Awareness with recall during general anaesthesia: a prospective observational evaluation of 4001 patients

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Background. We have prospectively evaluated the incidence and characteristics of awareness with recall (AWR) during general anaesthesia in a tertiary care hospital.

Methods. This study involves a prospective observational investigation of AWR in patients undergoing general anaesthesia. Blinded structured interviews were conducted in the post-anaesthesia care unit, on postoperative day 7 and day 30. Definition of AWR was 'when the patient stated or remembered that he or she had been awake at a time when consciousness was not intended'. Patient characteristics, perioperative, and drug-related factors were investigated. Patients were classified as not awake during surgery, AWR, AWR-possible, AWR-not evaluable. The perceived quality of the awareness episode, intraoperative dreaming, and sequelae were investigated. The anaesthetic records were reviewed to search for data that might explain the awareness episode.

Results. The study included 4001 patients. Incidence of AWR was 1.0% (39/3921 patients). If high risk for AWR patients were excluded, the incidence was 0.8%. After the interview on the seventh day, six patients denied having been conscious during anaesthesia; hence, the incidence of AWR in elective surgery was 0.6%. Factors associated with AWR were: anaesthetic technique incidence of 1.1% TIVA-propofol vs 0.59% balanced anaesthesia vs 5.0% O2/N2O-based anaesthesia vs 0.9% other anaesthetic techniques (mainly propofol boluses for short procedures), χ2=0.008; age (AWR 42.3 yr old vs 50.6 yr old, χ2=0.041), absence of i.v. benzodiazepine premedication (χ2=0.001), Caesarean section (C-section) (χ2=0.019), and surgery performed at night (χ2=0.013). More than 50% of patients reported intraoperative dreaming in the early interview, mainly pleasant. Avoidable human factors were detected from the anaesthetic records of most patients. Subjective auditory perceptions prevailed, together with trying to move or communicate, and touch or pain perception.

Conclusions. A relatively high incidence of AWR and dreams during general anaesthesia was found. Techniques without halogenated drugs showed more patients. The use of benzodiazepine premedication was associated with a lower incidence of AWR. Age, C-section with general anaesthesia, and surgery performed at night are risk factors.


Keywords: anaesthesia, general; anaesthesia, depth; complications, awareness; monitoring, depth of anaesthesia

Accepted for publication: April 11, 2008
Awareness with recall (AWR) during general anaesthesia is a known anaesthesia-related problem. However, the actual incidence is unclear but previous studies suggest a rate of intraoperative AWR between 0.02 and 1.0%, for adults and children. For patients, the possibility of being awake during the operation is a primary cause of worry and they score this event as a cause of dissatisfaction. AWR is a source of complaint against anaesthetists. In Spain, apart from isolated case reports, there are no data on this topic.

We undertook this study to evaluate the incidence and characteristics of AWR in patients undergoing general anaesthesia, in an unselected surgical population of a tertiary care hospital in Spain.

Methods

Design of the study and setting

We conducted a prospective observational study of the incidence of AWR during general anaesthesia. The study was conducted at the Consorcio Hospital General Universitario de Valencia, a tertiary care hospital with 600 beds serving a population of 200 000. We enrolled patients scheduled for elective or urgent surgery requiring general anaesthesia during two separate periods: from April 1995 to April 1997, and from December 1998 to November 2001. Consent from the Ethics Committee of our hospital was obtained. The verbal consent of physicians in the department of anaesthesia was requested.

Sample size

This study was designed to establish the incidence of AWR. During the time of study design, reviews estimated incidences of 0.2% or higher. As no national or local reference was available, an incidence of 0.2–0.4% of intraoperative AWR was assumed and a sample size of 4000 was selected to provide a 95% confidence interval of 0.09–0.37% with a mean value of 0.2%. The first 4000 patients were enrolled on April 1, 1995, and enrolment continued until 4000 patients had been recruited. Subjects were excluded from enrolment if they were transferred to the Critical Care Unit for postoperative care, if they were <15 yr, or were undergoing cardiac surgery.

Patient interview, detection, and evaluation

Our definition of AWR was ‘when the patient (spontaneously or at interview) stated or remembered that he or she had been awake at a time when consciousness was not intended’. Evaluation of awareness was based upon three consecutive interviews. The protocol for patient detection and follow-up is presented in Table 1. Patients were interviewed, in the postanaesthesia care unit (PACU) immediately after the surgery was complete and when they were clinically stable, by interviewers blinded to both the anaesthetic procedure and drugs used.

