Part 3 of a 3-Part Series

Perioperative Patient Monitoring: Utilizing BIS in Total Intravenous Anesthesia Procedures

Faculty

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Introduction

In order to optimize short- and long-term outcomes, anesthesia providers typically monitor the level of drug delivery to best achieve the most appropriate depth of anesthesia while ensuring that incidence of adverse events (AEs) due to anesthetic administration will be low. Thus, the use of techniques, such as total intravenous anesthesia (TIVA), has expanded and increased the need for precise anesthetic monitoring. The BIS™ (bispectral index) Brain Function Monitoring System is designed to illustrate anesthetic depth even when specialized techniques like TIVA are employed.

Total Intravenous Anesthesia: Procedure and Outcomes

In contrast to the use of inhalation agents for general anesthesia, TIVA involves the use of different IV drugs: one for the hypnotic effect (eg, propofol, ketamine, midazolam, dexmedetomidine) and another for analgesia (eg, remifentanil or other opioids).[1-3] TIVA is often used in Europe—employing target-controlled infusion (TCI) devices—although some countries outside of Europe require regulatory approval for the use of TCI devices and certain anesthesia medications in special populations (ie, pediatric patients).[4] However, even without TCI, TIVA has been shown to be effective in establishing general anesthesia and may be associated with fewer AEs compared with inhalation agents.[1,5] Particularly, TIVA has been shown to be useful for patients with a history of severe cardiovascular instability,[6] patients with asthma,[7] those who have a known susceptibility to malignant hyperthermia,[4] or patients who experience frequent postoperative nausea and vomiting (PONV).[4]

In fact, multiple studies have shown that TIVA is associated with decreased PONV compared with inhalation agents: For example, Visser et al studied 1,447 elective inpatient surgeries and 563 outpatient surgeries, and reported that TIVA with propofol reduced the absolute risk for PONV up to 72 hours by 15% among inpatients (from 61% to 46%; $P<0.001$) and by 18% among outpatients (from 47% to 29%; $P<0.001$) compared with inhalation anesthesia.[5] Furthermore, the median length of stay in the postanesthesia care unit was 135 minutes after isoflurane versus 115 minutes after TIVA for inpatients ($P<0.001$) and 160 minutes after isoflurane versus 150 minutes after TIVA for outpatients in the hospital day care unit ($P=0.039$).[5] Other studies have shown a decreased rate of PONV with TIVA compared with inhalation agents in patients undergoing minor elective gynecologic or orthopedic interventions,[8] robot-assisted laparoscopic radical prostatectomy,[9] maxillofacial surgery,[10] and laparoscopic cholecystectomy,[11] among other surgical populations.

Table. Advantages of TIVA

Can be administered to maintain anesthesia in patients undergoing airway procedures
Improved quality of emergence from anesthesia
Method of choice for some patients with muscle disorders (ie, Duchenne's muscular dystrophy)
Method of choice for patients at risk for malignant hyperthermia
No risk for environmental pollution
Possible use in off-site and office-based locations
Rapid offset using propofol
Rapid onset of action independent of alveolar ventilation
Reduction in incidence of postoperative nausea and vomiting

TIVA, total intravenous anesthesia
Adapted from references 2 and 4.

TIVA may have other advantages over inhalation agents (Table).[2,4] Chandler et al reported that TIVA with propofol and remifentanil was associated with a lower rate of emergence delirium (38.3% vs 14.9%; $P=0.018$) and a lower median postoperative pain score (1 vs 3; $P=0.033$) compared with the use of sevoflurane in a study of 112 children undergoing strabismus repair.[12] Hofer et al reported that measures of psychological well-being at 90 minutes after surgery were higher with TIVA than with inhalation anesthesia.[8] Finally, in contrast to inhalation anesthetics, the use of TIVA does not result in operating room air pollution.[2]

Monitoring Level of Consciousness During TIVA Procedures

Despite the benefits of using TIVA, the method can present a challenge when clinicians seek to measure anesthetic depth as effectively as possible. When using inhalation anesthetics, measures such as minimum alveolar concentration or end-tidal volatile anesthetic concentration supplement standard monitoring[13]; however, due to the form of administration, these methods are not applicable during TIVA procedures.

