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Effects of different methods of general anesthesia on intraoperative awareness in surgical patients

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Abstract

The purpose of the study was to investigate the effects of total intravenous anesthesia (TIVA) and combined of intravenous and inhaled anesthesia (CIIA) on intraoperative awareness in surgical patients.

A total of 678 patients were recruited in the CIIA group, while TIVA group included 566 patients. The clinical characteristics and the occurrence of intraoperative awareness were compared between the groups. Mini-Mental State Examination, Generalized Anxiety Disorder 7, and Patient Health Questionnaire 9 tests were performed to estimate cognitive and psychological functions of the patients. In addition, logistic regression analysis was applied to identify the risk factors for intraoperative awareness in surgical patients.

In CIIA group, 3 patients (0.44%) were confirmed with intraoperative awareness, while 11 patients (1.94%) in TIVA group underwent intraoperative awareness. The occurrence rate of intraoperative awareness was significantly higher in VITA group than that in the CIIA group ($P = .029$). Awareness classification demonstrated that intraoperative awareness mainly included auditory, tactile, and pain perceptions. Moreover, 4 patients showed distress after operation. Patients with intraoperative awareness exhibited poor performance in cognitive and psychological tests ($P < .001$ for all). Logistic regression analysis demonstrated that CIIA (odds ratio [OR] = 0.198, 95% confidence interval [CI] = 0.047–0.827), age (OR = 0.951, 95% CI = 0.908–0.997), midazolam application (OR = 0.158, 95% CI = 0.034–0.736), awareness history (OR = 10.131, 95% CI = 2.206–45.517), and duration of surgery (OR = 1.016, 95% CI = 1.001–1.032) were significantly associated with intraoperative awareness.

Intraoperative awareness can significantly influence the cognitive and psychological functions of surgical patients. CIIA and midazolam application may lower the risk of intraoperative awareness.

Abbreviations: ASA = American Society of Anesthesiologists, CI = confidence interval, CIIA = combined of intravenous and inhaled anesthesia, GAD-7 = Generalized Anxiety Disorder 7, ICU = intensive care unit, MiAC = Michigan Awareness Classification, MMSE = Mini-Mental State Examination, OR = odds ratio, PHQ-9 = Patient Health Questionnaire 9, PTSD = post-traumatic stress disorder, TIVA = total intravenous anesthesia.

Keywords: combined of intravenous and inhaled anesthesia, general anesthesia, intraoperative awareness, total intravenous anesthesia

1. Introduction

Intraoperative awareness, also named general anesthesia awareness with recall, is described as postoperative recall of the consciousness and events during the general anesthesia.[1] Despite of the low occurrence rate, intraoperative awareness is a severe complication of anesthesia that may significantly influence the cognitive and psychological functions of the patients, even causing post-traumatic stress disorder (PTSD).[2,3] Until now, the commonly used methods for intraoperative awareness monitoring include depth of anesthesia monitoring and brain-function monitoring. However, the advantages of the methods remain unclear, due to the diverse anesthetic conditions, such as age, race, gender, acid–base imbalances, drug administered to the patients, and so on.[4–6] Therefore, identification of the risk factors regarding awareness may be an effective approach to guide intraoperative awareness intervention.

According to the epidemiological studies, 3 types of factors may contribute to the occurrence of intraoperative awareness, including patients, surgical procedures, and anesthetic techniques.[1] It was reported that the incidence of intraoperative awareness was higher in women than that in men.[7,8] Moreover, the patients with the age of <60 years were more likely to undergo anesthesia awareness of recall after operation.[9] However, some researchers suggested that the morbidity of awareness was higher among elder surgical patients.[10] Besides, surgical procedures might also influence the occurrence of intraoperative awareness, and caesarean section is considered as a high-risk operation for awareness.[11] Recently, intravenous anesthesia application was recognized as a risk factor for intraoperative awareness. It was reported that at the same depth of anesthesia, combined of intravenous and inhaled anesthesia (CIIA) exhibited well performance in suppressing the stress response during laparoscopic radical gastrectomy for patients

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with gastric cancer.[12] However, the effects of total intravenous anesthesia (TIVA) and CIIA on intraoperative awareness in patients undergoing other surgeries had been rarely reported.

