Int J Clin Exp Med 2016;9(2):5077-5082
www.ijcem.com /ISSN:1940-5901/IJCEM0018277

Original Article

Dezocine in patients during recovery after anesthesia for thoracotomy: a prospective randomized controlled trial

Qinfang Cai, Xiaofei Gu, Jun Li, Zhe Zhang

Department of Anesthesiology, Navy General Hospital, Beijing 100048, China

Received October 22, 2015; Accepted January 16, 2016; Epub February 15, 2016; Published February 29, 2016

Abstract: Objective: To study the safety and efficacy of dezocine in patients during recovery from general anesthesia after thoracic surgery. Methods: A total of 90 patients (ASA physical status I and II) receiving thoracotomy were randomly divided into three groups. Fifteen minutes before the end of operation, patients in the control group were given 2 mL saline intravenously, patients in sufentanil group received 0.2 μg/kg sufentanil diluted in 2 mL saline, and those in dezocine group received 0.1 mg/kg dezocine diluted in 2 mL saline. Results: Compared with control group, the MAP and HR of patients in sufentanil and dezocine groups were significantly reduced at the time points T1 to T4 ($P<0.05$). The time of tracheal extubation and orientation recovery time did not differ significantly among the three groups ($P>0.05$). The dwelling time in PACU of patients from dezocine group was significantly reduced compared with those from the control group and sufentanil group (56±11 min vs. 73±12 min and 68±12 min, $P<0.05$). In addition, patients from dezocine group had significantly reduced sedation-agitation scale and Ramsay sedation scale compared with those from sufentanil group at all time points during the time of extubation ($P<0.05$). Conclusion: The use of dezocine in patients during anesthesia recovery period after thoracotomy can maintain hemodynamic stability, ensure a smooth recovery, and lead to a low rate of respiratory depression.

Keywords: Dezocine, injection, intravenous, surgery, thoracotomy

Introduction

Thoracotomy can be performed in a variety of severe diseases, such as esophageal cancer, lung cancer, cardiac disease, etc. It is invasive, but is widely applied in clinical settings. Acute pain after surgery is a common feature of this kind of invasive surgery, and it can be severe enough to cause complications, such as agitation and disorder of circulation, during recovery after anesthesia, thus affecting patients' recovery after surgery and even endangering their life [1]. In the past, the clinicians always use opioids to prevent related complications. However, traditional opioid analgesics can inhibit respiration, thus aggravating the above complications during the recovery period after the surgery [2]. Dezocine is a kind of synthetic mixed agonist-antagonist, and is characterized by quick action, strong analgesic effect, long-duration analgesia, etc. [3]. Thus, it is widely used clinically. This study aims at investigating the effect of intravenously injected dezocine on patients receiving thoracotomy during the period of anesthesia recovery.

Patients and methods

Patients

Ninety patients receiving thoracotomy in our hospital were included in this study, among whom there were 76 males and 14 females. This study was approved by the People's Liberation Army (PLA) Navy General Hospital Research Ethics. They were American Society of Anesthesiology (ASA) physical status I-II patients, with an age from 39-71 years old and a weight from 45-78 kg [4]. The patients had no severe heart, liver and kidney diseases, no history of long-term use of opioids, no blood coagulation disorders and no neuropsychiatric diseases. The patients were randomly divided into

Table 1. General information of patients

	Dezocine group (n=30)	Sufentanil group (n=30)	Control group (n=30)	*P* value
Male/female	26/4	25/5	24/6	*P*=0.45
Age (years)	63.2±5.4	59.5±7.1	61.3±6.2	*P*=0.28
BMI (kg/m^2)	21.4±2.5	22.2±2.3	22.6±2.1	*P*=0.33
Operating time (min)	170.8±11.4	154.9±19.3	163.5±17.6	*P*=0.19

Table 2. Changes in HR, MAP and SpO_2 at different time points ($\bar{x}\pm s$)

