Tutorial of the Week: Awareness under Anaesthesia

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Questions:

1. The incidence of awareness under general anaesthesia is currently thought to be:

    - 1 to 2 per 10000 people
    - 1 to 2 per 1000 people
    - 1 to 2 per 100 people

2. What questions should you ask a patient post-operatively if you wish to reliably detect awareness under general anaesthesia?

3. True or false – the following are risk factors for awareness under anaesthesia:

    - Difficult airway
    - ASA IV patients
    - Muscle relaxants
    - Neurosurgery
    - Previous history of awareness

4. True or false - regarding depth of anaesthesia monitoring:

    - A BIS reading of 30 to 50 is thought to prevent awareness under anaesthesia
    - The use of depth of anaesthesia monitoring will prevent awareness under anaesthesia
    - The effect of nitrous oxide and volatile anaesthetic agents on BIS readings are the same
    - Forehead galvanometry is an alternative reliable depth of anaesthesia monitor

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Introduction:

Many patients are more afraid of their anaesthetic than their surgery and one of their main concerns is "I won't wake up during the operation, will I doctor?" [1]

There is a growing acknowledgement amongst anaesthetists that the true incidence of awareness is greater than many previously thought. Public awareness of this issue is increasing, with cases involving healthcare problems receiving a higher profile in the media than ever before.

The release of the Hollywood film "Awake" (30 November 2007, MGM) will undoubtedly raise the profile further and we may be faced with increasing numbers of enquiries about the problem from our patients.

This article aims to describe types, incidence, sequelae, contributing factors and management of awareness.

Definitions:

The word anaesthesia comes from the Greek *an* + *aesthesis* meaning "without sensation". Of course, anaesthesia is a continuum whereby consciousness, recall and reflexes – both somatic and autonomic – are gradually lost.

Awareness generally occurs where there is an imbalance between the depth of anaesthesia and the stimulus to which a patient is exposed. In surgery performed under local or regional anaesthesia this may deliberate, although there should not be awareness of the anaesthetised region. Other examples include surgery that involves a "wake-up test", e.g. some spinal or neuro-surgery.

"Explicit awareness" – this refers to the conscious recollection of events, either spontaneously or as a result of direct questioning.

"Implicit awareness" – implicit memories exist without conscious recall but they can alter patients' behaviours after the event.

Incidence:

Large trials have demonstrated that around 1 to 2 per 1000 patients experience some form of awareness [2, 3]. The majority of these do not feel pain although around one third did, be it a sore throat from an endotracheal tube or pain from the incision site. The incidence is halved in the absence of neuro-muscular blockade [3].

One of the difficulties in identifying the true incidence of awareness is the ability to detect it accurately and specifically.

Some patients may dream around the time of surgery and although this is common (3 to 6%), it does not constitute awareness yet may cause diagnostic uncertainty [3, 4]. Patients may also recall sounds or conversations as well as the presence of airway devices still in situ as they regain consciousness. These may also be falsely interpreted as awareness.

On the other hand, true awareness may actually be quite difficult to detect. Whilst some patients are able to report awareness immediately post surgery, others may not realise they were aware until days or even weeks after the event [2]. An acknowledged and well established method of detecting awareness involves the use of a structured Brice interview which asks the following questions [5]:

1. What was the last thing you remembered happening before you went to sleep?
2. What was the first thing you remembered happening on waking?
3. Did you dream or have any other experiences whilst you were sleep?
4. What was the worst thing about your operation?
5. What was the next worst thing?

Variations in the content and timing of such interviews may lead to differing pick-up rates for awareness.

Sequelae of awareness during general anaesthesia:

Awareness can be complicated by a spectrum of psychological symptoms that are dependent upon both the individual patient and their specific experience. These may range from anxiety, fear of surgery and anaesthesia and sleep disturbances to flashbacks, nightmares and post-traumatic stress disorder or depression [6].