The pharmacokinetic effects of certain TIVA drugs also can affect standard hemodynamic measurements including mean arterial pressure (MAP) and heart rate (HR). Guignard et al found noncranial patients exhibited a hemodynamic response (changes in MAP and HR) when receiving large doses of remifentanil with propofol.[14] In this study, the authors also used BIS to monitor anesthetic depth and found no change in BIS levels to correspond with changes found in MAP and HR. Therefore, the study authors concluded that measuring depth of anesthesia only using hemodynamic variables may be unreliable when opioids, hypnotics, and other drugs can alter these variables. Instead, the appropriate anesthesia amount was maintained with the help of BIS, which was unaffected by the specific drugs administered.[14]

BIS

A statistically based, complex index, BIS is unique because it integrates several disparate descriptors from a single channel of frontal electroencephalographic (EEG) data into a single variable, based on a large volume of clinical data, to synthesize an index that correlates behavioral assessments of sedation and hypnosis,[15] yet is insensitive to the specific anesthetic or sedative agent chosen. BIS was derived empirically by recording EEG data from healthy adults who underwent repeated transitions between consciousness and unconsciousness using several different anesthetic regimens.[15] The BIS monitor generates a number on a continuous scale of 0 to 100, with 100 representing alert cortical electrical activity and 0 indicating cortical electrical silence.[16] Validation studies have demonstrated that a BIS value between 45 and 60 is considered suitable for surgical anesthesia and reflects a very low probability of consciousness.[17]

BIS Monitoring During TIVA Procedures

Regarding the use of BIS to monitor intraoperative awareness during TIVA procedures, although some studies have found either no benefit[18]—or discovered a benefit after secondary analysis[19]—other studies have shown that BIS is effective in reducing awareness incidence in TIVA procedures.[20] Zhang et al performed a prospective, double-blind, randomized controlled multicenter trial of BIS monitoring in 5,228 patients undergoing surgery with TIVA.[20] The authors observed 4 cases of confirmed awareness (0.14%) reported in the BIS-guided group and 15 (0.65%) in the control group (odds ratio, 0.21; 95% confidence interval, 0.07-0.63; $P=0.002$). Overall, this study found that the incidence of awareness was reduced by 78% when TIVA was guided by BIS.[20]

Positive results have been found irrespective of agent used with TIVA. Researchers in Germany studied 42 patients scheduled for microlaryngoscopy.[21] Patients were randomly assigned to 1 of 2 groups: IV remifentanil or IV alfentanil; hypnosis was managed using propofol in both groups.[21] The researchers noted that using BIS during the procedure provided a clear determination of how much propofol to administer in order to not only ensure adequate anesthesia, but also to achieve equal BIS values to investigate the difference in recovery from anesthesia between the 2 agents.[21] Results showed that use of remifentanil/propofol with TIVA managed by BIS provides a more rapid recovery of ventilatory function.[21] Khafagy et al reported that study coadministration of clonidine or magnesium as adjuvants to TIVA, guided by BIS, reduced anesthetic consumption and was associated with improved hemodynamic values and enhanced postoperative analgesia.[22] Overall, Akçali et al reported that the use of BIS resulted in lower consumption of propofol and shorter time to extubation in patients undergoing lumbar discectomies under TIVA.[23]

Case Study: 72-Year-Old Woman With Colon Cancer Scheduled for Colectomy With Planned Colostomy

The patient's medical history included hypertension, type 2 diabetes, myocardial infarction 15 years ago, depression, and chronic back pain. The patient noted that her blood pressure (BP) was not very well controlled despite medication. Her American Society of Anesthesiologists (ASA) classification was 3. Surgical history included gynecological laparoscopy, total hip replacement, and laparoscopic cholecystectomy and appendectomy. She experienced postoperative nausea and vomiting (PONV) after each surgery, and she related that her anesthesiologist tried every antiemetic known without success. She is currently on atenolol for her hypertension; glipizide to control diabetes; sertraline for depression; and hydrocodone, pregabalin, and ibuprofen for back pain.

The patient was scheduled for a colectomy with planned colostomy. She received a laxative as part of the routine bowel preparation that her surgeon ordered and did not have any fluid from midnight of the day of surgery. In view of her previous history of PONV, a total intravenous anesthesia (TIVA) technique with propofol was planned. Additionally, dexamethasone 4 mg IV was administered at induction of anesthesia and ondansetron 4 mg IV was planned for administration toward the end of the surgery.

