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Review Article

Accidental awareness during general anaesthesia – a narrative review

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Summary

Unintended accidental awareness during general anaesthesia represents failure of successful anaesthesia, and so has been the subject of numerous studies during the past decades. As return to consciousness is both difficult to describe and identify, the reported incidence rates vary widely. Similarly, a wide range of techniques have been employed to identify cases of accidental awareness. Studies which have used the isolated forearm technique to identify responsiveness to command during intended anaesthesia have shown remarkably high incidences of awareness. For example, the ConsCIOUS-1 study showed an incidence of responsiveness around the time of laryngoscopy of 1:25. On the other hand, the 5th Royal College of Anaesthetists National Audit Project, which reported the largest ever cohort of patients who had experienced accidental awareness, used a system to identify patients who spontaneously self-reported accidental awareness. In this latter study, the incidence of accidental awareness was 1:19,600. In the recently published SNAP-1 observational study, in which structured postoperative interviews were performed, the incidence was 1:800. In almost all reported cases of intra-operative responsiveness, there was no subsequent explicit recall of intra-operative events. To date, there is no evidence that this occurrence has any psychological consequences. Among patients who experience accidental awareness and can later remember details of their experience, the consequences are better known. In particular, when awareness occurs in a patient who has been given neuromuscular blocking agents, it may result in serious sequelae such as symptoms of post-traumatic stress disorder and a permanent aversion to surgery and anaesthesia, and is feared by patients and anaesthetists. In this article, the published literature on the incidence, consequences and management of accidental awareness under general anaesthesia with subsequent recall will be reviewed.

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Introduction

Unintentional or accidental return of consciousness during intended general anaesthesia represents a failure to achieve the primary aim of anaesthesia, and is thus a serious complication of general anaesthesia that is feared by patients and anaesthetists alike.

It is difficult to define and describe consciousness. Although thought of as a binary phenomenon, many

now consider that consciousness may occur during one of the graded spectra of states [1–5]. Similarly, anaesthesia is also difficult to define, and is more commonly defined by what is absent, in particular, with reference to attributes that are desirable or undesirable. The surgeon usually wants the absence of movement (immobility), the patient does not want to be conscious (what is described as 'hypnosis' in anaesthetic parlance) and does not want to remember intra-operative events (amnesia); and generally, the surgeon and anaesthetist want to avoid haemodynamic responses to pain (for which analgesia or antinociception is required).

In the anaesthetic literature, an episode of unintentional or accidental consciousness during intended general anaesthesia has been referred to for many years as 'awareness,' although more recently the term 'accidental awareness during general anaesthesia' (AAGA) has become popular [6]. Different grades of anaesthetic awareness can be described and classified according to the method of discovery and consequences of an episode of 'awareness' (Table 1). For the purposes of this review, the term AAGA will refer to AAGA with subsequent explicit recall of intra-operative events, whether the experience is spontaneously reported by the patient, or detected by direct questioning or prompting.

Intra-operative return of consciousness is not always clinically obvious. Traditionally described indicators of awareness and distress, such as sweating and signs of sympathetic activation, are not always present, and when present, they are not specific. Likewise, although movement in response to noxious stimuli may be caused by inadequate anaesthesia, this sign is not sensitive or specific for consciousness. Patients who have received muscle relaxants are unable to move in response to noxious stimuli, whereas in non- (or partially) paralysed patients, movement is commonly the result of reflex activity [7–9]. Studies using the isolated forearm technique (IFT) have shown that a high proportion of patients respond to command during supposed adequate anaesthesia, and of these patients, most do not move spontaneously, even during a noxious stimulus such as laryngoscopy [10–13]. In some situations, such as after administration of high doses of opiates, patients who have not received neuromuscular blocking agents (NMBAs) may not move during surgery, despite later providing convincing evidence of AAGA [14].

Intra-operative use of an electroencephalogram (EEG)-based depth of anaesthesia monitor may give some indication that anaesthesia is inadequate, but

Table 1 Wang's classification of intra-operative cognitive states, presented with permission from John Wiley and Sons [58].

