The application of dexmedetomidine combined with dezocine in thoracoscopic radical resection of lung cancer and its effect on awakening quality of patients

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Abstract. – OBJECTIVE: The paper aims to explore the application of dexmedetomidine combined with dezocine in thoracoscopic radical resection of lung cancer and its effect on the awakening quality.

PATIENTS AND METHODS: 122 patients undergoing thoracoscopic radical resection of lung cancer in The Affiliated Hospital of Qingdao University from April 2009 to January 2012 were selected as the subjects of the study. Among them, 68 patients were anesthetized with dexmedetomidine combined with dezocine as a study group, 54 patients with midazolam combined with fentanyl as a control group. The onset of anesthetic, operation time, awakening time, extubation time, and recovery time was compared. The mean arterial pressure (MAP), central venous pressure (CVP), and heart rate (HR) were compared before anesthesia (t0), at extubation (t1), 10 min after extubation (t2), and when patients left anesthesia recovery room (t3). The postoperative sedation score (Ramsay), modified the objective pain score (MOPS), and the pediatric anesthesia emergence delirium (PAED) score were compared at the time of the postoperative awakening (b1), 30 min after awakening (b2), 1 hour after awakening (b3), and 3 hours after awakening (b4).

RESULTS: There was no significant difference in MAP, CVP, and HR between the study group and the control group at t0 ($p > 0.05$). The scores of PAED at b3 and b4 in the study group were lower than those in the control group ($p < 0.05$).

CONCLUSIONS: The anesthesia effect of dexmedetomidine combined with dezocine in thoracoscopic radical resection of lung cancer is better and safer than other drugs, and it can produce good sedation and analgesic effect.

Key Words:
Dexmedetomidine combined with dezocine, Thoracoscopic radical resection of lung cancer, Awakening quality.

Introduction

Lung cancer is a common cause of cancer death in the world. About 1.8 million people are diagnosed with lung cancer every year[1], and about 1.6 million people die from this disease. Non-small cell lung cancer (NSCLC) is the most common lung cancer, mainly composed of squamous cell carcinoma and adenocarcinoma, and the incidence of non-small cell lung cancer accounting for 85-90% of lung cancer[2]. Surgical resection remains to be a clinical method for the treatment of early stage of lung cancer[3]. Compared with traditional open surgery, laparoscopic surgery can avoid the chest wall muscle division and rib diffusion, thus reducing pain and postoperative complications, shortening hospital stay, and improving the quality of life[4]. But the pain still remains, so analgesia is essential. However, anesthetics are indispensable in surgery. Due to a wide range of wounds, extensive use of general anesthetics, and slow drug metabolism, the delayed awakening after anesthesia is common[5].

Dexmedetomidine is a selective epinephrine agonist with anti-anxiety, anti-sympathetic nerve, and little effect on respiratory function, sedation, and analgesia[6]. Dexmedetomidine is an important choice for short- or long-term sedation in the intensive care unit[7]. In laparoscopic surgery, it can reduce the hemodynamic response of pneumoperitoneum[8], reduce the duration of coma, and shorten the duration of the mechanical ventilation[9]. Dezocine is a mixed agonist/antagonist of opioids that has been used to control the postoperative pain. Some common side effects have been significantly reduced due to partial μ receptor-activation[10]. Dezocine has good effects on spinal

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sedation and analgesia, including low respiratory inhibition, high safety, low drug dependence, and high tolerance[11]. It has been reported that dexmedetomidine combined with dezocine is a safe and effective method in gynecological thoracoscopic surgery under general anesthesia, which can make the blood circulation of patients more stable and improve the recovery rate of patients[12].

At present, there are few studies on the treatment of lung cancer with dexmedetomidine combined with dezocine under thoracoscopy. This study aims to a provide reference for the treatment of lung cancer by observing the anesthetic effect and the effect on the awakening quality of patients with lung cancer treated with dexmedetomidine combined with dezocine under thoracoscopy.

