

Original Article

Clinical research of dexmedetomidine combined with target-controlled infusion of propofol for surgery under general anesthesia in elderly patients

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Abstract: Objective: To evaluate the anesthetic efficacy and adverse reactions of dexmedetomidine combined with target-controlled infusion (TCI) of propofol in elderly patients scheduled for surgery under general anesthesia. Methods: A total of 60 elderly patients scheduled for surgery under general anesthesia were recruited and randomly divided into the observation group (30 cases) and the control group (30 cases). For general anesthesia, patients in the control group and the observation group were given sufentanil combined with TCI of propofol, and dexmedetomidine combined with TCI of propofol, respectively. The anesthetic efficacy and the incidence of adverse reactions were evaluated and compared between the two groups. Results: Our study showed that there were no significant differences between the two groups at different time points and time duration with respect to pulse oxygen saturation (SPO₂) (T0: $P=0.091$, T1: $P=0.201$, T2: $P=0.106$, and T3: $P=0.266$, respectively). And heart rate (HR), respiratory rate (RR) and mean arterial pressure (MAP) in the observation group at T1, T2 and T3, were all higher than those in the control group ($P=0.013$, 0.040 , and 0.031 , respectively). What's more, anesthetic onset time, breathing recovery time, extubation time and time of Observer's Assessment of Alertness/Sedation Scale (OAAS) which reached grade 5 in the observation group were all shorter than those of the control group ($P=0.007$, 0.031 , 0.003 and 0.019 , respectively). The incidence of adverse reactions in the observation group was 26.6%, which was significantly lower than that of the control group (56.6%) ($P=0.039$). Conclusion: Dexmedetomidine combined with propofol target-controlled infusion presented good anesthetic efficacy for surgery under general anesthesia in elderly patients, which can stabilize blood flow dynamics, shorten anesthetic onset and recovery time, and reduce the incidence of adverse reactions.

Keywords: General anesthesia, dexmedetomidine, propofol, target-controlled infusion

Introduction

General anesthesia is one of the common methods of anesthesia in clinical practice, which is widely used in thoracic, abdominal, lower extremity surgery, etc. Propofol and sufentanil are commonly used anesthetics and have been widely used in general anesthesia for a long period. However, previous studies have indicated that propofol had an inhibitory effect on cardiovascular system, especially in elderly patients [1-3]. Sufentanil provides rapid effective pain relief in surgery under general anesthesia, but it also produces undesirable side effects, including respiratory depression, delayed recovery from anesthesia, etc. What's more, cumulative studies have demonstrated that the combined use of these two may

increase the risk of these complications, which threw a threat to patients' safety [4], especially in elderly patients who were more sensitive to these anesthetics. Therefore, it is of great significance to maintain stable vital signs during the operation for elderly patients.

Dexmedetomidine is a new type of alpha-2 adrenergic receptor agonist, which presents good efficacy in analgesia and sedation by inhibiting the sympathetic nerve mainly in the central and peripheral nervous system. What's more, less adverse reactions have been reported previously by using dexmedetomidine in general anesthesia [4-6]. Target-controlled infusion (TCI) is a simple and easy intravenous anesthetic method, and has been developed as a standardized infusion system for the adminis-

Table 1. Clinical characteristics in the two groups

	The observation group (n=30)	The control group (n=30)	P
Gender (male/female)	18/12	17/13	0.919
Age (year)	68.9±5.3	68.8±4.9	1.091
The type of surgery (case)			0.633
Thoracic surgery	5	4	
Abdominal surgery	12	11	
Spinal surgery	6	9	
Lower extremity surgery	7	6	

tration of propofol and other anesthetics by target controlled infusion [7-10].

A limited number of previous studies have demonstrated dexmedetomidine combined with target-controlled infusion of propofol was safer with better anesthetic efficacy and less side effects than fentanyl analgesic combined with target-controlled infusion of propofol in surgery, such as painless artificial abortion [11, 12], etc. however, few studies have compared the anesthetic efficacy and adverse reactions of these two anesthetic modalities in elderly patients.

In the current report, we evaluated and compared the anesthetic efficacy and adverse reactions of dexmedetomidine combined with TCI of propofol and sufentanil combined with propofol TCI in elderly patients who were scheduled for surgery under general anesthesia. The findings in our report will provide a theoretical basis for clinical treatment.

Materials and methods

Participants

Inclusion criteria: (1) patients with age >65; (2) patients without obvious respiratory system diseases and circulatory system diseases; (3) patients without lung, liver, kidney, or other diseases. Exclusion criteria: (1) patients with a history of substance abuse; (2) patients with a history of the use of opioid narcotic drugs in the past 2 months; (3) patients with mental illness, neurological disease or intellectual disabilities.