Intra-operative states			Postoperative state		
			Immediate	Late (> 1 month)	Descriptor
0	Unconscious	No signs; no response to command	No recall	No recall	Adequate anaesthesia
1	Conscious	Signs/response to command	No recall	No recall or emotional sequelae	Intra-operative wakefulness with obliterated explicit and implicit memory
2	Conscious; word stimuli presented	Signs/response to command	No explicit recall, implicit memory for word stimuli	No explicit recall; implicit memory for word stimuli but no emotional sequelae	Intra-operative wakefulness with subsequent implicit memory
3	Conscious	Signs/response to command	No recall	PTSD/nightmares but no explicit recall	Intra-operative wakefulness with implicit emotional memory
4	Conscious	Signs/response to command	Explicit recall with or without pain	Explicit recall but no emotional sequelae	Awareness but resilient patient
5	Conscious	Signs/response to command	Explicit recall with distress and/or pain	PTSD/nightmares with explicit recall	Awareness with emotional sequelae

PTSD, post-traumatic stress disorder.

once again, the output of such systems is not highly sensitive and specific for consciousness [15, 16].

As mentioned, several studies have sought to detect awareness in 'real time' using the IFT. Some of these have shown surprisingly high incidences of intra-operative responses to command (up to 40%) [4]. In these studies using the IFT, almost none of the responsive patients had postoperative recall of intra-operative events. This is probably because most anaesthetic agents are potent amnesics, even when present in sub-anaesthetic doses [4, 17]; it is, however, also possible that responsiveness during the IFT represents an intermediate state, which Pandit has termed 'dysanaesthesia' [3]. To date, no studies have indicated any strong evidence that awareness without recall has important psychological or other consequences, and so the significance of responsiveness to command with the IFT is currently uncertain and is debated [2, 18].

Most studies of AAGA have relied on post hoc detection of awareness, based on either prompted or spontaneous recall of intra-operative events. This reliance on recall has significant limitations. A problem of this reliance on recall is that, as stated by Robert Veselis [19], 'memory is a behaviour', since it requires a behavioural output once the 'victim' has decided to report an experience. There are many factors that determine whether or not patients will decide to, and indeed report their experiences, either prompted or spontaneously; as will be seen later, the choice of method of identifying awareness has a large effect on the reported incidence [20].

It is clear, however, that awareness with subsequent recall is associated with adverse consequences, such as postoperative dissatisfaction and long-lasting post-traumatic stress disorder (PTSD) [21–25]. We aim to review the literature concerning the incidence, consequences and management of accidental awareness under general anaesthesia, with a focus on cases when there is subsequent recall of intra-operative events.

Methods

We performed a PubMed search for all peer-reviewed English language articles published between 1 January 2000 and 1 March 2017. The following MESH key words were used: 'Intra-operative Awareness', AND ('General Anaesthesia' OR 'General Anesthesia'). This strategy yielded only 121 articles, and did not capture several key studies. We therefore included the non-MESH term 'awareness'. A search using the terms ('Intra-operative Awareness' OR 'Awareness' OR 'Intra-operative Consciousness'), AND ('General Anaesthesia' OR 'General Anesthesia') yielded 899 articles (see Supporting Information, Appendix S1 for a list). After screening the titles, abstracts and content, we sought out, and have considered in this review, articles discussing the incidence, risk factors, consequences, prevention and management of accidental awareness. Studies where awareness was a planned and expected part of the procedure, were excluded. In the following review, we will highlight the studies deemed to be the largest and most influential.

Definition and detection of AAGA

Table 2 contains a summary of the results of key studies investigating the incidence of awareness. In particular, it summarises the method used to detect or identify awareness. As can be seen, the reported incidence of AAGA strongly depends on the method of detection. Mashour et al. compared two methods of postoperative assessment (structured interview with direct questions vs. a routine quality assurance approach conducted one day postoperatively, where the patient was only asked if they had any problems with their anaesthetic), and showed that the two methods produced a five-fold difference in incidence: 0.1% with the structured interview vs. 0.02% with the quality assurance approach [20]. Given this strong link between study methodology and reported incidence, the results of the identified studies will be grouped according to the method of detection.