Groups		HR (times/min)	MAP (mmHg)	S_pO_2 (%)
Dezocine group (n=30)	T0	76±4	83±5	99.5±0.4
	T1	72±4[a,b]	77±6[a,b]	99.5±0.4
	T2	82±5[a,b]	88±12[a,b]	99.4±0.5
	T3	87±7[a,b]	95±13[a,b]	98.4±0.5
	T4	86±7[a,b]	90±8[a,b]	96.9±0.4[b,c]
Sufentanil group (n=30)	T0	76±4	81±6	99.4±0.4
	T1	71±3[a,b]	78±6[a,b]	99.4±0.7
	T2	79±6[a,b]	87±10[a,b]	99.3±0.6
	T3	85±7[a,b]	94±12[a,b]	98.3±0.6
	T4	84±6[a,b]	89±8[a,b]	96.4±0.4[b]
Control group (n=30)	T0	77±5	82±9	99.4±0.6
	T1	78±5	85±9	99.3±0.7
	T2	86±7[a]	95±10[a]	99.4±0.6
	T3	93±10[a]	108±16[a]	97.9±0.6
	T4	90±9[a]	103±13[a]	94.7±0.5

Note: a: compared with T0, *P*<0.05; b: compared with the control group, *P*<0.05; c: compared with sufentanil group, *P*<0.05; T0: before drug administration; T1: 5 min after drug administration; T2: at the end of the surgery, and T4: 5 min after removing the tube.

three groups according to random number table, to receive either dezocine (n=30), sufentanil (n=30), and no drug as control (n=30). For the dezocine group, the ratio of male to female was 26/4, with an age of 63±5 years; for the sufentanil group, the male to female ratio was 25/5, with an age of 59±7 years; for the control group, the male to female ratio was 24/6, with an age of 61±6 years (**Table 1**). The patients of the three groups did not differ significantly in each aspect (*P*>0.05).

Methods

Scopolamine (0.3 mg) was intramuscularly injected 30 min before anesthesia in all patients. After the patients were sent into the operation room, the veins were opened, radial artery catheterization was used to monitor invasive mean artery pressure (MAP), the heart rate (HR), and pulse oxygen saturation (SpO_2), electrocardiogram (ECG) was monitored routinely, and bispectral index (BIS) monitoring was performed. For anesthetic induction, 0.3 mg/kg etomidate, 0.3-0.5 μg/kg sufentanil, and 0.8 mg/kg rocuronium bromide (for rapid induction) were used. After topical pharyngeal anesthesia with lidocaine, a double-lumen endotracheal tube was inserted. The S_pO_2 was maintained at above 95%, while $P_{ET}CO_2$ was maintained at 35-45 mmHg. Before surgery, 0.2 μg/kg sufentanil was added. For maintenance of anesthesia, 50-120 μg/(kg·min) propofol and 0.15-0.2 μg/(kg·min) remifentanil were intravenously injected, and BIS was maintained between 40-50. Cisatracurium besylate (0.2 mg/kg) was discontinuously added if it was needed in surgery. Fifteen minutes before the end of the operation, the patients in control group were injected with 2 ml saline, those in sufentanil group were intravenously injected with 0.2 μg/kg sufentanil that was diluted in 2 ml saline, and those in dezocine group were intravenously injected with 0.1 mg/kg dezocine that was diluted in 2 ml saline. Thirty minutes before the end of the surgery, muscle relaxant was discontinued, 5 min before the end, propofol was discontinued, and at the end of the surgery, sufentanil was discontinued. When the patients had spontaneous respiration, neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg) were used for reversal of muscle relaxation. When the patients were conscious, the spontaneous respiration rate was more than 12 times/min, and tidal volume was over 8 ml/kg. During respiration, SpO_2 was maintained at >95% for over 5 min. Swallowing and reflection of tussis were recovered. When the endotracheal tube was removed, the patients were sent into post anesthesia care unit (PACU), and a disposable perfusion pump was connected for patient-controlled intravenous analgesia.

For the formula of analgesia pump, we used 2 μg/kg sufentanil and 0.2 mg/kg ondansetron

Table 3. Comparison of indicators during the recovery period

Groups	Time of tracheal extubation (min)	Orientation recovery time (min)	Dwelling time in PACU (min)	Incidence of nausea and vomiting (%)	Incidence of respiratory depression (%)
Dezocine group (n=30)	11.5±1.6	19±4	56±11[a,b]	1 (3)	2 (7)
Sufentanil group (n=30)	11.6±2.0	19±4	68±12	3 (10)	5 (17)
Control group (n=30)	10.9±1.2	17±3	73±12	2 (7)	4 (13)

Note: compared with the control group, [a]P<0.05; compared with sufentanil group, [b]P<0.05.

