Opioid free. propofol ketamine for ambulatory surgery: the transition from art to science

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Ambulatory surgery patients are expected to be discharged to home following their surgery. The three main problems facing their anesthesiologists are 1) delayed emergence, 2) pain, 3) postoperative nausea and vomiting (PONV). The last two problems are well-recognized causes for unintended hospital admissions after day surgery. Ambulatory discharge is predicated on discharge-ready emergence in about an hour following surgery. When patients take longer to emerge, discharge is delayed, increasing nursing hours and decreasing cost-effectiveness. (Patients' ride delays, while another frustrating problem, are rarely in the purview of the anesthesiologist.)

The patient's brain cannot respond to information it does not receive. Failure to saturate critical sub-cortical NMDA receptors pre-local anesthetic injection is a major cause of post-operative pain. (1) Following an incremental propofol induction, 50 mg IV ketamine 2-5 minutes pre-injection provides saturation of those NMDA receptors for about 10-20 minutes while the surgeon injects local analgesia (LA).

From March 26, 1992 to December 26, 1998, the technique was qualitative. Glycopyrrolate 0.2 mg IV was given prior to induction. No infusion pump was used. A micro-drip (i.e. 60 gtts $\cdot$ cc^{-1}) IV set was used. A 50 cc IV bag of normal saline or Ringers Lactate into which 50 cc 10 mg $\cdot$ cc^{-1} propofol was injected. The final propofol concentration was 5 mg $\cdot$ $cc.^{-1}$ The initial drip rate approximated the patient's baseline heart rate and adjusted based on response.

Propofol was titrated to the clinical endpoints of loss of lid reflex (LLR) and loss of verbal response (LVR). Incremental propofol induction preserves the muscles responsible for maintaining a patent airway; i.e. *genioglossus, orbicularis oris, masseter & temporalis.* More than half the patients required only the rhytidectomy position (i.e. chin extended, head lateral) with or without an IV bag under the shoulders to maintain a patent airway. Typical induction times were 2-3 minutes.

SpO_2 was maintained between 92-95% with spontaneous ventilation on room air. Oxygen was available but rarely needed to maintain SpO_2. Continuous EKG and NIABP was also monitored. Nasal and oral airways, as well as laryngeal mask airways (LMA) were available. Although anesthesia machines were not available, suction, crash carts and defibrillators were. No patients required endotracheal intubation or cardiopulmonary resuscitation.

The use of ketamine *without* opioids was the basis for the lowest published PONV rate (0.6%) in an Apfel-defined high-risk (i.e. non-smoking, female, PONV history, emetogenic surgery) patient population *without* anti-emetics. (2) Opioid postoperative rescue was also absent in this portion of the author's experience. However, there was no objective evidence with which the author could convince the surgeons to re-inject vasoconstricted fields when patients moved during surgery. Adding additional adjuvant drugs that failed to accurately address the issue of inadequate analgesia prolonged patients' emergence and discharge.

“If you cannot measure it, you cannot improve it.” Lord Kelvin’s quote originally referred to temperature but also provides the rationale for direct brain measurement of anesthetic response to avoid too much anesthesia with probable delayed emergence.

On December 26, 1998, bispectral (BIS) index monitoring was added to the technique along with *critical* real time electromyogram (EMG) as the secondary trend. (Fig. 1) Induction began with a baseline rate of
25 mcg $\cdot$ kg^{-1} $\cdot$ min^{-1} propofol with successive 50 mcg $\cdot$ kg^{-1} propofol boluses (i.e. shorturl.at/bsFP9 s). Again, induction times were between 2-3 minutes. After BIS <75 *with* baseline EMG, *then* 50 mg ketamine was administered followed by a 2 to 5 minutes wait, *then* subcutaneous LA was injected by the surgeon.

The BIS values (and trend) are delayed from real time by 15-30 seconds. Depending on this time-delayed information for propofol titration is akin to trying to drive an automobile with rear mirror values alone. EMG is the electrical activity of the *frontalis* muscle and is as real time as the EKG of the cardiac muscle. EMG spikes persist despite forehead Botox.® EMG spikes signal incipient arousal. (3) Arousal precedes nociception. (4) Pre-LA injection saturation of NMDA receptors is the basis of opioid free, preemptive analgesia. (1) Absence of EMG spikes with LA injection provides a *numerically reproducible* basis with which to confirm NMDA receptor saturation. (Fig. 1)

Numb patients rarely move during surgery. Patient movement under sedation is a vexing problem for the surgeon and the anesthesiologist. The epinephrine is in the same syringe (or tumescent solution) as is the lidocaine. Surgeons believe vasoconstriction equals *adequate* analgesia. Therefore, they believe patient movement means ‘too light,’ the risk of awareness with recall, as well as interference with the surgery.

Patient movement *without* EMG spike means movement is originating from a *sub-cortical* signal and is, therefore, without risk of awareness with recall. Re-injection of the immediate area of surgical dissection eliminates patient movement in 98-99% of cases. (1) The use of an objective patient movement origin definition was an effective, *dispassionate* method to educate the surgeons that vasoconstriction does *not* equal adequate analgesia. Simply, a little more LA provides adequate analgesia and eliminates the majority of patient movement. Emergence is not delayed by giving additional intravenous medications that do not accurately deal with the problem.

