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Review Article

Inhalation anesthesia combined with total intravenous anesthesia can alleviate pain response and reduce adverse reactions of patients undergoing radical mastectomy

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Abstract: To determine the effects of inhalation anesthesia combined with total intravenous anesthesia on the pain response and adverse reactions of patients undergoing radical mastectomy. A total of 73 patients clinically diagnosed with breast cancer who were to undergo radical mastectomy from November 2017 to June 2019 were enrolled as research subjects, and assigned to a observation group (obs group, n=41) and a control group (con group, n=32) according to the specific anesthesia methods used. The two groups were compared in anesthesia-related indexes, cortisol level, heart rate, blood pressure changes, pain degree, and adverse reactions, and the visual analog scale (VAS) was adopted to score the pain degree of the patients after anesthesia. There was a significant difference in the pain degree between the two groups ($P<0.05$). After anesthesia, the VAS score of the obs group was significantly lower than that of the con group ($P<0.05$), and after treatment, both groups showed decreased systolic blood pressure and diastolic blood pressure, and the decrease in the obs group was more significant than that in the con group ($P<0.05$). In addition, the incidence of adverse reactions in the obs group was significantly lower than that in the con group ($P<0.05$), and at 60 min after anesthesia, both groups showed significantly increased serum cortisol levels ($P<0.05$), and the increase in the con group was more remarkable than that in the obs group. Furthermore, the obs group experienced significantly shorter induction time, anesthesia time, drug withdrawal-extubation time, and spontaneous breathing recovery time than the con group. Inhalation anesthesia combined with total intravenous anesthesia can alleviate the pain response and reduce adverse reactions of patients undergoing radical mastectomy, which is worthy of clinical promotion.

Keywords: Inhalation anesthesia, total intravenous anesthesia, radical mastectomy, pain response, adverse reaction

Introduction

Breast cancer (BC) is a malignant tumor due to the invasion of malignant cells and the destruction of normal breast tissues, which has relatively high clinical incidence and complicated pathogenesis [1]. Recently, the incidence of BC is on the rise, and more and more young people are suffering from it [2, 3]. According to statistics, there were 1,670,000 new BC patients and 520,000 patients died of BC in 2012. BC is the most common cancer among women, accounting for 25.1% of all cancers. The incidence of BC is relatively high in developed countries, and its relative mortality is the highest in underdeveloped countries [4]. In order to control BC, many patients need a radical mastectomy [5]. However, BC patients are relatively weak, and they need nutrients and support for maintenance, so it is crucial to lower the pain of patients during surgery [6, 7].

Clinically, some anesthetics can relive the pain of patients during surgery, but they usually bring about many complications, and patients require a relatively long awakening time after surgery, which causes them great pain [8, 9]. Inhalation anesthesia allows strong control of drug flow. With inhalation anesthesia, the appropriate depth can be maintained and with

an increase in the dosage of inhalational anesthetics it can effectively reduce the required intravenous anesthetics, and it is relatively simple to operate, but it is accompanied by risks and complications [10, 11]. With the ability of shortening the recovery time, inhalation anesthesia combined with total intravenous anesthesia is considered to be one of the anesthesia methods with relatively good analgesic effects, and is currently widely used in the treatment of diseases including gastric cancer and rectal cancer [12, 13].

Therefore, this study was designed to investigate the anesthetic influence of inhalation anesthesia combined with total intravenous anesthesia on radical mastectomy by applying total intravenous anesthesia combined with inhalation anesthesia in some patients treated in our hospital and inhalation anesthesia alone in some other patients, respectively, and comparing their pain degree, adverse reactions, and anesthesia-related indexes; with the goal of providing reference for clinical practice.

Materials and methods

General data

A total of 73 patients clinically diagnosed with BC who were to undergo radical mastectomy from November 2017 to June 2019 were enrolled as research subjects, and assigned to a observation group (obs group, n=41) and a control group (con group, n=32) according to the specific anesthesia methods. The obs group consisted of patients between 26 and 57 years old, with an average age of (42.41±2.98) years, course of disease between 1 and 7 months, and average course of disease of (3.46±1.24) months, including 23 patients with left BC and 18 patients with right BC, 26 patients in I stage and 15 patients in II stage. The con group consisted of patients between 29 and 58 years old, with an average age of (42.85±3.41) years, course of disease between 1 and 6 months, and average course of disease of (3.51±1.37) months, including 19 patients with left BC and 13 patients with right BC, 18 patients in I stage and 14 patients in II stage. All patients were females who met the diagnostic criteria for BC and were confirmed by pathological examination, and all of them received radical mastectomy. The study was carried out after consent was obtained from the patients or their families and approval from the Ethics Committee of Yiwu Central Hospital and was in accordance with the Helsinki Declaration.

