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Original Article

Effects of dexmedetomidine on the recovery profiles from general anesthesia in patients undergoing endoscopic sinus surgery

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Abstract: Objective: The aim of the present study was to evaluate the effects of dexmedetomidine on the recovery profiles from general anesthesia in patients undergoing endoscopic sinus surgery (ESS). Methods: Sixty patients undergoing ESS under general anesthesia were randomly assigned to two groups. The dexmedetomidine group (Group D) received intravenous administration of dexmedetomidine 0.5 μg/kg after endotracheal intubation, while the control group (Group C) received volume-matched normal saline. Heart rate, mean arterial pressure, and recovery profiles were evaluated during emergence. Results: There was no significant difference between the two groups with respect to the demographic data, durations of surgery and anesthesia, time to eye opening, and time to extubation. The heart rate and mean arterial pressure were more stable in Group D compared with Group C during emergence ($P < 0.05$). The incidence of emergence agitation and postoperative pain scores were significantly lower in Group D than Group C ($P < 0.05$). Conclusion: Intraoperative infusion of dexmedetomidine may result in a smooth and favorable recovery profile in patients undergoing ESS under general anesthesia.

Keywords: Dexmedetomidine, general anesthesia, endoscopic sinus surgery, recovery

Introduction

Endoscopic sinus surgery (ESS) is currently an effective method in the surgical treatment of chronic rhinosinusitis [1]. For the purpose of providing optimal operating conditions, general anesthesia is preferred for most patients undergoing ESS [2]. However, emergence from anesthesia is often associated with hypertension, tachycardia, coughing, hypoxia and agitation, which may have significant impact on patients' recovery [3]. Thus, smooth recovery from anesthesia is desirable in these patients to decrease the risk of adverse events.

Dexmedetomidine is a highly specific α_2-adrenergic receptor agonist that has sedative, analgesic and sympatholytic properties without affecting respiratory status [4]. Intraoperative infusion of dexmedetomidine has shown to effectively reduce anesthetic requirements, postoperative pain and the hemodynamic response to intubation and extubation in surgery patients [5, 6]. Furthermore, it has been reported that intraoperative dexmedetomidine infusion attenuates the stress response and has the protective effects on organ function [7, 8]. These studies suggest that dexmedetomidine should be considered as a useful adjunct to general anesthesia.

In this randomized, double-blind, placebo-controlled study, we aimed to evaluate the effects of intravenous administration of dexmedetomidine on the recovery profiles in patients undergoing ESS under general anesthesia.

Materials and methods

General data

This study was approved by the Ethics Committee of Nanjing Medical University Affiliated Wuxi Second Hospital. Written informed consent was obtained from all participants. Sixty patients, with an American Society of Anes-

thesiologists physical status of I or II, aged 20-60 years, and scheduled for ESS for chronic sinusitis under general anesthesia, were enrolled between January 2015 and June 2015. All patients were allocated by computer-generated randomization to either the dexmedetomidine group (Group D, n = 30) or the control group (Group C, n = 30). Exclusion criteria included the presence of cardiovascular or respiratory dysfunction; any kind of cardiac conduction disorder; a history of renal or hepatic insufficiency; allergy to α_2-agonists; and chronic use of psychotropic medications. Assessment of preoperative symptoms was performed subjectively using a visual analogue scale (VAS; 0 = the absence of symptoms and 10 = the presence of extremely severe symptoms) to score symptoms of nasal blockage, alteration in the sense of smell, headache, facial pain, nasal discharge, and overall symptoms [9]. The patients' preoperative sinus computed tomography scores were evaluated according to the Lund-Mackay staging system [10].

