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Original Article

The incidence and risk factors of intra-operative awareness during general anesthesia

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Abstract: Objective: To investigate the incidence of intra-operative awareness during general anesthesia (GA), and the corresponding risk and protective factors. Methods: A total of 5,504 patients who underwent GA during different surgeries between May 2008 and December 2010 were included. Awareness during surgery was reported by the patients, and gender, age, body weight, use of opioid analgesics, volatile anesthetic, tracheal intubation, pre-medication, blood pressure changes during surgery, anesthetic time, and the American Society of Anesthesiologists' (ASA) classifications were recorded for a multiple logistic regression analysis. Results: The incidence of intra-operative awareness was 0.7% and was highest in cardiothoracic surgery (1.00%), followed by general surgery (0.58%), and neurosurgery (0.43%). A multifactorial logistic regression analysis found that female gender, advanced age, no use of opioid analgesic, and tracheal intubation were risk factors ($P < 0.05$), and complications were related to awareness (which could be based on dosage), while pre-medication was protective ($P < 0.05$). Conclusion: While intra-operative awareness during GA was rare, to avoid awareness in GA careful consideration should be given to female and advanced aged patients, so sufficient pre-medication and proper application of opioid analgesics are necessary, and laryngeal mask airway insertion is preferable to tracheal intubation.

Keywords: General anesthesia, incidence of awareness, influencing factors, surgery

Introduction

Anesthetics are pharmacological agents that target specific central nervous system receptors. Once they bind to their receptors, anesthetics modulate remote areas of the brain by acting upon global neuronal networks, leading to a controlled and reversible loss of consciousness [1]. Accidental awareness under general anesthesia (GA) has received a great deal of attention from the research community in the past few years, including a recent national audit [2]. Awareness under GA is defined as an experience of consciousness under GA which can be recalled after emergence (also known as awareness with explicit memory) [3]. Patients may recall intra-operative events spontaneously or after specific questioning, and recall can occur immediately or up to one month after the operation. While the controllability and safety of GA has increased dramatically as modern medical science and monitoring techniques have evolved, intra-operative awareness (awareness for short periods) cannot be entirely avoided [4]. These episodes can cause post-traumatic stress disorder (PTSD) [5, 6], and the symptoms may last for two years. According to a sentinel-event alert disseminated by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), between 20,000 and 40,000 cases of anesthesia awareness may occur in the United States each year [7].

Internationally, studies have indicated that the incidence of awareness is low, between 0.1% and 0.2% [8-10]. In high-risk patients, the incidence can be up to 1% [11], and the highest incidences have been observed in cardiac and obstetrical surgeries [12]. The incidence in domestic surgery cases, however, has been reported to be significantly higher [13]. One study with 1,874 cases of cardiac surgery demonstrated that the incidence was over 2.5% [14]. There is a consensus that human factors and anesthesiologists play a role in many of the

awareness cases, and that these issues should be addressed to decrease the incidences [15, 16]. In this study, 5,504 patients who underwent GA were studied, and the occurrence of awareness and possible contributing factors were investigated.

Materials and methods

Subjects

A total of 5,504 patients from different departments in our hospital between May 2008 and December 2010 were selected. These patients were between 35 and 79 years of age, with an average age of 52.6 years ± 13.4, and underwent surgery under GA only, but without neuroelectrophysiological monitoring methods, such as bi-spectral index (BIS) or auditory evoked potential (AEP). Of these subjects, 2,731 cases were male and 2,773 cases female, with an average body weight (BW) of 57.6 kg ± 21.5. There were 628 patients with previous surgeries, while the other 4,876 had their first surgery in this study. Hypertension was present in 17.9% of patients and diabetes was present in 10.4% of patients. The time in surgery was longer than two hours for 4,865 patients, and less than two hours for the remaining 639 patients. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the General Hospital of the Armed Police Forces. Written informed consent was obtained from all participants.

Analysis of the incidence of awareness

All patients were administered GA only. One to three days after surgery, the patients were visited by professional staff for their follow-up visits. During the visits, patients were interviewed using standardized questions (as previously described by Russell [17]) to assess the extent of recall during surgery, as patients that have experienced awareness can clearly and precisely recall various incidents occurring during their surgery. Surgery outcomes were also evaluated.