The inclusion criteria of the study: Patients meeting the diagnostic criteria for BC [14], patients with BC in I or II stage in TNM staging, patients equal to 65 years old or younger, patients undergoing the radical mastectomy for the first time, and those without infection who had not received radiotherapy and chemotherapy. The exclusion criteria of the study: Patients with dysfunction of important organs, endocrine system, or immune system, patients with thyroid diseases, patients with a history of drug allergy or contraindications for drugs, patients with severe liver, kidney, heart, or lung dysfunction, patients who had mental diseases or took drugs or hormones, and those who refused to participate in this study.

Treatment methods

Patients in the con group were given inhalation anesthesia as follows: They were asked to inhale 1.5%-3.0% isoflurane (H20059911, Abbott Laboratories, Shanghai, China) and then vecuronium bromide and fentanyl were added to the isoflurane according to the specific needs of each patient for anesthesia maintenance.

Patents in the obs group were given inhalation anesthesia combined with total intravenous anesthesia in addition to the treatment for the con group: The vital signs of each patient were detected and recorded in the operating room. Then 1.5-2.5 mg/kg propofol (H19990281, Libang Pharmaceutical Co., Ltd., Xi'an, China) was applied to each patient for anesthesia induction, and 0.2-0.5 μg/kg sufentanil citrate injection (H20054256, Humanwell Pharmaceutical Co., Ltd., Yichang, China) and 0.2-0.3 mg/kg cisatracurium (H20183042, Heng Rui Pharmaceutical Co., Ltd., Jiangsu, China) were injected intravenously into each patient for anesthesia. After successful intubation, each patient was asked to inhale 1.0-2.0% isoflurane, and then intravenously and continuously infused with 500 mg propofol mixed with 500 μg fentanyl at an adjusted infusion speed. The vital signs of each patient were closely monitored, and anesthesia maintenance was carried out according to the intraoperative condition of the patient. The main reference indexes included heart rate within the range of basic

Table 1. Comparison of clinical data between the observation group and the control group

Item	The observation group (n=41)	The control group (n=32)	χ^2-value	*P*-value
Age (Y)	42.41±2.98	42.85±3.41	0.588	0.559
Sex			0.140	0.708
Male	2	1		
Female	39	31		
Course of disease (Month)	3.46±1.24	3.51±1.37	0.163	0.871
Weight (kg)	58.47±4.51	56.91±3.78	1.572	0.120
Diseased site			0.079	0.779
Left	23	19		
Right	18	13		
TNM staging			0.385	0.535
Stage I	26	18		
Stage II	15	14		
Operation time (min)	71.55±4.6	72.84±5.31	1.111	0.270

heart rate ±20% and blood pressure within the range of the basic blood pressure ±20%, which were monitored to ensure the stable vital signs of patients. When a patient could breathe autonomously, and showed a pulmonary ventilation volume per minute recovered to 80% of the basic value, respiratory frequency ≥10 time/min, and recovery basic reflex including swallowing, cough, and consciousness, the trachea cannula of the were removed. If necessary, 0.03-0.06 mg/kg neostigmine and 15-30 μg/kg atropine were applied to the patients through intravenous drip for muscle relaxation and antagonism.

Outcome measures

Anesthesia-related indexes including anesthesia induction time, anesthesia time, drug withdrawal-extubation time, and spontaneous breathing recovery time of the two groups were analyzed, and the pain degree of the patients in the two groups at 90 min after anesthesia recovery was scored using the visual analog scale (VAS) with a full score of 10 points. A higher score indicates more serious pain. In addition, the adverse reactions of the two groups were assessed, including dysphoria and excessive sedation. The heart rate changes of patients in the two groups were analyzed at 30 min before anesthesia and 15 min after anesthesia, and the cortisol level was determined using the radioimmunoassay at 30 min before anesthesia and at 1 h after anesthesia. The pain degree was compared between the two groups.

Statistical analysis

All the data obtained in this study were analyzed statistically using SPSS 22.0. Measurement data were expressed as the mean ± standard deviation (x ± s), and analyzed using the t test. Enumeration data were analyzed using the χ^2. *P*<0.05 implied a significant difference.