Materials and Methods

General Materials

122 patients undergoing thoracoscopic radical resection of lung cancer in The Affiliated Hospital of Qingdao University from April 2009 to January 2012 were selected as the subjects of the study. Among them, 68 patients were anesthetized with dexmedetomidine combined with dezocine as a study group, and 54 patients with were treated with midazolam combined with fentanyl as a control group. There were 33 males and 35 females in the study group, with the age of 43-76 years old, and an average age of (61.24 ±9.11) years old. The tumor diameter of patients in the study group was 1.5-4.7 cm, with a mean diameter of (2.87±1.35) cm. According to the TNM staging, there were 36 cases in I+II stage and 32 cases in III stage. According to the pathological differentiation degree, there were 40 cases of high-medium differentiation and 28 cases of low differentiation. There were 26 males and 28 females in the control group, with the age of 41-74 years old, an average age of (60.57 ±9.28) years old. The tumor diameter of patients in the control group was 1.3-4.5 cm, with a mean diameter of (2.82±1.67) cm. According to the TNM staging, there were 34 cases in I+II stage and 20 cases in III stage. According to the pathological differentiation degree, there were 36 cases of high-medium differentiation and 18 cases of low differentiation.

Inclusion and Exclusion Criteria

Inclusion criteria: patients were diagnosed with lung cancer by preoperative pathological examination[13], and no distant metastasis was found by CT, color Doppler ultrasound, and MRI. The general clinical data of patients were complete. There was no contraindication in the treatment of patients. Patients were not treated with chemotherapy and radiotherapy. Patients were diagnosed for the first time, aged 43-75 years old. The expected survival time of the patient was more than or equal to 1 year.

This study was approved by the Ethics Committee of The Affiliated Hospital of Qingdao University. The subjects and their families were informed, and the fully informed consent form was signed.

Exclusion criteria: there was no sick sinus syndrome, bradycardia, other tumors, severe liver, kidney dysfunction, electrolyte disorder, hematopoietic dysfunction, infectious disease, neurological history, and addictive opioid history.

Surgical Method

Patients in the study group were anesthetized with dexmedetomidine combined with dezocine, while patients in the control group were treated with midazolam combined with fentanyl. After successful anesthesia induction, the double-lumen tracheal catheterization was performed in both groups. Three trocar needles were selected for opening. The lens was placed in the sixth or seventh intercostal part of the axillary midline, and the other two puncture holes were selected according to the location of the lesion. The three incisions were triangular and were pointed to different lesion sites in different directions. After the operation, the closed drainage tube was put into the chest and extubated after the recovering of spontaneous breathing, cough, and swallowing reflex.

Observation Indicator

The onset of anesthetic, operation time, awakening time, extubation time, and recovery time was observed and recorded. The mean arterial pressure (MAP), central venous pressure (CVP), and heart rate (HR) levels of the two groups were measured and recorded before anesthesia (t0), at extubation (t1), 10 min after extubation (t2), and when patients left anesthesia recovery room (t3).

Comparison of Postoperative Curative Effect Score Between the Two Groups

The postoperative sedation scores (Ramsay) of the two groups were measured and recorded at the time of postoperative awakening (b1), 30 min after awakening (b2), 1 hour after awakening (b3), and 3 hours after awakening (b4). Scoring criteria: 1 point=fidgety; 2 points=sober and quiet cooperation; 3 points=drowsiness, following the instructions of the medical staff; 4 points=rapid eye movement sleep; 5 points=fall asleep, slow response to calls; 6 points=deep sleep. The scoring criteria of the modified objective pain score (MOPS): 0 point=painless, 1-3 points=mild pain, 4-6 points=moderate pain, and 7-10 points=severe pain. The scoring criteria of the pediatric anesthesia emergence delirium (PAED): 1 point=sleep, 2 points=sober and quiet, 3 points=cry, 4 points=-cannot comfort and do not stop crying, and 5 points=serious restlessness.

