Pediatric Anesthesia and Critical Care Journal 2021;9(2):75-79
doi:10.14587/paccj.2021.13

PACCJ

Use of the bispectral index in an adolescent to assess depth of sedation during palliative care

R. Munch[1], J. D. Tobias[2]

[1]Ohio University Heritage College of Osteopathic Medicine - Dublin Campus, Dublin, Ohio, USA
[2]Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA

Corresponding author: J. D. Tobias, Department of Anesthesiology & Pain Medicine, Nationwide Children's Hospital and the Department of Anesthesiology & Pain Medicine, The Ohio State University College of Medicine, Columbus, Ohio, USA. E-mail: Joseph.Tobias@nationwidechildrens.org

Keypoints

1. The assessment of anesthetic depth traditionally relies on the measurement of end-tidal anesthetic gas concentration and changes in vital signs in response to surgical stimulation.
2. Depth of anesthesia monitors such as the bispectral index use a proprietary algorithm to interpret the electroencephalogram and provide an assessment of the depth of anesthesia.
3. Although used mostly in the operating room setting, there may be applications in the ICU or palliative care setting when clinical depth of sedation monitoring is not feasible due to the administration of neuromuscular blocking agents.
4. Practice standards for palliative care emphasize the administration of adequate sedation and analgesia to mitigate suffering. Neuromuscular blocking agents may interfere with the clinical assessment of sedation and analgesia. In such circumstances, the BIS index may be a useful adjunct to gauge the depth of sedation.

Abstract

Although not considered standard of care, depth of anesthesia monitors are frequently used in adults to ensure an appropriate level of anesthesia and potentially limit the incidence of intraoperative awareness. Although, there are several depth of anesthesia monitors available, the one that has seen the greatest use both in and out of the operating room is the bispectral index (BIS) monitor. The BIS monitor is a quantitative electroencephalogram device that provides a numerical value to quantify the depth of anesthesia. To date, its applications outside of the operating room (OR) setting remain limited. We present a 16-year-old patient in whom the BIS monitor was used to monitor sedation during the use of neuromuscular blocking agents in the Pediatric ICU during end-of-life care. The general principles of the BIS monitor are presented, its use in the OR reviewed, and its potential role outside of the OR including the palliative care setting discussed.

Keywords

Depth of anesthesia; bispectral index; end-of-life care

Introduction

Practice standards for end-of-life care emphasize the provision of adequate sedation and analgesia to mitigate suffering.[1] In the specific instances when patients are receiving mechanical ventilation, in addition to appropriate doses of sedative and analgesic agents, neuromuscular blocking agents (NMBAs) may be necessary to facilitate ventilation and oxygenation.[2] However, NMBAs mask a patient's physical exhibition of pain and agitation, thereby impeding the clinical assessment of the depth and

efficacy of sedation.[2,3] Without the ability to assess the patient's pain and agitation due to neuromuscular blockade, the measurement of cortical activity can provide insight into sedation level.

The bispectral index (BIS) uses a proprietary algorithm to interpret the processed electroencephalogram (EEG) and provide a numerical measure (0 to 100) of the depth of sedation.[4] To date, its applications outside of the operating room (OR) setting remain limited. We present a 16-year-old patient in whom the BIS monitor was used to monitor sedation during the use of neuromuscular blocking agents in the Pediatric ICU during end-of-life care. The general principles of the BIS monitor are presented, its use in the OR reviewed, and its potential role outside of the OR including the palliative care setting discussed.

