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REVIEW SPECIAL TOPICS

BIS Monitoring Transformed Opioid-Free Propofol Ketamine Anesthesia From Art to Science for Ambulatory Cosmetic Surgery

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Abstract Measurement is the essence of science. The BIS™ brain monitor provides direct propofol response measurement. Measuring transformed the propofol ketamine technique from a qualitative approach to a quantitatively reproducible one. Propofol was originally titrated with an IV bag and a micro-drip IV set. Propofol response was titrated to clinical signs. An infusion pump later replaced the IV bag, enabling the propofol *dose* enumeration. The propofol *effect* was measured with a BIS.™ A statistically significant 30% propofol reduction was achieved with BIS™ monitoring. Patient movement occurred during propofol sedation. Secondary EMG trending to BIS™ enabled the differentiation of cortically based movement (i.e., deeper sedation indicated) from spinal cord-based movement (i.e., more local indicated). Outcomes were improved when surgeons re-injected vasoconstricted field with patient movement.

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Introduction

Ambulatory cosmetic surgery patients are expected to be discharged to home following their surgery. The problems facing their anesthesiologists and surgeons are (1) delayed emergence, (2) pain, and (3) postoperative nausea and vomiting (PONV). These problems are causes for unintended hospital admission after day surgery. Ambulatory discharge is predicated on discharge-ready emergence in about an hour after surgery. When patients take longer to emerge, discharge is delayed, resulting in increased nursing hours and decreased cost-effectiveness. Discharge delays secondary to patients' rides are a different issue but not in the purview of the anesthesiologist.

A patient's brain cannot respond to information it does not receive. Failure to saturate *N*-methyl-D-aspartate (NMDA) receptors *prior* to local anesthetic (LA) injection is a major cause of postoperative pain [1]. From March 26, 1992, to December 26, 1998, after a *qualitative*, incremental propofol induction, a 50 mg IV ketamine dose was given 2–5′ before the surgeon's LA. The 2–5′ delay allows the ketamine to saturate the NMDA receptors. The saturation provides 10–20′ immobility for LA injections. After the initial LA injections, patient movement *during* the case was challenging. The 'too light' versus 'more local' discussion resulted in more IV drugs, instead of more local, being given to the patient. Discharge delays resulted.

Glycopyrrolate 0.2 mg IV was given prior to induction to eliminate laryngospasm potential by minimizing oropharyngeal secretions. The propofol initial drip rate was set to approximate the patient's baseline heart rate and then adjusted based on response. Patient variation in propofol sensitivity made it difficult to enumerate the effective dose that was administered. Variable propofol drip rates with the technique made it artful but challenging to reproduce.

Propofol sedation was defined by the clinical signs of loss of lid reflex and loss of verbal response. Propofol sedation blocks ketamine hallucinations [2]. The degree of airway intervention was dictated by patient response. The incremental propofol induction preserved the muscles responsible for maintaining a patent airway, i.e., *genioglossus, orbicularis oris, temporalis masseter.* Spontaneous ventilation was preserved by avoiding an initial propofol bolus. Approximately 30% of the patients required only the rhytidectomy position to keep a patent airway. With the chin extended and head rotated laterally, two vectors of *temporalis masseter* were exerted on the *genioglossus* kept the tongue off the back of the throat. In another 30% of patients, the rhytidectomy position proved inadequate. To open the airway, an IV bag was placed under the patients' shoulders. The IV bag added additional force to the *genioglossus* muscle. If neither of the first two airway maneuvers were adequate to keep the airway open, a nasal airway was used for another 30% of patients. Less than 10% of patients required laryngeal mask airway (LMA) to support their airway. No patients required bag and mask ventilation or endotracheal intubation. More than half the patients required no airway instrumentation, an advantage for avoiding postoperative sore throat complaints.

Typical induction times were between 2 and 3.' Propofol was deliberately titrated to produce an SpO_2 92–95% *with* spontaneous ventilation on room air. The oxygen concentration in room air is insufficient to support combustion during facial electrocautery [3]. Respiratory depression to this SpO_2 level was thought to prevent ketamine hallucinations. None were reported. Oxygen was available but rarely needed. Continuous EKG and NIABP were also monitored. Suction, Ambu® bags, crash carts and defibrillators were available. Only suction for persistent oropharyngeal secretions was used.