Statistical Analysis

The SPSS 22.0 (SPSS Inc., Chicago, IL, USA) software was used to statistically analyze the collected data. The intra-group counting data were represented by a number of cases/percentages [n (%)] and analyzed by the Chi-square test. The measurement data were represented by the mean ±standard deviation (x±sd). The measurement data between the two groups were compared by the *t*-test. The repeated measurement variance was used for comparison at the same time point. The Bonferroni method was used for pairwise comparison between different time points in the group. $p < 0.05$ was considered as indicating a statistically significant difference.

Results

General Materials of the Two Groups

There was no significant difference in sex, age, baric index, smoking history, drinking history, exercise, tumor diameter, TNM stage, and pathological differentiation between the study group and the control group ($p > 0.05$). See Table I.

Comparison of Operation Time of Anesthesia Induction Intubation between the Two Groups

There was no significant difference in the onset time of anesthesia between the two groups ($p > 0.05$). The awakening time, extubation time, and recovery time of the study group were lower than those in the control group ($p < 0.05$). See Table II.

Comparison Of MAP Between The Two Groups At Different Time Points During Operation

There were significant differences in MAP between the two groups at each time point ($p < 0.05$). There was no significant difference in MAP between the two groups at t0 ($p > 0.05$).

Table I. Comparison of general baseline data between the study group and the control group [n (%)]/($\bar{x} \pm$ sd).

Classification	Study group (n = 68)	Control group (n = 54)	t/χ^2	*p*-value
Sex			0.002	0.967
Male	33 (48.53)	26 (48.15)		
Female	35 (51.47)	28 (51.85)		
Age (years)	61.24 ± 9.11	60.57 ± 9.28	0.400	0.690
Weight (kg/cm^2)	22.34 ± 3.18	22.15 ± 3.13	0.330	0.742
Smoking history			0.243	0.622
Yes	45 (66.18)	38 (70.37)		
No	23 (33.82)	16 (29.63)		
Drinking history			1.347	0.236
Yes	37 (54.41)	35 (64.81)		
No	31 (45.59)	19 (35.19)		
Exercise			0.181	0.670
Yes	19 (27.94)	17 (31.48)		
No	49 (72.06)	37 (68.52)		
Tumor diameter (cm)	2.87 ± 1.35	2.82 ± 1.67	0.183	0.855
TNM stage			1.236	0.266
I+II	36 (52.94)	34 (62.96)		
III	32 (47.06)	20 (37.04)		
Pathological differentiation			0.788	0.375
High-medium differentiation	40 (58.82)	36 (66.67)		
Low differentiation	28 (41.18)	18 (33.33)		

Table II. Comparison of operation time of anesthesia induction intubation between the two groups ($\bar{x} \pm$ sd, min).

	Study group (n = 68)	Control group (n = 54)	*t*	*p*-value
Onset time of anesthesia	4.78 ± 1.04	5.02 ± 1.13	1.218	0.226
Awakening time	13.48 ± 2.53	14.89 ± 2.96	2.835	0.005
Extubation time	11.26 ± 3.12	12.56 ± 3.45	2.181	0.031
Recovery time	10.46 ± 2.78	11.56 ± 2.83	2.154	0.033

Table III. Comparison of the MAP of each time period during the operation of two groups of patients ($\bar{x} \pm$ sd, mmHg).

Group	t0	t1	t2	t3	F	*p*-value
Study group (n = 68)	81.09 ± 8.67	72.01 ± 7.12*	73.09 ± 7.91*	74.16 ± 8.35*	17.210	< 0.001
Control group (n = 54)	82.76 ± 8.77	74.88 ± 8.98*	75.99 ± 8.01*	77.99 ± 7.24*	9.559	< 0.001
t	1.051	1.969	1.978	2.667	–	–
p	0.295	0.012	0.048	0.009	–	–

Note: *Indicates that compared with t0, $p < 0.05$.

The MAP at t1, t2, and t3 in both groups was lower than that at t0 ($p > 0.05$). The MAP was lower in the study group than that in the control group at t1, t2, and t3 ($p < 0.05$). See Table III.