The patient received midazolam 2 mg and fentanyl 50 mcg as premedication. Anesthesia induction was accomplished with propofol 2 mg/kg with further 100 mcg of fentanyl. Neuromuscular blocking agent rocuronium 0.6 mg/kg was administered to facilitate tracheal intubation. Propofol infusion was initiated at 100 mcg/kg/min. Monitoring devices included ASA-recommended basic monitoring. Additionally, the patient had a BIS™ (bispectral index) sensor placed before induction of anesthesia.

Immediately following induction of anesthesia, her BP dropped precipitously to 60/40 mm Hg. At this point, the patient's BIS value was 30, with no interference from electromyogram (EMG) and high signal quality index (SQI). Propofol was reduced to 30 mcg/kg/min and a dose of phenylephrine 100 mcg was administered. Ventilation was supported with a facemask while awaiting onset of rocuronium. Three minutes later, the patient was intubated with a size 7.5-mm orotracheal tube and taped. While a second IV catheter was being placed, the BIS value trended up and now was reading 73.

A dose of propofol 50 mg was injected and propofol infusion rate was increased to 150 mcg/kg/min. A BIS value of more than 70 indicated a higher risk for patient awareness. Therefore, a bolus of propofol was appropriate to rapidly deepen anesthesia, and this was followed by a corresponding increase in propofol infusion rate to maintain adequate anesthesia.

Following induction, an esophageal Doppler was placed in the mid-esophagus to guide fluid and hemodynamic management. At 30 minutes, the patient's BP increased to 190/100 mm Hg with a heart rate (HR) of 100 beats per minute (bpm), and propofol was being infused at 150 mcg/kg/min. At this time, the patient's BIS value was 45. As the BIS level range was consistent with general anesthesia range, adjustment of propofol infusion rate was not appropriate and the increased BP was treated with an antihypertensive.

Following treatment with esmolol, her BP and HR reduced to 130/85 mm Hg and 85 bpm, respectively. After approximately 90 minutes into the surgery, her BP registered 80/50 mm Hg and her HR was 65 bpm. Propofol was infused at 150 mcg/kg/min. BIS values then were measured at 50, which indicated an adequate level of sedation. Therefore, causes of hypotension other than adjusting propofol infusion should be considered. For example, does the patient need plasma volume expansion with fluid? Could it be blood loss? What is the patient's hemoglobin level? If fluid or blood loss is not an issue, hypotension may be treated with a vasoactive drug (eg, phenylephrine). On the other hand, if the BIS value was 30, with the presence of hypotension, propofol infusion rate could be reduced further to provide appropriate level of sedation, between 45 and 60. This case illustrates using information from the BIS monitor to better manage the patient's hemodynamic response during anesthesia, and select the more appropriate strategy to treat hyper- and hypotension.

Conclusion

TIVA is an effective strategy for the establishment of general anesthesia and may be associated with fewer AEs compared with inhalation analgesia.[1,5] Use of the BIS Brain Monitoring System can help optimize delivery of anesthetics, including TIVA, and thereby may result in fewer AEs and improved outcomes.