Table 1 Protocol for patient detection and follow-up of the intraoperative awareness with recall (AWR) event. PACU, postanaesthesia care unit

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tr>
<td>1</td>
<td>Structured interview in the PACU, day of surgery (data available online, Annex I)</td>
</tr>
<tr>
<td>2</td>
<td>Proposal of psychological treatment or advice if indicated</td>
</tr>
<tr>
<td>3</td>
<td>Analysis of the possible cause of awareness in every patient from the data of the anaesthetic record form</td>
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</table>

Patient, anaesthetic and surgical characteristics, and the drugs used were recorded in a blinded manner on a database. Suspicion of an episode of AWR was registered together with its characteristics. The occurrence of intraoperative dreaming and its characteristics was also recorded. If awareness was detected or was considered a possibility (see definitions below), the first author conducted a second interview on the seventh day after operation to confirm the awareness episode. Thirty days after surgery, the third structured interview was conducted over telephone (Annex I, additional material online). Two months after operation, two blinded anaesthetists independently reviewed the anaesthetic records for perioperative incidents that may have related to the episode of AWR.

Evaluation of factors that could have influenced the incidence of awareness with recall

Persistent hypotension, a known cause of AWR, was defined to have occurred if a systolic arterial pressure of 80 mm Hg or less was recorded as consecutive entries over a 30-min period.

Surgery was classified as urgent if it was an emergency or urgent procedure. Duration of surgery was stratified into two groups: <180 min or >180 min. To analyse the influence of the time of day, patients were grouped as those operated between 08:00 and 22:59 (morning and evening work time), and those operated between 23:00 and 07:59 (night work time).

Other data recorded were: drugs given i.v. immediately before anaesthesia, anaesthetic induction and maintenance drugs; the mean inspiratory fraction of O₂ (FIO₂), and the mean per cent of inhaled anaesthetic agent used throughout the operation (mean Fi halogenated), or if this varied more than 30%, the mean of the two most frequently used concentrations.

Patients were classified by ‘anaesthetic technique’ as those receiving propofol as an i.v. induction and maintenance drug (TIVA group), any i.v. induction drug plus a halogenated agent for maintenance of anaesthesia.
(balanced anaesthesia, BA group), any i.v. induction drug with \( O_2-N_2O \) maintenance (mixed anaesthesia, MA group), and a miscellaneous anaesthetic technique group (other techniques of anaesthesia, OTA group). The latter comprised primarily bolus dose of propofol for short procedures, but also midazolam–ketamine induction and infusions and midazolam with high-dose opioids.

**Awareness and dreaming classification**
A positive finding of AWR (AWR-yes) was defined as occurring when the patient in response to the structured interview was certain of having been aware at any time during the operation. The patient when sure of having been asleep during anaesthesia was defined as (AWR-no). Awareness was considered as possible (AWR-possible) in those cases where the patient believed to have been awake during surgery, but was not completely sure. Patients who were unable to be evaluated, for example those with dementia, were defined as not verifiable (AWR-not evaluable). Patients with AWR because of erroneous administration of neuromuscular blocking drugs (NMBDs) before the hypnotic drug during the induction of anaesthesia were classified as AWR-no. Patients were also classified as having no dreams or remembering having had dreams during anaesthesia. Dreams were classified as pleasant, unpleasant or indifferent, and ‘do not remember’.

The second interview was designed as a modified ‘structured interview’ (Annex I, additional data available online), starting with some general questions and then focusing on the potential awareness episode. During the third structured interview, the earlier findings of AWR were confirmed and details of the episode were requested: physical (visual, auditory, movement or pain perception) and psychological characteristics: time perception, previous AWR episodes, and psychological sequelae. Finally, we asked about the communication of the event to other persons.

**Statistical analysis**
SPSS 11.0 (SPSS Inc., Chicago, IL, USA) was used to perform statistical analysis. A comparison of the first 300 patients with the last 300 was performed to evaluate possible changes in anaesthetic techniques or practices, drugs or doses used, and incidence of AWR. Differences in categorical variables were evaluated using Fisher’s exact test or the Pearson’s \( \chi^2 \) test, both two-sided. Differences in continuous variables were evaluated using Student’s \( t \)-test for independent samples, after verifying homogeneity of variance with Levene’s test. A value of \( P<0.05 \) was considered to be statistically significant.