Results

Comparison of clinical data between the groups

Comparison of clinical data between the obs group and the con group revealed that there was no significant difference between the two groups in age, sex, course of disease, weight, diseased site, TNM staging, and operation time (all P>0.05) **Table 1**.

Comparison of anesthesia-related indexes between the groups

The comparison of anesthesia-related indexes between the obs group and the con group showed that the obs group experienced significantly shorter induction time, anesthesia duration, drug withdrawal-extubation time, and spontaneous breathing recovery time than the con group (all P<0.05) **Table 2**.

Comparison of VAS score between the two groups at 90 min after anesthesia recovery

The VAS score of the obs group was significantly lower than that of the con group ((1.64±0.26) points *vs.* (2.42±0.48) points, P<0.05) **Figure 1**.

Comparison of blood pressure and heart rate between the two groups before anesthesia and at 15 min after anesthesia

Before anesthesia, there was no significant difference between the two groups in systolic

Table 2. Comparison of anesthesia-related indexes between the observation group and the control group

Group	Induction time	Anesthesia time	Drug withdrawal-extubation time	Spontaneous breathing recovery time
The observation group (n=41)	3.42±0.92	75.45±3.26	8.77±2.19	10.56±1.21
The control group (n=32)	2.67±0.88	85.41±3.37	15.72±3.26	6.58±1.47
t	3.522	12.76	10.87	12.69
P-value	<0.01	<0.01	<0.01	<0.01

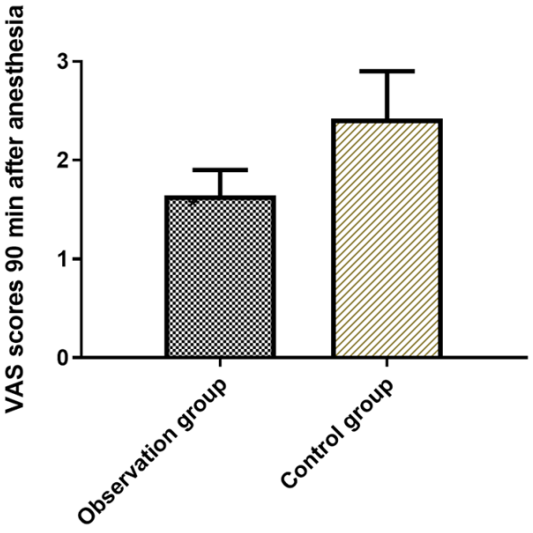

Figure 1. Comparison of VAS score between the observation group and the control group at 90 min after anesthesia recovery. The VAS score of the observation group was significantly lower than that of the control group ((1.64±0.26) points vs. (2.42±0.48) points, P<0.05).

blood pressure, diastolic blood pressure, and heart rate (both P>0.05). While at 15 min after anesthesia, both groups showed significantly decreased systolic blood pressure, diastolic blood pressure, and heart rate (both P<0.05), and the three indexes of the obs group were significantly lower than those of the con group (both P<0.05); so the decrease of systolic blood pressure, diastolic blood pressure, and heart rate in the obs group was more significant than that of the con group **Table 3** and **Figure 2**.

Comparison of adverse reactions between the groups

All the patients in the two groups recovered from anesthesia within 2 hours and suffered from different degrees of postoperative anesthesia complications. The obs group showed an incidence of adverse reactions of 9.76%, with dysphoria in 2 patients and excessive sedation in 2 patients. While the con group showed an incidence of adverse reactions of 40.63%, with nausea in 7 patients, dysphoria in 3 patients, and aspiration and reflux in 3 patients, so the incidence of adverse reactions in the obs group was significantly lower than that in the con group (P<0.05). The above adverse reactions are all mild and disappeared in a timely manner after treatment **Table 4**.

Comparison of serum cortisol level between the two groups before anesthesia and at 60 min after anesthesia

Before anesthesia, there was no significant difference in serum cortisol level between the two groups (P>0.05). While at 60 min after anesthesia, both groups showed significantly increased serum cortisol level (P<0.05), and the serum cortisol level of the obs group was significantly lower than that of the con group (P<0.05), so the increase in the con group was more significant than the obs group **Figure 3**.

Discussion

BC is a malignant tumor with high morbidity and mortality, and it has become a common disease threatening women's health [15, 16]. BC is mainly treated through surgery in clinical practice, and intraoperative anesthesia is a major factor affecting the efficacy of surgery [17, 18]. Some studies have shown that different anesthesia methods and anesthetics cause great differences in surgical stress response and bring about different effects on physiological indexes of patients during and after surgery [19, 20]. Therefore, it is particularly important to choose reasonable anesthesia methods [21].