Value assignment of influencing factors

In this study, ten factors that may influence the incidence of awareness were studied: gender, age, BW, use of opioid analgesics, volatile anesthetics, tracheal intubation, pre-medication, blood pressure changes during surgery, anesthetic time, complications, and American Society of Anesthesiologists' (ASA) classification.

Quality control

All data were entered using EpiData 3.0 with double data entry to ensure veracity and credibility.

Statistical analysis

SPSS 13.0 was used for the statistical analysis. Enumeration data was represented using the case number and χ^2 test or Fisher's exact test. Measurement data was represented using $\bar{x}$ ± s using the t-test. The Cochran-Armitage trend test was used to determine whether there was a linear trend between ASA grading and intra-operative awareness. Stepwise multifactorial logistic regression analysis was performed with inclusion criteria of 0.05 and exclusion criteria of 0.10.

Results

General data analysis

The average age of all 5,504 cases was 52.6 years ± 13.4. Awareness occurred in 23 patients (0.4%). Demographic and surgery variables are shown in **Table 1**. Demographic characteristics, type of surgery, and duration were compared in the awareness and non-awareness groups. There were no differences in age or gender between the awareness and non-awareness groups (age: $\lambda^2 = 0.696$, P = 0.404; gender: $\lambda^2 = 1.170$, P = 0.279). Complications and types of surgery were different in the two groups (complications: $\lambda^2 = 10.683$, P = 0.014; types of surgery: $\lambda^2 = 18.637$, P = 0.005). The two groups showed no difference in surgery duration, as measured by the ratio of longer than two hours: shorter than two hours ($\lambda^2 = 1.191$, P = 0.275).

Comparison of awareness incidence

The incidence of awareness was highest for cardiothoracic surgery, which was 1.00%. This was followed by general surgery and neurosurgery, which were 0.58% and 0.43%, respectively. No awareness was found from the

Table 1. Variables in patients with awareness and non-awareness

Variables		Awareness	Non-awareness	λ^2	
Age	Advanced ages(> 60 y)	4	645	0.696	0.404
	Young ages(≤ 60 y)	19	4836		
Gender	Male	14	2717	1.170	0.279
	Female	9	2764		
Complication	None	13	4307	10.683	0.014
	Hypertension	3	607		
	Diabetes	2	196		
	Hypertension+diabetes	5	371		
Types of surgery	Orthopedics	6	1381	18.637	0.005
	General	15	1579		
	Cardiothoracic	0	1201		
	Neurosurgery	2	734		
	Orbital	0	354		
	Urologic	0	11		
	Laparoscopic	0	221		
Duration	≥ 2 hours	22	4842	1.191	0.275
	< 2 hours	1	639		

Table 2. Value assignment of factors influencing the incidence of awareness

Factors	Value assignment
Gender	M = 0, F = 1
Age	The exact age of patient (Years)
BW	The exact BW of patient (Kg)
Usage of opioid analgesic	N = 0, Y = 1
Usage of volatile anesthetic	N = 0, Y = 1
Tracheal intubation	N = 0, Y = 1
Premedication	N = 0, Y = 1
Blood pressure changes during surgery	N = 0, Y = 1
Anesthetic time	The exact anesthetic time (min)
ASA classification	Class 1 and 2 = 0, The rest = 1

Department of Orbital Diseases, Urologic Surgery, or the Department of Laparoscopic Surgery.

Multifactorial logistic regression analysis

In this study, ten factors that might influence a patient's GA were investigated: gender, age, BW, use of opioid analgesics, volatile anesthetics, tracheal intubation, pre-medication, blood pressure changes during surgery, anesthetic time, and the ASA classification (**Table 2**). ASA has three grades: 1, 2 and 3; the proportions of intra-operative awareness are 0.004, 0.005 and 0.000 respectively. There was no linear trend between ASA classification and intra-operative awareness (P = 0.944). The analysis demonstrated that age, use of opioid analgesics, tracheal intubation, and pre-medication were all factors that could influence the patients' GA; advanced age, no use of opioid analgesics, and tracheal intubation were risk factors, while pre-medication was protective. We also found that complication was a related factor (P < 0.05, **Table 3**).