Isolated forearm test

A handful of studies have used the IFT, which enables detection of responsiveness to command in patients who have received NMBAs [26]. These studies were recently reviewed by Sanders et al., and so will only be briefly described here [4]. Many were performed by Russell, commonly in female patients undergoing gynaecological surgery [13, 17, 26, 27]. Using this technique, he found evidence of responsiveness in 23 (72%) out of 32 patients who had received an alfentanil/midazolam anaesthetic, leading him to question whether the

Table 2 Summary of studies investigating the incidence of accidental awareness during general anaesthesia (January 2000–March 2017). Values are number (proportion).

Authors	Trial name	Year	Number of subjects	Study design	Method of identification	Incidence of intra-operative awareness	Notes
Sandin et al. [14]		2000	11,785	Observational prospective case study	Modified Brice questionnaire: PACU, 1–3 days and 7–14 days postoperatively	18 (0.15%)	
Myles et al. [43]		2000	11,811	Observational prospective case study	Question and answer survey within 24 h of surgery	12 (0.11%)	
Russell and Wang [17]		2001	40	Randomised controlled trial	IFT and a formulated interview	7 (17.5%)	No cases of explicit postoperative recall
Schneider et al. [59]		2002	20	Observational prospective case study	IFT and patients were postoperatively asked to recall any awareness	8 (40%)	No cases of explicit postoperative recall
Slavov et al. [60]		2002	41	Observational prospective case study	IFT and patients were postoperatively asked to recall any awareness	10 (24%)	No cases of explicit postoperative recall
Myles et al. [18]	B-Aware	2004	Total: 2463 BIS: 1225 Routine care: 1238	Randomised controlled trial	Modified Brice questionnaire: 2–6 h, 24–36 h, and 30 days postoperatively	Total: 13 (0.52%) BIS: 2 (0.16%) Routine care: 11 (0.89%)	
Russell [27]		2006	Total: 12	Observational prospective case study	IFT and patients were postoperatively asked to recall any awareness	12 (100%)	44% explicit recalls
Avidan et al. [31]	B-unaware	2008	Total: 1941 BIS: 967 ETAC: 974	Randomised controlled trial	Modified Brice questionnaire: 0–24 h, 24–72 h, and 30 days postoperatively	Total: 9(0.4%) BIS: 6 (0.6%) ETAC: 3 (0.3%)	
Andrade et al. [28]		2008	184	Observational prospective case study	IFT and postoperative structured interview	2 (1.1%)	No cases of explicit postoperative recall
Avidan et al. [32]	BAG-RECALL	2011	Total: 5731 BIS: 2861 ETAC: 2852	Randomised controlled trial	Modified Brice questionnaire: 72 h and 30 days postoperatively	Total: 9 (0.15%) BIS: 7 (0.24%) ETAC: 2 (0.07%)	
Pandit et al. [6]	NAP5	2014	Estimated: 2,766,600	Cross-sectional observational study	Spontaneous complaints/ reports of awareness	471 (0.017%)	
Walker et al. [37]	SNAP-1	2016	16,222	Cross-sectional observational study	Modified Brice questionnaire	19 (0.12%)	
Sanders et al. [11]	ConsCIOUS1	2017	260	Observational prospective case study	IFT followed by modified Brice questionnaire	12 (4%)	No cases of explicit postoperative recall

PACU, post-anaesthetic care unit; IFT, isolated forearm technique; BIS, bispectral index; ETAC, end-tidal anaesthetic gas concentration; BAG-RECALL, Bispectral Index or Anaesthetic Gas to Reduce Explicit Recall; NAP5, 5th Royal College of Anaesthetists National Audit Project; SNAP-1, 1st Sprint National Anaesthesia Project; ConsCIOUS1, Connectedness and Intra-operative Unresponsiveness Study.

