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Original Article

Awakening from anesthesia using propofol or sevoflurane with epidural block in radical surgery for senile gastric cancer

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Abstract: Objective: To study the awakening of the elderly patients from propofol intravenous general anesthesia or sevoflurane inhalation general anesthesia combined with epidural block after radical gastric cancer surgery. Method: Eighty cases receiving selective radical surgery for gastric cancer were included. They were aged 65-78 years and classified as ASA grade I-II. Using a random number table, the cases were divided into 4 groups (n = 20): propofol intravenous general anesthesia (P group), sevoflurane inhalation general anesthesia (S group), propofol intravenous general anesthesia combined with epidural block (PE group), and sevoflurane inhalation general anesthesia combined with epidural block (SE group). For P and PE group, target controlled infusion of propofol was performed; for S and SE group, sevoflurane was inhaled to induce and maintain general anesthesia; for PE and SE group, before general anesthesia induction, epidural puncture and catheterization at T_{7-8} was performed. After surgery, perform patient controlled intravenous analgesia (PCIA) or patient controlled epidural analgesia (PCEA), and maintain VAS ≤ 3. The recorded indicators were as follows: time to recovery of spontaneous respiration, time to awakening, time of endotracheal tube removal, time to orientation, time to achieve modified Aldrete scores ≥ 9, modified OAA/S and Aldrete scores upon endotracheal tube removal (T_1), 5 min after removal (T_2), 15 min after removal (T_3) and 30 min after removal (T_4), dose of intraoperative remifentanil, intraoperative hypotension, and emergence agitation. Results: Time to awakening, time of endotracheal tube removal, time to orientation, and time to achieve modified Aldrete scores ≥ 9 in PE and SE group were obviously shortened compared with P and S group ($P < 0.05$); modified OAA/S and Aldrete scores at T_1 and T_2 in PE and SE group were significantly higher than those in P and S group ($P < 0.05$), and the scores of SE group at T_1 were much higher compared to PE group ($P < 0.05$). Dose of intraoperative remifentanil in PE and SE group was significantly lower than that in P and S group. Conclusion: Compared to propofol intravenous general anesthesia or sevoflurane inhalation general anesthesia, propofol or sevoflurane general anesthesia combined with epidural block was more conducive to increasing the awakening quality of the senile patients from anesthesia after radical gastric cancer surgery. Moreover, sevofluorane inhalation general anesthesia combined with epidural block achieved a more stable hemodynamics and a shortened time to awakening.

Keywords: Propofol, sevoflurane, epidural block, awakening, radical surgery for senile gastric cancer

Introduction

As the development of ageing tendency of population, the number of senile patients who require surgical treatment is increasingly growing, and which choice of anesthesia methods is more beneficial to early postoperative recovery of the senile patients is one of the important clinical concerns. Propofol is one of the most widely used intravenous anesthesia drugs in clinical practice, which is widely used in surgical anesthesia, analgesia or auxiliary analgesia. Sevoflurane is a halogenated fluorinated ether used in inhalation general anesthesia, which has been widely used in clinics with hemodynamic stability during anesthesia induction. The influence of propofol and sevoflurane on awakening from anesthesia was intensively investigated in recent years. We compared the awakening of the senile patients from propofol intravenous general anesthesia or sevoflurane inhalation general anesthesia and that from propofol or sevoflurane general anesthesia combined with epidural block after radical gastric cancer surgery, and aimed to provide optimal anesthesia regimen for the senile patients.

Table 1. Aldrete's scoring criteria

Item	Description	Scores
Mobility	Spontaneous or ordered movement of four limbs and head raising	2
	Spontaneous or ordered movement of two limbs and restricted head raising	1
	Inability to move the limbs or raise the head	0
Respiration	Capable of deep breath and effective cough, with normal breathing rate and amplitude	2
	Difficulty in breathing or restricted breathing, but capable of shallow and slow spontaneous breathing, probably through oropharyngeal airway	1
	Apnea or weak breathing, with the need for respirator or assisted respiration	0
Blood pressure	Before anesthesia ± 20%	2
	Before anesthesia ± (20%-49%)	1
	Before anesthesia ± 50% or above	0
Consciousness	Completely conscious (accurate response to calling one's name)	2
	Capable of being awakened, drowsiness	1
	No response	0
SpO_2	≥ 92% upon air breath	2
	≥ 92% upon oxygen breath	1
	≤ 92% upon oxygen breath	0

Note: Final scores were based on the sum of scores on mobility.

