

Prevention of awareness during general anesthesia

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F1000 Medicine Reports 2009, 1:9 (doi: 10.3410/M1-9)

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Abstract

Awareness during general anesthesia with subsequent explicit recall is a serious and frequently preventable problem that is gaining attention from clinicians and patients alike. Cost-effective interventions that increase vigilance should be implemented to decrease the likelihood of this complication.

Introduction and context

Awareness events can lead to post-operative psychological sequelae [1] but are also feared by patients presenting for surgery. As such, a reliable method of detecting or preventing awareness would be an important clinical advance. Although there are a number of candidate 'awareness monitors' based mainly on processed electroencephalograms (EEGs) or on evoked potentials, there has been considerable study and controversy regarding one particular processed EEG: the bispectral index (BIS) monitor.

Most of the research into awareness has focused on episodic consciousness during general anesthesia with subsequent explicit recall. Clinical investigators, however, have used Tunstall's isolated forearm technique to show that patients may have frequent episodes of awareness during anesthesia without forming explicit memories [2]. Even at low subanesthetic concentrations, both inhalational and intravenous anesthetic agents have been shown to block emotional and episodic memory before engendering loss of consciousness [3,4]. Debate has arisen as to whether it is acceptable for patients to have conscious perception with possible concomitant unpleasant sensations, even if they do not remember their experiences [5,6].

Current practices: what are the key considerations?

Prospective studies of unintended intra-operative awareness with subsequent explicit recall (AWR) in the general surgical population demonstrated an incidence of 1 to 2 cases per 1000 [7,8]. An increased risk for AWR has been attributed to specific patient and surgical risk factors [9]. Broadly speaking, these have been conceptualized as patients with resistance (genetic or acquired) to anesthetic agents, patients who do not tolerate high-dose anesthetic agents owing to poor cardiac reserve, and surgeries in which anesthetic dose has often been low, such as cardiac surgery and cesarean section using general anesthesia [9,10]. Beyond these risk factors, human error and machine malfunction may also lead to awareness events. Two landmark studies, a large Scandinavian observational study [11] and the B-Aware Study [9], found that incorporating BIS guidance into routine anesthetic practice could decrease the incidence of AWR. Since these studies, BIS monitoring has enjoyed widespread adoption in operating rooms and intensive care units worldwide. Interestingly, the utility of BIS monitoring in decreasing AWR was not found in a large multicenter US study, but in this study patients who received BIS monitoring may not have been well matched with those who did not [8]. In the B-Unaware randomized controlled trial, conducted in patients who were anesthetized with exclusively inhalational agents, a

BIS-guided protocol was not found to confer an advantage in preventing AWR compared with a protocol using end-tidal anesthetic gas concentration [10]. The possibility of a small but clinically important benefit attributable to the BIS monitor was not excluded by this study. The B-Unaware Trial raises the question of whether the reduction in awareness reported previously with processed EEG guidance is attributable predominantly to an 'awareness monitor' or to a protocol that increases clinical vigilance.

BIS values have been shown to correlate with propofol blood concentrations [12], and routine intra-operative measurement of propofol levels is not presently available. It is therefore plausible that processed EEG-guided adjustment of propofol infusion might decrease the likelihood of awareness with total intravenous anesthesia (TIVA). There are, however, no randomized controlled trials assessing the efficacy of a processed EEG-guided protocol for preventing awareness with subsequent recall in the context of TIVA. Although 43% of patients in the B-Aware Study received TIVA [9], the incidence of definite awareness in this group was not reported separately, nor was this a pre-specified subgroup analysis. If the incidence of awareness had been significantly lower in this subgroup among those who received the BIS protocol, this result would have been hypothesis-generating.

The incidence of AWR in children (5 to 12 years old) has been estimated to be 0.8% [13]. In a survey of European pediatric anesthesiologists, more than 60% identified awareness as a problem in current practice [14]. In the pediatric population, the BIS has demonstrated some degree of correlation with anesthetic concentration using sevoflurane [15,16,17] as well as isoflurane [18]. The BIS has also demonstrated some degree of correlation with propofol sedation and anesthesia [19]. Thus, the use of the BIS or perhaps another 'awareness monitor' could potentially provide evidence that consciousness is unlikely in a child. There are no data, however, suggesting that the use of processed EEG or evoked potentials can prevent awareness in the pediatric population. Whether using any 'awareness monitor' provides a higher probability of unconsciousness and amnesia compared with other indices, such as movement or respiratory rate, is currently unknown.

Recent advances

In the last decade, there have been important advances in our understanding of anesthetic mechanisms [20], sleep circuits in the brain [21,22], consciousness [23], functional brain imaging [3,5], advanced electroencephalography analysis [24,25], and memory formation [3,4,26]. Recent

evidence suggests that anesthetic drugs exert amnestic and hypnotic actions at different receptor subtypes in different brain regions [27]. This raises the possibility that some patients may have genetic resistance to the memory-blocking actions of anesthetic agents, which may increase their susceptibility to the complication of AWR. Improved detection of unconsciousness with general anesthesia has been facilitated by brain monitors based on processed EEG analysis [2,24,25,28] and evoked potentials [29,30]. While the BIS is reasonably good at predicting unconsciousness [2], new approaches, such as permutation entropy, Hilbert-Huang spectral entropy, bicoherence, weighted spectral median frequency, and combination techniques [24,25,28,29,30,31], may be superior at discriminating between consciousness and unconsciousness.

Implications for clinical practice

While methodological approaches may confound the detection of AWR, the vast range from 1/100 [32] to 1/14,000 [33] in the reported incidence of awareness suggests that it may not be only high-risk patients or surgeries that determine the likelihood of AWR, but also high-risk anesthetic techniques. This notion was reinforced by the results of a recent study in 1095 women undergoing cesarean section with general anesthesia [34]. Historically, this has been considered high-risk surgery and anesthesia for explicit recall, with an estimated incidence of awareness of 1% [9]. But only two women experienced awareness with explicit recall in this study, and both cases could likely have been prevented with the implementation of a simple protocol designed to increase vigilance. Inhalational anesthesia may carry less risk for awareness than TIVA since the practitioner can routinely monitor exhaled anesthetic gas and alarms can be set for low concentrations; this hypothesis warrants further examination.

At this time, it is unclear whether current 'awareness monitors', or indeed newer and potentially superior technologies, will be both efficacious and cost-efficient in the prevention of awareness during general anesthesia or other related settings [35]. Voss and Sleight [35] have written an excellent and thought-provoking review on the challenges and limitations associated with EEG-based monitors of 'depth of anesthesia'. Large prospective randomized trials without commercial influence or bias are currently under way to evaluate BIS guidance both in high-risk patients (NCT00682825) and in all-comers (NCT00689091). The major advance in the past 10 years has been the validation of awareness as a serious problem that requires rigorous study.

Abbreviations

AWR, awareness with recall; BIS, bispectral index; EEG, electroencephalogram; TIVA, total intravenous anesthesia.

Competing interests

The authors declare that they have no competing interests.

Acknowledgments

The authors thank Rachel Wilson for her editorial and proofreading contributions to this article.

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