Awareness Under General Anesthesia

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Summary: The incidence and causes of awareness under general anesthesia are reviewed, as well as principles of prevention and management. Although intra-operative awareness is rare, occurring in 0.2-0.4% of all operations done under general anesthesia, it causes severe peri-operative and post-operative complications.[1] Moreover, the incidence of awareness is higher in certain patients (e.g. those who are drug-tolerant), and certain procedures (e.g. cardiac surgery). Preventing awareness has been difficult because depth of hypnosis is difficult to measure. However, the bispectral index (BIS) system offers a new way to objectively measure depth of hypnosis. In most cases, BIS is not necessary, but in patients and procedures where the risk of awareness is high, BIS is a useful clinical tool.
Methods: A Medline search was performed, crossing the medical subject headings "Awareness" and "General Anesthesia", and limiting the results to reviews or meta-analyses in English. This search yielded five relevant papers. The reference sections of these papers were searched to obtain other relevant papers.

Introduction

Awareness under general anesthesia occurs in 0.2% to 0.4% of patients.[1] Awareness can be defined as consciousness while under general anesthesia, revealed by explicit or implicit memory of intra-operative events.[2] Awareness during anesthesia can result in the formation of explicit or implicit memory.[2] Explicit (state-independent) memory is expressed as direct recall of an experience. Implicit (state-dependent) memory cannot be stated explicitly in a normal state of consciousness.[3] Implicit memory is displayed as a change in task performance as a result of having direct recall of a stimulus. Both explicit and implicit learning are stored in long-term memory and may lead to post-operative complications such as inadequate pain control, post-traumatic stress disorder, and generalized anxiety/apprehension concerning future operations.[4] Intra-operative experiences during awareness episodes may include hearing sounds or voices, having visual perceptions, and/or sensations of touch or pain. Hearing is the last sense to be obliterated and the first to return, and this accounts for a great deal of awareness. The incidence of awareness under general anesthesia varies because:[2]

1) It is dependent on the diagnostic criteria used to identify awareness (i.e. criteria for explicit and implicit memory are different, and different criteria detect varying degrees of awareness).
2) Different combinations of drugs depress consciousness to a varying extent.
3) The intensity of the noxious stimuli may alter the patient's required depth of anesthesia.
4) Different procedures require different levels of anesthesia.

The most important factor in the incidence of explicit awareness is the nature of the surgical procedure and major differences in rates of explicit memory formation are seen between different types of procedures. Among patients undergoing "routine" surgery, spontaneous recall, as elicited in post-operative interviews, occurs in 0.2% to 0.4% of patients.[2] However, the incidence is much higher in obstetrics and cardiothoracic surgery (up to 23%[5]) and major trauma (43%[6]).

The post-operative interview of the patient is ubiquitous in awareness studies because the absence of recall of events is the only objective criterion for unconsciousness. Below are some examples of questions that may be asked during such an interview:[3]

- What is the last thing you remember before going to sleep?
- What is the first thing you remembered after waking up?
- Is there anything you remember about the period between going to sleep and

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waking up?
- Have you had dreams about your operation?
- What was the worst thing about the operation?

The conventional post-operative interview is the most commonly used tool to detect intra-operative awareness, but it measures only explicit memory. Determining the incidence of all awareness, both implicit and explicit, is problematic, because there is no objective measurement for either. Indeed, even eliciting implicit awareness subjectively is difficult.[1] Many awareness studies include only explicit recall as awareness episodes since little is known about implicit awareness.

However, psychological testing can be used to detect implicit awareness. One useful tool for studying implicit awareness is hypnosis, which mimics the effects of general anesthesia. Implicit memory can often be described explicitly if the patient is placed in a similar state of consciousness as when the stimulus occurred. However, this is still a relatively new technique, and dangers such as false memory syndrome[7] must be avoided.

Causes of awareness, complications, and extent of the problem

Intra-operative awareness occurs because the risk of awareness associated with light anesthesia must be balanced with the higher morbidity and mortality of deeper levels of anesthesia. Unfortunately, there is no clear clinical end-point that can serve as a basis for rational administration of drugs to achieve unconsciousness. Usually, when a patient experiences spontaneous recall of intra-operative events, one of the following has occurred:[8]

1) Anesthetic drugs have been intentionally administered in limited quantities for specific clinical reasons (e.g. hypovolemic trauma patients, intra-operative hemorrhage, etc).
2) A machine malfunction or inadvertent syringe swap has occurred, resulting in an inadequate dose administration.
3) Apparently adequate quantities of anesthetic agents as judged by measurements such as blood pressure, are delivered to a patient who post-operatively describes awareness.
4) The patient has altered pharmacokinetics/ pharmacodynamics (e.g. tolerance).