patients were actually undergoing 'anaesthesia' at all [26]. In two subsequent studies involving patients undergoing propofol/remifentanil anaesthesia, he found similar results. In one, all 12 (100%) patients responded at some time during surgery, and in the other, 16 out of 22 patients (72%) [13, 27]. Studies using the IFT were also undertaken by several other groups, with variable results. For example, Andrade et al. found that only two out of 184 children undergoing maintenance of anaesthesia using volatile agents (isoflurane or sevoflurane, with N_2O or air) responded to command [28]. In 2012, Sanders et al. reviewed the findings of the published IFT-based studies, and concluded that among the patients enrolled in those studies, a median of 37% responded to command during supposedly adequate anaesthesia [4]. As mentioned earlier, almost none of the patients responding to command during anaesthesia were able to recall intra-operative events. Most previous studies using the IFT were performed in one of a small number of centres, involved small numbers of patients and light anaesthesia in the context of a study attempting to validate the ability of an EEG-based monitor to detect return of consciousness. Sanders et al. thus performed the Connectedness and Intra-operative Unresponsiveness Study (ConsCIOUS1), a multi-centre study of patients undergoing standard anaesthesia as practised in their local institution [11]. The IFT was used, and patients were tested for responsiveness immediately before and after laryngoscopy and tracheal intubation. Postoperatively, a structured questionnaire was used to detect recall (modified Brice), and later a Bauer patient satisfaction questionnaire was completed [29, 30]. Out of the 260 patients enrolled, 12 (4.6%) responded to command. This is a conservative estimate, as situations where the hand of the patient moved spontaneously before command, were not studied. Interestingly, of the patients who responded to command, none had postoperative explicit recall, although they reported less satisfaction with their pain after surgery when compared with non-responders.

Prospective use of questionnaires to identify explicit recall of intra-operative events

As mentioned, most studies of AAGA have identified it after the fact – postoperatively – by prospectively asking a cohort of patients to complete a structured questionnaire and interview. The details of likely cases were then reviewed by a committee, who, depending on the study, commonly classify the likelihood of awareness as: 'No awareness'; 'Possible awareness'; 'Probable awareness'; or 'Definite/confirmed awareness'.

The first large study since the turn of the century used this approach during an observational study of AAGA among 11,785 patients undergoing elective procedures under general anaesthesia [14]. Participating patients were interviewed on three occasions, using a modified version of the Brice questionnaire (Table 3), which has since become the gold standard for prospective observational studies of AAGA [30]. The investigators conducted the first interview while the patient was in the post-anaesthesia care unit, the second after 1–3 days and the third at 7–14 days postoperatively. Of the participating patients, 325 had received total intravenous anaesthesia, of whom none had suspected awareness, whereas of the 11,454 who received volatile maintenance of anaesthesia, 18 had probable awareness. Overall, the incidence of probable awareness was 0.15% (or 1:600). Out of the 18 with AAGA, 14 had received neuromuscular blockade and tended to be those that suffered the worst psychological consequences [14, 23]. No difference was found in the incidence of awareness between men and women. Interestingly, most of the patients first reported awareness during the second or third interview.

The next major study was the B-Aware trial, which was a randomised controlled trial published in 2004 [18]. The goal of this study was to evaluate the efficacy of the bispectral index (BIS) in reducing intra-operative awareness among patients at high risk of awareness (e.g. cardiac surgery). The modified Brice questionnaire was used to interview patients on three

Table 3 Modified Brice questionnaire [30].

