Review Article

Awareness; why is it important for anaesthetist?

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Abstract
Awareness while under general anaesthesia can be experienced by patients as horrific events that leave lasting mental trauma behind. For some patients it leaves no sequelae but for others can lead to post traumatic stress disorder consisting of complex psychopathological phenomena such as anxiety, insomnia, nightmares, irritability, and depression possibly leading to suicidality. The aim of this review is to evaluate awareness during general anaesthesia in term of its incidence, risk, and possible prevention and management. In case of intraoperative awareness our aim is to gather information from patient and verify the patient’s statement. The patient should be assured that his or her claims are taken seriously and possible explanation should be provided; psychological support to be given.

Key words: Awareness, anaesthesia, brain function monitoring, bispectral index monitoring

1. Introduction
Awareness during anaesthesia is uncommon. The thought of being awake during an operation despite anaesthesia is a worry often expressed by the patients about to undergo surgery. These concerns are not entirely unfounded, for despite the most modern of anaesthetic technology. Awareness is a repeated occurrence. The frequency has gone down sharply almost to tenth of what it was in 1970’s. The most common complaints are auditory perception and loss of motor power. The major causes of awareness are overly light anaesthesia at the time of the episode. Anaesthetic machine malfunction or misuse and increased anaesthetic requirement are much less frequent.

A strategy for avoiding awareness phenomenon under anaesthesia includes training of staff to know about its problem. If awareness occurs despite all preventive measures patient must be given expert disciplinary treatment as soon as after the event.

The term “awareness” during anaesthesia, as used in the anaesthesia literature, implies that during a period of intended general anaesthesia, the brain is aroused by stimuli that are stored in memory for future explicit recall. Patients who experience awareness will recall such experience during a state of inadequate anaesthesia.

2. Classification
a) Explicit or conscious memory.
   b) Implicit or unconscious memory.

Explicit memory- Refers to conscious recollection of previous experiences.
Implicit memory- Refers to changes in performances or behavior that are produced by previous experiences but without any conscious recollection of those experiences.

Incidence: In recent times, the incidence of awareness with explicit recall of severe pain has been estimated at 0.03% of general anaesthetics (1 in 3000).

3. Definitions
Consciousness is a state in which patient is able to process information from his or her surroundings.
Recall is the patient’s ability to retrieve stored memories.

“Awakefulness” has been used to describe patients who are able to react meaningfully to stimuli during general anaesthesia but are not able to recall either the stimuli or their reactions postoperatively. There is evidence of large number of existence of these patients. There is also evidence that wakefulness without explicit recall might be detrimental for the patient but this has not been definitely proven.

4. Contributing factors
- Problems with patient dose requirement variability.
- Problems tolerating side effects of anaesthetic agents.
- Problems detecting the clinical signs of awareness, or light anaesthesia.
- Problems with equipment and drug delivery mechanisms.
5. Causes

Light anaesthesia: Light anaesthesia is required in some cases like caesarean section, patients with minimal cardiac reserve or hypovolemic patients. In these circumstances, consciousness and recall is not surprising because judgments of depth of anaesthesia are not precise. Muscle relaxant also may lead to problem. This is probably the most common cause of awareness, and represents, in a sense, an iatrogenic mishap.8

Increased requirement: Younger age, tobacco, smoking, long term use of certain drugs (alcohol, opiates or amphetamines) may increase the anaesthetic dose needed to produce unconsciousness.9

Machine malfunctions or misuse resulting in an inadequate delivery of anaesthetic, for example- by empty vaporizer or malfunctioning intravenous pump or disconnection of its tubing.

6. Detection of awareness

Intraoperative detection: There are many methods used to monitor depth of general anaesthesia. These methods do not measure learning or possibility for later recall, but consciousness. There is a thorough review of methodology and an update including most recent methods by Bruhn et al.10 and Drummond.11

Clinical signs: Signs are generated through sympathetic activation. Heart rate and blood pressure are routinely used to monitor depth of anaesthesia. It has been shown that these methods are unreliable, meaning that these parameters are not bound to indicate anaesthesia depth correctly.11,12 Signs of increased autonomic activity may be absent during treatment with many drugs like opioids, cholinergic and β adrenergic antagonists, vasodilators and antihypertensive agents.13

Perceptions of awareness:

Most common are

- Sounds of conversation
- Sensation of paralysis
- Anxiety & panic
- Helplessness and powerlessness

Least common:

- Visual perceptions
- Intubation or tube in the throat
- Feeling of operation without pain

Patients of awareness present in following way:

“Suddenly I felt that I could not breath, I was totally alert. I could not feel my chest rising and I had no sensation of air moving in or out. It was a terrifying feeling.”14

Why awareness is important??