The purpose of the present study was to investigate the effects of different anesthetic methods on intraoperative awareness, as well as the risk factors for intraoperative awareness in surgical patients. In addition, we discussed the influences of intraoperative awareness on cognitive and psychological functions of the patients.

2. Materials and methods

2.1. Patient population

The study was approved by the Ethic Committee of Beijing Luhe Hospital. The patients or their family signed informed consents in advance.

The study was carried out in Beijing Luhe Hospital. The patients collected in the study should be met the following inclusion criteria—Age: older than 18 years; undergoing general anesthesia for surgery; with normal metal status; American Society of Anesthesiologists (ASA) classification: I to II; and without drug abuse. In addition, the patients did not meet the inclusion criteria, or presented the following conditions should be excluded from the research: with anesthetic contraindications; died in the hospital (intraoperation or postoperation); could not complete the postoperative questionnaire within 48 h; and presentation with severe mental disorders after surgery.

2.2. Methods

The patients received routine monitoring after entering the operation room. All the patients received similar anesthesia induction strategies. During the operation, sevoflurane combined with propofol was used for maintaining anesthesia for patients in CIIA group. The VTi of sevoflurane was 2.5% to 4%, and the propofol was infused at the speed of 2 mg/(kg h). Among patients in TIVA group, the anesthesia was maintained with propofol, and the target concentration was 3 to 4 μg/mL.

2.3. Intraoperative awareness estimation

After operation, all the patients were transferred to intensive care unit (ICU) for postoperative sedation and ventilation. Then the patients were transferred to wards where the patients were awakened.

Each patient was interviewed within 48 h after operation according to the modified Brice Interview.[13] Based on their answers, the patients were defined as: confirmed awareness, possible awareness, and no awareness.[14] The occurrence of awareness during ICU stay would be excluded. Michigan Awareness Classification (MiAC) was used to evaluate the experience of patients confirmed with intraoperative awareness. It included 5 points: Class 1 referred to isolated auditory perceptions; Class 2 pointed tactile perceptions; Class 3 was related with pain; Class 4 was paralysis; and Class 5 included paralysis and pain. In addition, if the patients were with the presentation of fear, anxiety, suffocation, sense of doom, sense of impending death, and so on; an additional "D"-for distress was added.[15]

2.4. Cognitive function assessment

The cognitive function was estimated by Mini-Mental State Examination (MMSE).[16] MMSE was a commonly used method for cognitive status evaluation, including the following aspects: orientation to place and time, the short-term memory, episodic long-term memory, subtraction, as well as the ability to construct a sentence and oral language ability. The maximum score of the examination was 30, and patients with the score <24 was defined as cognitive impairment.[17]

The examination was performed for the patients before surgery and within 2 weeks postoperative.

2.5. Psychiatric evaluation

Two weeks after operation, the patients received psychiatric examination, including anxiety and depression. The anxiety symptoms of the patients were evaluated by Generalized Anxiety Disorder 7 (GAD-7) questionnaire,[18] while the Patient Health Questionnaire 9 (PHQ-9) was used to estimate their depression status.[19]

2.6. Statistical analysis

The medical information of the patients as well as the results of postoperative evaluation were recorded. The continuous variables were shown as mean ± standard deviation, and analyzed by Student *t* test. Chi-squared test was used for categorical data analyses. Logistical regression analysis was applied to identify the risk factors for intraoperative awareness. All the statistical analyses were performed in SPSS 18.0 software (SPSS Inc., Chicago, IL). *P* values <.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics of the included patients

According to the selection criteria, 1244 surgical patients including 698 men and 546 women were recruited in the present study; 678 of them received combined of intravenous and inhaled anesthesia (CIIA), while 566 patients were treated with TIVA. The average age of the patients was 53.67 ± 11.67 years, and their mean body mass index value was 22.78 ± 3.64 kg/m^2. According to ASA classification, 558 patients were classed to ASA I, while 686 patients were at ASA II. Among the patients, 14 (1.12%) patients were diagnosed with confirmed awareness, and 23 (1.85%) patients were confirmed as possible awareness. The detailed information of the patients were summarized in Table 1.