There are also consequences for the anaesthetist too. As well as being distressing, there are medico-legal implications. An analysis of the American Society of Anesthesiologists (ASA) Closed Claim Project showed that 1.9% of claims were for awareness and blamed substandard care, specifically deficiencies in drug labelling and administration [7].

Contributing factors:

The causes of intra-operative awareness are, not surprisingly, multi-factorial. They can be placed into the following groups:

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

Patient variability:

Pharmacogenetics can alter people's dose requirements. Both animal experiments and human genome analysis have shown polymorphisms in neurotransmitters and their receptors. The actual implications of this are not known.

Our delivery of inhaled anaesthetic agents is analysed in terms of minimum alveolar concentration (MAC). MAC is defined as the minimum alveolar concentration of vapour in the lungs, at one atmosphere, required to prevent a motor response to a standardised surgical stimulus in 50% of patients. It is one of the measures that we often use to help determine depth of anaesthesia and useful because it allows us a real-time measurement of effect site concentration (assuming the end-tidal measurement equates to the brain value).

There are a few problems with the use of MAC to help with preventing awareness. The value is a median one and therefore 50% of patients may still move in response to the surgical stimulus. In addition, MAC is refers to the

concentration required to prevent a motor response – predominantly a spinal reflex. It does not refer to a patient's level of arousal and therefore the likelihood of them being aware; patients lose consciousness at levels well below 1 MAC. MAC was determined in un-premedicated patients in their 30s and 40s.

MAC is clearly only applicable to inhaled agents. An equivalent concept of minimum inhibitory concentration (MIC) has been proposed for intravenous agents but studies have shown an even greater inter-patient variability for dosage requirements with these agents and this is compounded by the fact that we have no means of measuring real-time blood concentrations whereas it is possible to monitor end-tidal concentrations of inhaled agents. These are two of the reasons that intravenous anaesthesia can be associated with a greater risk of awareness.

Many factors alter MAC. It is decreased at the extremes of age, decreasing gradually above the age of 1, at a rate of approximately 10% per decade of life[8]. It is also decreased by hypothermia, hypocapnia, hypothyroidism and pregnancy, as well as by other sedatives, analgesics and regional anaesthesia. Conversely, it is increased by the hyperthermia, hyperthyroidism, anxiety and the chronic use of certain drugs (sedatives, recreational drugs and enzyme inducing agents such as nicotine and alcohol).

Identification of such factors pre-operatively can reduce the risk of intra-operative awareness. This is the recommendation of a 2006 ASA Task Force [9] and patients are advised of this fact in the Royal College of Anaesthetists' patient information leaflet [10].

Problems with anaesthetic side effects:

It is well known that general anaesthesia may cause cardiovascular depression by decreasing systemic vascular resistance as well as by direct myocardial depression. As a result, there are certain types of surgery during which anaesthetic doses may be deliberately reduced in the interests of safety, in order to maintain blood pressure.

These typically include cardiac surgery, emergency or trauma surgery and Caesarean section. In the latter, there are also concerns about the effects of general anaesthetic agents upon the unborn, and often compromised, child.

Clinical signs of awareness:

In the absence of specific depth of anaesthesia monitoring, cardiovascular parameters are usually relied upon to gauge adequacy of anaesthesia. It is assumed that light anaesthesia will manifest itself by causing hypertension and tachycardia as well as other signs of sympathetic nervous system stimulation, such as lacrimation, papillary dilatation and sweating.

It is important to put these variables into the context of the specific patient and their anaesthetic. There are many factors that may cause blunting of these responses and therefore delay or prevent the suspicion of inadequate anaesthesia.

Many of these are pharmacological. Anti-cholinergic medications may dry secretions such and reduce sweating or lacrimation as well as causing mydriasis. Opioids can cause meiosis. Many anti-hypertensive and anti-anginal medications may reduce a patient's ability to mount a tachycardic and hypertensive response to stress (e.g. β-blockers, calcium channel antagonists, ACE-inhibitors). The presence of an epidural can also lead to relative hypotension as can hypovolaemia from any number of causes.