Case report

Preparation of this case report followed the guidelines of the Institutional Review of Nationwide Children's Hospital (Columbus, Ohio). The patient was a 16-year-old, 53.2 kilogram adolescent who presented for allogenic (haploidentical, from biological mother) bone marrow transplant (BMT) with natural killer (NK) cell therapy for refractory myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). Prior to BMT, the patient underwent reduced-intensity conditioning with total body irradiation (TBI) and NK cell infusion. Post-BMT, the patient underwent chemotherapy, immune suppression, and additional NK cell infusions. After conclusion of BMT-related treatments (hospital day 23), the patient was transferred to the Pediatric ICU (PICU) for concern of sepsis. Discharge from the PICU occurred the following day. On hospital day 28, the patient required increased respiratory support and was again admitted to the PICU. The patient remained in the PICU for 93 days until his death on hospital day 121. During this time, endotracheal intubation and mechanical ventilation were required for respiratory failure. Sedation and analgesia were provided by dexmedetomidine (1.4 µg/kg/hour), ketamine (0.5-2 mg/kg/hour), and midazolam (1-2 mg/hour) infusions. Neuromuscular blockade with vecuronium was necessary to provide effective mechanical ventilation. Further sedation and analgesia was provided by additional as needed doses of fentanyl and midazolam prior to noxious patient care procedures. Due to concerns of inadequate sedation and difficulties with assessing the depth of sedation during neuromuscular blockade, a BIS monitor was placed to assess the depth of sedation. BIS ratings were maintained at 40-50 by adjustment of midazolam and fentanyl infusions and bolus doses. The BIS monitor was used for a total of 7 days prior to the patient's death with measurements ranging from 21-48 during that time. No sedation issues or concerns were noted during the use of the BIS monitor. After a prolonged hospitalization, the patient expired on hospital day 121 due to bradycardia and asystole as a result of fungal sepsis associated with a blood culture that was positive for *Candida parapsilosis*.

Discussion

The key components of general anesthesia include hypnosis (lack of awareness and recall), analgesia (lack of nociceptive response), skeletal muscle relaxation, and control of the autonomic nervous system response to noxious stimuli.[1] The measurement of anesthetic depth traditionally relies on monitoring end-tidal anesthetic gas concentration and an assessment of changes in vital signs in response to surgical stimulation. Although, there are several "depth of anesthesia" monitors available, the one that has seen the greatest use both in and out of the operating room is the first one introduced into clinical practice, the BIS monitor. The BIS monitor is a quantitative EEG instrument which can be used to monitor the level of hypnosis during the administration of specific anesthetic agents (volatile anesthetic agents, benzodiazepines, barbiturates, and propofol). Although demonstrated to decrease the incidence of intraoperative awareness, the BIS monitor's superiority over other intraoperative monitors such as end-tidal gas monitor as a means of limiting awareness has not been clearly demonstrated.[5-7]

The BIS monitor includes a sensor (placed on the patient's forehead), digital signal converter, and monitor

display. The sensor receives EEG signals from the patient, which are then transferred to the digital signal converter which uses a proprietary algorithm to provide a numerical readout ranging from 0-100. Complete suppression of cortical activity would register a score of 0, while an awake patient would typically register 90-100. A BIS rating less than 60-70 has generally been shown to correlate with a low probability of intraoperative awareness.[4] The data conversion algorithm of the monitor was developed from the analysis of data from approximately 1,500 anesthetic administrations with nearly 5,000 hours of data collection.[4,8,9] Conversion of raw EEG data to a single numeric output is based on multivariate statistical analysis conducted of EEG data collected from patients transitioning from awake to fully anesthetized.[4] The BIS algorithm derivation process involved retrospective analysis of EEG changes with incrementally increasing doses of anesthetic agents that are known to act through the γ-amino butyric acid (GABA) system, including isoflurane and propofol, as the patients transitioned from awake to fully anesthetized.[10]

The BIS monitor and its EEG algorithm was originally developed for use with inhalational anesthetic agents and not the myriad of sedative and analgesic agents used for sedation in the ICU setting. Therefore, its correlation with depth of sedation and prevention of awareness may not be as accurate with medications other than those that work through the GABA system (inhalational anesthetic agents, barbiturates, benzodiazepines, and propofol). Although the BIS correlated with the University of Michigan Sedation Score when pentobarbital or benzodiazepines were used for sedation, it did not correlate with a regimen that included chloral hydrate, meperidine, hydroxyzine, or ketamine.[11] Other studies have demonstrated the inaccuracy of the BIS monitor with the administration of etomidate or agents such as xenon or nitrous oxide which act through the N-methyl-D-aspartate (NMDA) system.[12-14] Dexmedetomidine, a highly selective α_2-adrenergic receptor agonist, induces sedation that resembles non-REM sleep with spindle wave activity in the frontal cortex.[15] Studies regarding the feasibility of using BIS monitoring to judge the depth of sedation with dexmedetomidine has yielded mixed results.[16,17]

