

AWARENESS UNDER GENERAL ANESTHESIA

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General anesthesia aims to eliminate patients' awareness of excruciating pain during surgery. Nevertheless, rare occurrences of patient awareness continue because the problem is not yet completely preventable. One study puts the incidence of awareness at 0.18% for patients receiving muscle relaxants and at 0.10% for patients not given relaxant drugs. Awareness experiences frighten patients and impact their implicit and explicit memories in ways that can leave a lifetime of residual emotional and psychological problems ranging from sleep disturbances, nightmares, and daytime anxiety that may subside with time to development of post-traumatic stress disorder.

Most anesthetists monitor depth of anesthesia by

assessing intraoperative hemodynamic responses to surgical stimuli—an approach questioned by some authors. Several depth-of-anesthesia monitors are available, but there is no ideal monitor that is 100% reliable.

This review provides an overview of literature that reports findings associated with the monitoring and occurrence of intraoperative awareness. These studies indicate assessment methods that can be trusted when we provide general anesthesia and what measures can be taken to prevent recall by patients under general anesthesia.

Key words: Anesthesia, awareness, monitoring, prevention, recall.

“**T**he operative course was uneventful and the total operation time was 2 hours and 50 minutes. Two days after the operation, there was surprise to learn that the patient complained of awareness during the surgery.”¹ This is one example of awareness under anesthesia reported in one anesthesia journal, but it is not an isolated incident. The goals for the anesthesia provider when administering general anesthesia are to help the patient avoid pain and to provide a state of sedation, hypnosis, and unconsciousness. Accomplishing these goals will go a long way toward preventing patient awareness.

The scientific explanation of awareness under general anesthesia is the patient's sensitivity, occurring in the form of explicit or implicit memory.² *Explicit memory* refers to the spontaneous or conscious recollection of previous experiences or intraoperative events.^{2,3} The recollection of intraoperative events may occur with or without the sensation of pain.² The term *awareness*, as used here, describes the explicit memory during anesthesia.³ *Implicit memory*, by contrast, refers to changes in performance or behavior that are produced by previous experiences but without conscious recollection of those experiences.³ Together with the fear of death, experiencing awareness while under general anesthesia is the next most common apprehension conveyed by patients before surgery and anesthesia.^{4,5} A vast number of studies have been conducted in an effort to find a method that would guarantee the absence of awareness under general anesthesia. Unfortunately, recall during general anesthesia still occurs, and the absolute solution for this dilemma is far from being found.

Literature review

Schwender and colleagues⁶ reported that all patients undergoing general anesthesia in their study (n = 45) recalled hearing sounds or voices, 33 of 45 patients understood and remembered conversations, 21 of 45 patients had visual recollection, 12 of 21 acknowledged objects and faces, 6 remembered the sensation of moderate pain, and 8 recalled having severe pain. A study conducted in Finland reported the following results: of 2,612 patients involved in interviews following general anesthesia, 10 (0.4%) experienced awareness and 9 (0.3%) additional patients possibly experienced awareness.⁷ A Swedish study found the incidence of awareness to be 0.18% when muscle relaxants were used and only 0.10% when no relaxants were administered.⁸ Differences in the anesthetic techniques used in these countries may account for variations in the incidence of awareness. According to a study from the University of Iowa, the incidence of recollection in nonobstetrical and noncardiac surgical patients was 0.2% and was 0.4% in obstetric cases.³ The same study found the incidence of awareness to be much higher in cases in which patient's cardiopulmonary and vascular functioning was compromised: 1.1% to 1.5% in patients undergoing cardiac surgery and 11% to 43% in major trauma cases.³

