CHAPTER
9

AAGA during the maintenance phase of anaesthesia


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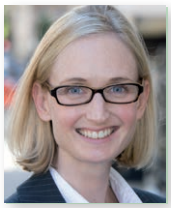
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HEADLINE

9.1 Although previous studies of AAGA have focussed on events during the maintenance phase ('during surgery') of anaesthesia, only a third of NAP5 cases fell into this category. Many of the AAGA reports during surgery were in fact due to contributory factors at or soon after induction or transfer (e.g. failure to turn on vaporiser after transfer). Other contributory factors identified were deficiencies in monitoring or responding to levels of end-tidal volatile agent, stopping volatile delivery too soon and intentionally low doses of agent. Superficially, 'TIVA' was over-represented in this group of reports, but non-TCI TIVA techniques predominated. Shorter perceived experiences did not reduce the psychological harm that was reported.

BACKGROUND

9.2 In NAP5 we defined maintenance as the period between the start of the surgical intervention up to when it was complete. Ghoneim et al. (2009) suggested that three-quarters of episodes of AAGA may have occurred during the maintenance phase, but timing an event, which may be brief, is not necessarily easy even in a prospective study (Errando et al., 2008).

9.3 Accidental awareness during surgery was, in a sense, first demonstrated in public by Horace Wells. The *Connecticut Hartford Courant* (9 Dec 1846) prints Wells's description of his (in)famous public demonstration of dental extraction during nitrous oxide administration in January 1845: "*A large number of students, with several physicians, met to see the operation performed – one of their number to be the patient. Unfortunately for the experiment, the gas bag was by mistake withdrawn much too soon, and he was but partially under its influence when the tooth was extracted. He testified that he experienced some pain, but not as much as usually attends the operation.*" This seems to be a case of stopping administration of anaesthesia too soon before the start of surgery.

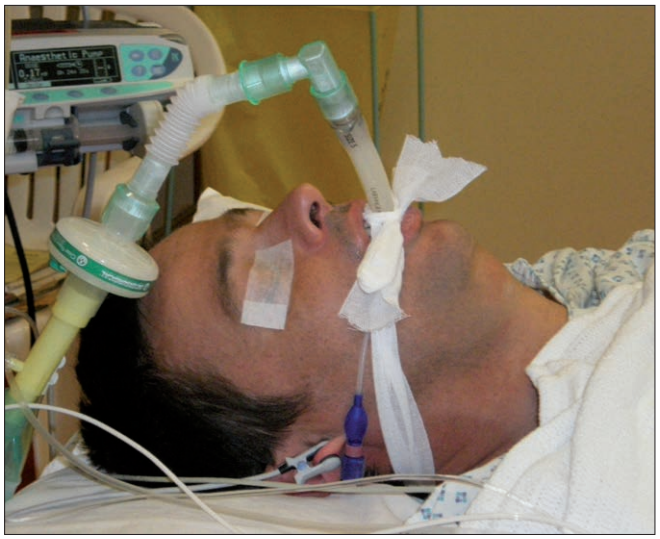
9.4 Existing literature discussing AAGA during maintenance can be grouped into: (a) case collections in cohort studies or sometimes detailed individual reports (Aaen & Moller, 2010; Rampersad, 2005), (b) assessments of implicit (Schacter, 1987) or explicit memory (Deeprose et al., 2004), (c) studies of depth of anaesthesia monitor use including isolated forearm technique studies (Russell, 2013a and b), or review or guidance articles (e.g. Apfelbaum, 2006). All the above studies attribute AAGA to three broadly separate causes:

(a) Overly light anaesthesia in patients at risk; especially in those undergoing emergency or obstetric procedures or in those with cardiovascular impairment, including in sepsis or trauma.

(b) Equipment malfunction (or human error in the use of equipment).

(c) Patients with a 'physiological resistance' to anaesthetic agents (e.g. tobacco smoking, heavy alcohol consumption, possible interaction with other centrally acting medication). Innate (e.g. genetic) resistance is also a possibility.

Maintenance is the phase when inherent resistance to anaesthetic agents may be most likely to present



NAP5 CASE REVIEW AND NUMERICAL ANALYSIS

9.5 Of the 141 Certain/probable and Possible (Class A and B) reports of AAGA, 51 (36%) involved AAGA during the maintenance phase (four of these involved AAGA at induction and maintenance, and one at maintenance and emergence).