Modified Brice questionnaire
1. What is the last thing you remember before your surgery?
2. What is the first thing you remember after waking up?
3. Can you recall anything between under anaesthesia and waking up?
4. Did you dream anything during surgery? If so, was it disturbing?
5. What did you find most unpleasant about the surgery?
6. Did you have problems going to sleep or waking up?

occasions: at 2–6 h; 1–2 days; and 30 days after surgery. A total of 1225 patients were assigned to BIS monitoring and 1238 patients to routine care. There were 13 reports of confirmed awareness, two (0.16%) in the BIS-guided group and 11 (0.89%) in the routine care group. In the routine care group, the higher incidence of awareness was consistent with expectations based on the selection criteria and the results of previous studies. Use of the BIS monitoring system was thus associated with an 82% risk reduction in the incidence of awareness [18].

In 2008, however, Avidan et al. were unable to reproduce these results, when comparing BIS monitoring to end-tidal anaesthetic gas concentration (ETAC) monitoring in the 'B-unaware' trial [31]. After randomly assigning 2000 general patients to either BIS- or ETAC-guided anaesthesia, they found an awareness incidence of 0.6% and 0.3%, respectively. In response to suggestions that the 2008 study was underpowered (the patients were probably at lower risk than in the study by Myles et al. [18]), Avidan et al. performed an even larger study using similar methodology in higher risk patients – the so-called Bispectral Index or Anaesthetic Gas to Reduce Explicit Recall (BAG-RECALL) trial using similar methodology to the 'B-unaware' trial [32]. Once again, patients were randomly allocated to either BIS monitoring (with low and high BIS alarms set at 40 and 60, respectively) or ETAC monitoring (with low and high alarms set at 0.7 and 1.3 MAC, respectively). As with the B-Unaware trial, the modified Brice questionnaire was completed at 0–24 h, 24–72 h and 30 days after tracheal extubation. A total of seven out of 2861 (0.24%) of BIS monitored patients and two out of 2852 (0.07%) of ETAC monitored patients were found to have been aware. BAG-RECALL was unable to demonstrate the superiority of BIS over ETAC with regard to preventing awareness. Nevertheless, the general incidence of awareness was in line with previous studies.

The following year, from the same group, Mashour et al. published an even larger study (the Michigan Awareness Control Study) of the incidence of AAGA in an unselected surgical population (i.e. not at high risk of awareness) [33]. Once again, patients recruited to this trial were randomly assigned to alerting algorithms for the BIS or ETAC concentration, and the Brice questionnaire was applied. This study was stopped early, however, due to futility. It showed that BIS alarms were associated with an incidence of definite awareness of 0.12% (11 out of 9376 patients), whereas anaesthetic concentration alerts were associated with an incidence of 0.08% (eight out of 9460 patients). Of note is that, in this study, of the patients assigned to the BIS group, there was a high rate of failure to actually perform BIS monitoring due to technical reasons, and absence of BIS monitoring was associated with a 4.7-fold increase in the incidence of awareness when compared with those in whom BIS monitoring was feasible [33].

Although most incidence rates for awareness cited by research papers are based on studies conducted in the UK or the USA, there have also been large studies conducted elsewhere. In 2009, a multi-centre observational study on 11,101 patients in China, found 46 (0.41%) cases of definite awareness, and an additional 47 (0.41%) cases of possible awareness [34]. As with other studies, the researchers conducted a modified Brice interview at the first and fourth day after general anaesthesia with muscle relaxant. Indeed, it appears that AAGA rates in China are two or three times higher than those reported by similar studies in the UK or USA. A study of 1259 patients undergoing general anaesthesia in Brazil also identified higher rates of AAGA (32 patients, 2.5%) [35]. Similarly, a Spanish multi-centre study of 4001 patients identified 39 (1.0%) cases of definite awareness, and an additional five (0.1%) cases of possible awareness, again indicating that incidence rates of AAGA differ between countries [36].

The most recently published study involving awareness was an observational study of patient-reported outcomes performed by the 1st Sprint National Anaesthesia Project (SNAP-1) investigation of patients undergoing general anaesthesia in 257 hospitals in the UK on 13 and 14 May 2014 [37]. The 16,222 enrolled patients underwent a postoperative interview (within 24 h) using the modified Brice questionnaire, and this yielded an incidence of awareness of 0.12% (1:800). There was no association between AAGA and anaesthetic care, or with dissatisfaction with anaesthetic care.