Comparison of CVP Between The Two Groups At Different Time Points During Operation

There were significant differences in CVP between the two groups ($p < 0.05$). There was no significant difference in CVP between the two groups at t0 ($p > 0.05$). The CVP at T1, T2, and T3 in both groups was lower than that at t0 ($p < 0.05$). The CVP was lower in the study group than that in the control group at t1, t2, and t3 ($p < 0.05$). See Table IV.

Comparison of HR Between The Two Groups At Different Time Points During Operation

There were significant differences in HR between the two groups at each time period ($p < 0.05$). There was no significant difference in HR between the two groups at t0 ($p > 0.05$). The HR at T1, T2, and T3 in both groups was lower than that at t0 ($p < 0.05$). The HR was lower in the study group than that in the control group at t1, t2, and t3 ($p < 0.05$). See Table V.

Ramsay Sedation Score in Both Groups at Different Time Points after Operation

There were significant differences in the Ramsay sedation score between the two groups at b1-b4 after the operation ($p < 0.05$). The Ramsay sedation score at b2-b4 was lower than that at b1 ($p < 0.05$). The Ramsay sedation score of the two groups significantly decreased with the prolongation ($p < 0.05$). The Ramsay sedation score of patients in the study group was lower than that in the control group at b1-b4 after the operation ($p < 0.05$). See Table VI and Figure 1.

MOPS Pain Score in the Two Groups at Different Time Points after Operation

There were significant differences in MOPS between the two groups at b1-b4 after operation ($p < 0.05$). The MOPS at b1-b3 was lower than

Table IV. Comparison of the CVP of each time period during the operation of two groups of patients ($\bar{x} \pm$ sd, cm H_2O).

Group	t0	t1	t2	t3	F	*p*-value
Study group (n = 68)	4.67 ± 1.14	3.54 ± 1.43*	3.68 ± 1.48*	4.01 ± 1.35*	9.372	< 0.001
Control group (n = 54)	4.87 ± 1.11	4.03 ± 1.23*	4.22 ± 1.14*	4.45 ± 1.01*	5.579	0.001
t	0.974	1.998	2.210	1.992	–	–
p	0.332	0.048	0.029	0.047	–	–

Note: *Indicates that compared with t0, $p < 0.05$.

Table V. Comparison of the CVP of each time period during the operation of two groups of patients ($\bar{x} \pm$ sd, times/min).

Group	t0	t1	t2	t3	F	*p*-value
Study group (n = 68)	85.37 ± 4.31	79.31 ± 4.01*	81.18 ± 4.13*	82.87 ± 4.01*	25.920	< 0.001
Control group (n = 54)	85.99 ± 4.19	77.57 ± 3.96*	82.68 ± 4.18*	84.35 ± 4.19*	6.052	0.006
t	0.799	4.320	3.819	4.466	–	–
p	0.426	< 0.001	0.002	< 0.001	–	–

Note: *Indicates that compared with t0, $p < 0.05$.

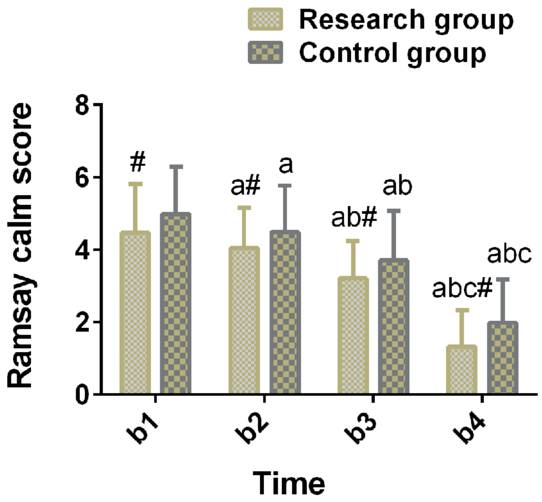

Figure 1. Ramsay sedation score of the two groups at each time period after the operation. The Ramsay sedation score at b2-b4 was lower than that at b1 ($p < 0.05$). The Ramsay sedation score at b3 and b4 was lower than that at b2 ($p < 0.05$). The Ramsay sedation score at b4 was lower than that at b3 ($p < 0.05$). The Ramsay sedation score of patients in the study group was lower than that in the control group at b1-b4 after operation ($p < 0.05$). Note: [a] indicates that, compared with b1, $p < 0.05$; [b] indicates that, compared with t2, $p < 0.05$; [c] indicates that, compared with t3, $p < 0.05$; [#] indicates that, compared with the control group, $p < 0.05$.

that at b4 ($p < 0.05$). The MOPS of the two groups significantly increased with the prolongation ($p < 0.05$). The MOPS of patients in the study group was lower than that in the control group at b1-b4 after the operation ($p < 0.05$). See Table VII and Figure 2.

