Awareness under general anaesthesia

Awareness under anaesthesia is a rare but important phenomenon which has become a source of fear – and of fascination – to the public and anaesthetists alike. This article discusses the incidence, aetiology, sequelae and prevention of awareness.

Accidental awareness under general anaesthesia ('awareness') has received a great deal of attention from researchers over the last few years, the most recent example being a national audit. This interest has been stimulated in part by news and other media bringing it to the attention of the public (such as the 2007 film *Awake*), but also by a greater understanding of the psychological and medicolegal consequences of awareness. Furthermore, new technologies which purport to measure the 'depth' of anaesthesia have brought hope that many cases of awareness could be prevented, although their efficacy remains uncertain. This article examines recent evidence on this topic and considers how awareness is relevant to anaesthetists and non-anaesthetists alike.

Definitions

Awareness is defined as an experience of consciousness under general anaesthesia, which can be recalled after emergence (also known as awareness with explicit memory). Patients may recall intraoperative events spontaneously or after specific questioning, and recall can occur immediately or as late as 1 month after the operation (Goddard and Smith, 2013). Awareness experiences range from vague recollections of sounds, to full consciousness and pain during surgery. The feeling of being conscious but paralysed and unable to communicate is distressing, even if there is no pain.

Research on awareness is difficult for several reasons: first, there is no objective indicator of consciousness, therefore its detection is retrospective and based on patient reports. Second, awareness can occur without memory formation at all. For example, in one study, patients under a light plane of general anaesthesia were given verbal commands to squeeze an observer's hand. Sixty-six per cent of patients responded unequivocally to the commands, but only 24% of those patients who responded could recall their experiences when interviewed after recovery (Kerssens et al, 2003). Third, awareness with explicit recall must be distinguished from implicit memory, and from dreams. Implicit memory refers to experiences that cannot be consciously recalled but still cause changes in behaviour or performance. For example, patients who are presented with the word 'pension' (usually played to them via headphones) while anaesthetized would be more likely to complete the stem 'pen–' as 'pension' rather than 'pencil' or 'peninsula' after waking (Ghoneim, 2000).

Awareness with implicit memory is of unknown clinical significance; in any case it is difficult to measure. Consequently, research has focussed on awareness with explicit recall. Nevertheless, obtaining an accurate estimate of the incidence of awareness has been a challenge.

Incidence

The reported incidence of awareness varies greatly – as much as one order of magnitude – between different studies. Several studies in which patients were interviewed in the recovery unit and up to 30 days later have found 1–2 cases of awareness per 1000 general anaesthetics administered (Sandin et al, 2000; Sebel et al, 2004). Interviews consisted of a modified 'Brice protocol' *(Table 1)* that was conducted after recovery, then repeated in follow-up sessions up to a month after the surgery.

However, data from a nationwide audit, released in September 2014, suggest a much lower incidence of awareness than that found in earlier studies. The fifth National Audit Project (NAP5), the result of a collaboration between the Royal College of Anaesthetists and the Association of Anaesthetists of Great Britain and Ireland, aimed to definitively answer several questions: how many patients spontaneously reported awareness in the year 2012, to whom did patients report their experiences, and what are the most important risk factors for awareness?

NAP5 is the largest study on awareness to date, with 471 patient reports of awareness gathered from all public hospitals in the UK and Ireland. These reports were assessed by a multidisciplinary panel and classed according to their likelihood of representing a true case of awareness

Table 1. Modified Brice protocol

What was the last thing you remember before going to sleep?
What was the first thing you remember after waking up?
Can you remember anything between these periods?
Did you dream during your operation?
What was the worst thing about your operation?

From Sebel et al (2004)

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ness (Pandit et al, 2014a). Disregarding all classes except 'certain' and 'probable' gave an incidence of one case of awareness per 25 000 general anaesthetics administered; far lower than most earlier studies of awareness (Pandit et al, 2014b). This lower incidence may be the result of the methodology of NAP5, which relies on spontaneous patient reports, rather than actively interviewing patients after emergence from anaesthesia.