Anesthesia regimen

All patients received premedication with intramuscular phenobarbital sodium (0.1 g) and atropine (0.5 mg) 30 min before the induction of anesthesia. Routine monitors included the use of the electrocardiogram (ECG), pulse oximetry, capnography and noninvasive blood pressure. General anesthesia was induced with intravenous ropofol (1.5-2 mg/kg) and fentanyl (3 μg/kg). Rocuronium (0.6 mg/kg) was intravenously injected to facilitate oral tracheal intubation. Anesthesia was maintained with inhalation of 2.0%-3.0% sevoflurance in 50% oxygen/air and intravenous infusion of remifentanil 0.1-0.2 μg/kg/min. Muscle paralysis was maintained with intermittent injection of rocuronium (0.15 mg/kg). Mechanical ventilation was adjusted to maintain end-tidal pressure of CO_2 ($P_{ET}CO_2$) between 35-45 mmHg. Heart rate (HR) and mean arterial pressure (MAP) were kept between 80% and 120% of the preanesthetic baseline levels by adjusting the anesthetic concentrations. Bradycardia (HR < 40 beats/min) was treated with atropine (0.5 mg i.v. bolus). Hypotension (MAP < 60 mmHg) was treated with ephedrine (6 mg i.v. bolus).

The study drugs were prepared by an anesthetist who was not involved in the perioperative management. For Group D, dexmedetomidine was diluted with normal saline to a concentration of 4 μg/ml in a 50 ml syringe. For Group C, normal saline was also prepared in a 50 ml syringe. After intubation, patients in Group D received intravenous administration of dexmedetomidine (0.5 μg/kg bolus given over a 10 min period), whereas those in Group C received volume-matched normal saline.

At the insertion of nasal packing, all patients had sevoflurance inhalation and remifentanil infusion stopped, and the patient's lungs were ventilated with 100% oxygen at 8 litre/min. Residual neuromuscular blockade was reversed with atropine 0.02 mg/kg and neostigmine 0.04 mg/kg. Extubation was performed when spontaneous ventilation was deemed sufficient and patients were able to open their eyes and follow verbal commands. After extubation, each patient was transported to postanesthesia care unit (PACU) and observed by nurses blinded to this study.

HR and MAP values were recorded before anesthesia induction (T_0), at the end of surgery (T_1), at the time of eye opening (T_2), at extubation (T_3), and 5 min after extubation (T_4). Emergence was defined as the period from discontinuation of anesthetic to 5 min after extubation. During emergence, the following variables were recorded: time to eye opening, time to extubation and the Ricker sedation-agitation scale. The sedation-agitation scale consists of seven grades (1 = No response to noxious stimuli; 2 = Arouses to physical stimuli but does not follow commands; 3 = Difficult to arouse; awakens to verbal stimuli; 4 = Calm, awakens easily, follows commands; 5 = Anxious or restless, calms down to verbal instructions; 6 = Requires frequent verbal reminding of limits or physical restraints; 7 = Pulling at endotracheal tube, striking at staff, thrashing side-to-side) [11]. Agitation was defined as a sedation-agitation scale score of ≥ 5, and the incidence of emergence agitation was recorded. After arrival in the PACU, postoperative pain was assessed with a visual analogue scale (VAS; 0 = no pain and 10 = the worst imaginable pain). Rescue fentanyl (0.5 to 1 μg/kg) was given when the pain score was > 4. Adverse events such as nausea, vomiting, and desaturation (SpO_2 <