Sequelae

Undetected intraoperative awareness remains a significant problem for anesthesia providers. Dauderer and Schwender⁹ claim that recall during anesthesia can adversely impact patients postoperatively. Incidences of awareness are associated with measuring the depth of

anesthesia in patients with individual characteristics. Anesthesia providers use such terminology as “too light,” “too deep,” or “deep enough”—degrees of depth that are neither quantifiable nor consistent among providers. Without a quantitative measurement of awareness, no one, except the patient with a recollection of intraoperative awareness following surgery, can state to any degree of certainty exactly how “deep” the anesthesia was. Using a depth-measuring device in the practice of anesthesia has many advantages, one of which is a medicolegal advantage. Despite the litigious nature of our society, the primary reason for using some type of depth-of-anesthesia monitor should be to improve patient care. Although the incidence of awareness is as low as 0.18%,^{7,8} when it does happen, with explicit recall of pain as the direct result of inadequate anesthesia, it frequently is expressed by patients as the worst experience of their lives.¹⁰ After waking up and remembering different stimuli, voices, or feelings, people may develop a variety of psychological responses. According to Osterman et al,¹¹ 56% of 16 patients interviewed who experienced intraoperative recall also experienced significant postoperative distress related to inability to communicate and to feelings of helplessness, terror, pain, insecurity, abandonment, and betrayal. In some patients, serious self-limiting symptoms, such as sleep disturbances, nightmares, and daytime anxiety, or even a posttraumatic stress disorder (PTSD) may develop. In patients in whom PTSD develops, manifestations include recurring nightmares, instability, anxiety, and preoccupation with death.³

Patients who experience recall during surgery often sue the anesthetist for not having provided sufficient pain control in administering the anesthetic, so there can be legal consequences for the anesthetist whenever an incident of recall occurs.⁶ However, it is the patient who more often suffers the long-term sequelae of a recall experience. Waking up with pain during surgery is shocking for the patient and puts the patient at high risk for developing PTSD. Patients who have experienced recall and seek mental health treatment following surgery should be evaluated for PTSD.⁶ Given such traumatizing risks, anesthesia experts agree that the possible advantages of using “light” anesthesia must be balanced carefully against the risk of the patient experiencing intraoperative recall or possible PTSD during the postoperative period.⁶ The detection and prevention of intraoperative recall is necessary to minimize the development of serious psychiatric complications, such as PTSD.¹²

Causes

According to most studies, recall results from inade-

quate levels of anesthesia.^{3,6,7,13} A continuum has been discussed in the literature, from adequate anesthesia resulting in complete absence of awareness, to lighter anesthesia resulting in an implicit memory, to even lighter anesthesia resulting in explicit recall.³ Intraoperative awareness, as it is commonly perceived, relates to poor judgment or inattention by the anesthesia provider leading to inadequate levels of anesthesia or explicit recall. Increased anesthetic requirement by some patients, machine misuse, or, less frequently, malfunction also result in an inadequate delivery of anesthesia.³ As any anesthesia provider knows, there is wide variability in anesthetic needs of patients. More recollection incidences occur when muscle relaxants are used, probably due to the increased difficulty of patient assessment.^{3,8} As Sandin and colleagues described,⁸ specific recall symptoms in patients without intraoperative muscle relaxation lacked anxiety and delayed neuroses. In contrast, the patients who had awareness when muscle relaxation was used developed both anxiety and postponed neurotic symptoms.⁸

According to the closed claims analysis from the database of the American Society of Anesthesiologists, awareness under general anesthesia (1.9% [79 of 4,183 claims]) was observed more commonly in women (77%), adults younger than 60 years (89%), patients with an ASA physical status of I or II (68%), and patients who received anesthesia with nitrous oxide, narcotic, and muscle relaxant techniques (without the addition of a halogenated inhalation agent).¹³ Of 79 awareness claims, there were 18 claims for awake paralysis and 61 claims for recall during general anesthesia.¹³ Most claims for awake paralysis (94%) represented substandard care involving errors in labeling and administration of drugs.¹³ “Infusion errors involved succinylcholine drips in 10 claims (56% of awake paralysis claims) caused by unlabeled succinylcholine bags (2 cases), mislabeled succinylcholine bags (2 cases), and failure to check the label on unintended succinylcholine drips (6 cases). Syringe swaps occurred with mislabeled drugs (2 cases) and failure to check the label on a properly labeled syringe (6 cases).”¹³ “In several of the cases, the practitioner injected a benzodiazepine after the muscle relaxant in an unsuccessful attempt to achieve retrograde amnesia.”¹³ The errors occurred mostly during induction periods when a muscle relaxant was administered instead of a sedative or hypnotic agent.¹³