Although light levels of anesthesia are sometimes medically required (e.g. in trauma patients) unintentional light anesthesia can usually be avoided by the use of good anesthetic technique. The most obvious complication of awareness is the pain and discomfort a patient may feel from undergoing surgery with inadequate analgesia and hypnosis. The following quotation from a patient who experienced awareness during surgery illustrates this point:[3]

> *"The surgeon then made an incision straight down into my stomach. I just started to scream inside my head and prayed that I would not die. I could hear my skin tearing and ripping, and it felt like someone took a blowtorch to my stomach...I felt as if I was trapped in my brain, and screaming and praying to God and telling myself to hold on."*

While not all episodes of awareness are so dramatic, they all can lead to post-operative complications. These include feelings of apprehension, helplessness, anxiety, panic, nightmares and anterograde amnesia. Post-traumatic stress disorder (PTSD) is a serious psychiatric side effect of awareness episodes in some patients. PTSD may develop in persons who have experienced a traumatic event that has involved experiencing, witnessing, or being confronted with actual or threatened death, serious physical injury, or a threat to one's physical integrity.[9] Symptoms include anxiety, irritability, insomnia, repetitive nightmares, depression and preoccupation with death. In addition, patients may develop a fear of physicians and other health care professionals that hinders post-operative treatment and follow-up.

Both conscious and unconscious awareness, leading to formation of explicit and implicit memory, respectively, can cause complications. The negative effects of explicit memory of pain are fairly well known. Up to 90% of patients who experienced and were able to recall pain during an operation suffered after-effects such as daytime anxiety and sleep disturbance.[5] The effect of unconscious awareness (leading to implicit memory formation) on post-operative behavior is not as well studied, and little is known. However, case reports suggest that rude remarks about the patient made intra-operatively may adversely affect the patient's outcome even if the patient has no explicit recall of such remarks.[10] In contrast, some studies show that positive intra-operative suggestion is beneficial, reducing post-operative analgesic requirements and hospital stay.[11]

Prevention of awareness

Several principles of good anesthetic technique are effective in preventing awareness and reducing the harmful effects of awareness on both the patient and physician:[2,8]

1) The patient-anesthetist relationship is critical in reducing pre-operation anxiety and post-operation complications. The patient must be informed about the possibility of awareness and be reassured of the measures that will be taken to prevent it. In some studies, 50% of patients had concerns about being awake.
2) Unintentional light anesthesia should be avoided. Equipment should be checked. Agents with particular amnestic qualities, such as a benzodiazepines or scopalamine, should be given as a premedicant or a supplement to general anesthesia. Intubation, which is very stimulating, requires a relatively deep level of anesthesia. Anticipating difficult intubations is of utmost importance, and patients susceptible to protracted laryngoscopy should be given supplemental doses of induction agents. As well, individual patient physiological variation, such as smoking or alcohol consumption, must be considered.
3) Depth of anesthesia should be assessed. Somatic

Table 1. The Components of Anesthesia, Including Drugs Used and Techniques for Intra-operative Measurement[14]

Component	Example of drugs used to induce/maintain	Measurement technique for level of anesthesia
Anxiolysis	Benzodiazepines (e.g. diazepam)	Not measured intra-operatively
Analgesia	Opioids (e.g. fentanyl)	Autonomic reflexes (HR, BP)
Muscle relaxants	Depolarizing: succinylcholine Non-depolarizing: pancuronium	Somatic reflexes (muscle twitch) Conventional: MAC
Unconsciousness (part of hypnosis)	Hypnotics (e.g. propofol)	Novel: BIS
Amnesia (part of hypnosis)	Benzodiazepines (e.g. diazepam)	Not measured
Non-Specific (inhalational agents)	halothane, enflurane, isoflurane, sevoflurane, desflurane, nitrous oxide	MAC (specific end-tidal concentration measurement)

(movement) and autonomic (heart rate [HR], blood pressure [BP], lacrimation, pupil dilation) reflexes should be monitored. However, no firm relationship has been established between autonomic reflexes and awareness.

4) Muscle relaxants should be avoided or administered in doses that do not produce complete paralysis. Thus, patients who experience awareness can still move.
5) Volatile vs. N_2O-opioid (NO) vs. total intravenous anesthesia: Volatile anesthetics are less associated with awareness. N_2O-opioids should be supplemented with an inhalational agent, because N_2O alone in non-hypoxic mixtures cannot guarantee lack of awareness.

Detecting awareness:

Measuring depth of anesthesia is an important way to prevent awareness. Anesthesia is complex, and Kissin defined its components as:[12]

1) anxiolysis
2) analgesia (with suppression of somatic and autonomic responses to noxious stimulation)
3) hypnosis (which consists of amnesia and unconsciousness), and
4) muscle relaxation

However, this breakdown is somewhat artificial as there is a great deal of overlap in the function of different drugs. The drugs are given in polypharmacy, where the primary action of each drug is different. Polypharmacy lends a great deal of flexibility to the anesthetic regimen, because there is overlap in the function of different drugs. The risk of awareness must always be balanced against the risk of morbidity/mortality.