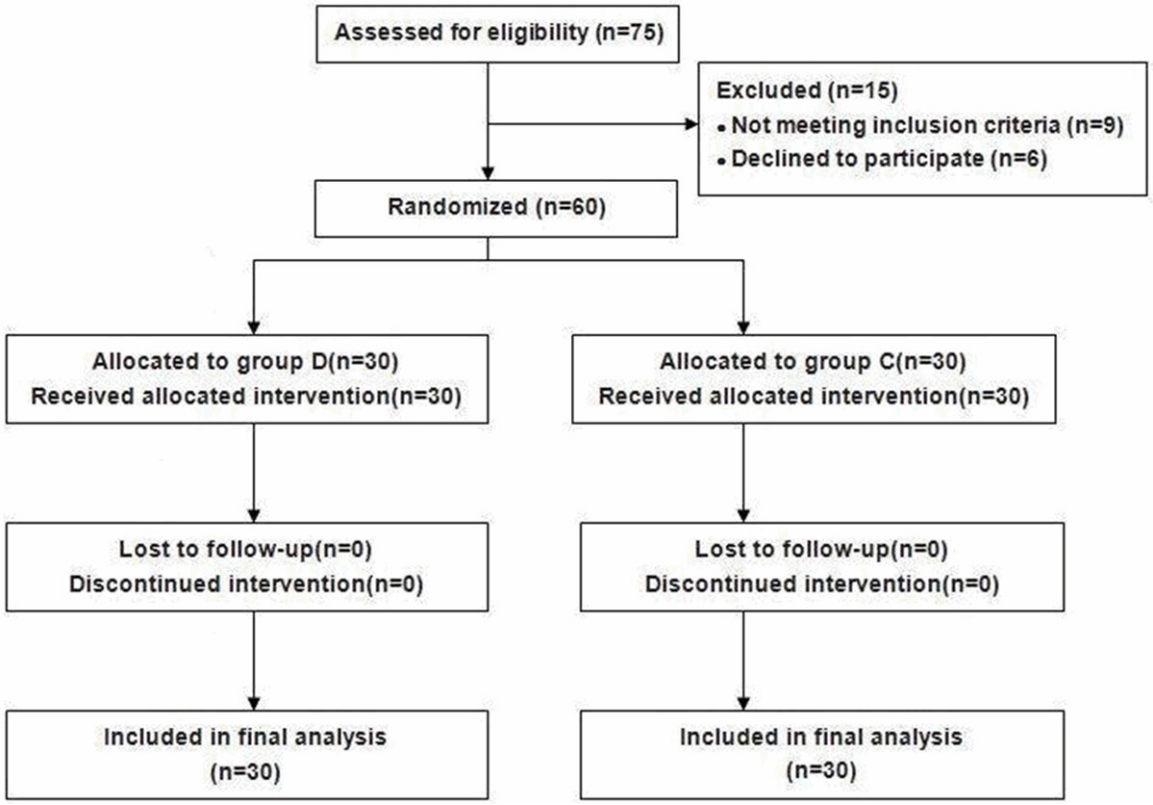

Figure 1. CONSORT diagram of patient recruitment.

Table 1. Demographic and clinical characteristics of patients

Clinical parameters	Group C (n = 30)	Group D (n = 30)	*P*-value
Age (yr)	40.2±11.5	37.5±12.3	0.389
Weight (kg)	61.8±8.6	64.6±9.1	0.229
Gender (male/female)	19/11	21/9	0.584
ASA classification (I/II)	24/6	23/7	0.754
Preoperative symptom scores	28.9±4.1	30.5±3.1	0.099
Preoperative Lund-Mackay scores	15.5±2.3	16.4±3.0	0.192
Duration of surgery (min)	86.2±17.5	79.6±13.2	0.104
Duration of anesthesia (min)	99.8±15.6	93.7±12.1	0.096

90%) were also recorded during anesthetic recovery.

Statistical analysis

All statistical analyses were performed with SPSS version 11.0 (SPSS Inc., Chicago, Illinois, USA). The normally distributed continuous variables were analyzed with Student's t-test. Data not normally distributed was compared using Mann-Whitney U-test. Categorical variables were compared using Chi-square tests. Data were presented as mean ± standard deviation, or number (%) as appropriate. $P < 0.05$ was considered statistically significant.

Results

A total of 75 patients were assessed for eligibility and 60 subjects completed the study (**Figure 1**).

There was no significant difference between the two groups in demographic data, preoperative clinical characteristics, duration of surgery, and duration of anesthesia (**Table 1**).