9.6 The patient characteristics in this group of patients were similar to those in the overall group of AAGA reports (see Chapter 5, Methods). Thirty-two (64%) of reports classified were from female patients. Of the 51 patients, 23 (46%) were of normal body habitus, 19 (38%) were overweight or obese, one patient was underweight and in 8 (16%) the body habitus was not recorded. 18 reports (36%) related to patients undergoing NCEPOD urgent or emergency procedures, compared with 23.6% in the Activity Survey. ASA classes were: 1 and 2, 76%; 3, 20% and 4 and 5, 4%: i.e. there did not seem to be an excess of patients with significant comorbidity.

9.7 In 39 cases (78%), maintenance was with a volatile agent, using nitrous oxide in 14 (27%); an identical proportion of use found as in the Activity Survey. Possibly because some reports were historical, volatile agents were the principal drug in different proportions in the reports vs the Activity survey (sevoflurane 46%, desflurane 12%, isoflurane 12%, halothane 2%, enflurane 4% vs 57%, 13%, 21%, 0%, 0% respectively).

9.8 In 11 (22%), maintenance involved a TIVA technique, including nitrous oxide in one case. Of these, seven cases (14% of maintenance cases) used a TCI regime (two following or with volatile agents), three by calculated IV infusion, and one by repeated manual IV boluses. This exceeded the proportion of TIVA use in the Activity Survey (~8%). Intravenous anaesthesia is discussed elsewhere (Chapter 18).

9.9 The grade of the most senior anaesthetist was known in 49 cases. In 36 reports (71%), care was delivered by a consultant, in ten (20%) by SAS grades, and in three by senior trainees. The distribution is similar to the Activity Survey, with 71% of anaesthetics delivered by consultants and 85% by non-trainees. In seven (14%) cases the anaesthetist was in a locum post: compared with 7% of anaesthetics delivered by a locum anaesthetist in the Activity Survey.

9.10 EEG-based depth of anaesthesia (DOA) monitoring was used in 3 of the 51 cases (6%); all used bispectral analysis (BIS); i.e. double the use reported in the Activity Survey). In some cases, there appeared to be conflicting information about depth of anaesthesia as based on interpretation of information provided by the BIS monitor and end-tidal monitoring.

9.11 End-tidal volatile monitoring was recorded or implied in the majority of reports (33 of 40; 83%) of volatile anaesthetic cases.

An elderly patient with cardiovascular co-morbidities underwent general surgery, and two months after surgery reported AAGA. The patient recalled the presence of the tracheal tube, the abdomen being sutured closed, pain, hearing people talking, a sensation of paralysis and being unable to move. The patient was not distressed and gave a neutral report of the experience. The anaesthetic (intravenous induction with volatile maintenance) included BIS monitoring and remifentanil TCI. End-tidal concentrations of sevoflurane (in 50% oxygen) ranged between MAC 0.6-0.9. BIS values were recorded in the 40s and briefly in the low 50s.' (MAC 0.6 at this point).

9.12 Patients reported a wide range of durations of experience of awareness, from a few seconds to 60 minutes (median five minutes); AAGA lasted an estimated <1 min in 34%. The eight patients who subsequently reported a PTSD-like condition had broadly similar durations of experience (median five minutes).

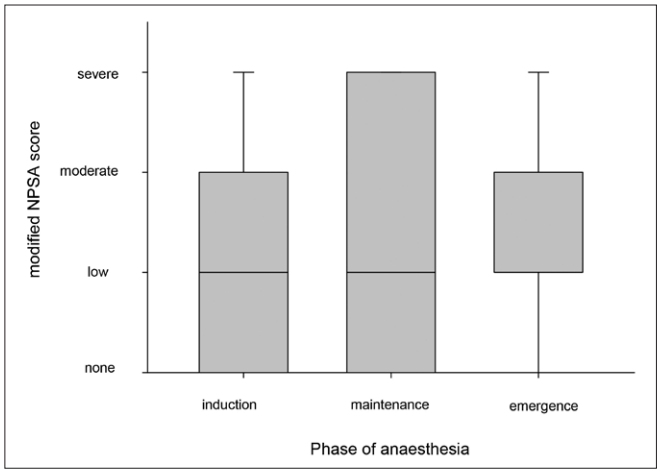
9.13 Of the patients who described the phase of surgery during which they experienced AAGA, 20 (40%) described it as the start of surgery (knife-to-skin) and 27 (54%) at a later period of surgery. In six patients the AAGA experience was reported to last for most of the procedure.

