcg/kg ⁻¹ minibolus repeated to $60 < \text{BIS} < 75$ with baseline EMG
Propofol infusion rate start 25 mcg/kg ⁻¹ /min ⁻¹
Adjust infusion rate as needed to maintain $60 < \text{BIS} < 75$ with baseline EMG
Ketamine 50 mg IV 3 minutes prior to local analgesia injection
Lidocaine 1 mg/lb ⁻¹ or 2 mg/kg ⁻¹ IV STAT for laryngospasm
Labetalol 10 mg iv for HR > 100–110. Avoid if patient asthmatic

Table 4. Clinical pathway.

that it is resolved when the ointment is wiped from their eyes. One patient in the author's 40-year career became panic-stricken upon emergence thinking something bad had happened to her eyes. Full disclosure to avoid repetition of this unfortunate patient's experience is strongly recommended.

Ketamine increases salivation. Glycopyrrolate causes less tachycardia and, for that reason, is chosen as an antisialagogue in preference to atropine. Because propofol can sometimes cause patient discomfort, lidocaine is added to the glycopyrrolate. The patient is advised to tell the anesthesiologist if there is additional aching during induction so that more lidocaine can be administered. Propofol ache is more common with distally placed IV.

Between 1992 and 1997, a 50-ml IV bag with 400 mg (40 ml) propofol was connected to a 60 drops/ml IV set (mini-drip, pedi-drip, micro-drip). The initial rate was set to the patient's heart rate and adjusted until **loss of lid reflex** and **loss of verbal response** were observed. This was a **qualitative** approach that was far more subjective and less reproducible. After the demand for the propofol numbers for publication, the author began using an infusion pump. A completely programmable, albeit more expensive, infusion pump is better than less expensive, commonly found pumps that only permit settings of 25, 50, 75 or 100 mcg/kg/min. The ability to deliver a separate bolus in addition to maintaining an infusion rate is also important. This **quantitative** approach along with BIS/EMG monitoring makes "Goldilocks" anesthesia numerically reproducible.

Set the pump to deliver propofol for 50 mcg/kg minibolus. Induce with miniboluses given in *one after another* until a decrease in the real-time frontalis muscle electromyogram (EMG) is observed (see YouTube Going under with Goldilocks anesthesia). The BIS value and trend line will display behind the EMG as it is based on algorithm-derived information that is delayed from real time by 15–30 s.

The induction goal is to observe whether or not 25 mcg/kg/min basal infusion rate is sufficient to maintain $60 < \text{BIS} < 75$ with baseline EMG. Bolus with 50–100 mcg/kg to maintain $\text{BIS} < 75$ and upwardly adjust the basal propofol rate to 35–50 mcg/kg/min to maintain that level PRIOR to administering ketamine. Most patients have been maintained at $60 < \text{BIS} < 75$ with baseline EMG with propofol 25–50 mcg/kg/min. However, as little as 2.5 mcg/kg/min and as much as 200 mcg/kg/min propofol have also been observed by the author in his 20-year, >4000 patient clinical experience.

Avoid the textbook advice of 1–2 mg/kg propofol bolus for induction. A bolus will produce peak propofol levels in the brain quickly and just as quickly begin to redistribute, decreasing a protective level just as the ketamine arrives to the brain. The brain may then not be protected from ketamine side effects when that drug is administered. The value of the brain monitored, incremental induction is providing a **numerically reproducible, stable propofol brain level to prevent negative ketamine side effects** [13]. The very sensitive as well as the very resistant patient can be identified from the outset of the case rather than trying to understand a body weight–derived dose effect. Lastly, the incremental propofol induction preserves baseline blood pressure as well as the muscles that maintain a patent airway, *i.e. the temporalis, masseter, orbicularis and genioglossus*. Nevertheless, one must always be prepared with available bag mask ventilation and suction for the exceptional patient, no matter how often it will be unnecessary.

Only after the patient's propofol level has stabilized should the 50 mg ketamine, **independent of body weight**, be given, **3 minutes prior** to local analgesia injection. Any patient movement accompanied with an EMG spike during injection must be given more propofol to drive the EMG spike back to the baseline. As little as repeated 100 mcg/kg propofol boluses or as much as 200–400 mcg/kg propofol boluses may be required. An upward basal rate should be considered to maintain the patient's propofol level at $60 < \text{BIS} < 75$ *with* baseline EMG.

The surgeon should inject as much of the proposed surgical field(s) with the initial ketamine dose whenever possible. Review of 1000 patient records demonstrated 80% were performed with one or two 50 mg ketamine doses. **Aggregate ketamine doses greater than 200 mg were associated with prolonged emergence.** Many surgeons are concerned that the lidocaine or epinephrine effect will not last if a lengthy procedure is contemplated. Long experience with Klein's ultradilute solution [21] has shown that concern is unwarranted even in 6-hour cases. Ketamine is to facilitate a painless injection of '**virgin**' surgical fields and is not necessary for reinjections when needed.

