EDITORIAL

Depth-of-Anesthesia Monitor and the Frequency of Intraoperative Awareness

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More than 21 million patients in North America alone receive general anesthesia each year,[1] and thanks to increasing knowledge, skill, and sophisticated technology, the vast majority of anesthetic procedures are uneventful. However, a rare but serious adverse event is the explicit recall of sensory perceptions during general anesthesia, termed "awareness" or "intraoperative awareness." The incidence of awareness may be as high as 1 or 2 for every 1000 patients, possibly higher among children.[2-5] Awareness occurs more frequently among patients who have received neuromuscular-blocking drugs, who cannot signal to the medical team that they are conscious.[3] In most cases, awareness is not associated with pain, but some patients have excruciating pain and long-term psychological consequences.[6]

Devices that monitor the depth of anesthesia offer the prospect of reducing anesthesia awareness. The global market leader is the bispectral index system (BIS, Aspect Medical Systems), which relies on a proprietary algorithm for processing an electroencephalogram and alerts the anesthesiologist if the depth of anesthesia is inadequate. The simplicity of the concept, together with the showcasing of patients who have had awareness (e.g., in *USA Today*,[7] the *Larry King Live* television show,[8] and a recent Hollywood movie[9]), has contributed to a demand from patients for use of this technology. Even a regulatory agency, the Joint Commission, has entered the discussion by posting a sentinel-event alert.[1]

Certainly anesthesiologists have been seeking ways to effectively titrate general anesthetics and measure neurologic depression since the introduction of ether in 1846. These factors have contributed to the use of the BIS monitoring system. According to the manufacturer,[10] 23 million patients in operating rooms around the world have been monitored with the BIS. In the United States, approximately 60% of all operating rooms use BIS technology. Approximately 17% of surgical procedures that required general anesthesia or deep sedation over the past 12 months were monitored with the use of the BIS system.

Has there been any compelling evidence to justify widespread adoption of depth-of-anesthesia monitors? In its review, the Food and Drug Administration determined that "use of BIS monitoring . . . may be associated with the reduction of the incidence of awareness with recall in adults during general anesthesia and sedation."[1] However, a recent Cochrane review[11] identified only two relevant prospective, randomized, controlled trials. One (supported in part by the manufacturer) concluded that BIS monitoring was of benefit to high-risk patients[5]; the other was underpowered to detect an effect.[12]

In this issue of the *Journal*, Avidan and colleagues report their findings from a study of 1941 patients at high risk for awareness.[13] A BIS-guided protocol was added to a standard protocol in which the concentration of anesthetic vapor was measured in the expired gases. The addition of the BIS-guided protocol did not reduce the frequency of definite or possible awareness. There was no difference in the amount of inhaled anesthetic delivered to patients in the two groups. Specifically, four patients, two in each group, had definite awareness (an overall incidence of 0.21%), and five additional patients (four in the BIS group and one in the control group) had possible awareness. Notably, the observed incidence of awareness was similar to that reported previ-

ously,[5] which confers external validity to this study and confirms its relevance to practice.

What else does this study tell us about anesthesia awareness? First, it showed that many patients reported the episode of awareness many hours and even days after the procedure. As such, anesthesiologists are unlikely to be directly involved in the patient's care at the time of disclosure. Nurses and surgeons need to be educated about awareness and refer patients back to an anesthesiologist for follow-up. The study also points to possible disadvantages of noninvasive depth-of-anesthesia monitoring. For example, Avidan and colleagues estimated that if BIS monitors were used for all patients in the United States who received a general anesthetic, the cost of disposable electrodes alone would exceed $360 million annually.[13]

Although it was not studied in the trial, it is plausible that awareness monitors could lead to overdosing or underdosing of anesthetic agents. The recommended dose of anesthetic was maintained for 45% of patients in the BIS group but for only 26% of those in the vapor-monitored group. This result will not surprise experienced anesthesia providers, who recognize that simple dosing protocols must often be modified to address unforeseen circumstances. Clinicians rely on judgment to select doses and prevent common adverse effects such as hypotension. General anesthetics have effects on multiple systems, and titrating doses to a single parameter such as the BIS value is dubious, particularly when we do not yet understand the underlying mechanisms of the drugs, the algorithms of the electroencephalogram analysis, or the validity of the monitor.