Without anti-emetics, the *opioid-free,* propofol-then-ketamine-then-LA paradigm achieved the lowest published PONV rate (0.6%) in an Apfel-defined high-risk patient population (i.e., non-smoking, female, PONV/motion sickness history, emetogenic cosmetic surgery) [4]. A 50 mg ketamine dose produced immobility (i.e., dissociative effect) for approximately 10–20′ in patients between 35 and 145 kg. Opioid postoperative rescue was also absent.

A brain is not required to produce movement. A headless chicken still moves. *Non-purposeful* movement was generated in the spinal cord, not the brain. Prior to BIS™ brain monitoring, all propofol sedation movement was treated *as if* patient awareness was a possible cause. Surgeons regard any non-purposeful patient movement during sedation as 'too light.' Based on the surgeons' belief that vasoconstriction equals *adequate* analgesia, the request for 'deeper' anesthesia was made when patients moved. When 'deeper' anesthesia was requested, this author responded with 'more local.' Prior to BIS™ monitoring, the author was unable to persuade the surgeons; the non-purposeful movement was generated from the spinal cord, *not* the brain. The author was unable to convince the surgeons to re-inject vasoconstricted fields in the immediate area of dissection. Adding additional drugs (i.e., more propofol or ketamine) failed to accurately address the issue of inadequate analgesia. Prolonged emergence and discharge followed.

"If you cannot measure it, you cannot improve it." Lord Kelvin's temperature quote also provides the rationale for direct brain measurement of propofol response. Measuring prevents too much or too little propofol. On December 26, 1998, bispectral (BIS™) index monitoring was added to the technique along with *real-time* electromyogram (EMG) secondary trending (Fig. 1). Induction began with a baseline rate of 25 mcg kg^{-1} min^{-1} propofol with successive 50 mcg kg^{-1} propofol boluses (i.e., shorturl.at/bsFP9 s). Induction times remained between 2 and 3 min. Propofol hypnosis was defined by BIS < 75 *with* baseline EMG. After induction, a 50 mg IV ketamine dose was administered followed by a 2–5′ wait, and *then*, subcutaneous LA was injected by the surgeon.

The BIS™ values are delayed from real time by 15–30 s. Relying on BIS™ numbers alone for propofol titration is akin to driving an automobile with rearview mirror information alone. BIS™ values alone are not

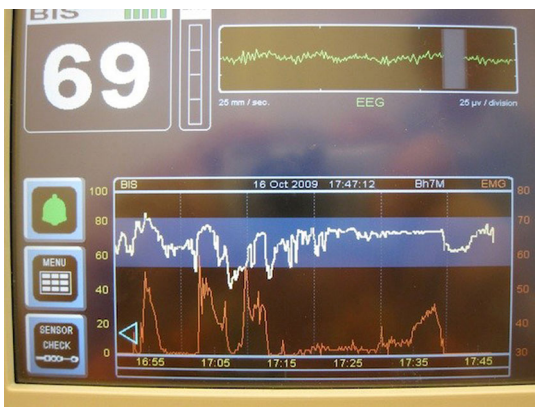

Fig. 1 Bispectral (BIS) index. BIS upper trend, real time EMG lower trend

useful to *predict* changing patient requirements during surgery. The EMG is the electrical activity of the facial *frontalis* muscle and is as real time as the EKG. Trended EMG spikes persist even when patients have forehead Botox.® EMG spikes signal incipient arousal of the brain [5]. More propofol is indicated to maintain sedation. Arousal precedes pain (nociception) [6]. Pre-LA injection saturation of NMDA receptors is the basis of *opioid-free*, preemptive analgesia [1]. In addition to patient immobility, the absence of EMG spikes with LA injection provides a *reproducible* basis with which to diagnose NMDA receptor saturation and *opioid-free* preemptive analgesia. See Fig. 1.

Numb patients rarely move during surgery. Non-purposeful patient movement under sedation has been a vexing problem for both the surgeon and the anesthesiologist. Is the movement purposeful or brain-originating with possible awareness. More sedation would be indicated? Or is the movement *non-purposeful,* meaning spinal cord-originating *without* possible awareness? More LA is indicated. Lidocaine–epinephrine is injected. Surgeons believe the epinephrine produced vasoconstriction equals *adequate* analgesia. Therefore, they believe patient movement means 'too light,' awareness risk and 'deeper' sedation indicated.