Studies of awareness not involving structured questionnaires

Pollard et al. reported the results of a study conducted by a continuous quality improvement group, during

which quality improvement data from 177,000 patients were reviewed. In addition, the patients were subjected to an abbreviated Brice questionnaire once in the recovery room, and once during the first two days thereafter [38]. Only open, non-leading questions from the Brice questionnaire were asked, and therefore questions 3 and 5 shown in Table 3 were omitted, and a shortened form of question 4 was asked. Of the 87,361 patients who met the inclusion criteria (adults who underwent general anaesthesia and did not die during surgery), only six reported instances of recall, an incidence of 0.0068% (1:14,560).

The 5th National Audit Project (NAP5) was a large-scale audit of all patients who spontaneously complained of AAGA during or after their admission to hospital in the UK and Ireland between June 2012 and May 2013 [6]. Of the 300 reported cases of awareness, a committee judged 141 to be certain or probable cases of awareness. Based on the results of a previous activity survey, the authors estimated the incidence of spontaneously reported awareness to be 0.005% (1:19,600) [39].

Causes of and risk factors for awareness

The NAP5 study showed that two-thirds of spontaneously reported cases of AAGA occurred during the dynamic phases of anaesthesia (induction and emergence), and only one-third during maintenance of anaesthesia [6]. The NAP5 group reported that many, but certainly not all, cases of AAGA during induction and emergence were caused by obvious errors such as 'syringe swaps', mixing of drugs, NMBA administered before hypnotics, drug administration discontinued during emergence despite residual paralysis or hopelessly inadequate propofol infusion rates during intensive care unit (ICU) transfer after volatile anaesthesia [6].

Ghoneim et al. reported that, during the maintenance phase of anaesthesia, overly light anaesthesia and misuse or malfunction of the anaesthesia delivery system were the major causes of AAGA [40]. Depth of anaesthesia represents a dynamic balance between the intensity of noxious stimulation and the pharmacodynamic sensitivity of the patient to the effect-site concentrations of administered drugs (which in turn depend on the pharmacokinetics of the drugs administered in the individual patient). Considerable inter- and even intra-individual pharmacokinetic and pharmacodynamics variability exist. Presumably, some of this variability is caused by genetic polymorphisms, and can result in lower than expected plasma and effect-site concentrations and/or pharmacodynamic sensitivity to otherwise reasonable concentrations. These factors may be responsible for some of the cases of AAGA during both the static and dynamic phases of anaesthesia.

The NAP5 group reported similar findings for the maintenance phase [6]. Most cases of AAGA during this phase could be explained by failure to turn on the vaporiser or adequately monitor the end-tidal levels of volatile anaesthetics, stopping inhalational agent delivery too soon before the end of surgery and the intentional use of low doses in favour of haemodynamic stability. However, in some cases, no explanation was found.

Risk factors for AAGA have been previously identified, and were again confirmed by the NAP5 study [6, 38, 40]. Major risk factors in current practice include: the use of thiopentone (followed by maintenance with a volatile anaesthetic); rapid sequence induction; obesity; difficult airway management; use of NMBAs; and interruptions of anaesthetic delivery during patient transport into the operating theatre. Additional factors associated with an increased the risk of AAGA were: female sex; young age (but not children); anaesthetist seniority; previous history of intra-operative awareness; out-of-hours operating; emergencies; and type of surgery (obstetric, cardiac, thoracic). The association between thiopentone use for induction and awareness, was presumed to be caused by a combination of dwindling familiarity with the use of thiopentone, its rapid kinetics, and insufficient attention to ensuring adequate end-tidal concentrations of a subsequently administered inhalational anaesthetic; this resulted in AAGA during the so-called 'valley of no anaesthesia'.

It is likely that other risk factors identified by the NAP5 study, such as young age and obesity, may be explained by the effect of these latter factors on the pharmacokinetic and pharmacodynamic properties of the hypnotic agents, although no studies have been performed to investigate this.