References

1. Hogue CW Jr, Bowdle TA, O'Leary C, et al. A multicenter evaluation of total intravenous anesthesia with remifentanil and propofol for elective inpatient surgery. *Anesth Analg*. 1996;83(2):279-285.
2. Lerman J, Johr M. Inhalational anesthesia vs total intravenous anesthesia (TIVA) for pediatric anesthesia. *Pediatr Anesth*. 2009;19(5):521-534.
3. Mani V, Morton NS. Overview of total intravenous anesthesia in children. *Paediatr Anaesth*. 2010; 20(3):211-222.
4. Lerman J. TIVA, TCI, and pediatrics: where are we and where are we going? *Paediatr Anaesth*. 2010;20(3):273-278.
5. Visser K, Hassink EA, Bonsel GJ, et al. Randomized controlled trial of total intravenous anesthesia with propofol versus inhalation anesthesia with isoflurane-nitrous oxide: postoperative nausea with vomiting and economic analysis. *Anesthesiology*. 2001;95(3):616-626.
6. Suryaprakash S, Chakravarthy M, Muniraju G, et al. Myocardial protection during off pump coronary artery bypass surgery: a comparison of inhalational anesthesia with sevoflurane or desflurane and total intravenous anesthesia. *Ann Card Anaesth*. 2013; 16(1):4-8.
7. Radosic N, Nikolic J. Comparative study of two types of anesthesia (TIVA and balanced NLA) in asthmatic patients undergoing functional endoscopic sinus surgery (FESS). Presented at: Euroanaesthesia 2005: Annual Meeting of the European Society of Anesthesiologists; May 28-31, 2005; Vienna, Austria. Abstract A-262.
8. Hofer CK, Zollinger A, Büchi S, et al. Patient well-being after general anaesthesia: a prospective, randomized, controlled multi-centre trial comparing intravenous and inhalation anaesthesia. *Br J Anaesth*. 2003;91(5):631-637.
9. Yoo YC, Bai SJ, Lee KY, et al. Total intravenous anesthesia with propofol reduces postoperative nausea and vomiting in patients undergoing robot-assisted laparoscopic radical prostatectomy: a prospective randomized trial. *Yonsei Med J*. 2012;53(6):1197-1202.
10. Gecaj-Gashi A, Hashimi M, Sada F, et al. Propofol vs isoflurane anesthesia-incidence of PONV in patients at maxillofacial surgery. *Adv Med Sci*. 2010;55(2):308-312.
11. Khalid A, Siddiqui SZ, Aftab S, et al. Recovery profile-a comparison of isoflurane and propofol anesthesia for laparoscopic cholecystectomy. *J Coll Physicians Surg Pak*. 2008;18(6):329-333.
12. Chandler JR, Myers D, Mehta D, et al. Emergence delirium in children: a randomized trial to compare total intravenous anesthesia with propofol and remifentanil to inhalational sevoflurane anesthesia. *Paediatr Anaesth*. 2013;23(4):309-315.
13. Sessler DI, Sigl JC, Kelley SD, et al. Hospital stay and mortality are increased in patients having a "triple low" of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anesthesia. *Anesthesiology*. 2012;116(6):1195-1203.
14. Guignard B, Menigaux C, Dupont X, et al. The effect of remifentanil on the bispectral index change and hemodynamic responses after orotracheal intubation. *Anesth Analg*. 2000;90(1):161-167.
15. Sinha PK, Koshy T. Monitoring devices for measuring the depth of anaesthesia – an overview. *Indian J Anaesth*. 2007;51(5):365-381.
16. Covidien. BIS™ Brain Monitoring Technology. www.covidien.com/rms/pages.aspx?page=OurProducts/BrainMonitoring/Technology. Accessed August 27, 2013.
17. Yeganeh N, Roshani B, Almasi A, et al. Correlation between bispectoral index and predicted effect-site concentration of propofol in different levels of target-controlled, propofol induced sedation in healthy volunteers. *Arch Iran Med*. 2010;13(2):126-134.
18. Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008;358(11):1097-1108.
19. Mashour GA, Shanks A, Tremper KK, et al. Prevention of intraoperative awareness with explicit recall in an unselected surgical population: a randomized comparative effectiveness trial. *Anesthesiology*. 2012;117(4):717-725.
20. Zhang C, Xu L, Ma YQ, et al. Bispectral index monitoring prevent awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial. *Chin Med J (Engl)*. 2011;124(22):3664-3669.
21. Wuesten R, Van Aken H, Glass PS, et al. Assessment of depth of anesthesia and postoperative respiratory recovery after remifentanil- versus alfentanil-based total intravenous anesthesia in patients undergoing ear-nose-throat surgery. *Anesthesiology*. 2001;94(2):211-217.
22. Khafagy HF, Ebied RS, Osman ES, et al. Perioperative effects of various anesthetic adjuvants with TIVA guided by bispectral index. *Korean J Anesthesiol*. 2012;63(2):113-119.
23. Akçali DT, Ozköse Z, Yardim S. Do we need bispectral index monitoring during total intravenous anesthesia for lumbar discectomies? *Turk Neurosurg*. 2008;18(2):125-133.

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