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Original Article

Application value of conventional anesthesia combined with dexmedetomidine in thoracoscopic radical resection of lung cancer

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Abstract: Objective: To explore the effect of dexmedetomidine combined with conventional anesthesia on thoracoscopic radical resection of lung cancer (LC). Methods: From January 2019 to June 2020, 217 patients undergoing thoracoscopic radical resection of LC in our hospital were selected and separated into two groups in accordance with different anesthesia methods, of which 96 patients received conventional anesthesia (control group, CG) and 121 patients received conventional anesthesia combined with dexmedetomidine (experimental group, EG). The clinical indicators and adverse reactions were analyzed in both groups. The visual analogue scale (VAS) was used to assess the degree of postoperative pain. The score of emergence agitation (PAED) was used to compare the postoperative inflammatory response and immune function between the two groups. The oxygen index (OI), respiratory index (RI) and arterial-alveolar oxygen partial pressure ratio (PaO_2/PAO_2) were calculated by arterial blood gas. The postoperative quality of life was compared in both groups. Results: After operation, the incidence of postoperative adverse effects, VAS score and PAED score, the expression levels of IL-8, IL-6 and TNF-α in the EG were obviously lower than those in the CG. After surgery, the levels of CD3+, CD4+, CD8+ and the ratio of CD4+/CD8+ in the EG were obviously better than those in the CG. The postoperative OI, RI and PaO_2/PAO_2 in the EG were obviously better than those in the CG. After operation, the quality of life score in the EG was obviously higher than that in the CG. Conclusion: Conventional anesthesia combined with dexmedetomidine can improve immune function, reduce stress response and emergence agitation, and ameliorate the postoperative quality of life of patients undergoing thoracoscopic radical resection of LC.

Keywords: Application value, lung cancer, dexmedetomidine, conventional anesthesia

Introduction

LC is a common malignant tumor, with an incidence rate of 11.6% and a mortality rate of 18.4%, accounting for the leading form malignant tumors [1]. At present, surgery is the most effective clinical treatment for LC. With the continuous development of minimally invasive surgery technology and the wide application of endoscopic technology, total thoracoscopic radical resection of LC has gradually become an important clinical treatment for patients with LC [2, 3]. However, pain, excitement and urethral canal issues can cause severe hemodynamic fluctuations and even induce cardiovascular events in the process of thoracoscopic radical resection of LC [4, 5]. Therefore, it is of great significance to explore suitable drugs to maintain the relative stability of hemodynamics in patients with LC during the perioperative period.

Dexmedetomidine is a 2-adrenoceptor agonist, which can directly inhibit the activity of the sympathetic nerve and cause sedative effects. It is widely used in clinical anesthesia at present [6, 7]. During thoracoscopic radical resection of LC, hypoxia and ischemia of tissues, decreased scavenging function of oxygen free radicals and lung atrophy can develop in the non-ventilated lung, and a large amount of oxygen free radicals are produced; which is a main cause of reperfusion injury [8]. Related studies have revealed that dexmedetomidine can inhibit oxidative stress and inflammatory reactions and reduce blood reperfusion injury [9]. Studies by Dong et al. [10] have shown that dexmedetomidine can reduce the perioperative inflammatory response and improve immunological function in patients undergoing radical gastrectomy for gastric cancer, but there are few studies on patients undergoing thoracoscopic radical surgery for LC.

Therefore, dexmedetomidine was used in one-lung ventilation during thoracoscopic radical resection of LC to observe the changes of inflammatory factors and lung function in this study. The results are as follows.

Materials and methods

Baseline data

From January 2019 to June 2020, 217 patients undergoing thoracoscopic radical resection of LC in The First People's Hospital of Zunyi were selected and separated into two groups in accordance with different anesthesia methods, of which 96 cases received conventional anesthesia (CG) and 121 patients received conventional anesthesia combined with dexmedetomidine (EG). There were no statistically significant differences in age, body mass, gender, operation time and duration of one-lung ventilation between the two groups ($P > 0.05$). This research was ratified by the hospital ethics Committee and all patients were informed of the study, agreed to participate and signed the informed consent form.

Inclusion criteria: patients with early non-small cell lung cancer who underwent thoracoscopic pulmonary lobectomy at an optional date were included; class was determined as I-II according to American Society of Anesthesiology (ASA) [11]; body mass was within ± 20% of the standard body mass; no contraindication to the operation; no ventilation dysfunction after preoperative examination; ages ranged from 18 to 65 years old.

Exclusion criteria were as follows: atients with organ dysfunction such as in the heart, liver and kidney; patients with obvious lung inflammation before operation; patients with severe ventilation issues before operation; those who did not cooperate with this study; patients with serious liver and kidney dysfunction; patients with diseases of the immune system or endocrine system.