9.14 The commonest experience during maintenance was pain and paralysis (19; 37%) which was almost always distressing (in 84% of these). Paralysis alone was experienced by ten (20%) and pain alone by six (12%). Isolated tactile or auditory sensations were reported by six and ten patients (12% and 20%) respectively.

9.15 Distress was reported more commonly if pain or paralysis were present: 50% of those reporting pain and 75% of those reporting paralysis. Nearly half the patients experiencing tactile sensation also reported distress. None of those who reported only auditory experiences were distressed by them.

9.16 Despite the higher incidence of pain and paralysis in this phase of anaesthesia compared to the induction or emergence phases (Chapters 8 and 10, respectively), the overall proportion of patients distressed during maintenance was lower than at emergence (54% during maintenance vs 46% at induction and 73% during emergence). There was a broadly similar longer-term impact as judged by modified NPSA scores (Figure 9.1).

Figure 9.1. Boxplots for modified NPSA scores by phase of anaesthesia



9.17 About half the patients (28; 55%) had been offered follow up contact or more formal psychological support following their report of AAGA. In terms of impact, eight reports (16%) made reference to a PTSD-like state, and 14 (28%) described lesser anxiety symptoms. Eleven patients (22%) had initiated a process of formal complaint at the time of the report to NAP5.

9.18 In 37 patients (74%) there were elements of inadequate care identified:

(a) Errors with a vaporiser in 13 patients (26%).

(b) An intentionally (but inappropriately) low dose of anaesthesia in 17 (34%).

(c) Inappropriately early cessation of anaesthesia in 4 (8%).

9.19 Vaporiser errors included being left switched off after transfer (ten instances (20%), an empty vaporiser unnoticed (two cases) or incorrectly mounted (one case). Distraction was specifically cited as contributing to vaporiser errors in four (8%) reports.

A middle-aged patient underwent a short procedure under intended general anaesthesia. Immediately post-operatively, the patient reported recall of being positioned but could not move, and that there was a feeling of violation. The patient was panicked and very scared. The patient estimated that an interval of 15 minutes elapsed before everything went blank. The patient developed symptoms of PTSD. The anaesthetic had been an intravenous induction, with neuromuscular blockade for insertion of a supraglottic airway. On transfer to theatre the volatile agent was inadvertently not restarted and the expired concentrations were <0.5 MAC for ~ 15 minutes. The patient was tachycardic and hypertensive during this period. Distraction by a malfunctioning pulse oximeter was cited.

A patient underwent an emergency operation and immediately reported having heard the stapling of the skin whilst paralysed. The patient also recalled a discussion about 'sweating'. The experience lasted ~30 minutes. There was distress, sleep disturbance and unpleasant dreams. The anaesthetist had mistakenly turned off the vaporiser prematurely at the end of surgery.

9.20 However, in 13 (26%) of reports no cause of the episode of AAGA could be ascertained. In nine (18%) patients, AAGA was reported while documented care appears to have been of good quality.

An obese patient underwent general surgery. Later, the patient reported having seen lights, people overhead and experienced pain (like 'animals biting'). The patient tried to (but couldn't) speak; all this lasted about one minute. The patient developed new sleep disturbance, a new anxiety state, nightmares, flashbacks, PTSD-type symptoms and has was referred for psychology assessment and therapy. The anaesthetic maintenance included apparently appropriate opioids, local anaesthetic infiltration and appropriate levels of volatile agent.

9.21 The cases involving TIVA are discussed in detail in Chapter 18, but contributory factors included low dosing, non-standard or erroneous use of TIVA machines, omission of opioids when apparently required and disconnections.

A healthy patient undergoing elective ENT surgery reported that they had been awake during surgery but unable to move. They reported a strange feeling of being asleep but being able to see and know what was going on. In addition to recall of events in the anaesthetic room, they remembered that they tried to cry so that they could show people that they were awake. Then they recall being transferred on to the operating table, people talking and the pressure and pain of a needle being inserted, then an intense burning sensation and thinking that they couldn't survive this. Then they lost consciousness. The anaesthetist had used propofol TCI target (between 3 and 7 mcg/ml plasma target) and tramadol and ketamine boluses combined with lignocaine and magnesium infusions. The patient received psychology review for a newly established post-traumatic stress disorder.