The significance of this marked disagreement between studies is controversial; some claim that NAP5 is unable to detect awareness which the patient does not report spontaneously – for example as a result of fear of appearing ungrateful – but which may cause psychological harm (Ghoneim, 2007; Avidan and Mashour, 2013b). Others question the significance of awareness in such cases (Irwin and Schraag, 2013).

The SNAP-1 audit will be another source of information about the incidence of awareness in the UK. Postoperative outcomes reported by patients (including awareness incidents) were collected over a 2-day period in May 2014.

Risk factors

Although most studies are underpowered to define risk factors with certainty, there is some agreement in the literature. NAP5 has strengthened some of these assumptions and qualified others; nevertheless, inadequate delivery of anaesthetic agent is probably the most significant risk factor (Ghoneim et al, 2009), and this may occur intentionally (e.g. in obstetric surgery) or unintentionally. The major risk factors are listed in *Table 2*.

The authors of NAP5 have added an intriguing new take on the discussion of awareness by emphasizing the importance of neuromuscular blockers in awareness. Although neuromuscular blockers were used in 46% of general anaesthetics, they featured in 97% of awareness cases reported to NAP5. Indeed, the authors suggest that awareness should now be viewed as 'cases of unintended awareness during neuromuscular block' rather than during anaesthesia in general (Pandit et al, 2014b). This is in keeping with earlier studies; Sebel et al (2004) found the rate of awareness in patients given muscle relaxants to be nearly double that in patients to whom they were not given. This is probably the result of reduced patient movements which would normally signal an anaesthetist to increase the delivery of anaesthetic. Additionally, muscle relaxants can make awareness more distressing by producing paralysis, even if no pain is felt (Ghoneim et al, 2009).

Table 2. Risk factors for awareness

Inadequate anaesthetic	Equipment misuse	
	Equipment failure	
	Difficult intubation	
	Hypovolaemia	
	Relating to surgery type	Cardiac
		Obstetric
		Trauma
Neuromuscular blocking agents		
Increased anaesthetic requirements	Chronic alcohol or opiate abuse	
	Obesity	
	Younger patient	
	Female patient	
History of awareness		
Total intravenous anaesthesia (unclear)		

Obstetric and cardiac surgery carry a high risk of awareness. When general anaesthesia is used in obstetrics, it is generally at a low dose to reduce the depressant effects of the anaesthetic agent on the newborn. Cardiac surgery also uses a low dose of anaesthetic, to reduce its effect on myocardial contractility. Similarly, hypovolaemic patients are often given a lighter plane of anaesthesia to avoid haemodynamic compromise. Awareness can also occur if intubation takes longer than anticipated and the dose of anaesthetic is not increased to make up for the delay (Ghoneim, 2007).

A review of 271 cases of awareness published from 1950 to 2005 suggested that patients with a history of awareness are at higher risk of awareness in subsequent surgeries (Ghoneim et al, 2009). Although this could be caused by confounding factors, such as obesity, a study which controlled for such risk factors found the relative risk of awareness to be five times greater in patients with an awareness history compared to controls (Aranake et al, 2013). This could be the result of inherited genetic factors causing resistance to anaesthetic agents. Alternatively, an episode of awareness could, in itself, increase future anaesthetic requirements by an unknown mechanism, and thus predispose to awareness in future.

Total intravenous anaesthesia

Total intravenous anaesthesia is a technique in which intravenous rather than inhaled agents are used for maintenance of anaesthesia. It boasts the advantages of a faster recovery and less postoperative nausea and vomiting compared to inhalation anaesthesia. However, some investigators have suggested that total intravenous anaesthesia carries a higher risk of awareness than inhalation anaesthesia, notably Errando et al (2008) and Xu et al (2009). This is confirmed by NAP5, with the caveat that most cases were caused by an inadequate rate or dose of infusion (Pandit et al, 2014b). Others have found no association (Ghoneim et al, 2009).