3.2. Effects of anesthetic methods on intraoperative awareness in surgical patients

In this study, we compared the clinical characteristics between the TIVA and CIIA groups. Analysis results suggested that the clinical parameters such as gender, age, complications, ASA, surgery type, and so on were similar between the 2 test groups ($P > .05$ for all) (Table 1). We also compared the occurrence of intraoperative awareness between the 2 groups. In CIIA group, 3 patients (0.44%) were diagnosed with confirmed awareness, and 8 patients were confirmed as possible awareness. Eleven patients (1.94%) in TIVA group underwent intraoperative awareness, and 15 possible awareness patients (2.65%) were identified. The occurrence rate of intraoperative awareness was significantly higher in VITA group than that in the CIIA group ($P = .007$) (Table 1).

3.3. Classification of intraoperative awareness

According to MiAC, 4 patients were classed to Class 1, and Class 2 included 2 patients. Three patients felt pain during operation and

Table 1

Basic characteristics of the study population.

Characteristics	Totally (n = 1244)	Anesthetic methods		P
		CIIA (n = 678)	TIVA (n = 566)	
Gender				.599
Male	698	385	313	
Female	546	293	253	
Age, y	53.67 ± 11.67	53.89 ± 11.52	53.40 ± 11.27	.456
BMI, kg/m^2	22.78 ± 3.64	22.90 ± 3.30	22.64 ± 4.00	.224
ASA				.830
I	558	306	252	
II	686	372	314	
Midazolam application				.986
Yes	681	371	310	
No	563	307	256	
Intraoperative awareness history				.810
Yes	30	17	13	
No	1214	661	553	
Types of surgery				.113
Neurosurgery	100	45	55	
Otolaryngology surgery	78	34	44	
Gynecology	33	19	14	
Orthopedic surgery	184	109	75	
Urology	103	54	49	
General surgery	271	160	111	
Thoracic surgery	320	173	147	
Oral surgery	155	84	71	
Duration of surgery, min	96.69 ± 36.68	97.33 ± 38.90	95.91 ± 33.85	.496
Complications				
Hypertension	530	295	235	.479
Hyperlipidemia	501	277	224	.647
Diabetes mellitus	509	275	234	.780
Alcohol	421	234	187	.584
Smoking	425	232	193	.965
Intraoperative awareness				.007
Confirmed awareness	14	3	11	
Possible awareness	23	8	15	
No awareness	1207	667	540	

ASA = American Society of Anesthesiologists, BMI = body mass index, CIIA = combined of intravenous and inhaled anesthesia, TIVA = total intravenous anesthesia.

were grouped into Class 3. There was 1 patient in each of Class 4 and Class 5. In addition, 4 patients were confirmed as "Distress" (Fig. 1).

3.4. Effects of intraoperative awareness on cognitive function and psychiatric status of the patients

The cognitive and psychiatric functions of the patients were estimated in the present study. We compared the MMSE, GAD-7, and PHQ-9 scores between intraoperative awareness patients and no or possible awareness patients. Analysis results demonstrated that patients with intraoperative awareness exhibited significantly poor performance in MMSE, GAD-7, and PHQ-9 examinations ($P < .001$ for both; Table 2).

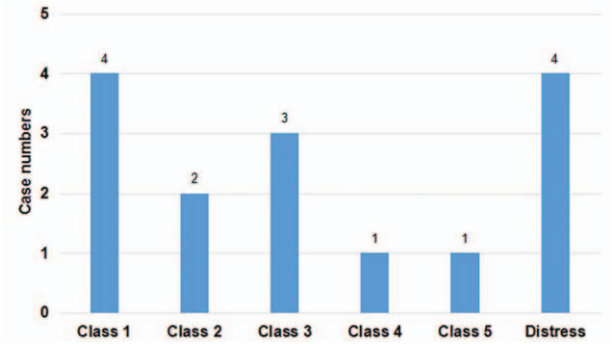

Figure 1. The classification of awareness among confirmed awareness patients. Class 1 referred to isolated auditory perceptions; Class 2 pointed tactile perceptions; Class 3 was related with pain; Class 4 was paralysis; and Class 5 included paralysis and pain. In addition, if the patients were with the presentation of fear, anxiety, suffocation, sense of doom, sense of impending death, and so on; an additional "D"-for distress was added. The classification demonstrated that the major patients with confirmed awareness exhibited in auditory perceptions, tactile perceptions, and pain. Moreover, 4 of them showed distress after operation.