The hemodynamic changes at each time point were shown in **Figure 2**. HR and MAP values were comparable between the two groups before anesthesia induction. At the end of surgery, MAP remained comparable between the two groups while HR was lower in Group D than in Group C in same period ($P < 0.05$). HR and

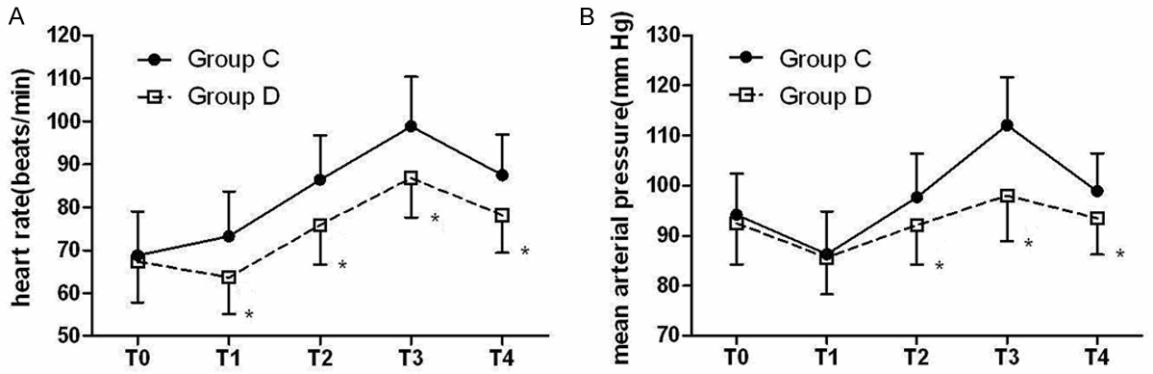

Figure 2. Changes in (A) heart rate and (B) mean arterial pressure for the control group (Group C) and the dexmedetomidine group (Group D) (T_0, before anesthesia induction; T_1, end of surgery; T_2, eye opening; T_3, extubation; T_4, 5 min after extubation). *P<0.05, when compared with Group C.

Table 2. Comparison of recovery data in 2 groups

Clinical parameters	Group C (n = 30)	Group D (n = 30)	*P*-value
Time to eye opening (min)	11.7±2.5	12.6±2.9	0.223
Time to extubation (min)	14.3±2.8	15.2±3.0	0.219
Emergence agitation [n (%)]	16 (53)	7 (23)	0.017
Postoperative pain scores	3.1±1.7	2.2±1.4	0.039
Rescue fentanyl [n (%)]	8 (27)	2 (7)	0.038
Nausea [n (%)]	7 (23)	5 (17)	0.519
Vomiting [n (%)]	2 (7)	1 (3)	0.554
Desaturation [n (%)]	0	0	–

MAP were significantly lower in Group D compared with Group C at the time of eye opening and extubation, and 5 min after extubation (P < 0.05). There was no severe hypotension (MAP < 60 mmHg) or bradycardia (HR < 40 beats/min) observed during the study period in both groups.

After discontinuation of anesthetic, the times to eye opening and extubation did not differ between the two groups. The incidence of emergence agitation was significantly lower in Group D compared with Group C (P < 0.05). Postoperative pain scores were significantly lower in Group D than Group C (P < 0.05). In addition, the percentage of patients who required rescue treatment with fentanyl for postoperative pain in the PACU was significantly lower in Group D compared with Group C (P < 0.05). There was no difference in the incidence of postoperative nausea and vomiting between the two groups. No episodes of desaturation were observed in both groups (**Table 2**).

Discussion

ESS is the mainstay for the management of chronic rhinosinusitis resistant to medical therapy. Because of the risk of nasal bleeding and pulmonary aspiration, awake extubation is preferred after surgery [12]. However, awake extubation may be associated with tracheal and laryngeal irritation that can cause coughing, agitation, laryngospasm, hypertension, and tachycardia. To attenuate airway and circulatory responses to extubation, prophylactic use of intravenous anaesthetics, benzodiazepines or opioid analgesics may be beneficial, but can prolong recovery and produce unpleasant side-effects, such as nausea and vomiting [13-15].