Data and methods

General data

The protocol was approved by Ethics Committee in the hospital. Signed informed consent was obtained from all subjects and their relatives. The subjects were 80 senile gastric cancer patients receiving selective radical surgery. They were aged 65-78 years, weighted 50-72 kg, and graded I-II based on ASA (American Society of Anesthesiologists). Those who had mental disorder, severe dysfunction of heart, lung, liver kidney, spinal deformity, contraindications of epidural anesthesia, and a history of severe trauma or surgical treatment were excluded. The subjects were divided into 4 groups using a random number table (n = 20): propofol intravenous general anesthesia (P group), sevoflurane inhalation general anesthesia (S group), propofol intravenous general anesthesia combined with epidural block (PE group), and sevofluorane inhalation general anesthesia combined with epidural block (SE group). Cases which underwent palliative operation or severe hemorrhage during surgery would get out of the study.

Anesthesia method

Conventional preparations were made. Before surgery, infusion of lactated Ringer's solution of 8 $ml \cdot kg^{-1} \cdot h^{-1}$ was given via venous approach of the forearm. ECG, heart rate (HR), oxygen saturation (SpO_2) and bispectral index (BIS) were monitored. Arterial pressure was monitored by right radial artery puncture and catheterization, and central venous pressure (CVP) was monitored by right internal jugular vein puncture and catheterization. Epidural puncture and catheterization were performed at T_{7-8} before induction of general anesthesia in PE and SE group. Then 3 ml 2% lidocaine was administered. It was confirmed that anesthesia level occurred without adverse reactions. At 30 min before skin incision, 10 ml 0.25% ropivacaine and 2 μg/ml fentanyl were injected into the epidural space. Induction of general anesthesia: for P and PE group, target controlled infusion (TCI) of propofol, target plasma concentration (Cp) 4.0 μg/ml. After the loss of consciousness, 3-4 μg/kg fentanyl and 0.2 mg/kg cisatracurium were intravenously injected. Endotracheal intubation was performed 3 min later. For S and SE group, 8% sevoflurane was inhaled at high flow rate (oxygen flow rate 8-10 L/min). After the loss of consciousness, oxygen flow rate was adjusted to 2 L/min. The end-tidal sevoflurane concentration of 2% was maintained, and mechanical ventilation was performed with the tidal volume of 6-8 ml/kg, respiratory rate of 12 breaths/min, exhalation: inhalation = 1:2, and oxygen flow rate of 2.0 L/min. Anesthesia maintenance: for P and PE group, fentanyl was intravenously infused at 0.15-0.35 $\mu g \cdot kg^{-1} \cdot min^{-1}$ with TCI of propofol, Cp1.5-3.0 μg/ml or continuous inhalation of sevoflurane (S and SE group), end-

Table 2. Comparison of dose of baseline data, dose of intraoperative remifentanil, incidence of hypotension and emergence agitation among the four groups

Group	Cases	Age (years, $\bar{X}\pm s$)	Body weight (kg, $\bar{X}\pm s$)	Gender composition (cases, male/female)	ASA Grade composition (cases, I/II)	Surgical time (min, $\bar{X}\pm s$)	Remifentanil (μg, $\bar{X}\pm s$)	Hypotension (case, %)	Agitation (case, %)
P group	20	71.4±5.6	60.6±8.1	15/5	4/16	135.3±26.6	2225.5±90.3	3 (15)	2 (10)
S group	20	67.9±7.2	58.4±10.8	16/4	5/15	141.6±23.2	2015.6±75.0	0 (0)	7 (35)[b]
PE group	20	69.0±6.6	58.1±10.7	15/5	3/17	132.7±27.5	1188.7±50.3[**]	8 (40)[a]	1 (5)
SE grouP	20	70.4±5.9	60.3±9.8	14/6	4/16	140.4±21.9	1060.4±80.6[**]	2 (10)	3 (15)

Note: Compared with P or S group, [**]P < 0.01; compared with P, S or SE group, [a]*P < 0.05*; compared with P, PE or SE group, [b]P < 0.05.

Table 3. Comparison of safety indicators among the four groups (min, $\bar{x}\pm s$)

Group	Cases	Time to spontaneous respiration recovery	Time to awakening	Time to endotracheal tube removal	Time to orientation	Time to achieve Aldrete scores ≥ 9
P group	20	15.4±2.1	33.2±6.4	34.6±5.3	36.6±5.6	40.6±6.2
S group	20	14.9±1.8	32.3±4.9	33.9±6.2	35.2±4.8	39.3±7.2
PE group	20	15.2±1.9	20.7±5.2*	21.2±4.4*	22.6±5.4*	22.9±5.7*
SE group	20	15.1±2.3	18.2±7.6*	19.4±5.6*	20.8±5.1*	21.4±8.0*

Note: Compared with P or S group, *P < 0.05.