A total of 60 elderly patients who were scheduled for surgery under general anesthesia were recruited into the current study from October 2015 to October 2016 at our hospital. Among them, 9 patients underwent thoracic surgery,

23 abdominal surgery, 15 spinal surgery and 13 lower extremity surgery. All the 60 patients were randomly divided into the observation group and the control group, with 30 patients in each group. In the observation group, there were 18 male patients and 12 female patients, with the mean age of 68.9±5.3 years old (ranging from 66 to 79 years old). Among them, 5 patients underwent thoracic surgery, 12 abdominal surgery, 6 spinal surgery

and 7 lower extremity surgery. And in the control group, there were 17 male patients and 13 female patients, with the mean age of 68.8±4.9 years old (ranging from 67 to 78 years old). Among them, 4 patients underwent thoracic surgery, 11 abdominal surgery, 9 spinal surgery and 6 lower extremity surgery. There were no significant differences between the two groups with respect to gender, age and the type of surgery ($P>0.05$) (Table 1). The study protocol was approved by the medical ethical committee of our hospital, and written informed consent was obtained from all participants before the study started.

Anesthesia

All patients underwent surgery under general anesthesia following conventional fasting for 8-12 h and abstinence from liquids for 4-6 h preoperatively. In addition, the venous channels were established, heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP) and pulse oxygen saturation (SpO₂) were monitored before the operation as well.

For patients in both groups, midazolam (0.05 mg/kg), propofol (2~2.5 mg/kg), cisatracurium (0.2 mg/kg), and sufentanil (0.2 µg/kg) were infused intravenously for anesthesia induction before the operation. For patients in the observation group, intravenous infusion of dexmedetomidine (0.1~0.2 g/kg min) (2 ml: 200 ug, Jiangsu Hengrui Pharmaceutical Co., Ltd., China), combined with target-controlled infusion of propofol (AstraZeneca Co., Ltd., Italy) with a final plasma concentration of 1 g/mL was given for anesthesia maintenance during the operation. For patients in the control group, intravenous infusion of sufentanil (0.5 g/kg) (Jiangxi Yichang humanwell Pharmaceutical Co., Ltd., China), combined with target-con-

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Table 2. Vital signs at different time points in both groups

	Group	T0	T1	T2	T3
SPO ₂ (%)	The observation group	99.6±0.6	98.6±0.6	98.3±0.3	99.0±0.5
	The control group	99.1±0.7	98.9±0.5	98.0±0.2	98.9±0.4
HR (beat/min)	The observation group	79.1±9.2	68.6±6.6* [*]	77.9±8.1* [*]	75.9±8.9* [*]
	The control group	76.1±9.5	64.7±7.0* [*]	72.2±9.6* [*]	73.3±8.1* [*]
RR (beat/min)	The observation group	17.6±1.0	16.1±1.8* [*]	15.6±1.2* [*]	16.9±1.3* [*]
	The control group	17.9±1.6	13.0±2.1* [*]	13.7±1.3* [*]	13.1±1.0* [*]
MAP (mmHg)	The observation group	85.1±6.6	71.9±6.8* [*]	72.8±9.6* [*]	81.1±11.2* [*]
	The control group	86.5±6.9	66.9±7.1* [*]	68.6±9.3* [*]	73.7±9.0* [*]

Note: compared with the control group, * $P < 0.05$; compared with T0, * $P < 0.05$.

trolled infusion of propofol (AstraZeneca Co., Ltd., Italy) with a final plasma concentration of 1 g/mL was used for anesthesia maintenance. After the operation, patients in both groups were given self-controlled analgesia pump for pain treatment (sufentanil 100 g, dezocine 10 mg and tropisetron 5 mg diluted in 100 mL of saline) at a dose of 1.6 mL/h (additional volume: 0.5 mL/dose, lock time: 15 min).

Monitoring and measures

For both groups, HR, RR, MAP and SpO₂ were monitored at different time points and time duration, including before anesthesia (T0), loss of consciousness (T1), duration of anesthesia maintenance (T2), and anesthetic recovery time (T3). Anesthetic onset time, breathing recovery time, extubation time, and time of Observer's Assessment of Alertness/Sedation Scale (OAAS) reaching grade 5 (fully awake) in both groups were measured. In addition, the incidence of adverse reactions in both groups was observed and recorded.

Statistical analysis

Statistical analysis was conducted by using SPSS 21.0 statistical package. Continuous variables were presented as mean ± standard deviation and analyzed by using unpaired Student's *t* test. Categorical variables were presented as percentage and analyzed by chi-square test or Fisher's exact test. $P < 0.05$ was considered significant.