Total intravenous anaesthesia could confer an increased risk for three reasons. First, the variation in dose requirements between patients may be greater for intravenous agents compared to inhaled agents (Hardman and Aitkenhead, 2005). Second, intravenous anaesthesia is more susceptible to equipment failure or misuse, for

example by dislodgement of the cannula. Third, it is not currently possible to monitor the concentration of intravenous agents in real time, which may result in inadequate drug delivery. Inhalation anaesthesia has the advantage that the concentration of exhaled agent can be monitored (discussed below).

Sequelae

Psychological

A prospective study by Samuelsson et al (2007) of 2861 patients who received a general anaesthetic found 46 cases of awareness. During their awareness experience, nearly two thirds of these patients suffered an acute emotional response (such as fear or helplessness) and nearly half experienced pain. One third reported late psychological symptoms, such as anxiety, nightmares and flashbacks. One patient was diagnosed with post-traumatic stress disorder after the awareness incident.

Somewhat encouragingly, this study found a lower prevalence of late psychological symptoms (33%) than had previously been suggested by earlier studies (as high as 89%) which were retrospective and therefore subject to selection bias. This is supported by data from NAP5, which indicate that 41% of incidents of awareness caused moderate-to-severe long-term harm (Cook et al, 2014). However, post-traumatic stress disorder remains a well-recognized complication of awareness. Awareness can also cause phobias and chronic fear associated with surgery or health care in general (Bruchas et al, 2011).

Medicolegal

Between 2005 and 2007, awareness accounted for 9% of all anaesthesia-related claims made to the NHS Litigation Authority. Eighty-seven per cent of claims for awareness resulted in a payout, with an average cost of £32 680 per successful claim (Mihai et al, 2009).

Prevention

Assess risk factors

Controllable risk factors should be avoided if possible. Equipment must be checked to ensure that it is functional, and education of anaesthetic trainees may prevent awareness events arising from simple errors. Anaesthetic dosing should be increased if a patient is anticipated to have increased anaesthetic requirements (*Table 2*).

Drug administration

A small dose of benzodiazepine pre-surgery does not prevent awareness but may inhibit formation of memories during surgery. Muscle relaxants should be avoided if possible.

Physical signs

Purposeful responses to surgical stimuli or voluntary movements can indicate that awareness is occurring or is imminent, and that anaesthetic delivery should be increased. Autonomic responses to surgery – such as hypertension, tachycardia or pupillary dilatation – are unreliable indicators of consciousness (Ghoneim, 2000).

End-tidal anaesthetic gas monitoring

Under inhalation anaesthesia, the concentration of the exhaled anaesthetic agent is monitored as part of routine practice and acts as a proxy for the amount of anaesthetic delivered to the patient. A certain minimum exhaled concentration is believed to inhibit the formation of memories and therefore prevent awareness (Avidan et al, 2011). By setting an alarm at this concentration, anaesthetists can be alerted to increase anaesthetic delivery.

Depth of anaesthesia monitoring

In the last decade, new technologies have allowed anaesthetists to monitor the level of consciousness in a more objective way, based on cortical electrical activity. There are currently two types of depth monitors: those which use algorithms to process spontaneous electroencephalography signals (Bispectral Index, Covidien, Mansfield, MA; Narcotrend, MonitorTechnik, Bad Bramstedt, Germany; E-Entropy, GE Healthcare, Little Chalfont, UK)(*Figure 1*), and those which measure electrical activity in response to auditory stimuli (aepEX, Medical Device Management Ltd, Braintree, UK). Bispectral index is the most studied depth of anaesthesia monitor. Bispectral index calculates a dimensionless figure from 0 to 100 indicating the probability of consciousness (from 0 = flat trace to 100 = fully conscious).