tidal sevoflurane concentration of 1.5-3.5%; intermittent intravenous infusion of cisatracurium, 0.05-0.1 mg/kg; end-tidal carbon dioxide partial pressure (P_{ET} CO_2) 30-40 mmHg (1 mmHg = 0.133 kPa), BIS40-60, CVP ≤ 12 cm H_2O (1 cm H_2O = 0.098 kPa). The fluctuation of BP and HR should not exceed 20% of the baseline. At 30 min before the end of surgery, muscle relaxant was disused. For PE and SE group, the mixed anesthesia solution of 10 ml was injected into the epidural space; for P and S group, 0.6-1 μg/kg fentanyl was injected intravenously. Remifentanil infusion, propofol infusion or sevoflurane inhalation was stopped 10 min before the end of surgery. For S and SE group, the airway was flushed by oxygen at high flow rate (4 ml/min). Perform PCIA (PE and SE group) or PCEA (P and S group), and maintain VAS scores ≤ 3. When swallowing reflux was recovered, with spontaneous breathing rate ≥ 12 breaths/min, P_{ET} CO_2 < 45 mmHg and SpO_2 ≥ 95%, endotracheal tube was removed. The patients were observed for 30 min. If SpO_2 < 92%, oxygen mask was used with 5 L/min. No conventional preventive measures were adopted for nausea and vomiting, but medications would be prescribed if symptoms deteriorated. The patients were returned to the ward after achieving modified Aldrete scores ≥ 9 [1] (see **Table 1** for scoring criteria).

Observation indicators

The following observation indicators were recorded: time to spontaneous respiration recovery (interval from the stopping of propofol infusion or sevoflurane inhalation to recovery of spontaneous respiration), time to awakening (interval from the stopping of propofol infusion or sevoflurane inhalation to awakening), time of endotracheal tube removal (interval from the stopping of propofol infusion or sevoflurane inhalation to endotracheal tube removal), time to orientation (interval from the stopping of propofol infusion or sevoflurane inhalation to saying one's name accurately), time to achieve modified Aldrete scores ≥ 9 (interval from the stopping of propofol infusion or sevoflurane inhalation to achieving modified Aldrete scores ≥ 9); modified OAA/S (Observer's Assessment of Alertness/Sedation) scores upon endotracheal tube removal (T_1), 5 min after removal (T_2), 15 min after removal (T_3), and 30 min after removal (T_4), and modified Aldrete scores. The scoring criteria for modified OAA/S scores were as follows: 5, complete consciousness and normal response to normal calling one's name; 4, delayed response to normal calling one's name; 3, no response to normal calling one's name, but showing response to calling one's name with a high voice repetitively; 2, no response to calling one's name with a high voice repetitively, but showing response to gentle tapping; 1 point, no response to tapping, but showing response to noxious stimuli. The dose of intraoperative remifentanil and incidence of hypotension were recorded. Hypotension was defined as SP ≤ 90 mmHg or reduction ≥ 20% of baseline for ≥ 5 min, and intravenous injection of 6 mg ephedrine was performed. Symptoms of emergence agitation were recorded and evaluated by using Riker Sedation-Agitation Scale (RSAS).

Statistical analysis

All statistical analysis was performed using SPSS17.0 software. Measurement data were expressed as mean ± standard deviation ($\bar{x}\pm s$). One-way ANOVA was used for inter-group comparison, and LSD method for pairwise comparison. Count data were compared using χ^2 test. P < 0.05 indicated statistically significant difference.

Results

Baseline data

Four groups showed no significant differences in distribution of age, body weight and gender, ASA grade composition and surgical time. The

Table 4. Comparison of modified OAA/S and Aldrete scores at different time points among the four groups (min, $\bar{x}\pm s$)

Indicator	Group	Cases	T_1	T_2	T_3	T_4
OAA/S scores	P group	20	3.1±0.4	3.6±0.7	4.3±1.0	4.5±0.6
	S group	20	3.2±0.5	3.8±0.6	4.5±0.7	4.7±0.6
	PE group	20	3.8±0.5[a]	4.2±0.8[a]	4.6±0.9	4.7±0.4
	SE group	20	4.2±0.4[a,b]	4.6±0.5[a,b]	4.7±0.8	4.8±0.5
Aldrete scores	P group	20	7.7±0.7	8.3±0.8	9.0±0.8	9.6±0.5
	S group	20	7.8±0.9	8.4±0.8	9.1±0.6	9.7±0.4
	PE group	20	8.4±0.8[a]	9.0±0.7[a]	9.5±0.5	9.7±0.5[a]
	SE group	20	9.0±0.6[a,b]	9.1±0.5[a]	9.6±0.4	9.7±0.5

Note: Compared with P or S group, [a]$P < 0.05$; compared with PE group, [b]$P < 0.05$.

dose of remifentanil in PE and SE group was significantly lower than that in P and S group ($P < 0.01$). PE group had a significance increase in incidence of hypotension, while S group had an increase in incidence of emergence agitation ($P < 0.05$) (**Table 2**).