Consequences

Accidental awareness during general anaesthesia may predispose patients to psychological sequelae that require treatment. The most common consequences appear to be nightmares, flashbacks and anxiety [41]. Other common consequences include: sleep disturbances; fear of future anaesthetics; late psychological symptoms [40]; impaired daily relationships and job performance; and the tendency to avoid necessary medical care [42].

Lennmarken performed a follow-up study of the patients who experienced AAGA in the study by Sandin et al. [14, 23]. Of the original 18 victims of AAGA, the authors were able to interview nine subjects. For up to two years after the episode, they found that four of the nine were still severely disabled by psychological consequences of their AAGA experience. The incidence of PTSD due to AAGA is difficult to determine, but may depend on multiple factors such as the surgical intervention itself, postoperative ICU admission, earlier traumatic experiences during chronic illnesses, and environmental, biological and psychological characteristics [24, 25, 42]. Although Ghoneim et al. reported that pain experienced during AAGA was not associated with the development of psychological symptoms [40], other studies have suggested that pain in association with muscle relaxation is a risk factor for severe psychological disturbances [6, 43, 44].

Although published studies suggest that awareness can have severe consequences, and case reports of awareness can make harrowing reading, studies suggest that fear of awareness does not rank highly among patients [45]. A review of nine studies dating from 1972 to 1994 by Klafta and Roizen, found that the proportion of patients fearing 'Waking up during surgery (awareness)' ranged from 0.8% to 54%, although these data were not discussed further [46]. Later, a study by Kindler et al. showed that before surgery, patients ranked 'Awareness during anaesthesia' the lowest of 10 specified fears [47].

Management of awareness

The NAP5 group has made available a support pack providing postoperative guidance for the management of cases of AAGA [48], and this is broadly similar to previous advice, such as that offered by Ghoneim [49, 50]. The NAP5 advice covers three stages of management: meeting; analysis; and subsequent support. The meeting stage consists of an interview with the patient, where the goal is to classify the extent and severity of AAGA. It is important that the interviewing clinician shows empathy, accepts the story as genuine, expresses regret and offers psychological support. Ideally, this interview should be conducted in the presence of an independent witness. A careful written record of the interview is essential. In the analysis phase, it is important to verify and confirm the details of the AAGA. Identifying the cause of awareness is essential. It should be determined if there was a drug error, or an issue with the sedation. Checking the details of the patient's story is also important in determining if the story as a whole seems likely. Seeking an independent opinion may also be helpful. In the final support stage, it is important to detect the potential consequences of AAGA early on. A follow-up consultation should be performed after 24 h, and should include an enquiry about nightmares, flashbacks, or new anxiety symptoms, which may indicate the need for the advice of psychologists and/or psychiatrists. After two weeks, a similar follow-up interview should be conducted. If the patient continues to show signs of adverse psychological consequences, the case manager should consider a formal psychological review and treatment for PTSD.

Treatment of the severe psychological sequelae of AAGA is similar to that of PTSD, although the literature available on this subject is limited to case reports, and is thus, not validated. Psychotherapy, pharmacotherapy, cognitive behaviour therapy, eye movement desensitisation and reprocessing, and exposure therapy are claimed to be important strategies [42, 48]. Pryor and Root have recommended that debriefing patients after AAGA and immediate referral to PTSD experts should be considered, along with a management protocol [51].

Prevention

The American Society of Anaesthesiologists published an advisory document on intra-operative awareness and brain function monitoring in 2005 [52]. This report summarised some of the literature concerning prevention of awareness, issued guidance based on expert opinion and strongly emphasised checking

of equipment (such as vaporisers, infusion pumps and sets) and drugs to prevent drug errors; routine use of depth of anaesthesia monitoring was not recommended, but should be considered on a case-by-case basis.