BIS^{TM} < 75 *with* baseline EMG provides *objective* evidence the patient *is* asleep and will *not* remember the surgery. Patient movement with propofol @ BIS < 75 *without* EMG spike equals spinal cord movement and is *without* awareness risk. Re-injection in the immediate area of surgical dissection eliminates *non-purposeful* patient movement in 98–99% of cases [1]. The use of objective evidence of the origin of patient movement was an effective; *dispassionate* means of helping surgeons understand vasoconstriction may *not* equal adequate analgesia. Improved emergence and discharge followed.

During surgery, propofol was maintained $60 <$ BIS < 75 *with* baseline EMG at 25–50 mcg$\cdot$ kg$^{-1\cdot}$ min^{-1} with a range between 2 and 200 mcg$\cdot$ kg$^{-1\cdot}$ min,$^{-1}$ a *100-fold variation* to achieve the same *numerical* level of sedation. The use of body weight, vital signs variation, body mass index (BMI), target-controlled infusion (TCI) or pharmacokinetic/pharmacodynamic (PK/PD) as the basis for propofol dosing is unlikely to account for this 100-fold variation. The effect of directly measuring with *real-time* EMG/BIS^{TM} brain monitoring yielded a statistically significant 30% reduction in propofol [7]. Delayed emergence secondary to excess propofol or ketamine was eliminated [1].

Eighty percent of patients required one or two 50 mg ketamine doses to satisfactorily complete the cases, many of which were 5 h. Aggregate ketamine doses exceeding 200 mg were not incompatible with one-hour discharge times. The brain size of a 100 kg male is not twice that of a 50 kg female, yet both remain immobile for LA injection with the same 50 mg ketamine dose. The heaviest patient to remain immobile from the 50 mg ketamine dose was this 145 kg liposuction patient. See Fig. 2. Therefore, the number of NMDA receptors does *not* vary with body weight.

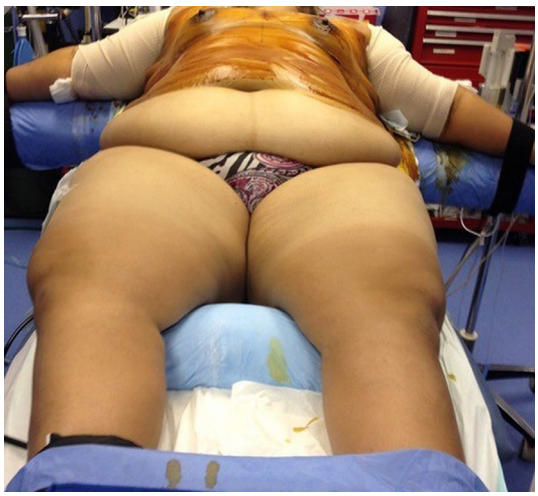

Fig. 2 A 145 kg female liposuction patient. 1500 ccs removed from each upper arm

Table 1 BIS values and sedation levels

98–100	Awake
78–85	Minimal sedation
70–78	Moderate sedation
60–70	Deep sedation
45–60	Sedation compatible with general anesthesia
< 45	Over medicated

LA was administered in volumes not to exceed 5000 ccs of tumescent solution or less than 55 mg kg^{-1} [8]. Postoperative bupivacaine was sprayed, not injected, on the surgical field not to exceed 50 ccs of 0.25%. Cases included liposuction, sub-pectoral breast augmentation, body implants, reduction mammoplasty, abdominoplasty and all facial cosmetic cases, i.e., rhytidectomy, browlift, facial implants and laser facial resurfacing. *N.B.,* Small volumes of 2% lidocaine with epinephrine were used for rhinoplasty and blepharoplasty cases (Table 1).

Conclusion

Over 26 years, more than 5000 patients received propofol *then* 50 mg ketamine *then* LA for ambulatory cosmetic surgery. All were discharged to home without requiring

professional aftercare givers. No patients were admitted to the hospital for either pain, PONV or prolonged emergence. There were no opioid addicts or opioid overdose deaths. The transition from qualitative to *quantitative* propofol ketamine sedation allowed the paradigm to evolve from an art to a science-based technique. *Real-time* EMG/BIS^{TM} monitoring helped surgeons understand vasoconstriction may not guarantee *adequate* analgesia.

Compliance with Ethical Standards

Conflict of interest The author has no conflicts of interest to disclose.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

informed consent For this type of study, informed consent is not required.

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