Discussion

Evolving modern medical science requires not only physical rehabilitation, but also maximal reduction of adverse effects to the patient's mental health. Awareness is rare during surgery under GA, but once it occurs, its occurrence will leave severe psychological and physiological effects on the patient [18, 19]. Therefore, intra-operative awareness and effective clinical intervention are gaining more attention from anesthesiologists and researchers [20]. Thanks to increasingly sophisticated technologies and a foundation of excellent research, researchers have successfully developed widely accepted criteria for ideal anesthesia, which is, in other words, leading the patient to complete analgesia and amnesia of surgery pain [21].

Intra-operative awareness includes implicit memory and explicit memory. In this study, we dealt with the memory status of patients after

Table 3. Multifactorial logistic regression analysis of factors influencing GA of population studied

Factors studied	B	Wald	*P*	OR	95% CI
Female	-0.157	0.115	0.734	0.855	0.345~2.119
Advanced age	1.286	3.547	0.018	2.167	1.287~4.658
Opioid free	2.657	12.964	0.000	17.648	5.498~78.325
Non-tracheal intubation	3.687	8.978	0.002	8.674	2.651~23.153
Premedication	-2.486	6.879	0.008	0.521	0.147~0.896
Complication	0.533	10.142	.001	7.704	1.228~2.366
Weight	0.061	0.033	0.066	1.063	0.996~1.134
Duration	0.866	0.704	0.401	2.378	0.314~17.995
Surgery Types	0.189	1.364	0.243	1.208	0.880~10659

surgery, which belongs to explicit memory and can result in various degrees of adverse effects [22]. Domestic studies have indicated that the incidence of awareness is approximately 0.91%, and might be influenced by multiple factors [23]. In this study, the incidence of awareness was 0.7%, and we examined potential influential factors by selecting ten factors for further investigation. The results revealed that the incidence was higher in female patients, those with advanced age, patients without opioid analgesics, and tracheal intubation, but lower for those with pre-medication. This indicates that the risk factors for awareness are female gender, advanced age, no use of opioid analgesic, and tracheal intubation, while premedication is protective. We also found that complication was a related factor; it has been suggested that the dosage of sedative and anesthesia drugs would be higher in patients with hypertension, which can prevent awareness [24]. We speculate that the absorption efficiency of anesthetic drugs may be low in female or aged patients, and even lower in patients undergoing GA without opioid or tracheal intubation. On the other hand, mild anesthesia may lead to awareness during surgery in female or aged patients because of poorer tolerance to anesthesia and the small amount of drug required for maintaining stable circulation. In this study, scopolamine, morphine, and tranquilizers, et al. were selected as the drugs for pre-medication for their anterograde amnesia effect [25], demonstrating that pre-medication could significantly reduce the incidence of awareness.

Similar studies have drawn various conclusions throughout the world. Sebel et al. proved that the incidence of awareness was chiefly related to ASA classification, based on their study of 19,575 cases with an incidence of 0.13% [26], while Davidson et al. demonstrated an incidence of 0.8% in their study of 864 pediatric surgery cases [27]. Errando et al. examined 4,001 awareness cases and found that usage of benzodiazepine before surgery and inhaled narcotics during surgery were protective factors for awareness, while advanced age, cesarean section under GA, and night surgery were risk factors [28]. Aranake et al. demonstrated that awareness occurred more frequently in patients who had previously experienced awareness [12, 29], and domestic studies have observed that the incidence of awareness could be reduced by monitoring the end-expiratory minimal alveolar concentration (MAC) of sevoflurane (in this case 0.7-1.3) [30, 31]. Low narcotic dose may also lead to awareness. Low narcotic dose can occur if the anesthesiologist reduces the dose to maintain the patient's hemodynamics during cardiac, open wound, or obstetric surgeries, and when intravenous anesthesia or neuromuscular-blocking drugs are used during surgery. Although the conclusions are different, each of these factors can be classified as an individual pharmacodynamic difference, a surgical procedure, gender, pre-medication, the patient's mental status, the application of neuromuscular-blocking drugs, surgery time, and so on [2]. The results from this study are also in contrast with other studies, indicating that a multitude of factors may result in awareness, and much more surgery data is needed for further, definite conclusions.

Disclosure of conflict of interest

None.

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