St Pierre et al¹⁴ determined the incidence of awareness during induction of anesthesia, which is one of the most stimulating parts in a surgical case, to be dose dependent. The study recommended that when

combining a short-acting induction agent with a delayed-onset neuromuscular blocker, the continuous infusion of the hypnotic drug may help to avoid awareness during induction.¹⁴

Hemodynamic responses

Many anesthesia providers currently rely on monitoring of patient hemodynamic responses as a method of awareness assessment. This practice relies on such hemodynamic measurements as blood pressure and heart rate to monitor the sedative-hypnotic state of the patient's brain during general anesthesia. This is based on a theory that a patient's hemodynamic responses are an indirect assessment of awareness in that they have a general correlation to brain perfusion. Extensive studies have revealed a close relationship between neuronal activity and regional cerebral blood flow.^{15,16} Many technologies, such as single-photon emission computed tomography, positron emission tomography, and transcranial Doppler sonography, are used commonly in these studies for assessment of the dynamics of cerebral blood flow changes at different states of functional brain activity.^{15,16} Klingelhofer et al¹⁵ reported that "...simple sensory stimulation (visual, acoustic and tactile) and complex mental tasks (viewing of complex pictures, tactile differentiation of objects) changed the blood flow velocity in the basal intracranial arteries." These authors recorded hemodynamic changes taking place in response to modifications of neuronal activity within less than 1 second. The findings of this study suggest that the coupling between alterations of neuronal activity and the regional cerebral blood flow response is mediated by a remarkably rapid mechanism.¹⁵

However, some authors argue that hemodynamic responses are not reliable for assessing awareness.^{9,17} Halliburton¹⁷ disputes the reliability of hemodynamic responses for predicting or quantifying awareness, logically stating that blood pressure and heart rate are not directly indicative of a patient's level of consciousness. Daunderer and Schwender⁹ reported that although the vital signs do not directly measure a patient's level of perception and awareness, they are used, almost exclusively at times, in our judgments. According to Miller,¹⁸ many factors can alter the hemodynamic profile, including β -adrenergic or calcium channel blockers, volume status, patient habits, preoperative ventricular function, and others. At present, hemodynamic values contribute to our evaluation of the patient's level of anesthesia.

Awareness monitoring

- *Bispectral index monitor*: The bispectral index

(BIS) monitor was developed by Aspect Medical Systems, Newton, Mass, to measure patient response to the administration of potent sedative and hypnotic agents. By equipping the anesthesia provider with a BIS monitor that provides a quantitative assessment associated with the hypnotic state of the patient, the risk of intraoperative recall may be decreased.⁴ The BIS, a noninvasive monitor with a sensor that is attached to the patient's forehead, provides a reading between zero (i.e., no brain activity) and 100 (ie, the patient is fully awake). The monitor's assessment is based on a parameter derived from the electroencephalogram (EEG). An algorithm is used to transform EEG data generated from the analysis into the BIS number.¹⁹ The monitor development team recommends certain values to avoid awareness: values between 40 and 60 are suggested by the manufacturer for surgery under general anesthesia.²⁰

This relatively new awareness monitor has received a variety of reviews regarding its effectiveness. One of the studies reported positive results, concluding that use of the BIS monitor will lead to cost containment and prevention of awareness in outpatient surgical patients.²¹ According to this study, the BIS monitor helps with propofol titration that leads to an average 32.6% reduction in the propofol dose and a decrease of mean time until eye opening of patients, without reducing patient satisfaction or causing intraoperative awareness.²¹ According to Glass and Johansen,¹⁹ clinical studies and routine hospital use demonstrate that "...BIS is an effective way to more accurately measure patients' anesthetic states and to customize medication delivery for each patient, resulting in faster, more predictable recovery without the problems associated with inadequate anesthesia."