Inhalation anesthesia is a commonly used anesthesia method in clinical practice, which

Table 3. Comparison of blood pressure and heart rate between the two groups before anesthesia and at 15 min after anesthesia

Group	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Heart rate (Times/min)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
The observation group (n=41)	123.16±10.54	103.57±9.28	79.41±8.14	62.76±6.39	83.89±8.56	71.42±7.25
The control group (n=32)	121.23±13.42	115.62±10.42	78.41±8.18	68.43±5.62	84.27±13.42	79.41±6.58
T	0.689	5.216	0.519	3.963	0.147	4.863
P-value	0.493	<0.01	0.605	<0.01	0.884	<0.01

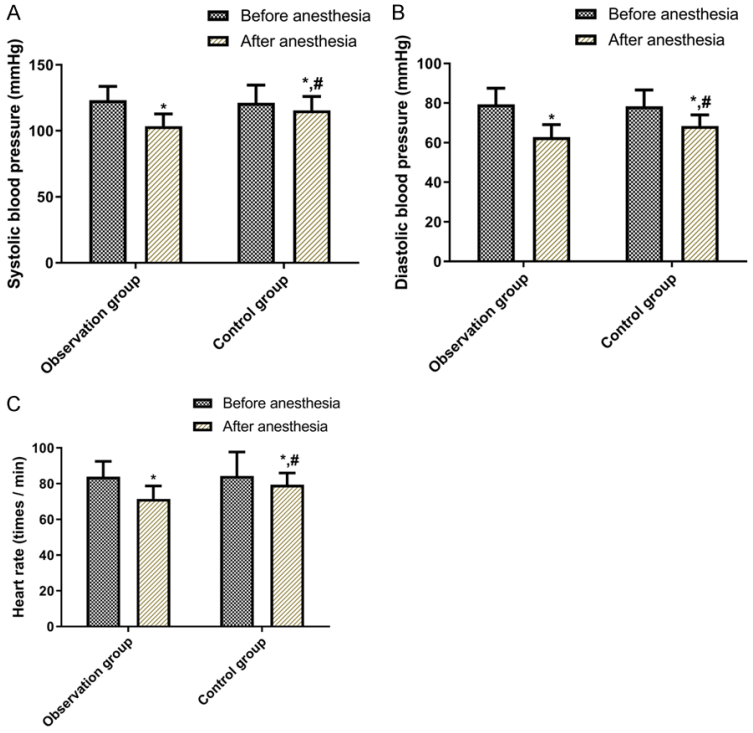

Figure 2. Comparison of heart rate and blood pressure between the observation group and the control group before anesthesia and at 15 min after anesthesia (A). Before anesthesia, there was no significant difference in systolic blood pressure between the two groups (P>0.05), while at 15 min after anesthesia, both groups showed significantly decreased systolic blood pressure, and the decrease in the observation group was more significant than that in the control group. The systolic blood pressure of the observation group was significantly lower than that of the control group (P<0.05) (B). Before anesthesia, there was no significant difference in diastolic blood pressure between the two groups (P>0.05), while at 15 min after anesthesia, both groups showed significantly decreased diastolic blood pressure, and the decrease in the observation group was more significant than that in the control group. The diastolic blood pressure of the observation group was significantly lower than that of the control group (P<0.05) (C). Before anesthesia, there was no significant difference in heart rate between the two groups (P>0.05), while at 15 min after anesthesia, both groups showed significantly decreased heart rate, and the heart rate of the obs group was significantly lower than that of the con group (P<0.05). Notes: *P<0.05 vs. the situation before anesthesia. #P<0.05 vs. the observation group after anesthesia.

adopts a laryngeal mask airway that facilitates insertion and operation, and does not usually affect muscle relaxant during operation. It is often applied to operations with lower requirements for muscle relaxation in clinical practice. Radical mastectomy is a surgery with relatively short operation times and relatively low requirements for muscle relaxation, so inhalation anesthesia is suitable for it [22]. However, clinical application shows that gas can easily leak out of the ventilation hood and enter the stomach of the patient during inhalation anesthesia, resulting in complications such as aspiration and reflux [23]. Compound anesthesia takes effect quickly, and brings about no pain with small irritation during induction. In addition, it can be performed with simple equipment and intravenous injection, after which patients usually recover relatively fast. With the continuous improvement in clinical research, due to the application of a variety of intravenous anesthetics, syringe pumps, and high-frequency ventilation devices, the clinical application of total intravenous anesthesia is more fruitful [24]. Therefore, this study applied total intravenous anesthesia combined with inhalation anesthesia on some patients treated in our hospital and inhalation anesthesia alone on some other patients. It came out that there was a remarkable difference in the pain degree between the two groups (P<0.05), and the VAS score of the