Bispectral index is also the most widely used monitor. Despite a 2007 Cochrane review (Punjasawadwong et al, 2007) finding that the use of bispectral index significantly reduces the incidence of awareness compared to

Figure 1. One of the authors attached to the E-Entropy system (GE Healthcare, Little Chalfont, UK). Screen shows calculated baseline consciousness derived from electroencephalography in white and a fast-reacting figure based on frontalis muscle activity in red.

monitoring physical signs, a later study found no difference in the incidence of awareness between using bispectral index compared to setting an end-tidal anaesthetic gas alarm (Avidan et al, 2008).

Depth of anaesthesia monitors may be useful in certain situations. For example, they could be used in total intravenous anaesthesia to titrate drug delivery to consciousness level, in the absence of any method to calculate real-time intravenous drug concentration. Indeed, three studies have supported the use of bispectral index in patients given total intravenous anaesthesia (Myles et al, 2004; Zhang et al, 2011; Mashour et al, 2012). However, evidence does not appear to support the use of bispectral index in high-risk patients, unless they are also given total intravenous anaesthesia (Avidan and Mashour, 2013a). Depth monitors could also be used with inhaled anaesthetics to titrate the dose to individual patient requirements, thereby decreasing anaesthetic side effects. In one study, bispectral index monitoring reduced the dose of anaesthetic used and reduced the risk of postoperative delirium and postoperative cognitive dysfunction (Chan et al, 2013).

National Institute for Health and Care Excellence (2012) guidelines have recommended the use of depth of anaesthesia monitors in high-risk patients and those receiving total intravenous anaesthesia. However, this guidance has been controversial (Pandit and Cook, 2013) and the use of electroencephalography monitoring is limited in the UK; NAP5 revealed that only 2.8% of general anaesthetics involve any form of depth monitoring (Pandit et al, 2014b).

Conclusions

Awareness under anaesthesia has become less common since the mid-20th century, however, large prospective studies have estimated its incidence at approximately 1–2 patients per 1000 general anaesthetics administered. Although this does not reflect the experience of most anaesthetists, the clinical relevance of unreported cases is unknown. Awareness is associated with several risk factors, most of which are related to an inadequate dose of anaesthetic agent and therefore are relatively easy to circumvent. Recent technological advances in electroencephalography processing has created the hope that the incidence of awareness could be drastically reduced; unfortunately the efficacy of depth of anaesthesia monitors is unclear. The fifth National Audit Project has produced many detailed and wide-ranging recommendations, beyond the scope of this article, which may help to reduce the incidence of awareness (full report available at www.nationalauditprojects.org.uk/NAP5_home).

KEY POINTS

- Awareness is an uncommon but distressing phenomenon which is preventable in most cases.
- Patients may not recall an awareness event for months, and may not report it at all unless directly questioned.
- Most awareness is avoidable by careful pre-assessment of risk factors, then ensuring that adequate anaesthetic agent is delivered.
- The efficacy of depth of anaesthesia monitors is unclear.
- All clinicians should be responsive to patient reports of awareness, and should arrange follow up for therapeutic and medicolegal purposes.

Future work

Greater understanding of the neurobiology of consciousness and memory may help to refine depth of anaesthesia monitors and overcome some of their limitations. For example, in all depth monitors there is a delay of 30 seconds to 2 minutes before the figure updates to reflect a change in conscious level. Awareness could occur during this period. Future work in neuropharmacology could produce new anaesthetic agents, or new methods of delivering anaesthetic agents, which could reduce the risk of awareness (see Mashour et al, 2011).

Relevance to non-anaesthetists

Patients presenting to any specialty may have experienced awareness, and this may affect their mental health as well as their engagement with clinicians. It is important that any claims of awareness are taken seriously and are documented meticulously, as recall may not occur until a month or more after the event. More importantly, these patients may require psychological or psychiatric treatment. Finally, awareness may result in claims for litigation, which have a high likelihood of success. **BJHM**

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