The detailed reports of the cases of awareness found by the NAP5 study provide useful insights into methods of preventing AAGA [53]. The study confirmed the strong association between NMBA use and awareness [6]. Where possible the use of NMBAs should be avoided or minimised. Furthermore, when NMBAs are used, neuromuscular function monitoring (e.g. train-of-four monitoring) is important to prevent (unsuspected) residual neuromuscular blockade during the emergence phase [6]. Medication errors due to syringe swaps and drug error can be prevented by clear and uniform labelling of syringes, use of standard syringe sizes and concentrations, and verbal double check of syringes before use. Depth of anaesthesia monitoring may be useful, and is particularly recommended for patients undergoing total intravenous anaesthesia and neuromuscular blockade [6, 53, 54]. As mentioned previously, the evidence for a reduction of the incidence of awareness with depth of anaesthesia monitoring is not consistent [18, 32, 33].

Discussion

Over the past few decades, attention has been focused on the issue of AAGA by clinicians, academics and the lay press. In comparison with other areas of interest to academic anaesthetists, studies of awareness have included large numbers of patients from a multitude of hospitals, and have resulted in highly read and cited publications [6, 18, 31–33].

In many cases of awareness, the cause is obvious – for example, a technical failure or error – and is thus preventable by improved preparation and monitoring. Nonetheless, there still remain cases where no rational explanation can be found for why someone receiving drugs known to be potently amnestic at subsedative doses, should regain consciousness and subsequently be able to recall intra-operative events [6]. Currently, one can only speculate that some cases of awareness are because of significant interindividual differences in pharmacokinetics and dynamics, possibly genetically determined; that perhaps some individuals are less susceptible to the amnestic effects of hypnotics, and that perhaps pain can activate memory functions sufficiently to enable encoding and subsequently retrieval of memories of intra-operative events.

A wide range of incidences of AAGA have been published – from as common as 1:600 patients to only 1:17,000. The breadth of this range can in part be explained by differences in the patient population, such as the prevalence of risk factors (e.g. critical illness, cardiac or emergency surgery, and NMBA administration). In several of the larger studies, the majority of patients received midazolam pre-operatively [18, 31–33]. Given that benzodiazepines are potent amnestics, and that current techniques of identification of AAGA rely critically on memory function, this is a significant confounder; it is likely that the proportion of patients receiving benzodiazepines will also influence the outcome.

However, most important are the differences in study methodology used. Although the NAP5 study was unique in the fact that it involved two whole countries (and thus a vast number of patients), and in the rigour applied to the analysis and reporting of the suspected cases, it is likely that the study failed to identify 80% or more of the cases that occurred during the study period [2]. It is most likely that the NAP5 study identified only the most serious and significant cases of AAGA during the study period.

The rigorously performed studies, involving structured interviews, suggest incidence rates of ≥ 1:1000 patients. Given the number of anaesthetics performed daily in the UK and elsewhere, it is surprising that many experienced and busy anaesthetists are only aware of small numbers of their own patients who have reported AAGA [55]. There are several potential reasons why some patients may choose not to spontaneously report their experiences, or may only form consolidated memories of their experience after several days or weeks [2, 20, 56].

Likewise, one would expect that litigation claims for AAGA would be common, and that compensation amounts would be high, considering the harrowing nature of some of the experiences of the victims. In fact, an analysis of the claims submitted to the NHS Litigation Authority between 1995 and 2007 showed that there were only 99 claims for 'brief awake

paralysis' or intra-operative awareness, that these were a small proportion of the total number of claims; the mean costs of claims for intra-operative awareness was also somewhat moderate (£32,680, £36,291, US $43,004) [57]. Finally, it is interesting to note that in the recently published study by the SNAP-1 group, which showed a high incidence of awareness (1:600), there was no association between AAGA and dissatisfaction with anaesthetic care.

In summary, AAGA appears to be relatively common, and mostly preventable. AAGA can be associated with severe psychological consequences, although this seems to be rare, and does not often translate into complaints and/or litigation. Nonetheless, it is important that all anaesthetists and anaesthetic departments implement and maintain strategies to limit the incidence of AAGA.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Reference list.