3.5. Risk factors for intraoperative awareness in surgical patients

In order to investigate the risk factors for intraoperative awareness in surgical patients, we compared the clinical characteristics between the intraoperative awareness group and no or possible awareness group. From Table 3, we found that age ($P = .025$), intraoperative history ($P = .000$), midazolam application ($P = .002$), surgery time ($P = .022$), hyperlipidemia history ($P = .011$), and anesthetic methods ($P = .029$) were significantly correlated with intraoperative awareness (Table 3).

Logistic regression analysis demonstrated that CIIA (odds ratio [OR] = 0.198, 95% confidence interval [CI] = 0.047–0.827, $P = .026$), elder age (OR = 0.951, 95% CI = 0.908–0.997, $P = .038$), and midazolam application (OR = 0.158, 95% CI = 0.034–0.736, $P = .019$) were protective factors for intraoperative awareness in surgical patients. While intraoperative awareness history (OR = 10.131, 95% CI = 2.206–45.517, $P = .003$) and duration of surgery (OR = 1.016, 95% CI = 1.001–1.032, $P = .039$) were identified as risk factors for intraoperative awareness (Table 4).

Table 2

Effects of intraoperative awareness on cognitive and psychiatric functions in surgical patients.

Factors	Preoperation			Postoperation		
	Confirmed awareness	No awareness or possible awareness	P	Confirmed awareness	No awareness or possible awareness	P
MMSE score	26.36 ± 2.13	26.51 ± 2.08	.777	19.79 ± 1.89	24.81 ± 3.13	<.001
GAD-7 score	4.14 ± 1.17	3.94 ± 2.45	.763	9.36 ± 2.84	5.50 ± 3.22	<.001
PHQ-9 score	4.93 ± 1.73	5.21 ± 2.73	.700	9.78 ± 2.64	5.79 ± 3.18	<.001

GAD-7 = Generalized Anxiety Disorder 7, MMSE = Mini-Mental State Examination, PHQ-9 = Patient Health Questionnaire 9.

Table 3

Association between medical characteristics and intraoperative awareness in the study population.

Features	Confirmed awareness	No awareness or possible awareness	*P*
Gender			.643
Male	7	691	
Female	7	539	
Age, y	46.86 ± 6.07	53.75 ± 11.43	.025
BMI, kg/m^2	22.00 ± 4.37	22.79 ± 3.63	.418
ASA			.697
I	7	551	
II	7	679	
Midazolam application			.002
Yes	2	679	
No	12	551	
Intraoperative awareness history			.000
Yes	3	27	
No	11	1203	
Types of surgery			.371
Neurosurgery	3	97	
Otolaryngology surgery	2	76	
Gynecology	0	33	
Orthopedic surgery	3	181	
Urology	1	102	
General surgery	1	270	
Thoracic surgery	2	318	
Oral surgery	2	153	
Duration of surgery, min	118.93 ± 20.52	96.43 ± 36.75	.022
Complications			
Hypertension, yes/no	7/7	523/707	.574
Hyperlipidemia, yes/no	1/13	500/730	.011
Diabetes mellitus, yes/no	7/7	502/728	.487
Alcohol, yes/no	4/10	417/813	.675
Smoking, yes/no	5/9	420/810	.902
Anesthetic methods			.029
CIIA	4	674	
TIVA	11	555	

ASA = American Society of Anesthesiologists, BMI = body mass index, CIIA = combined of intravenous and inhaled anesthesia, TIVA = total intravenous anesthesia.

Table 4

Logistic regression analysis of risk factors for intraoperative awareness.

Parameters	OR	95% CI	*P*
Gender	0.946	0.301–2.979	.925
Age, y	0.951	0.908–0.997	.038
BMI, kg/m^2	0.951	0.825–1.095	.483
ASA	1.369	0.432–4.336	.594
Midazolam application	0.158	0.034–0.736	.019
Intraoperative awareness history	10.131	2.206–46.517	.003
Duration of surgery, min	1.016	1.001–1.032	.039
Hypertension	1.285	0.408–4.051	.668
Hyperlipidemia	0.120	0.015–0.955	.045
Diabetes mellitus	1.721	0.555–5.333	.347
Alcohol	0.860	0.250–2.957	.811
Smoking	0.746	0.223–2.494	.634
Anesthetics (CIIA vs. TIVA)	0.198	0.047–0.827	.026

ASA = American Society of Anesthesiologists, BMI = body mass index, CI = confidence interval, CIIA = combined of intravenous and inhaled anesthesia, OR = odds ratio, TIVA = total intravenous anesthesia.