However, others question the claims made for new technology such as the BIS monitor. Reported cases of awareness despite BIS monitoring convinced the authors of an independent study of BIS efficacy that the usefulness of the monitor is less than 100%.²² Several other authors question the effectiveness of BIS monitoring for the detection of awareness.^{1,22,23} According to Kurehara and coworkers,²³ a patient was able to substantiate claims of complete awareness despite an intraoperative BIS value of 40. In this case, investigators concluded that the BIS may be a helpful indicator of a patient's hypnotic state, but awareness might still occur, even with low BIS values.²³ One recent study, done to evaluate the usefulness of BIS monitoring for preventing recall during intubation, found that BIS values between 50 and 60 before intubation were insufficient to prevent awareness of the stimulation of intubation during propofol or alfentanil anesthesia.²⁰

An additional study was performed to assess the usefulness of BIS monitoring during cardiopulmonary bypass and to focus on preventing awareness. The authors reported that the BIS was the only EEG measurement (other modalities also were tested) that paralleled the patient's sedation level and that increasing body temperature to normal levels during cardiopulmonary bypass considerably elevated the BIS reading.²⁴ As a result, it became difficult to state to any degree of certainty whether a decrease in the BIS reading could be attributed to higher serum propofol levels (from slower circulation during cardiopulmonary bypass) or just hypothermia. Doi et al²⁵ reported that hypothermia significantly decreased BIS levels and that this decrease was to be expected because other EEG parameters also decreased when brain temperature decreased.²⁴ However, a follow-up study by Schmidlin et al²⁴ did not find variation in BIS values in the hypothermic group.

One of the setbacks with the BIS monitor is that it provides different results when different drugs are used. Moreover, such results do not necessarily correlate with the absence or presence of awareness during general anesthesia. A study that compared changes in the BIS value noted on induction of anesthesia with ketamine vs thiamylal found that given the dissociative nature of ketamine anesthesia, use of this drug produced persistently elevated BIS values, which is in direct contrast with values for thiamylal and for other conventional anesthetic agents.²⁶ Consequently, according to this study, the established range of recommended BIS values for surgery does not seem to apply in patients receiving ketamine anesthesia.

A clinical trial was done to assess the value of using a BIS monitor for preventing awareness during nitrous oxide anesthesia. Nitrous oxide at concentrations of 33% and 66% caused no change in BIS readings.²⁷ Barr and colleagues²⁷ reported in their study of the BIS and nitrous oxide use that "...pharmacological unconsciousness-hypnosis can also be reached by mechanisms to which BIS is not sensitive. Thus BIS is a sufficient but not a necessary criterion for adequate depth of anaesthesia or prevention of awareness."

- *Electroencephalogram.* To prevent recollection of events and sensations during general anesthesia, many other monitors have been tested. Electroencephalogram monitoring has been used to monitor EEG waveform changes with the use of anesthetic agents; characteristic EEG waveforms are a direct indication of the patient's level of consciousness. On the basis of this knowledge, both unprocessed and computer-processed EEG recordings have been used to elucidate the patient's level of consciousness during

general anesthesia. However, problems arise because raw, unprocessed EEG signals are complex, easily affected by artifact, and require a dedicated interpreter.¹⁷ Routine use of EEGs as awareness monitors is costly and problematic owing to the complexity of the equipment and the difficulty reading and interpreting the waveforms.