Propofol was maintained 60<BIS<75 *with* baseline EMG at 25-50 mcg $\cdot$ kg$^{-1.}$ min^{-1} with a range 2-200 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, BMI, TCi or pharmacokinetic/pharmacodynamic (PK/PD) basis for propofol dosing is unlikely to account for this observed 100-fold variation in requirements to achieve identical *measured* sedation levels.

Eighty percent of patients required one or two 50 mg ketamine doses to satisfactorily complete the case, many of which take as long as 5 hours. 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. Conclusion? The number of NMDA receptors *do not* vary with body weight. A 145 kg female liposuction patient was the biggest patient this author administered 50 mg ketamine to achieve immobility. (Fig. 2)

Local analgesia was administered in volumes not to exceed 5,000 ccs of Klein's tumescent solution; i.e. 500 mg lidocaine per liter or 2,500 mg or less than 55 mg $\cdot$ kg.$^{-1}$ (5) Postoperative bupivacaine was sprayed, not injected, on the surgical field not to exceed 50 ccs of 0.25% or 125 mg.

Cases included liposuction (5,000 ccs maximum), sub-pectoral breast augmentation, reduction mammoplasty, classical abdominoplasty (i.e. pubis to xiphoid skin reflection, rectus sheath imbrication) & all facial cosmetic cases; i.e. rhytidectomy, rhinoplasty, blepharoplasty, browlift (open and endoscopic) facial implants and facial resurfacing. *N.B.,* Small volumes of 2% lidocaine with epinephrine, not tumescent solution, were used for rhinoplasty and blepharoplasty cases only.

Conclusion

This author's office-based, ambulatory practice began on March 26, 1992 and ended on November 28, 2018. Over those 26 years, more than 5,000 patients received incremental propofol *then* 50 mg ketamine *then* subcutaneous ultra-dilute 0.05% lidocaine with epinephrine (Klein's tumescent solution) 2-5 minutes *after* the ketamine. All were discharged to home without requiring professional aftercare givers. Not a single patient was admitted to the hospital for either pain or PONV. There were no pulmonary embolisms despite the absence of sequential compression stockings for abdominoplasty. There were no opioid addicts or opioid overdose deaths.

The transition from qualitative propofol ketamine to quantitative, real time EMG/BIS brain monitoring of propofol *then* ketamine *then* local analgesia transformed an artful technique into a scientifically based, reproducible paradigm.

References

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Fig. 1 Bispectral (BIS) index

BIS upper trend, real time EMG lower trend

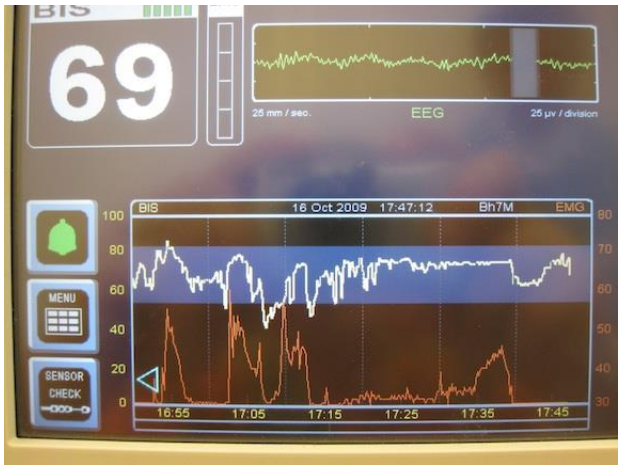
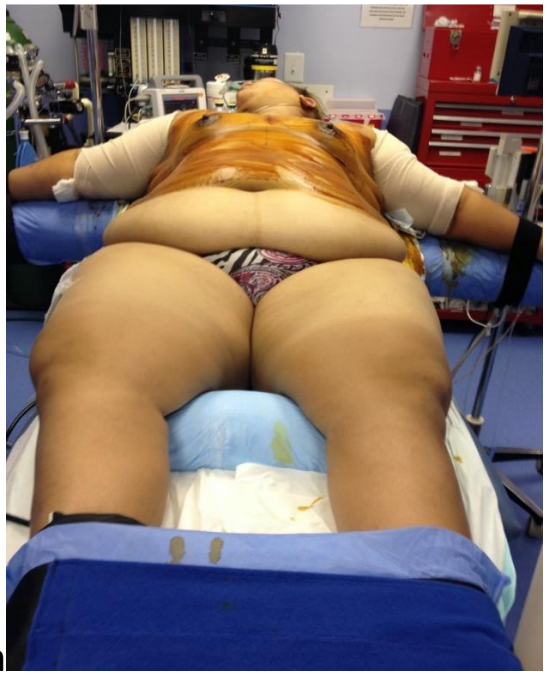


Fig. 2 145 kg female liposuction patient



1500 ccs removed from each upper arm