PAED Score at Each Time Period after Operation in Two Groups

There were significant differences in PAED score between the two groups at b1-b4 after the operation ($p < 0.05$). The PAED score at b1-b3 was lower than that at b4 ($p < 0.05$). There was no significant difference in the PAED score between the study group and the control group at b1 and b2 ($p > 0.05$). The PAED score of patients in the study group was lower than that in the control group at b3 and b4 after the operation ($p < 0.05$). See Table VIII and Figure 3.

Discussion

Lung cancer is the most common fatal cancer. It causes 18% death of all cancer deaths, and the progression of lung cancer decreases the survival rate[14]. For the early stage of lung cancer treatment, surgical resection is still the main method. The traditional thoracotomy with large incision and

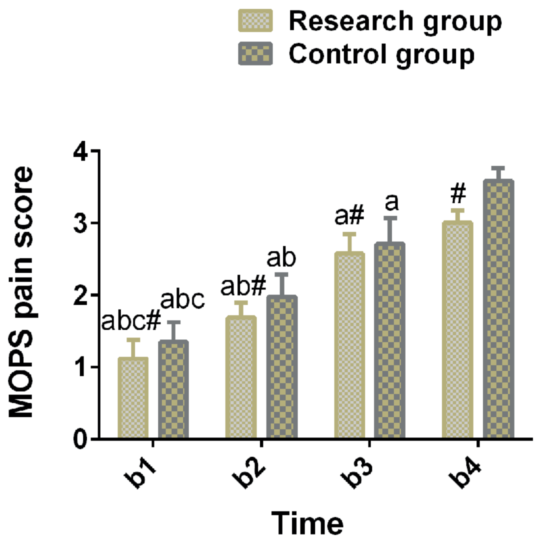

Figure 2. MOPS of the two groups at each time period after the operation. The MOPS at b1-b3 was lower than that at b4 ($p < 0.05$). The MOPS at b1 and b2 was lower than that at b3 ($p < 0.05$). The MOPS at b1 was lower than that at b2 ($p < 0.05$). The MOPS of patients in the study group was lower than that in the control group at b1-b4 after operation ($p < 0.05$).
Note: [a] indicates that, compared with b4, $p < 0.05$; [b] indicates that, compared with b3, $p < 0.05$; [c] indicates that compared with b2, $p < 0.05$; [#] indicates that, compared with the control group, $p < 0.05$.

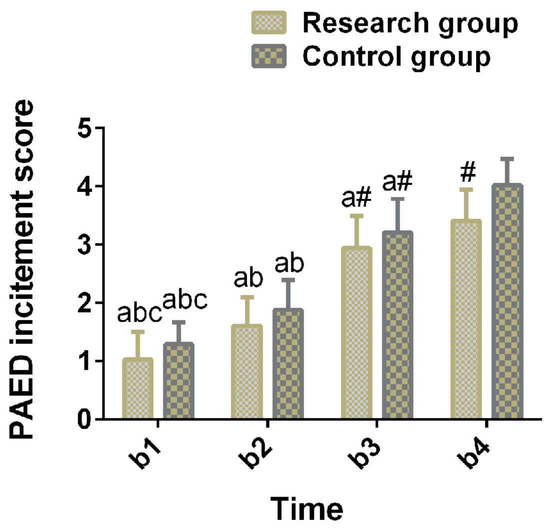

Figure 3. PAED score of the two groups at each time period after operation. The PAED score at b1-b3 was lower than that at b4 ($p < 0.05$). The PAED score at b1 and b2 was lower than that at b3 ($p < 0.05$). The PAED score at b1 was lower than that at b2 ($p < 0.05$). There was no significant difference in the PAED score between the study group and the control group at b1 and b2 ($p > 0.05$). The PAED score of patients in the study group was lower than that in the control group at b3 and b4 after the operation ($p < 0.05$).
Note: [a] indicates that, compared with b4, $p < 0.05$; [b] indicates that, compared with b3, $p < 0.05$; [c] indicates that, compared with b2, $p < 0.05$; [#] indicates that, compared with the control group, $p < 0.05$.