It is important because of the distress that patient may experience during the episode itself and because of the long term complications that the episode may cause.

The patients also may be tormented, if they were in an obtunded state, by doubts about whether what they experienced really happened or whether there is something wrong in their minds.15

Of the long term effects, the most important is post traumatic stress disorder (PTSD). Several criteria have been identified in diagnosis of post traumatic stress disorder.16,17

1. Intense fear, helplessness, horror.
2. Recurrent and intrusive recollections of traumatic event, including images, thoughts, perception, or dreams.
3. Persistent avoidance of thoughts, feelings, conversations, or activities associated with the event.
4. Persistent symptoms of increased arousal (not present before the trauma) by two or more of the following
   - Difficulty falling or staying asleep
   - Irritability or outburst of anger
   - Difficulty concentrating
   - Hypervigilance
   - Exaggerated startle response
5. Duration of the disturbance (symptoms in criterion 2-4) is more than one month.
6. The symptoms caused clinically significant distress or impairment in social, occupational or other important areas of functioning.

| Signs of Awareness       | Factors masking the signs                                                                 |
|--------------------------|------------------------------------------------------------------------------------------|
| Tachycardia              | Heart block, β-blockers, hypothyroidism, autonomic neuropathy (eg: diabetes, renal failure) |
| Hypertension             | Heart block, β-blockers, hypothyroidism, vasodilators, epidural analgesia, blood loss, autonomic neuropathy |
| Sweating                 | Anti muscarinic drugs (eg: atropine, glycopyrrolate)                                      |
| Tear production          | Anti-muscarinic drugs, eye tapes/ointment                                                  |
| Movement/grimacing       | Neuromuscular blocking agents, sheets covering the patient                                 |
| Tachypnea                | Neuromuscular blocking agents                                                             |
| Pupillary dilation and reactivity to light | Anti muscarinic drugs, opioids, ocular pathology, eye tape/ointment |

Monitors for measuring depth of anaesthesia:

The most commonly used method of monitoring for awareness is measurement of the patients end tidal volatile agent concentration.14 Assurance of 0.8-1 MAC of exhaled anaesthetic agent is likely to assure lack of awareness.

Modalities of monitoring Depth of Anaesthesia (DoA):

1. Clinical techniques and conventional monitoring
   - Clinical signs
   - Skin conductance
   - Isolated forearm technique
   - Spontaneous surface electromyogram
   - Lower esophageal contractility
   - Heart rate variability

2. Percussion and auscultation
3. Oropharyngeal assessment
4. Measurement of end tidal volatile agent
5. Clinical signs

Table 1: The clinical signs of awareness and factors that mask these signs
2. Spontaneous EEG activity monitors:
   - EEG
   - Bispectral index
   - Entropy
   - Patient state analyzer
   - SNAP index
   - Cerebral state monitor/ Cerebral state index
   - Evoked AEP

Skin conductance:
Goddarch et al found a reasonable correlation with anaesthetic depth in 67 patients. Initially low and increased as anaesthetic depth was increased, reducing again with surgical incision.

Limitation:
Atropine, autonomic neuropathy can reduce the accuracy of this monitoring.

Isolated forearm technique:
Isolated forearm technique has been used to evaluate depth of anaesthesia in the presence of neuromuscular blocking drugs.18,19
   - Originally described by Tunstall
   - A tourniquet is applied to the patient’s upper arm, inflated above Systolic blood pressure-before muscle relaxants.
   - Movement of the arm either spontaneously or to command indicated wakefulness.
   - Some argue that response to command during surgery is a late sign when attempting to prevent awareness.
   - In the past it is used to detect awareness during caesarean section under general anaesthesia.
   - Limitation- Limited time available before patients is unable to move their arm due to tourniquet induced ischemia.

Lower Oesophageal Contractility:
   - Evans et al first proposed it as DoA
   - Now striated muscles of lower oesophagus retain their activity even after paralysis by NMB.
   - Two prime derivatives: SLOC & PLOC

SLOC (Spontaneous Lower Oesophageal Contractility):
   - Induced by stress, emotion in awake individual
   - Detected by pressure transducer.
   - SLOC are under the control of a central oesophageal motility centre, the activity of which is influenced by higher centre.