What are the roadblocks to the development of reliable depth-of-anesthesia monitors? Although we now understand what anesthetics do in terms of both desirable effects (e.g., unconsciousness, immobility, and memory blockade) and undesirable effects (e.g., cardiovascular depression and blunting of the hypoxic drive), we have only a rudimentary understanding of their sites and mechanisms of action. One subtype of γ-aminobutyric acid receptor ($GABA_A$) that is predominantly expressed in the hippocampus has been identified in animal models as a potential target for the memory-blocking actions of general anesthetics.[14,15] Surface electrodes for cortical electroencephalographic measurements are unlikely to reveal drug action at the level of the hippocampus or other critical memory centers. Thus, it is not surprising that patients can have awareness despite low (i.e., "desirable") BIS values. Adding to the complexity, different types of memory (e.g., auditory, fear-associated, short-term, and long-term) are mediated by different neuronal pathways in different regions of the brain,[16] so the anesthetic dose required to suppress each type of memory may differ.

The study by Avidan and colleagues points to several important lessons. First, the widespread adoption of devices and other interventions must be based on ample peer-reviewed data. All too often, we discover that strategies that intuitively appear to be valuable fail to perform as predicted. Professionalism demands that care plans be based on a critical evaluation of the best available data, not on pressure from external forces such as fear of litigation[17] or public demand. Second, the delegation of critical elements of patient care to a "black box" approach, in which decisive factors are under proprietary control, must be avoided. Third, we must remember that the signals detected by monitors may or may not represent physiological processes of interest, such as learning and consciousness. Finally, general anesthesia has come a long way, but future advances will depend on the development of a better understanding of how and where anesthetics act.

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1. The Joint Commission. Preventing, and managing the impact of, anesthesia awareness. (Accessed February 22, 2008, at http://www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea_32.htm.)
2. Sebel PS, Bowdle TA, Ghoneim MM, et al. The incidence of awareness during anesthesia: a multicenter United States study. Anesth Analg 2004;99:833-9.
3. Sandin RH, Enlund G, Samuelsson P, Lennmarken C. Awareness during anaesthesia: a prospective case study. Lancet 2000;355:707-11.
4. Lopez U, Habre W, Laurençon M, Haller G, Van der Linden M, Iselin-Chaves IA. Intra-operative awareness in children: the value of an interview adapted to their cognitive abilities. Anaesthesia 2007;62:778-89.
5. Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. Lancet 2004;363:1757-63.
6. Samuelsson P, Brudin L, Sandin RH. Late psychological symptoms after awareness among consecutively included surgical patients. Anesthesiology 2007;106:26-32.

7. Doheny K. When patients wake up — during surgery. USA Today. October 22, 2004.
8. Larry King Live Radio Show. Awake during surgery. December 12, 2007 (transcript). (Accessed February 22, 2008, at http://www.westwoodone.com/pg/jsp/larryking/transcript.jsp?pid=19780.)
9. Awake. (Accessed February 22, 2008, at http://www.awakethemovie.com.)
10. Aspect Medical Systems home page. (Accessed February 22, 2008, at http://www.aspectmedical.com.)
11. Punjasawadwong Y, Boonjeungmonkol N, Phongchiewboon A. Bispectral index for improving anaesthetic delivery and postoperative recovery. Cochrane Database Syst Rev 2007;4:CD003843.
12. Puri GD, Murthy SS. Bispectral index monitoring in patients undergoing cardiac surgery under cardiopulmonary bypass. Eur J Anaesthesiol 2003;20:451-6.
13. Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. N Engl J Med 2008;358:1097-108.
14. Cheng VY, Martin LJ, Elliott EM, et al. Alpha5GABA$_A$ receptors mediate the amnestic but not sedative-hypnotic effects of the general anesthetic etomidate. J Neurosci 2006;26:3713-20.
15. Caraiscos VB, Newell JG, You-Ten KE, et al. Selective enhancement of tonic GABAergic inhibition in murine hippocampal neurons by low concentrations of the volatile anesthetic isoflurane. J Neurosci 2004;24:8454-8.
16. Linden DE. The working memory networks of the human brain. Neuroscientist 2007;13:257-67.
17. Kent CD, Domino KB. Awareness: practice, standards, and the law. Best Pract Res Clin Anaesthesiol 2007;21:369-83.