trauma and serious postoperative pain makes the quality of life of lung cancer patients seriously declining[15]. With the development of endoscopic technology, the minimal invasive, the reduction of the postoperative complications, and the improvement of the quality of life of patients with lung cancer are the clinical research foci[16]. Postoperative pain is common due to the elimination of the efficacy of anesthetics[17]. To avoid all kinds of postoperative complications and reduce postoperative pain, it is particularly important to find an efficient anesthetic for laparoscopic surgery.

Thoracoscopic surgery has been widely used in the clinic and replaces the conventional laparotomy step by step. However, the instruments of the thoracoscopic surgery support the ribs, resulting in the compression of the intercostal nerve by the thoracic cannula and the stimulation of the pleura by the thoracic drainage tube, so that the patients still have a moderate degree of pain[18]. The pain will increase the stress response of patients and has adverse effects on immune function and endocrine. Acute postoperative pain and chronic postoperative pain will increase the incidence of postoperative patients and have an impact on postoperative recovery. Therefore, effective postoperative pain relief has a positive effect on postoperative recovery[19]. In this study, two groups of patients with lung cancer under laparoscopy were anesthetized with two different anesthetic methods, namely, the study group of dexmedetomidine combined with dezocine and the control group of midazolam combined with fentanyl.

Dexmedetomidine has been used clinically as a general anesthetic, painkiller, and sedative for more than 30 years[20]. More than 30% of the patients suffered from adverse reactions such as anxiety, delirium, and stress after the operation, while dexmedetomidine played a role in regulating the psychology and physiology of postoperative patients and reducing the incidence of delirium[21]. In the study of Kang et al[22], dexmedetomidine in lung cancer resection can reduce the incidence of restlessness and improve the recovery of patients. Dezocine is an effective analgesic, which has been widely used in the treatment of pain[23]. As an auxiliary analgesic with small side effects and dependence, dezocine can enhance the analgesic effect of morphine and reduce the consumption and side effects of opioids in laparotomy and thoracotomy[24]. Goldfarb et al[25] demonstrated that dexmedetomidine combined with dezocine is a safe and effective anes-

Table VI. Ramsay sedation score in each time period after operation in both groups ($\bar{x} \pm$ sd, point).

Group	b1	b2	b3	b4	F	*p*-value
Study group (n = 68)	$4.47 \pm 1.34^{\#}$	$4.05 \pm 1.11^{a\#}$	$3.21 \pm 1.03^{ab\#}$	$1.32 \pm 1.01^{abc\#}$	103.900	< 0.001
Control group (n = 54)	4.99 ± 1.31	4.49 ± 1.28^{a}	3.71 ± 1.37^{ab}	1.98 ± 1.21^{abc}	56.050	< 0.001
t	2.150	2.032	2.301	3.283	–	–
p	0.034	0.044	0.023	0.001	–	–

Note: [a]Indicates that, compared with b1, $p < 0.05$; [b]Indicates that, compared with t2, $p < 0.05$; [c]Indicates that, compared with t3, $p < 0.05$; [#]Indicates that, compared with the control group, $p < 0.05$.

Table VII. MOPS in each time period after operation in both groups ($\bar{x} \pm$ sd, point).