Table 4. Sedation-agitation scale and Ramsay sedation scale during extubation period ($\bar{x}\pm s$)

Groups		Sedation-agitation scale	Ramsay sedation scale
Control group (n=30)	0 min	2.65±0.17	3.88±0.17
	10 min	2.32±0.14	3.54±0.13
	20 min	2.15±0.08	2.96±0.11
	30 min	0.98±0.11	2.31±0.08
Sufentanil group (n=30)	0 min	2.21±0.13[a]	3.04±0.15[a]
	10 min	2.07±0.09[a]	2.89±0.16[a]
	20 min	1.56±0.10[a]	2.32±0.13[a]
	30 min	0.45±0.07[a]	2.07±0.12[a]
Dezocine group (n=30)	0 min	1.87±0.32[a,b]	2.34±0.57[a,b]
	10 min	1.03±0.18[a,b]	2.13±0.48[a,b]
	20 min	0.89±0.10[a,b]	2.01±0.13[a,b]
	30 min	0.32±0.13[a,b]	1.99±0.16[a,b]

Note: compared with the control group, [a]P<0.05; compared with sufentanil group, [b]P<0.05.

hydrochloride which were diluted in 100 mL saline. The infusion rate was 2 mL/h, PCIA was 0.5 ml and the duration was 15 min.

Observed indexes

MAP, HR and S_pO_2 of the three groups were recorded before drug administration (T0), 5 min after drug administration (T1), at the end of the surgery (T2), and 5 min after removing the tube (T4). We also recorded the time of tracheal extubation, orientation recovery time, dwelling time in PACU, sedation-agitation scale 10 min, 20 min and 30 min after extubation, Ramsay sedation scale, and the incidence of adverse reactions, such as nausea, vomiting and respiratory depression. The time of tracheal extubation refers to the period between the withdrawal of anesthetics and the time of removing the tube, the orientation recovery time refers to the period between the withdrawal of anesthetics and the time when the patients can accurately tell their birthday; the dwelling time in PACU refers to the time period during which the patients stayed in PACU.

Scoring criteria

The scoring criteria for agitation: 0 point for quiet cooperation, 1 point if there was body movement caused by stimulation such as sputum suction, 2 points if there was extremity agitation when stimulation was absent, 3 points for fierce struggling and difficulty in control. The scoring criteria for Ramsay sedation scale: 1 point for restlessness, 2 points for quiet cooperation, 3 points for somnolence, responsiveness to instructions but slurred speech, 4 points if the patients can be woken up from sleeping, 5 points for slow response to calling; 6 points for deep sleep or anesthetic status, unresponsiveness to calling. 2-4 points means that satisfactory sedation was achieved; and 5-6 point means that excessive sedation was achieved.

Statistical analysis

SSPS 13.0 was used for data analysis. The qualitative data were presented as $\bar{x}\pm s$. The *t* Test and Variance Analysis were used for comparison between groups. The qualitative data were analyzed using chi-square test. $P<0.05$ was considered statistically significant.

Results

Changes in HR, MAP and SpO_2 in the three groups during the recovery period

The MAP and HR were significantly reduced in patients in sufentanil and dezocine groups ($P<0.05$) compared with those in the control group at time points T1-T4. MAP and HR almost remained unchanged in the control group ($P>0.05$) and reduced greatly in sufentanil and

dezocine groups at T1 compared to at T0, but remarkably increased in the three groups at T2, T3, T4 ($P<0.05$). At T0-T3, SpO_2 was not significantly different between three groups; at T4, SpO_2 in sufentanil and dezocine groups was greatly increased ($P<0.05$) (**Table 2**).

Comparison of the tracheal extubation time, orientation recovery time, dwelling time in PACU among the three groups

Patients from the three groups did not differ significantly in the time of tracheal extubation, orientation recovery time, and dwelling time in PACU ($P>0.05$). Dwelling time in PACU was greatly reduced in dezocine group compared with the control group and sufentanil group ($P<0.05$). The incidence of nausea and vomiting was lower in dezocine group (**Table 3**).

Sedation-agitation scale and Ramsay sedation scale at the time points during recovery

At the time of tracheal extubation, 10 min, 20 min and 30 min after extubation, Sedation-agitation scale and Ramsay sedation scale were superior to those of the control group ($P<0.05$). Sedation-agitation scale and Ramsay sedation scale of the dezocine group were superior to those of sufentanil group ($P<0.05$) (**Table 4**).