A multivariate modelling of the awareness endpoint was carried out with the data from patients classified as ‘AWR-yes’ or ‘AWR-no’ in the initial assessment. In the forward stepwise logistic regression model, the independent variables were those which were significantly different \((P<0.05)\) or approaching significant difference between the AWR-yes and AWR-no patient groups. The relative risk (RR) associated with each variable was calculated using the final fixed model with only the significant variables.

**Results**
Data from 4001 patients were included in the study (Table 2). Patients from a total of 42 anaesthetists were enrolled. In the interim analysis (first 300 patients vs last 300), the proportion of patients conducted with TIVA increased from 30.7% at the start of the study to 34.4% at the end, while BA decreased from 52.7% to 43.1% \((P=0.018)\). There were more Caesarean section (C-section) patients among the first 300 patients \(\text{13 vs three patients; } P=0.011\). No other differences were observed between these two groups, including the incidence of AWR.

**Incidence of awareness**
After the first interview, the ‘crude’ incidence of intraoperative AWR (AWR-yes) was 1.0%, 39 of 3921 evaluable patients reported an AWR episode, 3662 patients \((93.4\%)\) were AWR-no, five patients \((0.1\%)\) were classified as AWR-possible, and 215 \((5.4\%)\) could not be evaluated.

**Table 2** Patient characteristics, anaesthetic, and surgical procedures by specialty. Data are presented as number (%) or mean (SD). TIVA, total i.v. anaesthesia with propofol; BA, balanced anaesthesia; MA, mixed anaesthesia; OTA, other anaesthetic combinations (see text for additional explanation and definitions)

<table>
<thead>
<tr>
<th>Gender, male/female (n=3968)</th>
<th>1680 (42.3)/2288 (57.7)</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>51 (18)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71 (14)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162 (10)</td>
</tr>
<tr>
<td>ASA (I/II/III/IV)</td>
<td>669 (17.0)/2159 (54.9)/1087 (27.6)/19 (0.5)</td>
</tr>
<tr>
<td>Anaesthetic procedure duration (min)</td>
<td>120 (51)</td>
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<tr>
<td>Anaesthetic technique (n=3946)</td>
<td>TIVA 1469 (37.2)</td>
</tr>
<tr>
<td></td>
<td>BA 1787 (45.3)</td>
</tr>
<tr>
<td></td>
<td>MA 126 (3.2)</td>
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<tr>
<td></td>
<td>OTA 564 (14.1)</td>
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<tr>
<td>Type of surgery</td>
<td>General-gastrointestinal 1517 (38.1)</td>
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<td></td>
<td>Orthopaedic 679 (17.0)</td>
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<tr>
<td></td>
<td>Ear-nose-throat 379 (9.5)</td>
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<td></td>
<td>Gynaecologic 277 (6.9)</td>
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<td></td>
<td>Neurosurgery 250 (6.2)</td>
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<td></td>
<td>Plastic-reconstructive 181 (4.5)</td>
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<td></td>
<td>Thoracic 159 (4.0)</td>
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<td></td>
<td>Ophthalmic 157 (3.9)</td>
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<td></td>
<td>Ambulatory 93 (2.3)</td>
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<td></td>
<td>Urologic 87 (2.2)</td>
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<tr>
<td></td>
<td>Maxillofacial 59 (1.5)</td>
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<tr>
<td></td>
<td>Vascular 53 (1.3)</td>
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<tr>
<td></td>
<td>Obstetric (excluding Caesarean section) 29 (0.7)</td>
</tr>
<tr>
<td></td>
<td>Caesarean section 59 (1.5)</td>
</tr>
</tbody>
</table>
When patients at high risk for awareness were excluded (i.e. emergency surgery, intraoperative hypotension-shock, and C-section), the incidence of AWR-yes was 0.8% (28/3477). However, after the interview on the seventh post-operative day, six of these patients denied awareness; hence, incidence of AWR-yes during elective surgery was 0.6% in our study population.

The rates of awareness differed significantly between different anaesthetic techniques (Table 3).

In the whole study population and in those patients at high risk for AWR, gender (0.8% vs 1.2%, male/female, \(P=ns\)), weight, height, ASA physical status, and surgical procedure had no influence on the incidence of AWR. Patients who reported AWR tend to be younger [mean (sd); 42.3 (20.5) yr old vs 50.0 (18.1) yr old in the ‘all patients’ group, \(P=0.009\)], [42.3 (21.4) yr old vs 50.6 (17.8) yr old in the ‘elective surgery only’ patients, \(P=0.041\)].