DISCUSSION

9.22 It is perhaps surprising that AAGA during the maintenance phase, during surgery, is not more common as a proportion of all the AAGA reports. Whereas the level of stimuli during induction is likely to be relatively modest and brief, during surgery the levels of nociceptive stimulus rises dramatically and therefore might be expected to predispose to AAGA. The fact that ~40% of reports in the maintenance phase relate to the brief period of 'knife to skin' is consistent with a notion that the induction dose may have been (in retrospect) inadequate or may have worn off by time of surgery (see Chapter 8, Induction) or indicate an unpredicted stimulus.

9.23 Although the incidence of pain and paralysis as a combination of symptoms was more common during maintenance than in other phases of anaesthesia, this arose largely at the start of surgery, or less commonly towards the end of surgery, as brief experiences. There was therefore considerable overlap in the symptomatology of this group of patients as compared with induction and emergence cohorts (see Chapters 8 and 10).

9.24 In Chapter 8 (Induction) we propose use of a checklist to ensure anaesthesia is being delivered before surgery starts. Based on our findings it seems logical that this (or a similar) checklist might reduce the incidence of AGAA at the start of surgery. This could be tested by research. Any such checklist should be undertaken before the start of surgery, and the surgical team should formally confirm with the anaesthetist that it is appropriate to start surgery, before doing so.

9.25 However, over half the reports relate to a later phase of surgery. Speculatively (but logically), the intensity of surgical stimulus can vary during an operation, and there may be times when it is sufficient to overcome the unconsciousness induced by anaesthesia, unless this is always carefully titrated to stimulus.

9.26 It might be anticipated that, since lower doses of anaesthetic might be employed in patients who are more unwell or unstable, a worse ASA grade is associated with AAGA. There were some instances in which the Panel felt dosing had been intentionally (and inappropriately) reduced for this reason, but generally this was not the case. Reasons for this lack of apparent association might be that, generally anaesthetists are dosing appropriately in these cases, or that sensitivity to anaesthetic parallels physiological instability (i.e. the more unwell the patient, the more sensitive to anaesthetic). As referred to elsewhere, early use of vasoactive agents will in many cases obviate the need to inappropriately reduce anaesthetic doses, even in high risk patients (see Chapter 8 Induction, Chapter 17 ICU).

9.27 Strikingly, in about a quarter of reports in the maintenance phase, the Panel could find no cause or contributory factor. This finding differs from the analysis of induction and emergence phases, where causative/contributory factors were readily ascertained (e.g. related to difficulties in airway management or residual neuromuscular blockade). This raises the possibilities that (a) an inherent (possibly genetic) resistance to the effects of anaesthesia might exist, and (b) if it does, then it is revealed during the maintenance phase of anaesthesia.

9.28 The inherent difficulties of monitoring TIVA are discussed elsewhere, but it was surprising that several reports of AAGA during maintenance were associated with vaporiser problems that went undetected despite end-tidal monitoring. End-tidal monitoring is of value only if appropriate alarm limits are established, audible alarms are on, and these are acted on. In-depth analysis is required of the 'human factors' elements that promote likely distraction, or process disorders that lead to these oversights. However it is notable that studies that have concluded that end-tidal gas monitoring is as effective as DOA monitoring in preventing AAGA have used rigorous protocols that include

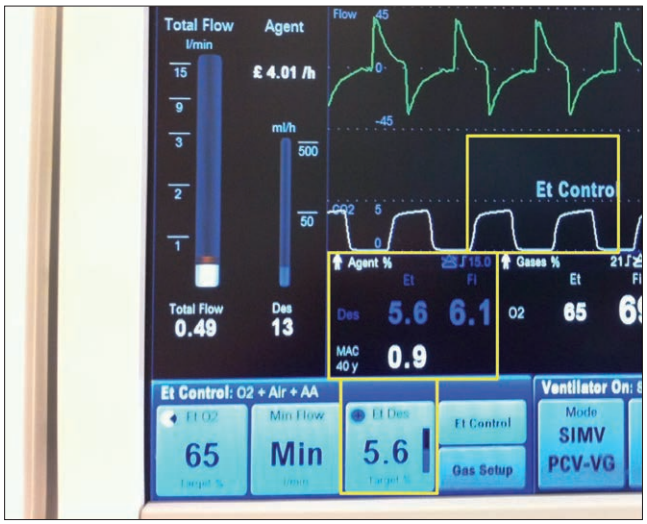
(a) enabled end-tidal gas alarms (b) audio alarms (c) in some cases text alert to the anaesthetist to inform them of alarm activation (d) protocolised responses to the alarm (Avidan et al., 2011; Mashour et al., 2012) .This rigour may not be reflected in 'standard care' (Myles et al., 2004).