There are a few disease conditions that may similarly cause uncertainty. Patients with hypothyroidism, autonomic neuropathy and limited cardiac reserve may have these cardiovascular responses masked.

Equipment and drug delivery mechanisms:

The delivery of volatile anaesthetic agents can obviously be compromised at a number of points such as inadequately filled vaporisers, failure to turn the vaporiser on and breathing system disconnections.

Similarly, TIVA delivery can be interrupted by blockages or "tissuing" of intravenous cannulae, disconnection of infusion lines or pump malfunction / misuse.

Many of these problems would be rapidly detected by default alarms (minute ventilation / airway pressure, "pump not infusing", "on hold" or occlusion alarms) but many would not. Many monitoring devices do not alarm for low end-tidal anaesthetic concentrations unless specifically set to do so and an infusion pump can happily deliver anaesthetic agents to the floor the wrong way past a three-way tap junction. This emphasises the importance of thorough checking of equipment and machinery as well as continuous vigilance throughout the case.

Managing awareness:

Pre-operative:

A thorough history and examination can identify potential risk factors for awareness. Specific patient factors may include a history of awareness, substance abuse (opioids, benzodiazepines), chronic pain with long term opioid use, limited cardiovascular reserve and a history of difficult intubation or anticipated difficult intubation [9]. Cardiac, Caesarean, emergency and trauma surgery have already been described as higher risk of awareness [9]. Lastly, the anaesthetic technique may also increase the risk of awareness if muscle relaxants are used or TIVA, in certain circumstances (e.g. rigid bronchoscopy) [9].

Having identified risk factors it may be appropriate to discuss this with the patient and it may be prudent to pre-medicate with benzodiazepines.

Intra-operative:

Benzodiazepines can be used at induction of anaesthesia to help reduce the incidence of awareness, particularly if difficulty is anticipated at intubation.

Titrating anaesthesia to blood pressure and heart rate may increase the risk of awareness. If anaesthetic agents are causing vasodilatation it should ideally be treated with a vasopressor or an inotrope rather than continually reducing the anaesthetic concentration.

It may also be worth considering using depth of anaesthesia monitoring when available (see below).

Despite precautions and good technique, some cases of awareness will still occur. It is therefore important that anaesthetists' records can stand up to scrutiny in a court of law. In particular, it should be clear when drugs were administered and in what dose. It should also be clear what forms of monitoring were used.

Post-operative:

If a patient complains of awareness, it is important to visit them and identify exactly what has happened. It may be necessary to differentiate between dreams or recall of events on emergence and genuine awareness.

Denying the patient's version of events may contribute to a worse psychological outcome for them so it is important to apologise for their experience and express

some sympathy. It should go without saying that detailed written records of these processes are vital.

The patient should receive adequate psychological support afterwards not only in the form of a regular visit by the anaesthetist but with the referral for counselling or psychotherapy if necessary. The patient's general practitioner should also be informed so that this information can be taken into account when future treatments may be planned.

Depth of anaesthesia monitoring:

One way to try and reduce the incidence of awareness is to use some form of depth of anaesthesia monitoring. For most anaesthetists, this takes the form of relatively continuous monitoring of physiological variables – requiring the continuous presence of an anaesthetist. However, as previously alluded to, this is not 100% reliable and does not have the sensitivity or specificity required.

This can be increased by the use of monitoring of end-tidal concentrations of inhaled anaesthetic agents. Despite the fact that MAC refers to a motor response, it is widely accepted that the risk of awareness is dramatically reduced if a patients are exhaling 0.8 to 1.0 MAC.

Specific "depth of anaesthesia monitors" are also available and they can broadly be classified as those that are based upon the EEG and those that are not.