PLOC (Provoked Lower Oesophageal Contractility):
   - Induced by a rapid inflation in balloon in lower esophagus.
   - Cause smooth muscle contraction
   - Detected by a distally placed transducer
   - SLOC & PLOC reduces in both latency & amplitude under GA
   - Oesophageal contractility index=SLOC rate + PLOC amplitude

Heart rate Variability:
   - Objective measurement of brain stem-mediated autonomic tone that is not affected by any factor other than anaesthetic depth.
   - HRV: 3 components
     - Low-circadian
     - Medium-baroreceptor reflex
     - High- Respiratory sinus arrhythmia.
   - Level of RSA reflects DoA:
     -Requires intact ANS & healthy heart conducting system
     -Surgical stimulation under light anaesthesia elicits more rises in RSA than lightening anaesthesia alone.
   - Limitations:
     -Β blockers, AV conduction abnormalities, sepsis can all affect RSA.
     -Both spontaneous EEG and mid latency auditory evoked responses(MLAEP) offer information about the hypnotic state of patient.10 Their monitoring systems can be subdivided into two groups; those that process spontaneous electroencephalographic and electromyographic activity, and those that acquire evoked responses to auditory stimuli(AEP).19

Bispectral Index Monitor: It is a machine that shows the depth of consciousness of the patient undergoing surgery. The BIS monitor (Aspect Medical systems, Newton, MA, USA) is complex, processed EEG that uses a computer algorithm to assign a numerical value to the probability of consciousness.21

BIS monitoring may reduce but not eliminate the risk of awareness.
1. Failure to respond adequately to changes in the index (i.e. allowing sustained BIS values above the recommended range).
2. Failure to recognize the possibility of misleading values or artifact
3. The possibility that awareness may occur in BIS-monitored patients.

BIS values with specific ranges of 40-60, are reported to reflect a low probability of consciousness under general anaesthesia . However, two case reports revealed patients experiencing intraoperative awareness despite monitored values indicating adequate depth of anaesthesia.21,22
When anaesthesia was guided with BIS, a 77% reduction in the incidence of awareness was found.23

BIS increases suddenly or is higher than expected, then the following things has to be checked:
-Is the sedative sufficient?
-Has the sedation been decreased?
-Is there an increase in stimulation?
-Is there any muscle shivering or patient motion?
-Is the NMBA wearing off?

BIS decreases suddenly or lower than expected, then there
-Has been a decrease in stimulation?
-Has patient recently received NMBA?
-Has there been an increasing in sedation?
-Is the patient sleeping?
-Has the patient recently received analgesic?
-Has there been a sudden significant drop in BP?

It remains unclear as to what BIS actually measures: Awareness? Hypnosis with recall? Delirium? Extent of brain injury, brain function or generalized cerebral electrical activity?

BIS number:
- What the numbers mean?
  0 = no electrical brain activity
  100 = fully awake
- For moderate sedation, aim for range from 60-70, below 60 is associated with a low probability of explicit recall.
- For deeper sedation, aim for range from 40-60. A patient with a BIS value of less than 45 is approaching a deep hypnotic state.
- The BIS algorithm may be altered by preoperative opioids and anticonvulsants use.
- Factors that alter BIS values:
  - Cerebral ischaemia or hypoperfusion
  - Gas embolism
  - Unrecognised hemorrhage
  - Inadvertent blockage of anaesthesia drug delivery.

Bispectral Index Monitors are useful for:
- Helping clinicians to formulate the precise type and optimal dosages of anaesthetic on sedative medication for each patient.
- Regulating anaesthetic drug use.
- Decreasing the incidence of postoperative side effects such as nausea and vomiting.
- Preventing intraoperative awareness.

BIS in children:
- Pediatric EEG reach adult pattern by 5 years
- BIS may be valid after 1 year of age

BIS is non-disruptive, easy to use depth of sedation monitor in children.
- Other uses of BIS:
  - At BIS score 60, LMA can be safely removed in children.
  - BIS reduces overall anaesthetic consumption and hence decreases cost.

Entropy:
- Mathematical concept of quantify non linear dynamics.
- Entropy describes the irregularity complexity or unpredictability characteristics of a signal.
- Entropy of signal has been shown to drop when a patient falls asleep and increase again when the patient wakes up.
- Entropy monitoring is based on requisition and processing of raw EEG and FEMG signals by using Entropy algorithm.
- State entropy-Index range 0-91 (awake)
- Response entropy-Index range 0-100 (awake)

Patient state analyzer:
- PSI is based on the observation that there are reversible spatial changes in power distribution of quantitative EEG at loss of consciousness and return of consciousness. PSI has a range of 0-100. It is a clinically validated measure of effect of anaesthesia and sedation & designed specifically for intra-op and ICU use to monitor patient sedation and drug effect.