9.29 End-tidal agent monitor alarms will provide an alert to indicate an unexpectedly low (or high) delivery of anaesthetic only if activated, at an appropriate level, for the whole duration of the anaesthetic procedure. The use of default alarm conditions should be considered. More sophisticated alarm process design may enable their use to be more keenly adopted.

9.30 For situations where an agent monitoring alarm is not employed there would be benefit from a vaporiser design which indicates an alarm when its contents are almost exhausted. Given that some vaporisers (desflurane) already have a power supply this should not prove impossible and is indeed available on some more modern machines. Reliance on a visual method for assessing the level of filling can lead easily to mistakes or omissions.

9.31 Newer anaesthetic machines are able to deliver 'targeted end-anaesthetic concentrations' even at low flows and this may also prove beneficial and is an avenue for future research.

Modern anaesthetic machines can maintain end-tidal gas concentrations at set levels (here 0.9 MAC of desflurane) which may help in reducing risk of AAGA



9.32 It is notable that over half of the reports were associated with pain. This suggests that, regardless of the dilemmas in monitoring the conscious state, when AAGA occurs during surgery pain is a prominent feature. This statistic would suggest that where AAGA is suspected during surgery, prompt deepening of anaesthesia should be coupled with administration of analgesia.

9.33 Consistent with data elsewhere in this Report, even short episodes of AAGA can be very distressing, and can be associated with longer term psychological morbidity and suffering.

9.34 The relatively stable maintenance phase of anaesthesia (in contrast to the more dynamic events at induction and emergence) should offer the most reliable conditions to test the possible impact of the use of DOA monitors. It is intriguing, and perhaps concerning, that 3 of 51 cases of AAGA during maintenance occurred during use of DOA monitors and further that there were episodes of AAGA when DOA monitoring data were reported to be in the recommended range throughout surgery. In one case, the depth of anaesthesia was judged more by the output of the DOA monitor than by the end-tidal volatile concentration (a dichotomy that can clearly create a genuine dilemma). However these three cases are too few on which to draw robust conclusions regarding the benefit (or harm) associated with DOA use. This is also discussed elsewhere (see Chapter 20, DOA). The risk of AAGA when end-tidal agent concentration is >0.7 MAC is extremely low (Aranake et al., 2013).

IMPLICATIONS FOR RESEARCH

Research Implication 9.1

The maintenance phase of anaesthesia most reliably offers a pseudo-steady state of anaesthesia, in which assessing the efficacy of DOA monitoring is less likely to be influenced by dynamic changes in conscious level. Research testing the utility of such monitoring should specify the phase of anaesthesia being examined, as outcomes may not be the same for induction, maintenance or emergence.

Research Implication 9.2

Research should seek to resolve the dilemma posed by the issue of how best to interpret a low DOA monitor output reading coupled with unexpectedly low anaesthetic concentration, since this can either indicate that the patient is sensitive to the anaesthetic agent, or that the DOA monitor output is incorrect.

Research Implications 9.3

Research should establish if there exists any inherent relative resistance to the effects of anaesthesia (e.g. genetic) and if so, which polymorphisms may be involved.

Research Implication 9.4
Perhaps in addition to monitors dedicated to measuring consciousness level (depth of anaesthesia), further research should be aimed at developing specific monitors for detecting the level of pain/nociception (analgesia or (anti)nociceptive monitoring).

Research Implication 9.5
Research should establish the optimum form of alarms to alert the anaesthetist to inadequate anaesthetic vapour delivery.

Research Implications 9.6
Further research should establish whether (and at what level) targeted (e.g. servo- or closed-loop) end-tidal volatile delivery can reduce AAGA.

RECOMMENDATIONS

RECOMMENDATION 9.1
An anaesthetic checklist should be conducted before the start of surgery to confirm (amongst other things) delivery of adequate anaesthesia. This might usefully be incorporated into the WHO checklist.

RECOMMENDATION 9.2
The surgical team should formally confirm with the anaesthetist that it is appropriate to start surgery, before doing so.

RECOMMENDATION 9.3
If AAGA is suspected during maintenance, then prompt attention should be paid to increasing analgesia, as well as deepening the level of unconsciousness. As recommended elsewhere, verbal reassurance should be given to the patient during this time.

RECOMMENDATION 9.4
Anaesthetists should exercise great caution in interpreting the outputs of processed EEG- based DOA monitoring as indicating adequate anaesthesia, in the face of unexpectedly low administered anaesthetic concentrations.

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