6. Laryngospasm

The traditional crowing sound of incompletely closed vocal cords is rarely seen with "Goldilocks" anesthesia. The type of laryngospasm is characterized by complete vocal cord closure. The only prodrome is a cough or a sneeze. The **traditional remedies** of anterior jaw thrust and positive pressure ventilation are **ineffective** in dealing with ketamine-associated laryngospasm. The author has consistently been successful treating this type of laryngospasm with IV lidocaine 1 mg/lb or 2 mg/kg given STAT whenever a cough or sneeze is observed.

Spontaneous ventilation preservation is a hallmark of successful "Goldilocks" anesthesia. The use of succinylcholine (SCh) will produce a patient with very painful postoperative muscle pains. SCh is not recommended as it is an MH trigger as opposed to nontriggering propofol or ketamine. Nondepolarizing rocuronium in small doses is a possibility but also defeats the value of spontaneous ventilation even with its short duration of action. Propofol elevates the lidocaine seizure threshold. The author has not observed lidocaine-induced seizures when treating laryngospasm with IV lidocaine. However, in *extremely* rare cases, severe bradycardia, even asystole, may be seen with multiple IV lidocaine injections. Preemptive lidocaine should be considered optional. Consider deepening propofol level after 2–3 lidocaine doses are required to break the laryngospasm.

7. Pitfalls to avoid

Anytime the words propofol and ketamine are used, readers too often think ketofol, the admixture of the two agents in the same syringe [22]. There are many permutations of the ideal ratio of propofol to ketamine. Mixing the two agents makes it very difficult, if not impossible, to differentiate when adequate hypnosis occurs as well as when midbrain NMDA receptor

saturation occurs. “Goldilocks” anesthesia provides numerically reproducible propofol levels to define adequate hypnosis as well as the absence of EMG spikes with local anesthesia injection to define midbrain NMDA receptor saturation (**Table 5**).

Propofol ketamine is like the martini cocktail wherein the propofol is the ‘vodka’ and the ketamine is the ‘olive.’ Ketofol is when the propofol is mixed with the ketamine. These are two very different approaches that should never be confused with one another. **Do not mix propofol with ketamine.**

Propofol hypnosis is protective of ketamine hallucinations [13]. **Do not give ketamine before propofol hypnosis.** Bolus propofol induction will not provide a stable CNS propofol level to protect against ketamine hallucinations. Do not induce with 1–2 mg/kg propofol boluses.

Propofol at BIS < 75 with baseline EMG is a numerically reproducible protection against ketamine hallucinations. **Do not give ketamine if BIS > 75 or EMG is not at baseline.**

Adequate local analgesia is critical to minimizing or eliminating the need for postoperative opioid pain rescue. Do not fail to have the surgeon reinject the immediate area of dissection when patient movement occurs *without* EMG spike and BIS < 75. More propofol or ketamine is an inadequate response for patient movement at BIS < 75 with baseline EMG. Adding opioids instead of more local analgesia is not only inadequate to correctly deal with insufficient local analgesia but also increases the probability of PONV.

Aggregate ketamine doses >200 mg is associated with prolonged emergence. **Do not exceed 200 mg ketamine or give ketamine in the last 20 minutes** of the case or use ketamine in cases less than 20 minutes. Spontaneous ventilation is a prized safety feature of “Goldilocks” anesthesia. **Do not introduce an MH trigger like SCH to treat laryngospasm.** Because of the

Do not mix propofol and ketamine. Titrate separately to define goals of adequate hypnosis and midbrain NMDA saturation.

Do not give ketamine before propofol.

Do not bolus propofol for induction. Incrementally induce.

Do not give ketamine at BIS > 75.

Do not fail to provide adequate local analgesia.

Do not give opioids in lieu of adequate local analgesia.

Do not give ketamine in lieu of adequate local analgesia.

Do not exceed an aggregate ketamine dose >200 mg.

Do not give ketamine in the last 20 minutes of a case or for cases <20 minutes duration.

Do not paralyze instead of using lidocaine to break laryngospasm.

Do not use succinylcholine instead of lidocaine to treat laryngospasm.

Table 5. Pitfalls to avoid.

subsequent need to support ventilation, rocuronium is not preferred over IV lidocaine even though postoperative muscle pain will not result from its use.

8. Conclusion

While many anesthesiologists have observed “Goldilocks” anesthesia administered for classical abdominoplasty, cognitive dissonance often prevents believing what they have witnessed. It is not unusual for anesthesiologists to observe patients recover in a manner totally unlike that of GA or neuraxial block for them to believe that what they formerly believed was a major invasive surgery performed with a minimally invasive anesthetic approach.

When the surgeon is properly prepared for his role giving adequate local analgesia, the stage is set for outstanding, reproducible anesthesia outcomes for elective cosmetic surgery. The anesthesiologist needs to understand the real-time value of BIS/EMG monitoring and use it for the benefit of the conduct of the case. It may also be necessary to overcome outdated, unproductive teaching about negative ketamine side effects.

Cosmetic surgery patients endeavor to improve their level of happiness by altering their body image. Propofol is a happy affect drug that nicely complements the mental recovery of these patients.

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