Given the similarities in the EEG pattern during deep sleep and pharmacologic sedation, the BIS algorithm may not differentiate between these states.[18] Thus, a patient in a state of deep sleep, although not be sedated, would register a BIS number that might suggest otherwise. Additionally, the BIS monitor measures sedation and not analgesia, so that patients may respond to a noxious stimulus with movement or a change in vital signs without being at risk for recall of such events.[19-21] Patient comorbid conditions or acute changes in cerebral blood flow may result in erroneous fluctuations in the BIS number. Asystole, as well as other factors that decrease cardiac output, alters CNS perfusion and EEG pattern, resulting in a decrease in the BIS number.[22] Anecdotal experience has reported similar changes with hypoglycemia.[23,24] Other patient-related issues that may impact the EEG pattern, and hence the BIS number, include dementia, Alzheimer's disease, recent electroconvulsive therapy, and a genetically-determined low voltage EEG.[22]

Despite these criticisms, the BIS monitor has demonstrated utility in assessing depth of sedation in the ICU setting and during procedural sedation.[11,25-29] Although the results have been mixed, the majority of reports have demonstrated a clinically acceptable correlation between the BIS number and commonly used ICU sedation scores such as the COMFORT score, Patient-State Index, and the Ramsay Score.[25-27] Furthermore, in patients receiving neuromuscular blocking agents, titration of sedation using the BIS monitor has been suggested to be effective in preventing over-sedation.[30] An additional advantage of the depth of anesthesia monitor is that it provides a continuous numeric readout using a simple 0-100 scale that is immediately and continuously available at the bedside as a guide to judge the depth of sedation. This is unlike sedation scoring systems that provide only an intermittent assessment and require time to assess and add various parameters. Furthermore, sedation scores frequently utilize

motor responses to tactile stimuli and therefore cannot be used in the presence of neuromuscular blocking agents. As such, the bedside clinicians and care givers must rely on physiologic parameters including heart rate and blood pressure, which may not be an accurate means of assessing sedation, especially in the critically ill patient.

Given the concerns of assessing the depth of sedation and ensuring amnesia during the administration of NMBAs in our patient, we chose to use the BIS monitor to assess the depth of sedation and ensure a level that would provide amnesia. The BIS monitor was used continuously without issue from hospital day 113 to our patient's death on hospital day 121. The monitor functioned effectively with limited to no technical issues. Given concerns of skin breakdown, the disposable forehead sensor was changed every 48-72 hours. To provide sedation and ensure amnesia, dexmedetomidine, ketamine, midazolam, and fentanyl were administered by continuous infusion, with as needed bolus doses of fentanyl and midazolam to provide additional comfort prior to noxious stimuli or when the BIS increased to greater than 60. Vecuronium was administered to allow for effective mechanical ventilation in our patient with altered respiratory compliance. Recorded BIS ratings ranged from 21-48. Our anecdotal experience suggests that BIS monitoring may be useful in guiding medication dosing during end-of-life care.

References

1. Olsen ML, Swetz KM, Mueller PS. Ethical decision making with end-of-life care: palliative sedation and withholding or withdrawing life-sustaining treatments. Mayo Clin Proc. 2010;85:949-54
2. Tobias JD. The use of neuromuscular blocking agents in children. Pediatr Ann. 1997;26:482-9.
3. Truog RD, Burns JP, Mitchell C, Johnson J, Robinson W. Pharmacologic paralysis and withdrawal of mechanical ventilation at the end of life. New Engl J Med. 200;342:508-11.
4. Medical Advisory Secretariat. Bispectral index monitor: an evidence-based analysis. Ont Health Technol Assess Ser. 2004;4:1-70.
5. Sebel PS, Lang E, Rampil IJ, et al. A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect. Anesth Analg. 1997;84:891-9.
6. Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. N Engl J Med. 2008;358:1097-1108.
7. Avidan MS, Jacobsohn E, Glick D, et al. Prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med. 2011;365:591-600.
8. Rampil IJ. A primer for EEG signal processing in anesthesia. Anesthesiology. 1998;89:980-1002.
9. Rosow C, Manberg PJ. Bispectral index monitoring. Anesthesiol Clin North Am. 2001;19:947-66.
10. Dahaba AA. Thinking outside the box. Off-label use of Bispectral Index within context and limitations for conditions other than depth of anesthesia. Minerva Anestesiol. 2019;85:189-93.
11. Brown McDermott N, VanSickle T, Motas D, Friesen RH. Validation of the Bispectral Index monitor during conscious and deep sedation in children. Anesth Analg. 2003;97:39-43.
12. Goto T, Nakata Y, Saito H, et al. Bispectral analysis of the electroencephalogram does not predict responsiveness to verbal command in patients emerging from xenon anesthesia. Br J Anaesth. 2000;85:359-63.
13. Barr G, Jakobsson G, Owall A, Anderson RE. Nitrous oxide does not alter bispectral index: study with nitrous oxide as sole agent and as an adjunct to IV anaesthesia. Br J Anaesth. 1999;82:827-30.
14. Lallemand MA, Lentschener C, Mazoit JX, et al. Bispectral index changes following etomidate induction of general anaesthesia and orotracheal intubation. Br J Anaesth. 2003;91:341-36.