4. Discussion

Intraoperative awareness is a serve complication associated with anesthesia. In this study, we found that the occurrence of intraoperative awareness was 1.12% in the surgical patients. These data were consisted with the previous investigations. A related reported based on Thai Anesthesia Incident Monitoring study database indicated that the incidence rate of intraoperative awareness was about 1.05%.[20] Despite the low morbidity, intraoperative awareness is a serious problem that may cause psychological side effects, such as sleep disturbances, depression, and anxiety, even PTSD.[21] In the present study, we compared the cognitive functions, depression, and anxiety status between confirmed awareness patients and no or possible awareness patients. Analysis results demonstrated that patients with intraoperative awareness had poor scores in cognitive and psychological examinations. Osterman et al[22] reported that surgical patients with the experience of intraoperative awareness had significant postoperative distress associated with unsafe, terrified, abandoned, and betrayed. In a words, intraoperative awareness patients were more likely to experience cognitive impaired, anxiety, or depression.

Prevention of intraoperative awareness remains a great challenge for anesthesiologists. Despite of the available methods for awareness monitoring during general anesthesia, intraoperative awareness can be only confirmed based on the postoperative information directly obtained from the patients.[1] To improve the management of awareness, various researches were aimed to identify the risk factors for intraoperative awareness. In the present study, we investigated the effects of anesthetic techniques on awareness in surgical patients. The data demonstrated that CIIA decreased the risk of intraoperative awareness compared with TIVA. A questionnaire survey in Japan done by Yasuhiro et al demonstrated that 24 intraoperative awareness cases were confirmed among 85,156 anesthetic cases; moreover, 88% (21/24) of the confirmed awareness cases received TIVA.[23] Wang et al[21] also reported that propofol maintenance was a risk factor for intraoperative awareness in general anesthesia. A multicenter observational study carried out by Xu et al[24] reported that anesthesia methods of TIVA might increase the risk of awareness. All the investigations indicated that anesthesia methods could influence the intraoperative awareness. CIIA might be an effective way for preventing intraoperative awareness caused in general anesthesia, and serious monitoring should be taken when TIVA was performed for the surgical patients.

In addition, we found that age, intraoperative history, midazolam application, surgery time, and hyperlipidemia history also showed close link with intraoperative awareness. Logistic regression analysis suggested that age, intraoperative history, midazolam application, surgery time, and anesthesia methods were independently correlated with intraoperative awareness in the study population. Age was a controversial factor for intraoperative awareness.[9,10] Based on our analysis, young patients were more likely to experience awareness compared with elder patients. The conclusion was consisted with the founding of Zheng et al.[25] In their study, patients with the age <60 years old were confirmed at high risk for awareness. Furthermore, they also found that duration of surgery was a risk factor for awareness. In addition, we found that patients with the experience of intraoperative awareness were more likely to undergo awareness. It was reported that the incidence of intraoperative awareness was significantly higher in patients with awareness history than those without.[26] Accumulating evidences have reported that midazolam application was a protective factor for intraoperative awareness.[27,28] The effects might dependent on its inhibitory

function in central nervous system. Taken together, the identified risk factors for intraoperative awareness might provide effective information for risk stratification of intraoperative awareness that guided the prevention of awareness in general anesthesia.

There were several limitations in the present study. First, considering the low morbidity of intraoperative awareness, the sample size was relatively small in the study. Further well-designed multicentral researches were still needed to investigate the issue. Second, various researches had reported that patients undergoing cardiac surgery were more likely to experience awareness. However, the association was not observed in the present study. The reason might be attributed to the gross classification of surgery types. Third, there was lack of standard tool to determinate if the patents regained consciousness, and it was hard to choose the appropriate time to initiate the first interview for the patients. In this study, awareness estimation was performed for the patients at 48 h postoperative. The time for interviews might cause the final result random error.

In conclusion, compared with TIVA, anesthesia method of CIIA can significantly lower the risk of intraoperative awareness. Young surgical patients are at high risk of intraoperative awareness compared with elder patients. In addition, midazolam application may be an effective approach for preventing intraoperative awareness. Long duration of surgery and awareness history are identified as risk factors for intraoperative awareness.

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