Table 4. Comparison of adverse reactions between the two groups

Item	The obs group (n=41)	The con group (n=32)	χ^2-value	*P*-value
Dysphoria	2 (4.88)	3 (9.38)	9. 928	0.002
Excessive sedation	2 (4.88)	0 (0)		
Nausea	0 (0)	7 (21.88)		
Reflux and aspiration	0 (0)	3 (9.38)		
The total incidence	4 (9.76)	13 (40.63)		

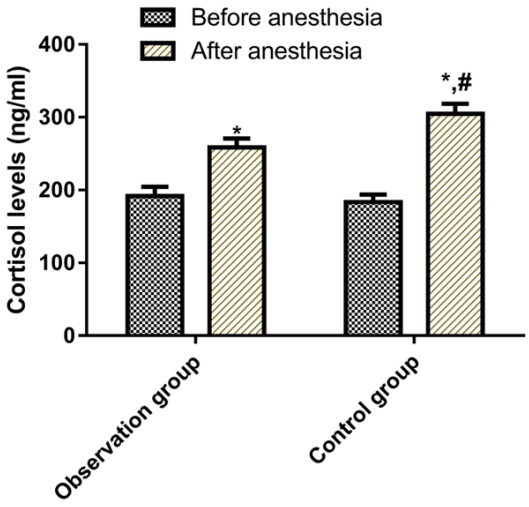

Figure 3. Comparison of serum cortisol level between the observation group and the control group before anesthesia and at 60 min after anesthesia. Before anesthesia, there was no significant difference in serum cortisol level between the two groups (P>0.05), while at 60 min after anesthesia, both groups showed significantly increased serum cortisol level (P<0.05), and the increase in the control group was more significant than that in the observation group. The serum cortisol level of the observation group was significantly lower than that of the control group (P<0.05). Notes: *P<0.05 vs. the situation before anesthesia. #P<0.05 vs. the observation group after anesthesia.

obs group was significantly lower than that of the con group at 90 min after anesthesia recovery, indicating that both anesthesia methods can relieve the pain of patients undergoing radical mastectomy, but inhalation anesthesia combined with total intravenous anesthesia was more effective, caused less pain in patients before and after surgery, and alleviated the pain of patients undergoing radical mastectomy. In addition, the blood pressure and heart rate of the patients in the obs group and the con group were evaluated before anesthesia and at 15 min after anesthesia, and it was found that the obs group showed a more remarkable decrease in the systolic blood pressure and diastolic blood pressure than the con group, and also showed a lower incidence of adverse reactions than the con group (all P<0.05) which indicated that inhalation anesthesia combined with total intravenous anesthesia can reduce adverse reactions of patients undergoing radical mastectomy.

Cortisol can be used to evaluate the stress levels of the body to help control an excessive inflammatory response. At the end of the study, we detected the serum cortisol level of patients in the two groups before and after anesthesia, finding that at 60 min after anesthesia, both groups showed significantly increased serum cortisol level (P<0.05), while the increase in the con group was more significant than that in the obs group, and the cortisol level in the obs group was significantly lower than that in the con group (P<0.05). The results implied that inhalation anesthesia combined with total intravenous anesthesia can reduce stress levels and surgical stimulation in radical mastectomy. Furthermore, the obs group experienced significantly shorter induction time, anesthesia time, drug withdrawal-extubation time, and spontaneous breathing recovery time than the con group, indicating that inhalation anesthesia combined with total intravenous anesthesia was a relatively good anesthesia method in radical mastectomy.

In this study, although we have confirmed the role of inhalation anesthesia combined with total intravenous anesthesia in radical mastectomy, we do not observe the long-term prognosis and adverse reactions of the two groups, so this study has certain limitations, and we hope to address them in future studies.

To sum up, inhalation anesthesia combined with total intravenous anesthesia can alleviate the pain response and reduce adverse reactions of patients undergoing radical mastectomy, which is worthy of clinical application.

Disclosure of conflict of interest

None.

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