Cerebral State Index/Monitor:
- CSI scaled from 0-100
- Energy of EEG is evaluated in specific frequency bands.
- Two energy ratios called α (alpha) and β (beta).

| Perception during intraoperative awareness | Prevalence (%) |
|------------------------------------------|----------------|
| Noises 85-100                            |                |
| Visual sensory impressions 27-46         |                |
| Fear 78-92                               |                |
| Helplessness 46                          |                |
| Details of operation 64                  |                |
| Paralysis 60-89                           |                |
| Pain 41                                  |                |

Post operative detection:
- If a patient complains in the postoperative period of intra operative awareness, the anaesthetist should visit the patient and obtain a detailed account of the patient’s experience. Awareness during general anaesthesia requires questioning the patient postoperatively for recall or recognition of intraoperative agents.
The anaesthetist should establish the perioperative timing of episode and distinguish between dreaming and awareness.\textsuperscript{13} The postoperative interview should be structured.\textsuperscript{9} In a study done by Sebel and colleagues, relevant questions in relation to awareness were asked in the postoperative interview.\textsuperscript{26}

Question asked in the postoperative interview\textsuperscript{27}
1. What is the last thing you remember before you went to sleep?
2. What is the first thing you remember when you woke up?
3. Do you remember anything in between?
4. Do you have any dreams?
5. What was the worst thing about your operation?

**Consequences**

There is no doubt that pain during surgery is the most distressing feature of awareness. It may be:

- Psychological
- Medico legal

Psychological: The after effects of intraoperative recall can be temporary and includes nightmares, sleep disorders and daytime anxiety. In worst cases awareness under anaesthesia leads to post-traumatic stress syndrome (PTSD) with repetitive nightmares, irritability and a preoccupation with death.\textsuperscript{28}

“The pain was like that of a tooth drilled without local anaesthetic-when the drill hits a nerve. Multiply these pains so that the area involved would equal a thumb-print, then pour a steady stream of molten lead into it”.

The quotation is from a physician describing her almost unbearable pain when she was aware during caesarean section.\textsuperscript{29}

Often patient needs consultation from psychiatrist.\textsuperscript{30}

**Medico legal consequences**

There are also medico legal consequences to awareness. Domino et al.\textsuperscript{31} recently analyzed claims from American Society of Anaesthesiologists closed claims project. The median payment for compensation after awareness during anaesthesia in the closed claims project was $18000.\textsuperscript{22}

**7. Prevention of Awareness**

Several recommendations have been published\textsuperscript{32,33,34} on avoiding awareness with recall. Prevention of recall of events during anaesthesia should be feasible in most cases. The methods include:

i. Premedication with benzodiazepines is common in modern anaesthesia management. Their primary goal is, of course, to relieve preoperative anxiety, but as these drugs are also associated with anterograde amnesia it can be assumed that prevention of awareness is also a goal, unfortunately there is no evidence to prove this effect.\textsuperscript{34}

ii. Administer more than a “sleep dose” of induction agents if they will be followed immediately by tracheal intubation.

iii. Training for anaesthetic personnel (training of vigilance, scientific discussion of awareness problem).

iv. No unnecessary use of muscle relaxants

v. Supplement N\textsubscript{2}O and opioids with volatile agents with end tidal concentrations of 0.6 minimum alveolar concentration or more.\textsuperscript{35}

vi. Provide extra monitoring (EEG) for risk patients

vii. Conduct periodic maintenance of anaesthesia machine and its vaporizers and meticulously check the machine and its ventilator before administering anaesthesia.

viii. In cases in which light anaesthesia is deemed necessary, the use of even small doses of amnesic drugs e.g., scopolamine, midazolam, sub anaesthetic doses of ketamine, or inhalation agents should be considered.\textsuperscript{9}

ix. Acoustic protection for the patient; quiet or silence in the operating room; avoid negative comments (negative suggestions).

x. Provide music via headphones

xi. Cobcroft and Forsdick, \textsuperscript{28} after reviewing a series of cases of awareness concluded that in most cases, understanding of the phenomenon and its management by medical personnel was poor or entirely lacking.

xii. Post operative evaluation of the patient (standardized interview)

xiii. Have a plan ready to deal with awareness, and work through it deliberately in a targeted manner. E.g., if it is suspected that the patient is aware; in this situation speak to patient calmly.

xiv. The anaesthetist should establish the perioperative timing of the episode and distinguish between dreaming and awareness.\textsuperscript{13}

**8. Conclusion**

Awareness or recall phenomena, with an incidence currently reported at 0.1% to 0.2%, can in some cases lead to long term neuropsychological disorders. To fail to take a patient complaint seriously is to commit a treatment error. Prognosis is good with early treatment. A basic knowledge of the awareness problem, together with a clear understanding of competent procedure, is a requirement in all medical fields in which consciousness is partially or completely depressed for diagnostic or operative interventions.

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