Dexmedetomidine, a potent α_2-adrenergic receptor agonist with sedative, analgesic and sympatholytic properties, has been widely used in clinical practice [6]. The sedative and analgesic effects of dexmedetomidine are mediated via central actions in the locus ceruleus of the brain stem and on the dorsal horn of the spinal cord, respectively [4]. Activation of postsynaptic α_2 receptors by dexmedetomidine leads to sympatholysis and results in decreases in blood pressure and heart rate, which helps to attenuate the stress response [16]. Guler et al. [17] reported that a single dose of dexmedetomidine given before extubation facilitated tolerance of the endotracheal tube and attenuated the airway and cardiovascular response to extubation. Talke et al. [18] investigated the hemodynamic and adrenergic effects of perioperative use of dexmedetomidine in patients

undergoing vascular surgery. They concluded that dexmedetomidine was associated with the attenuation of increases in heart rate and plasma norepinephrine levels during the recovery period after anesthesia. In our study, we found that heart rate and blood pressure were significantly lower in Group D compared with Group C during the periextubation period, suggesting dexmedetomidine was effective in blunting the sympathetic response to extubation and increased hemodynamic stability.

Emergence agitation (EA) is a troublesome phenomenon in the postoperative period. Although generally self-limited, EA can be severe and increase the risk of serious complications such as hypoxia, pulmonary aspiration, bleeding at the surgical site or even reoperation [19]. EA occurs frequently after ear, nose, and throat (ENT) surgery. Yu et al. [20] reported that the incidence of EA was 55.4% after ENT surgery. Multiple factors for development of EA include personal character, preoperative anxiety, postoperative pain, rapid awakening, and presence of tracheal tube [21, 22]. In addition, Eckenhoff et al. [23] speculated that a "sense of suffocation" during anesthetic recovery may provoke EA in patients undergoing head and neck surgery.

Previous studies have shown dexmedetomidine to be effective in decreasing the incidence of EA following general anesthesia in children [22, 24]. It has been demonstrated that dexmedetomidine can be used successfully to manage agitation in critically ill patients undergoing weaning from mechanical ventilation [25]. In our study, we found that intravenous administration of dexmedetomidine 0.5 μg/kg after intubation significantly reduced postoperative pain and EA. These effects may be due to the sedative and analgesic properties of dexmedetomidine. Moreover, dexmedetomidine offers a unique "conscious sedation" in which patients are readily aroused and communicative. In the present study, recovery times did not differ between the two groups. We believed that the unique "conscious sedation" along with minimal respiratory depression facilitated smooth recovery without delay in the dexmedetomidine group. A recent study suggested that prolongation of the extubation time in patients receiving dexmedetomidine was dose dependent [26]. In our study, dexmedetomidine was infused at a relatively small dose, achieving effective EA control without compromising recovery from anesthesia. Similar to our results, Kim et al. [12] reported that intraoperative use of dexmedetomidine (0.4 μg/kg/h) reduced EA after nasal surgery without delay of extubation.

Hypotension and bradycardia are common side effects of dexmedetomidine [5]. In our study, severe hypotension or bradycardia that required intervention was not observed in patients when a bolus of dexmedetomidine 0.5 μg/kg was infused over 10 min. This suggested that the incidence of dexmedetomidine-related cardiovascular adverse effects could be decreased by using a proper dosage and a slow infusion rate. Gurbet et al. [27] demonstrated that intraoperative use of dexmedetomidine did not increase postoperative nausea and vomiting. The finding in our study was similar to their study, and showed that there was no between-group difference in the incidence of postoperative nausea and vomiting. Dexmedetomidine has no respiratory depressant effects at clinically relevant doses [5, 28]. In our study, desaturation was not observed in both groups.

In conclusion, intravenous administration of dexmedetomidine 0.5 μg/kg after intubation attenuated the hemodynamic responses to extubation and decreased the occurrence of emergence agitation without delayed awakening. Therefore, the use of dexmedetomidine may result in a smooth and favorable recovery profile in patients undergoing ESS under general anesthesia.

Disclosure of conflict of interest

None.

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