EEG based monitors:

Anaesthetic agents suppress the normal EEG pattern is a dose related manner. A conventional EEG is complex and requires specialist interpretation. Therefore, a number of EEG processing devices exist on the market which attempt to analyse the raw EEG's component waveforms and present that data in a more easily interpretable way – either graphical or numerical.

One of the most well known is the BIS (Bi-spectral Index, Aspect Medical) monitor, which calculates and presents a single number on a scale of 0 to 100 (no activity to an awake patient). 40–60 is accepted as the range that corresponds to general anaesthesia. This number corresponds to the hypnotic state of the patient but not to motor responses to stimuli which are partially mediated at a spinal level.

Whilst processed EEG devices monitor cerebral function – which may be more closely related to awareness than MAC – there are limitations. At present, the devices are not widely available in many institutions in the UK. As with all

electrical signals, interference may occur, particularly in the electrically noisy theatre environment. The EEG is not suppressed by nitrous oxide whilst ketamine increases electrical activity.

In addition, BIS has been marketed as a tool which enables lower usage of anaesthetic agents, which in turn may lead to faster wake up times with shorter and better quality recovery stays and subsequent cost reductions [11, 12]. As yet, this has not been shown to translate into other outcomes such as a faster discharge from hospital. Some have expressed concern that the use of such monitoring may encourage lighter anaesthesia and actually increase the risk of awareness.

So does this sort of monitoring actually reduce awareness? There are many studies in the literature with varying conclusions. Some fail to detect any awareness at all whilst others demonstrate a reduction in awareness with depth of anaesthesia monitoring [13].

An interesting recent publication randomised 2000 high risk patients to receive either BIS guided anaesthesia (targeted range between 40 and 60) or end-tidal guided anaesthesia (maintained above 0.7 MAC – actually targeted range 0.7 to 1.3 MAC) [14]. The study showed an identical incidence of awareness in both groups leading the authors to suggest that their findings did not support the use of BIS monitoring in standard practice.

Another interpretation of this is that the use of an end-tidal guided anaesthetic (which was difficult in 74% of these patients) may actually be an effective method of reducing awareness and this may actually be a change in practice in itself, in certain groups of patients.

Other types of monitors:

Evoked electrical potentials have their uses in medicine. It is possible to detect nervous system activity as a result of central stimulation by measuring auditory or somatosensory potentials but these are little affected by anaesthetics and they are more commonly used to detect nervous system tissue integrity during spinal or neurosurgery.

The isolated forearm technique, measurement of oesophageal motility and forehead galvanometry are experimental techniques that are relatively unreliable and are now confined to history.

Summary:

Anaesthetic awareness is a rare but potentially devastating complication of general anaesthesia. It may not be possible to prevent every case from happening, but it is possible to identify high risk cases and modify anaesthetic technique accordingly. For all other cases, prevention of awareness requires meticulous attention to detail to eliminate errors.

Whilst depth of anaesthesia monitors that process EEG signals may help to reduce the incidence of awareness, they are not widely used in this country and the evidence is still not conclusive. This does not mean that they are not useful but it may be that a strict protocol driven anaesthetic delivery may be as good.

Answers to questions:

1. The incidence is thought to be 1 to 2 per 1000 patients.

2. The Brice Questionnaire is acknowledged to be the accepted tool for detecting awareness post operatively (see the text for the questions themselves).

3. All of the options are risk factors for awareness with the exception of neurosurgery.

Managing a difficult airway may interrupt delivery of inhaled anaesthetics and / or force the anaesthetist to rely on intravenous agents – which are difficult to monitor – at a time when stimulation may be high. This applies to rigid bronchoscopy as well. Poor physiological reserve may lead to the deliberate under-dosing of anaesthesia in an attempt to maintain blood pressure. Some studies have shown an increased incidence of awareness in the presence of neuromuscular blockade.

4. The recommended BIS reading for "anaesthesia" is 40-60 although awareness has been recorded within this range. Galvanometry is one of many historical or experimental methods of detecting awareness.

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