Comparison of perioperative safety indicators among the four groups

Time to awakening, time of endotracheal tube removal, time to orientation and time to achieve modified Aldrete scores ≥ 9 in PE and SE group were obviously shortened compared with P and S group ($P < 0.05$) (**Table 3**).

Comparison of modified OAA/S and aldrete scores at different time points for the four groups

Modified OAA/S and Aldrete scores in PE and SE group at T_1 and T_2 were obviously higher than those in P and S group ($P < 0.05$), and the scores in SE group at T_1 were higher than those in PE group ($P < 0.05$) (see **Table 4**).

Discussion

Delayed awakening from anesthesia and emergence agitation are common in radical surgery for senile gastric cancer due to extensive wound, intensive use of general anesthetics and slow drug metabolism. Propofol and sevoflurane are widely used in anesthesia for the elderly patients, which have the features of rapid anesthesia induction, quick awakening from anesthesia and good controllability. However, Murata et al. [2] found that long-term, high-dose intravenous infusion of propofol changed pharmacokinetics and enhanced analgesic effect, therefore prolonging the time to awakening and endotracheal tube removal. The most common adverse reactions after anesthesia using propofol are injection pain and inhibited circulation. Anesthesia induction using 2-2.5 mg/kg propofol may reduce SBP and stroke volume index (SVI) by 25%-40% and about 20%, respectively, regardless of cardiovascular diseases. Sevoflurane has a less inhibitory effect on circulation in a dose-dependent manner, and the main adverse reactions include blood pressure decline and dilation of peripheral blood vessels. However, sevoflurane is the risk factor of emergence agitation [3] which is independent on pain [4]. In the present study, although sevoflurane inhalation was already stopped during abdomen closing and airway was flushed by oxygen at a high flow rate, the incidence of emergence agitation was still high in S group. This phenomenon may be explained by slow circulation and metabolism in the elderly patients. However, residual anesthetics may delay functional recovery of cerebral cortex and awakening. The patients may show abnormal reactions, including emergence agitation [5].

Epidural block not only prevents the conduction of noxious stimuli to the central nervous system and reduces the damage to the central nervous system, but also reduces the dose of general anesthetics, such as propofol, sevoflurane and remifentanil, as may explain why it reduces emergence agitation during rehabilitation period after general anesthesia and increases awakening quality. Modified OAA/S scores can be used as the observation indicator of awakening quality and anesthesia depth changes [6]. We found that PE and SE group in which epidural block was adopted had an increase of awakening quality and a decrease of incidence of emergence agitation. However, PE group showed a much higher incidence of hypotension, probably due to sympathetic block caused by epidural anesthesia and circulation inhibition caused by propofol. Intraoperative hypotension is more likely to occur after anesthesia induction, with dilation of peripheral blood vessels; moreover, intraoperative blood volume is low due to long-term fasting. One research on anesthesia induction among the elderly patients indicated that after intrave-

nous infusion of 1.0 mg/kg propofol, MAP was decreased by 28.8% compared with the baseline; for inhalation anesthesia with 8% sevoflurane, MAP was decreased by 21.3% compared with the baseline [7]. Due to decline of myocardial chronotropism and inotropism, degeneration of cardiac valves and reduction of windkessel vessel elasticity, the elderly patients are more vulnerable to peri-anesthesia hypotension [8]. For the elderly patients combined with hypertension and atherosclerosis, vascular resistance must be maintained while dilating the blood vessels by reducing the rate of anesthesia induction and anesthetic concentration.

All the enrolled patients were classified as ASA grade I-II in the present study, who showed stable vital signs and consistent depth of anesthesia during operation. Effective analgesic measures and consistent postoperative management were performed. The awakening quality under four anesthesia regimes was evaluated. Compared with propofol intravenous general anesthesia and sevoflurane inhalation general anesthesia among the elderly patients, propofol or sevoflurane general anesthesia combined with epidural block contributed to an obvious shortening of time to awakening, time to endotracheal tube removal, time to orientation, and time to achieve modified Aldrete scores ≥ 9.

To conclude, propofol or sevoflurane general anesthesia with epidural block is more favorable for increasing the awakening quality of the senile patients from anesthesia after radical gastric cancer, which achieved higher hemodynamic stability and a shorter time to awakening.

Disclosure of conflict of interest

None.

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