- *Auditory evoked response.* The auditory evoked response monitor is yet another awareness monitor. Fluctuations in the middle latency auditory evoked response (AER) are a sign of changes in anesthetic depth and, to some extent, changes as a result of surgical stimulation.²⁸ One study investigated the presence of and the relationship of explicit and implicit memories to the AER after general anesthesia using nitrous oxide with and without opioid supplementation. Investigators reported a positive correlation between both the AER amplitude and wave latency and the incidence of awareness and memory priming, leading them to conclude that there may be a future use for AER in anesthesia to minimize awareness.²⁹ A follow-up study on the use of AER was conducted to evaluate whether the sensitivity exhibited by this technology could be used for awareness detection.²⁸ A correlation was found between the changes in the wave of the AER and changes in awareness, as measured using the isolated forearm technique. Unfortunately, complete results demonstrated decreased usefulness of this monitor during anesthesia for awareness prevention. No consistent correlation was demonstrated between patient responses and AER readings, although no evidence of memory for intra-anesthetic events was demonstrated either.²⁸ According to Kalkman and Drummond,³⁰ "while the auditory evoked response may provide a good correlation in individual patients with depth of anesthesia for one class of agents (and it appears to do so with volatile agents and propofol), it may offer a much less apparent correlation for others (e.g., narcotics, benzodiazepines) that have less effect on the auditory pathway." The clinical applicability of such findings remains doubtful.

- *Ocular microtremor.* A promising new device under investigation for monitoring intraoperative awareness is the ocular microtremor monitor. It measures a "...fine high frequency tremor of the eyes caused by extra-ocular muscle activity stimulated by impulses emanating in the brain stem."³¹ Bojanic et al³¹ reported that the frequency of eye tremor is reduced in patients whose consciousness is reduced by anesthesia or head injury; therefore, ocular microtremor monitoring might possibly be used to determine depth of anesthesia.

• *Patient state analyzer index.* Recently, Physiometrix (Billerica, Mass) introduced an EEG monitor, the Patient State Analyzer Index, for which the algorithms, like those of the BIS, were derived from multivariate analysis of retrospective data.³² The Patient State Analyzer Index is a "...self-normed QEEG [quantitative analysis of the EEG] derived index of level of awareness designed to predict loss and return of consciousness during anesthesia administration."³³ The first model based on this concept, the PSA 4000, works by processing the changes in the anterior-posterior distribution of the electroencephalogram, using a more extensive electrode sensor than that used for the BIS.³⁴ There currently are few completed studies on the PSA and its effectiveness as an awareness monitor. Gugino et al³³ reported the PSA to be a sensitive measure of the level of awareness during propofol induction. Drover et al³⁵ reported that Patient State Analyzer Index—"directed titration of propofol delivery resulted in faster emergence and recovery from propofol–alfentanil–nitrous oxide anesthesia, with modest decrease in the amount of propofol delivered, without increasing the number of unwanted events."

Ideal awareness monitor

Anesthesia providers are faced with the dilemma of which anesthesia depth monitor most reliably provides sensitive, reproducible information to aid in making clinical decisions. The literature concurs on specific requirements for an ideal monitor.³⁶ First, it should be applicable for any type of anesthesia—intravenous and inhalation alike. Second, the monitor must have enough sensitivity to reliably indicate when a patient may be awake. A high degree of sensitivity is crucial. If it is not exceptionally sensitive, the monitor itself might lead to an increasing number of patients being awake during anesthesia, with the provider relying on the monitor and refraining from increasing the level of anesthesia while the patient remains awake. Specificity is not as important as sensitivity.³⁶ The ideal monitor should not be expensive; otherwise, hospitals and surgery centers would not be able to afford this new technology. Finally, any new technology to monitor the depth of anesthesia should be easy to use. If the awareness monitor is too complicated to use, anesthesiologists would be less likely to use it or to use it correctly. This would lead to misinterpretations that would ultimately jeopardize the patient in terms of awareness prevention. If a device for monitoring the depth of anesthesia were developed that was simple, safe, accurate, and economical, every anesthesia provider would be able to use it as a

standard monitor, much as pulse oximeters have become standard monitoring devices.