Before operation, 2222 patients received benzodiazepines premedication, mainly midazolam (54.5%) and 3448 (86.2%) received opioids. Patients receiving benzodiazepines had a lower incidence of AWR (\(P<0.001\)) when compared with the other premedication groups. Use of NMBDs, and halogenated agents were not significant influences. C-section patients (\(P=0.019\)) and surgery performed at night time (\(P=0.013\)) showed a higher incidence of AWR. Data on the influence on AWR of the perianesthetic drugs used and perioperative factors are displayed in Supplementary material, Table S1.

Multivariate logistic regression analysis

The independent variables which were significantly different or had nearly significant difference between the AWR-yes and AWR-no groups (anaesthetic technique, premedication type, NMBD use, time of day of surgery, C-section, duration of surgery >180 min, emergency procedure, age, and mean Fi halogenated agent) were introduced in a forward stepwise logistic model. There were 1958 patients with data values for each of the independent variables. The final model included only the premedication type (\(P=0.041\)), the other variables being all non-significant when added to this model.

A fixed logistic model consisting of only premedication type was run using the 3701 patients having data for this variable. This model again was significant for premedication type (overall \(P=0.001, R^2=0.036\)). To calculate RR, we chose the reference to be the premedication type with the lowest incidence of awareness, that is midazolam and midazolam plus opioid. Then ‘no premedication’ was associated with a 6.1-fold increase in the odds of awareness (\(P=0.001\)), ‘other premedication’ was associated with a 4.9-fold increase (\(P=0.002\)), and ‘opioid premedication’ alone was associated with two-fold increase (\(P=0.115\)).

In order to exclude the possible bias of introducing emergency surgery patients (usually non-premedicated) in this model, both the type of premedication and emergency surgery (Yes/No) were included as variables, but the significance remained unchanged. A stratified analysis (separate logistic regressions) for emergency and non-emergency patients, although unbalanced, found that the only statistically significant predictor (vs premedication with midazolam or midazolam plus opioid) was ‘no premedication’ group, with a RR of 5.7 (\(P=0.012\)).

Intraoperative dreaming

At the first interview, 1920 out of 3644 patients (52.6%) reported dreams during surgery/anaesthesia (Table 3). By gender, 758 (48.6%) male vs 1163 (55.3%) female patients dreamt during the procedure (\(P<0.001\)). There was no influence of the type of anaesthesia on the perceived quality of the dreams other than a higher incidence of ‘pleasant’ in the MA group (Table 4).

Recall of the awareness episode and psychological sequelae

We were able to obtain a description of the episode of AWR from 22 of the patients who reported being conscious during anaesthesia. Descriptive data concerning some of the elective and emergency surgery patients are listed in Supplementary material, Table S2. Out of the 22 patients, 11 reported hearing noise and 18 reported hearing conversation. No patient reported hearing unpleasant expressions or comments. Only two patients reported
were detected only in delayed interviews. 41 01 21 9 at risk for AWR 15–17 were not included ‘per protocol’ as ill surgical, and hypovolaemic trauma patients) considered admitted to the Critical Care Unit (cardiac surgery, severely explicit recall of intraoperative events, may have been missed as this was not studied, 18 and up to 50% of patients recruited ruled out the influence of information to the staff on the management of the anaesthetic procedures, 20 21 and the decrease in the number of C-section patients performed under general anaesthesia was probably because of the trend to use regional anaesthesia and not to the perception of more patients of AWR in this group.

We observed a higher incidence of AWR in the TIVA group than in the BA group. This result has been suggested by others, 22 23 or indirectly demonstrated, 5 24 but no formal studies have been performed. The induction bolus or infusion rate of propofol was not standardized in this study, which could have influenced the incidence of AWR. The molecular mechanisms of action of inhaled and i.v. agents are different. 25 Recent multicentre studies using inhaled anaesthetics reported incidences of AWR between 0.13 and 0.91%. 4 10 12 14 However, some did not include ‘possible’ awareness 4 14 in the incidence.

Studies using BIS monitoring showed a low incidence of awareness to 0.17, 4 and 0.04%. 14 In the study with the lowest incidence reported to date, 0.0068%, 13 a ‘regular quality assurance analysis’ was performed through the investigation and this may have influenced the results.