Discussion

During anesthesia recovery period, the anesthetics are continuously degraded and excreted, and the degree of anesthesia is gradually reduced. Meanwhile, motor and sensory functions begin to recover, and the patients begin to respire spontaneously and become conscious. During this process, a variety of complications are likely to occur, such as high pressure, increased heart rate, hypoxemia, and agitation, which can endanger the patients' life [5]. Numerous factors contribute to these complications, including the pain caused by surgical incision, inadequate ventilation, hypoxia, sputum aspiration, mechanical stimulation caused by endotracheal tube and urinary catheter, etc., among which pain is the most common cause [6]. The pain is more intense after thoracotomy than after general surgeries, because the incision is large, the ribs need to be resected or cut off, and the damage to thoracic tissue is great. Therefore, effective inhibition of the pain during the recovery period plays an important role in reducing or avoiding the complications, and helping patients smoothly pass through the perioperative period [7]. Opioid receptor agonist is the primary drug that inhibits the cardiovascular responses during recovery period. Sufentanil is a strong opioid analgesics, which can effectively inhibit the cardiovascular stress [8]. Factors that may affect the efficacy of sufentanil are often accompanied by respiratory depression, delayed revival, and the adverse events, such as nausea and vomiting.

Dezocine is a new mixed agonist-antagonist, which can function as efficient analgesic by activating κ opioid receptor [9]. It can also serve as μ opioid receptor antagonists, relax gastrointestinal smooth muscle, and reduce the incidence of muscle spasm and gastrointestinal reaction [10]. Because dezocine has both agonistic and antagonistic effects on μ opioid receptor, it can inhibit the adverse reactions caused by the activation of this receptor, such as respiration depression. It is independent of μ opioid receptor, and does not cause much addiction [11]. Dezocine is equivalent to morphine in analgesia intensity, the action time and duration. It can function within 15 min after intravenous injection ($t_{1/2}$: 2.2-2.8 h), and its action lasts from 3-6 h. In this study, it was administered 15 min before suturing skin, because surgical stress response was the greatest during recovery, and analgesic effect of dezocine was strong enough at this moment [12]. It was found that the changes in HR and MAP in dezocine group were similar to those in the sufentanil group 5 min after administration, at the end of the surgery, at the time of extubation, and 5 min after extubation. Thus, we infer that the analgesic effect of the two drugs used in the two groups is similar. Li et al. [13] conducted research on the anesthesia in children, finding that dezocine has similar efficacy to sufentanil in reducing the agitation after the children recovered from anesthesia. Meanwhile, for the dezocine group, the incidence of post-surgical adverse reaction was lower. The study by Lu et al. [14] showed that if dezocine was used in advance, the pain caused by injection of propofol can be decreased, and dezocine can obtain similar analgesic effect to lidocaine.

Hypoxemia is a common complication after thoracotomy. Because some factors (such as the pain at the incision and the stimulation caused by closed thoracic drainage) directly affect cough and respiration of the patients, lung capacity declined during the exertion of force and secretions retained in the respiratory tract, leading to atelectasis and pneumonia and imbalanced ventilation/blood flow ratio, which will affect respiratory function and lead to hypoxemia after surgery. In addition, Kang et al. [15] also showed that probability of adverse events such as vomiting, retention of urine, skin itching and so on were significantly decreased by using dezocine after surgery. Effective analgesia can reduce the restriction of respiration by pain, promote early movement of diaphragm, and decrease the occurrence of hypoxemia. Sun et al. [16] also confirmed that prophylactic intravenous with dezocine (0.1 mg/kg) could inhibit the cough reflex induced by sufentanil completely. In this research, SpO_2 in dezocine group was superior to that in sufentanil group. However, extubation time and orientation recovery time in this group did not significantly different from sufentanil group, which can be explained by the agonistic-antagonistic dual effect of dezocine on μ opioid receptor [17]. Meanwhile, previous studies have confirmed that dezocine could agonize the κ opioid receptor, which represented analgesic effect by regulating visceral nerve function [18]. Therefore, the dezocine can provide a good postoperative analgesic effect, which was also indicated in our research.

In summary, the use of dezocine in the patients during recovery period after receiving thoracotomy can obtain good analgesic effect, slightly inhibit respiration, and does not prolong the dwelling time in PACU. Thus, it is a safe and effective analgesics after surgery of this kind. However, in the future study, randomized controlled study with a larger sample is needed to investigate the efficacy of dezocine and relevant adverse events.