15. Xi C, Sun S, Pan C, Ji F, et al. Different effects of propofol and dexmedetomidine sedation on electroencephalogram patterns: wakefulness, moderate sedation, deep sedation and recovery. PLoS One. 2018;13:e0199120.
16. Gu Y, Yang F, Zhang Y, et al. The effects of different doses of dexmedetomidine on the requirements for propofol for loss of consciousness in patients monitored via the bispectral index: a double-blind, placebo-controlled trial. BMC Anesthesiol. 2020;20:96.
17. Kasuya Y, Govinda R, Rauch S, et al. The correlation between bispectral index and observational sedation scale in volunteers sedated with dexmedetomidine and propofol. Anesth Analg. 2009;109:1811-15.
18. Sleigh JW, Andrzejowski J, Steyn-Ross A, Steyn-Ross M. The bispectral index: a measure of depth of sleep?. Anesth Analg. 1999;88:659-61.
19. Coleman RM, Tousignant-Laflamme Y, Ouellet P, e tal. The use of the bispectral index in the detection of pain in mechanically ventilated adults in the intensive care unit: a review of the literature. Pain Res Manag. 2015;20:e33-7.
20. Lysakowski C, Dumont L, Pellegrini M, Clergue F, Tassonyi E. Effects of fentanyl, alfentanil, remifentanil and sufentanil on loss of consciousness and bispectral index during propofol induction of anaesthesia. Br J Anaesth. 2001;86:523-7.
21. Ekman A, Brudin L, Sandin R. A comparison of bispectral index and rapidly extracted auditory evoked potentials index responses to noxious stimulation during sevoflurane anesthesia. Anesth Analg. 2004;99:1141-6.
22. Yousefi-Banaem H, Goharani R, Hajiesmaeili M, et al. A review of bispectral index utility in neurocritical care patients. Arch Neurosci. 2020;7:1-6.
23. Blaabjerg L, Juhl CB. Hypoglycemia-induced changes in the electroencephalogram: an overview. J Diabetes Sci Technol. 2016;10:1259-67.
24. Xi C, Pan C, Li T. Abnormally low bispectral index and severe hypoglycemia during maintenance of and recovery from general anesthesia in diabetic retinopathy surgery: two case reports. BMC Anesthesiol. 2018;18:45.
25. Aneja R, Heard AM, Fletcher JE, Heard CM. Sedation monitoring of children by the bispectral index in the pediatric intensive care unit. Pediatr Crit Care Med. 2003;4:60-64.
26. Triltsch AE, Nestmann G, Orawa H, et al. Bispectral index versus COMFORT score to determine the level of sedation in paediatric intensive care unit patients: a prospective study. Critical Care. 2005;9:R9-R17.
27. Berkenbosch JW, Fichter CR, Tobias JD. The correlation of the bispectral index monitor with clinical sedation scores during mechanical ventilation in the pediatric intensive care unit. Anesth Analg. 2002;94:506-11.
28. Powers KS, Nazarian EB, Tapyrik SA, et al. Bispectral index as a guide for titration of propofol during procedural sedation among children. Pediatrics 2005;115:1666-74.
29. Gill M, Green SM, Krauss B. A study of the bispectral index monitor during procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2003;41:234-41.
30. Tobias JD, Grindstaff R. Bispectral index monitoring during the administration of neuromuscular blocking agents in the Pediatric ICU patient. J Intensive Care Med. 2005;20:233-7.