Results

Vital signs at different time points in both groups

As shown in **Table 2**, There were no significant differences between the two groups at differ-

ent time points and time duration, with respect to SPO₂ (T0: $P = 0.091$, T1: $P = 0.201$, T2: $P = 0.106$, and T3: $P = 0.266$, respectively). And HR, RR and MAP at T1, T2, T3 were all lower than those before surgery (T0) in both groups, the differences were all statistically significant ($P < 0.05$). Additionally, HR RR and MAP in the observation group were higher than those of the control group at T1, T2 and T3, respectively, the differences were statistically significant ($P = 0.013$, 0.040, and 0.031, respectively).

Anesthetic onset time and postoperative status in both groups

As shown in **Table 3**, anesthetic onset time, respiratory recovery time, extubation time, and time of OAAS which reached grade 5 in the observation group were all shorter than those in the control group, the differences were statistically significant ($P = 0.007$, 0.031, 0.003 and 0.019, respectively).

The incidence of adverse reactions in both groups

As shown in **Table 4**, the incidence of adverse reactions in the observation group was 26.6%, which was lower than that of the control group (56.6%), and the difference was statistically significant ($\chi^2 = 4.240$, $P = 0.039$).

Discussion

Dexmedetomidine is a new alpha-2 adrenergic receptor agonist, which presents rapid and strong analgesic efficacy without sacrificing the safety [13]. The results of our study showed that HR, RR and MAP after surgery (T1, T2 and T3) were all significantly lower than those before surgery (T0) at both groups (**Table 2**, $P = 0.033$, 0.029, and 0.010, respectively). While,

Table 3. Anesthetic onset time and postoperative status in both groups

Group	Anesthetic onset time (min)	Respiratory recovery time (min)	Extubation time (min)	Time of OAAS reaching grand 5 (min)
The observation group	1.5±0.6	7.3±3.3	5.1±1.1	15.1±4.3
The control group	1.8±0.6	8.9±4.1	5.6±0.9	17.9±6.0
<i>t</i>	-2.311	-1.810	-2.877	-1.791
<i>P</i>	0.007	0.031	0.003	0.019

Table 4. The incidence of adverse reactions in both groups

Group	Anxiety	Nausea and vomiting	Cough reflex	Respiratory repression	Total
The observation group	3 (10)	1 (3.3)	4 (13.3)	0	8 (26.6%)
The control group	7 (23.3)	2 (6.7)	7 (23.3)	1 (3.3)	17 (56.6%)

HR RR and MAP in the observation group at T1, T2 and T3 were all higher than those of the control group (Table 2, *P*=0.013, 0.040, and 0.031, respectively), suggesting that dexmedetomidine combined with TCI of propofol for general anesthesia can favor to maintain the stability of hemodynamics during the operation. Our results were consistent with the findings in the previous reports [14, 15].

It is well known that long-term anesthesia post-operatively can damage the circulatory and nervous system [16, 17], therefore, it is vital to select suitable anesthetics and modality, which can promote the early recovery, reduce the extent of damage, especially for the nervous system [16, 17]. Our study showed that anesthetic onset time, respiratory recovery time, extubation time, and time of OAAS reaching grade 5 in the observation group were all shorter than those of the control group (Table 3, *P*=0.007, 0.031, 0.003 and 0.019, respectively), which was in accordance with previous study [18]. All these indicated that dexmedetomidine is safer than sufentanil for general anesthesia.

Previous study indicated that the incidence of adverse reactions increased in patients under general anesthesia, including nausea, vomiting, cough reflex and respiratory depression, due to its intravenous administration [13]. Our study showed that the overall incidence of adverse reactions in the observation group were significantly lower than that of the control group (*P*=0.039). It may be due to the fact that the half-life of dexmedetomidine in tissue and

blood is shorter than sufentanil, which helps to reduce the incidence of adverse reactions greatly. The results of our study were in line with the work by Mccutcheon, et al [19-22]. In addition, studies by Tadros and others [23, 24] also found that high dose of dexmedetomidine can cause respiratory depression, excessive sedation, nausea and vomiting and other adverse reactions, and even drug dependence,

which indicated us that caution should be paid to avoid the use of dexmedetomidine alone, or at a high dose.

Our study still has some limitations. Firstly, the number of patients enrolled in this study was small, which may cause statistical bias and limit the power to detect differences between groups. Secondly, the follow-up after surgery was not conducted to evaluate the long-term safety in elderly patients. All these will be modified in the future study.

To conclude, dexmedetomidine combined with TCI of propofol presented good anesthetic efficacy in elder patients undergoing surgery under general anesthesia, which can stabilize blood flow dynamics, shorten anesthetic onset and recovery time, and reduce the incidence of adverse reactions.

Disclosure of conflict of interest

None.

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