Comparing available technology

What technology, already available for monitoring awareness, can be trusted? Which awareness monitor is the best of all of available? The pressure, rate, sweating, and tears score is calculated from changes in the patient's blood pressure, heart rate, sweating, and tear production. However, just as tachycardia is no guarantee of light anesthesia, research disproves observation of clinical autonomic signs, even including the calculation of the pressure, rate, sweating and tears score, as sufficiently valid to indicate or predict intraoperative wakefulness.⁹ At present, an ideal monitor of awareness is unavailable. The isolated forearm technique, discussed earlier, has been regarded as the most reliable tool to detect intraoperative wakefulness.⁹ However, it can be used only for very short periods. The more complex devices (ie, median frequency processed EEG, spectral edge frequency index, and BIS) are important scientific tools for quantifying the central effects of anesthetics under various pharmacodynamic and pharmacokinetic models that try to explain how anesthetics work. Nevertheless, according to Daunderer and Schwwender,⁹ each of these sophisticated monitors seems to be less suitable for indicating intraoperative wakefulness or awareness. There is no technology available that can indicate changes in anesthetic depth from one surgical stimulus to the next. Available awareness monitors reflect patient changes in real time, meaning that anesthesia providers are treating responses to stimuli that have already occurred. Studies continually report the absence of a "golden number" that reliably predicts adequate depth of anesthesia.³⁶ Consequently, any technology facilitating monitoring of the depth of anesthesia must be considered supplemental—not absolute—in the anesthesiologist's judgment of the risk of awareness in a patient.

Conclusion

This extensive literature review on awareness monitors clearly demonstrates that an ideal awareness monitor does not yet exist and that the goal of reliably preventing awareness of patients receiving general anesthesia remains elusive. Anesthesiologists can use other modalities to assure safe anesthesia administration. Prevention of awareness can be accomplished in most cases through premedication with amnesic drugs, administration of more than sleep doses of induction agents, and avoidance of muscle relaxants, unless absolutely necessary.^{3,8,13} Supplementation of volatile

anesthetics with nitrous oxide and opioids to a minimum alveolar concentration of at least 0.8 to 1 (the percentage of delivered anesthetic required to prevent 50% of patients from responding to a surgical stimulus) reduces the chances that a patient will be awake during surgery.³ Similarly, light anesthesia should be supplemented with amnesic drugs to reduce the likelihood of intraoperative awareness.³

Reduction in the incidence of intraoperative awareness can be reduced further by ensuring that all equipment is functioning properly. This means the anesthesia machine should be maintained consistently and checked periodically by biomedical personnel. In addition, the anesthetist should check all equipment before administering each anesthetic. Discussions of awareness prevention with colleagues and in-service meetings on the topic are excellent tools to increase knowledge about prevention. As much as meetings are discounted, they serve their role in reminding people of the issue.

In some cases, anesthetic requirements are increased. Failure to identify those cases may lead to awareness by patients during anesthesia. Other well-known but sometimes forgotten facts include the following: multiple general anesthetics may produce long-term tolerance to subsequent anesthetics; chronic alcoholism, hypernatremia, and hyperthermia increase the minimum alveolar concentration; and drugs that increase central nervous system catecholamine levels (such as monoamine oxidase inhibitors, tricyclic antidepressants, cocaine, and amphetamines) also increase the minimum alveolar concentration of inhaled anesthetics.² The anesthetist can best help prevent intraoperative awareness by being knowledgeable about its possibility and conscientiously trying to prevent it. Most people make mistakes when they forget to be thorough and stop believing that these incidents may occur. Remember, vigilance is intrinsic to anesthesia.

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