A large study of patients receiving TIVA 26 for short-stay surgical procedures, found no patients of AWR in a cohort of 5053 patients, but smaller studies have reported rates of 0.07–1.2%. 9 11 92 0 These figures would increase by a factor of 2 or 3 if ‘possible’ AWR patients were included. 9 Therefore, depending upon the definition used or the agreement of evaluators, the true incidence could be closer to our results.

We found a significant relationship between AWR and the type of premedication with a reduced incidence of AWR following midazolam compared with opioid premedication, the groups that had a sufficient sample size to enable comparison. However, the reduction in the rate of AWR because of premedication accounts for a small amount of the overall variance in the data (R²), so the influence of benzodiazepines is limited. In some previous studies, the use of midazolam did not prevent AWR, 10 11 but in others the rate was reduced. 9 23 Anaesthetists were shown to be equivocal about the benefit of amnesic premedication in the prevention of AWR, 27 but, when informed about their own incidence of AWR, increased use and dosages of benzodiazepines reduced the incidence. 21

As in our MA group, a high AWR incidence was reported with only O₂/N₂O anaesthesia. 10

Only one study 13 has found ASA physical status to cause an influence on AWR. 9 11 This agrees with our findings.

We found no significant effect of gender on AWR which is in agreement with other studies, 9 10 12 although some have found a higher incidence in males 11 or in females. 11 A similar variation occurs with age and AWR with no relationship, 9 11 12 a higher incidence in younger, 21 as we observed, or in older patients. 13 Closed claim analysis shows a higher number of young, female, ASA I and II patients. 5

It is difficult to draw any conclusions from our emergency surgery patients because of the exclusion of the sickest patients and the small number studied. Emergency surgical procedures
have been investigated before, but we have found a higher incidence of AWR in patients who had surgeries performed at night compared with day time patients. Fatigue of the anaesthesia staff could have been involved. The incidence of AWR in C-section patients is well known. Smaller induction doses together with reluctance to use high concentrations of halogenated drugs may be the factors involved. A recent survey did not find a higher incidence of awareness in obstetric patients than in controls.

The value of clinical data in predicting awareness is not clear. BIS monitoring can be, but end-expiratory concentration of inhaled anaesthetics (MAC-related) is of limited value, as are haemodynamic changes or the isolated forearm technique. However, clinical signs and end-tidal concentration of inhaled agents are more commonly relied upon than neuror monitoring in practice, although recent recommendations may change this.

As it occurs with other critical incidents and sources of human error, it is difficult to convince some anaesthetists that explicit recall during anaesthesia exists and that it is an important clinical problem. In surveys, anaesthetists opinions of their own incidence of AWR is lower than that reported, and patients have noted doctors’ scepticism after describing their experience of awareness.

Dreaming has been interpreted by some as an expression of light anaesthesia (i.e. awareness without explicit recall), and patients with BIS-guided anaesthesia showed lower incidence of dreams. However, dreams have been excluded from the definition of intraoperative awareness by the Practice Advisory for intraoperative awareness of the ASA. We report an incidence of dreaming similar to a previous study. This may be attributable to the first interview, in PACU, being soon after the anaesthetics when compared with later interviews in other studies (incidence of 2–22%). as recall of dreams decreases in later follow-up interviews. Dreams were more frequent in younger, lower ASA status, elective surgery, and ambulatory patients. In our study, the MA group showed a lower incidence of dreams which may be due, in part, to these being mainly short procedures. The clinical importance of dreaming remains unknown.

Description of the reported experiences of awareness with recall

There have been few direct awareness descriptions written by patients in the medical literature, but these are dramatic and describe an awareness episode recognized as a real event distinct from dreams. Auditory perceptions are reported by 50% of the patients, in agreement with our study. It has been demonstrated that auditory processing and memory is possible under propofol anaesthesia, and that surgical stimulation facilitates learning during anaesthesia independent of its effects on anaesthetic depth.
anaesthetic techniques are factors to be considered. In a tertiary care hospital such as ours, the observed incidence translates from 30 to 50 AWR patients per year. AWR should be prevented, and, provided a patient is detected, treatment should be started as soon as possible, including explanation to the patient of the causes of the event.

Supplementary material
Supplementary material is available at British Journal of Anaesthesia online.

Acknowledgements
We are grateful to Gabrielle Sennholz, MD and Mr Ignacio González from Aspect Medical Systems for their personal support and encouragement. Results have been reported, in part, as an oral presentation, in the XXVIII Spanish National Anaesthesia Congress (Valencia, Spain, April 26–28, 2007).

Funding
Funding was provided only from departmental sources.

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