The various components of anesthesia are measured by different techniques. Ideally, depth of anesthesia should be assessed with respect to each of the specific components described above.[12] Because anxiolysis is more of a pre-operative concern, it will not be considered here in the intra-operative monitoring of depth of anesthesia. Analgesia can be measured by monitoring autonomic reflexes (HR and BP) and somatic reflexes (movement). Muscle relaxation can be measured by muscle twitch. However, these parameters do not measure the component of hypnosis very well.[2,13] Reflex responses are a very crude measure of unconsciousness, because the ablation of reflex responses is believed to occur below the level of the cortex and may therefore be unrelated to level of consciousness. With respect to muscle twitch as a measure of hypnosis, a patient may regain consciousness while still under full muscle relaxation.

Moreover, the mechanism of action of anesthetic agents is not well understood. Hypnosis is usually induced by a fast-acting agent such as propofol, and maintained using volatile anesthetic with or without N_2O. Adjusting the ratios of these agents affects depth of anesthesia. The components of anesthesia, the drugs used for each component, and methods of detection are summarized in Table 1.

Determining how much volatile anesthetic is needed to prevent awareness has traditionally been done using the MAC principle. MAC, or mean alveolar concentration, is a measure of the concentration of gaseous anesthetic in the lungs. MAC was originally defined as the minimum alveolar concentration required to prevent purposeful movement of head or extremities upon surgical skin incision in 50% of patients in the near steady-state situation.[15] MAC multiples are a convenient way to measure how much anesthesia a patient is receiving, but has shortcomings when it is the basis for determining anesthetic depth. First, the assumption is made that at an anesthetic depth where movement is unlikely (1.3 MAC), awareness is also unlikely.[2] However, MAC is based on statistical probabilities, so using it does not provide any objective way to individualize the patient's anesthetic needs. Moreover, the studies that determined MAC values were done on healthy patients. MAC is affected by many factors, such as drug tolerance (from prescription or street drugs), age, and other co-morbidities. Patients who are physiologically compromised or have increased tolerance will have a different depth of anesthesia from a particular MAC than the average patient. Therefore, MAC is a useful starting point for measurement of anesthetic depth, but is affected by many underlying conditions.

Bispectral index (BIS):

Bispectral index (BIS) is the first direct measure of hypnosis.[16] BIS is an empirical measure of patient hypnosis based on the EEG. It is patient and drug-independent and is a combination of power spectrum, bispectrum, and the time domain of the EEG. It is given on a scale of 0 to 100, where 100 is awake and 0 is a flatline EEG. Deep hypnosis corresponds to a BIS of 0 to 40, moderate hypnosis is 40-60, and 70-90 is light sedation.[13]

The proposed benefits of BIS are the following:[17]

1) Effective monitoring for risk of awareness
2) Reduced drug use (more precise titration of anesthetic agents, with better specificity in drug selection and reduced used of hypnotic drugs)
3) Decreased need for post-anesthetic care
4) Facilitation of phase-1 PACU bypass
5) Higher-quality recovery

BIS appears to be a good measure of patient hypnosis. It is not correlated with heart rate and mean arterial blood pressure, indicating that it is independent of these factors. The risk of patient recall is very low when the patient's BIS is less than seventy, and patients show signs of arousal with transient rises in BIS.[13]

BIS seems to correlate best with the effects of hypnotic drugs, whereas opioid analgesics attenuated movement at dose levels that had little effect on the EEG. In fact, the correlation of BIS to the level of sedation is equal to, or better than, using measured drug concentrations.[13] Glass *et al*. demonstrated that for propofol, midazolam, and isoflurane, the correlation between the BIS value and measured effect is independent of the drug administered to induce sedation.[13] However, the EEG signal can be contaminated by electrical activity in muscle, and there is some controversy over whether or not BIS is specific enough for all types of anesthesia.[17,1]

Because the risk of awareness is so low in most situations, BIS is generally not needed. However, it should be used in patients or procedures where risk of awareness is high. Having an objective measurement to guide specificity in selecting and dosage in administering anesthetics may be very useful in patients who are physiologically compromised or drug-tolerant. Titrating the dosage of anesthetics such as N_2O according to the BIS reduces intra-operative awareness while minimizing undesirable side effects. BIS can also be used in the ICU for monitoring sedation.

Management of awareness:

If awareness occurs, good management is essential. The physician should be aware that awareness can happen. The reasons for the incident should be explained to the patient should the need arise. The patient should be reassured that he/she is not irrational or imagining things. The patient should be educated about how to avoid awareness in the future. A good patient-physician relationship is essential to management of awareness, and may also reduce risk of litigation. Lawsuits against anesthetists for episodes of awareness are not uncommon in the United States. The incidence ranges from 1.5% to 7% of all claims against anesthetists.[3]

Conclusion:

Awareness can occur to different degrees and have different manifestations, such as implicit and explicit memory. The complications of awareness can range from pain during anesthesia to post-traumatic stress disorder, which may lead to poor patient compliance during follow-up. Awareness may be a problem in some patients or in situations where light anesthesia is unavoidable (e.g. cardiac surgery, trauma). Detecting awareness has been unsuccessful in the past, but the combination of EEG and computer processing has produced BIS, a useful technology in this problem. Because of the low incidence of awareness, BIS is not necessary in every patient, but is reasonable in patients or situations where awareness is more likely.

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