Group	b1	b2	b3	b4	F	p-value
Study group (n = 68)	$1.12 \pm 0.26^{abc\#}$	$1.69 \pm 0.21^{ab\#}$	$2.58 \pm 0.27^{a\#}$	$3.01 \pm 0.17^{\#}$	928.700	< 0.001
Control group (n = 54)	1.35 ± 0.28^{abc}	1.98 ± 0.31^{ab}	2.71 ± 0.36^{a}	3.59 ± 0.18	648.200	< 0.001
t	4.691	6.144	2.279	18.240	–	–
p	< 0.001	< 0.001	0.024	< 0.001	–	–

Note: [a]Indicates that, compared with b4, $p < 0.05$; [b]Indicates that, compared with b3, $p < 0.05$; [c]Indicates that, compared with b2, $p < 0.05$; [#]Indicates that, compared with the control group, $p < 0.05$.

Table VIII. PAED score in each time period after operation in both groups ($\bar{x} \pm$ sd, point).

Group	b1	b2	b3	b4	F	p-value
Study group (n = 68)	1.03 ± 0.47^{abc}	1.61 ± 0.49^{ab}	$2.94 \pm 0.55^{a\#}$	$3.41 \pm 0.53^{\#}$	322.9	< 0.001
Control group (n = 54)	1.29 ± 0.38^{abc}	1.88 ± 0.51^{ab}	3.21 ± 0.57^{a}	4.02 ± 0.45	357.2	< 0.001
t	0.001	0.004	2.650	6.744	–	–
p	3.298	2.969	0.009	< 0.001	–	–

Note: [a]Indicatesa that, compared with b4, $p < 0.05$; [b]Indicates that, compared with b3, $p < 0.05$; c indicates that, compared with b2, $p < 0.05$; [#]Indicates that, compared with the control group, $p < 0.05$.

thesia method in the gynecological laparoscopic surgery that can stabilize the blood circulation, improve the postoperative recovery rate, and prevent the adverse reaction to the patient after general anesthesia. In addition, Ni et al[26] showed that dezocine combined with dexmedetomidine could achieve ideal analgesic effect in patients with ICU mechanical ventilation, and that the anesthetic, sedation, and analgesic effect were better than those of dexmedetomidine alone and dexmedetomidine combined with fentanyl. In this study, there was no significant difference in the onset time of anesthesia between patients in the study group and the control group. However, the awakening time, extubation time, and recovery time after anesthesia in the study group were lower than those in the control group. MAP, CVP, and HR significantly decreased at t1, t2, and t3, and the study group was lower than those in the control group, indicating that dexmedetomidine combined with dezocine can provide more stable hemodynamics for patients with lung cancer.

Restlessness can lead to self-injury in patients undergoing general anesthesia, which may be related to indwelling catheter and organ intubation after the operation and may have an impact on the mental health of patients[27]. Mohite et al[28] detected that dexmedetomidine combined with dezocine can reduce the degree of restlessness and the incidence of restlessness after chest surgery and can inhibit the inflammatory reaction. The results of this study showed that the Ramsay sedation score, the MOPS at b1-b4, and the PAED score at b3 and b4 in the study group were lower than those in the control group, indicating that dexmedetomidine combined with dezocine can better inhibit pain, irritation, and transmission to the central nervous system. The combination of the two anesthetic drugs can lead to better postoperative analgesia and sedative effect so that it can reduce the occurrence of restlessness during the recovery of the lung cancer patient, and the mechanism may be related to the synergistic effect of the combined application of the two anesthetic drugs.

The object of this study was strictly screened according to the inclusion and exclusion criteria. There was no significant difference in sex, age, baric index, and other general clinical baseline data between the study group and the control group, which ensured the rigor and reliability of the study. This study had some limitations because it failed to compare the effects of different doses of two different anesthetics and failed to analyze the adverse reactions and quality of life of patients with two different combinations of anesthetics. In future reports, to support the results of this analysis, the study time will be extended, and the follow-up will be added.

Conclusions

The anesthesia effect of dexmedetomidine combined with dezocine in thoracoscopic radical resection of lung cancer is better and safer than other drugs. Dexmedetomidine combined with dezocine can produce good sedation and analgesic effect, and high quality of recovery after the operation, which can reduce the restlessness of patients after operation, and is worth promoting in clinical practice.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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