Disclosure of conflict of interest

None.

Address correspondence to: Jun Li, Department of Anesthesiology, Navy General Hospital, Beijing 100048, China. E-mail: lijundoc@sina.com

References

[1] Grosen K, Vase L, Pilegaard HK, Pfeiffer-Jensen M and Drewes AM. Conditioned pain modulation and situational pain catastrophizing as preoperative predictors of pain following chest wall surgery: a prospective observational cohort study. PLoS One 2014; 9: e90185.

[2] Bujedo BM. Current evidence for spinal opioid selection in postoperative pain. Korean J Pain 2014; 27: 200-209.

[3] Sun Q, Zhou W, Wu B, Ji MH and Peng YG. Dezocine: a novel drug to prevent fentanyl-induced cough during general anesthesia induction? J Anesth 2012; 26: 470.

[4] American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology 2012; 116: 248-273.

[5] Cavaliere F, D'Ambrosio F, Volpe C and Masieri S. Postoperative delirium. Curr Drug Targets 2005; 6: 807-814.

[6] Ugur B, Ogurlu M, Gezer E, Nuri Aydin O and Gursoy F. Effects of esmolol, lidocaine and fentanyl on haemodynamic responses to endotracheal intubation: a comparative study. Clin Drug Investig 2007; 27: 269-277.

[7] Apfelbaum JL, Silverstein JH, Chung FF, Connis RT, Fillmore RB, Hunt SE, Nickinovich DG, Schreiner MS, Silverstein JH, Apfelbaum JL, Barlow JC, Chung FF, Connis RT, Fillmore RB, Hunt SE, Joas TA, Nickinovich DG and Schreiner MS. Practice guidelines for postanesthetic care: an updated report by the American Society of Anesthesiologists Task Force on Postanesthetic Care. Anesthesiology 2013; 118: 291-307.

[8] Maciejewski D. Sufentanil in anaesthesiology and intensive therapy. Anaesthesiol Intensive Ther 2012; 44: 35-41.

[9] Fischer BD, Miller LL, Henry FE, Picker MJ and Dykstra LA. Increased efficacy of micro-opioid agonist-induced antinociception by metabotropic glutamate receptor antagonists in C57BL/6 mice: comparison with (-)-6-phosphonomethyl-deca-hydroisoquinoline-3-carboxylic acid (LY235959). Psychopharmacology (Berl) 2008; 198: 271-278.

[10] Lv Z, Fang J, Zhu J, Liang B, Li F, Jiang S, Li A, Cheng Z and Dong T. Intravenous dezocine pretreatment reduces the incidence and intensity of myoclonus induced by etomidate. J Anesth 2014; 28: 944-947.

[11] He L, Ding Y, Chen H, Qian Y and Li Z. Dezocine pretreatment prevents myoclonus induced by

etomidate: a randomized, double-blinded controlled trial. J Anesth 2015; 29: 143-145.
[12] Zhou X, Zhang C, Wang M, Yu L and Yan M. Dezocine for Preventing Postoperative Pain: A Meta-Analysis of Randomized Controlled Trials. PLoS One 2015; 10: e0136091.
[13] Li X, Xia Q and Li W. Comparison of the effects of dezocine, fentanyl, and placebo on emergence agitation after sevoflurane anesthesia in children. Int J Clin Pharmacol Ther 2015; 53: 241-246.
[14] Lu Y, Ye Z, Wong GT, Dong C and Yu J. Prevention of injection pain due to propofol by dezocine: a comparison with lidocaine. Indian J Pharmacol 2013; 45: 619-621.
[15] Kang L, Long W and Jingshan C. Comparison of clinic effect between dezocin and sufentanil for postoperative analgesia after cesarean section. Mil Med JS Chin 2013; 27: 802-804.
[16] Sun ZT, Yang CY, Cui Z, Zhang J and Han XP. Effect of intravenous dezocine on fentanyl-induced cough during general anesthesia induction: a double-blinded, prospective, randomized, controlled trial. J Anesth 2011; 25: 860-863.
[17] Liu R, Huang XP, Yeliseev A, Xi J and Roth BL. Novel molecular targets of dezocine and their clinical implications. Anesthesiology 2014; 120: 714-723.
[18] Kivell B and Prisinzano TE. Kappa opioids and the modulation of pain. Psychopharmacology (Berl) 2010; 210: 109-119.