Methods

In the conventional group, patients were anesthetized with propofol, midazolam, sufentanil and cisatracurium besylate. In the EG, patients were anesthetized with dexmedetomidine in addition to treatment in the conventional group. No patients were given non-study related medicine before surgery, and the peripheral veins of upper limbs were opened after entering the room. The blood pressure, blood oxygen saturation, electrocardiogram and heart rate were routinely monitored. In the conventional group, patients were intravenously injected with propofol (2 mg/kg) (Zhejiang Jiuxu Pharmaceutical Co., Ltd., H20084531), sufentanil (0.3 μg/kg) (Yichang Humanwell Pharmaceutical Co., Ltd., H20054171), midazolam (0.05 mg/kg) (Zhejiang Jiuxu Pharmaceutical Co., Ltd., H20113387) and cisatracurium besylate (0.15 mg/kg) (Jiangsu Hengrui Pharmaceutical Co., Ltd., H20060868). After induction, patients were intubated. In the conventional group, patients were injected with 15 mL of normal saline. In the EG, patients were treated with dexmedetomidine (0.4 g/kg) (Jiangsu Hengrui Pharmaceutical Co., Ltd., H20090251) in addition to treatment in the conventional group. During the operation, patients were intravenously given with dexmedetomidine (0.2 $g \cdot kg^{-1} \cdot h^{-1}$) for 10 min to maintain the anesthesia. During operation, patients were intravenously given propofol (4 $mg \cdot kg^{-1} \cdot h^{-1}$) (Zhejiang Jiuxu Pharmaceutical Co., Ltd., H20084531) and remifentanil (8 $\mu g \cdot kg^{-1} \cdot h^{-1}$) (8690258100083, Langfang Branch of Sinopharm Group Industry Co., Ltd., H20123422). Then, cisatracurium besylate (2 mg) was added intermittently to maintain anesthesia. The bispectral index (BIS) was kept between 40 and 60. When the incision was sutured, a patient controlled intravenous analgesia (PCIA) pump was turned on. The drug formula is as follows: sufentanil (2 μg/kg) and metoclopramide (20 mg) were added to 100 mL of normal saline (2 mL/h, a dose of 2 mL, 15 min).

Outcome measures

During operation, the adverse reactions were observed in both groups. The degree of postoperative pain [12] was assessed by visual analogue scale (VAS), and pain scores were based on a combination of self-description and pain cheek (0 was painless, 10 was severe pain,

Table 1. Baseline data in both groups

Factors	EG (n = 121)	CG (n = 96)	t	P
Gender			0.011	0.917
Male	90 (74.38)	72 (75)		
Female	31 (25.62)	24 (25)		
ASA grading			0.221	0.638
Grade I	68 (56.2)	57 (59.38)		
Grade II	53 (43.8)	39 (40.63)		
Age	42.15±1.34	41.88±1.56	1.371	0.172
Weight (kg)	64.79±1.33	65.04±1.23	1.421	0.157
Average operation time (min)	132.47±24.84	134.16±22.67	0.517	0.606
Average duration of one-lung ventilation (min)	117.52±27.46	119.34±25.58	0.500	0.618

Table 2. Comparison of the incidence of adverse effects between the two groups

Categories	Choking cough	Nausea and vomiting	Chill	Incidence of adverse effects
EG (n = 121)	5 (11.9)	0 (0)	0 (0)	5 (11.9)
CG (n = 96)	13 (36.11)	1 (2.78)	4 (11.11)	18 (50)
t value				12.07
P value				< 0.01

VAS < 3 was good analgesia, 3-4 was basically satisfaction, and > 5 was poor analgesia). The score of emergence agitation (PAED [13]) was used: (1) Kept their eye on the nursing staff; (2) Purposeful action; (3) Able to know their environment; (4) Uneasy; (5) Unable to be appeased. The scores of items 1, 2 and 3 were 4-0 (4 = none; 3 = less; 2 = more; 1 = much; 0 = always); The scores of item 4 and 5 were 0-4 (0 = none; 1 = less; 2 = more; 3 = much; 4 = always). The sum of each score was PAED score, and the higher the score, the more severe the degree of emergence agitation. The levels of interleukin-8 (IL-8), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were measured by taking peripheral blood before anesthesia induction (T0), at the end of operation (T1) and after surgery for 12 h (T2) and 24 h (T3). At T0, T1, T2 and T3, the oxygenation index (OI), respiratory index (RI) and arterial-alveolar oxygen partial pressure ratio (PaO_2/PAO_2) were calculated by arterial blood gas, and the postoperative T cell subsets were compared between the two groups.

Statistical methods

SPSS 22.0 was used for statistical analysis of the data obtained in this study. Graohpad was used to illustrate the figures. All the indicators of the quantitative data were in accordance with a normal distribution, which was represented by (x ± sd). Repeated analysis of variance was used to compare the levels of each indicator in both groups. The difference was statistically significant with (P < 0.05).

Results

Baseline data in the two groups

There were no statistically significant differences in age, body mass, gender, operation time and duration of one-lung ventilation between the two groups (P > 0.05) (**Table 1**).

Comparison of the incidence of adverse effects between the two groups

There were 5 cases with choking cough in the EG, and the incidence of adverse effects was 11.9%. In the CG, there were 13 cases of choking cough, 1 case of nausea and vomiting and 4 cases of chills, and the incidence of adverse effects was 11.9%. The incidence of postoperative complications in the EG was obviously lower than that in the CG (**Table 2**).

Comparison of postoperative pain and emergence agitation after operation between the two groups

By comparing the postoperative pain in the two groups, it was found that the VAS pain score of the EG was significantly lower than that of the CG (P < 0.05). By comparing the emergence agitation after operation in the two groups, it

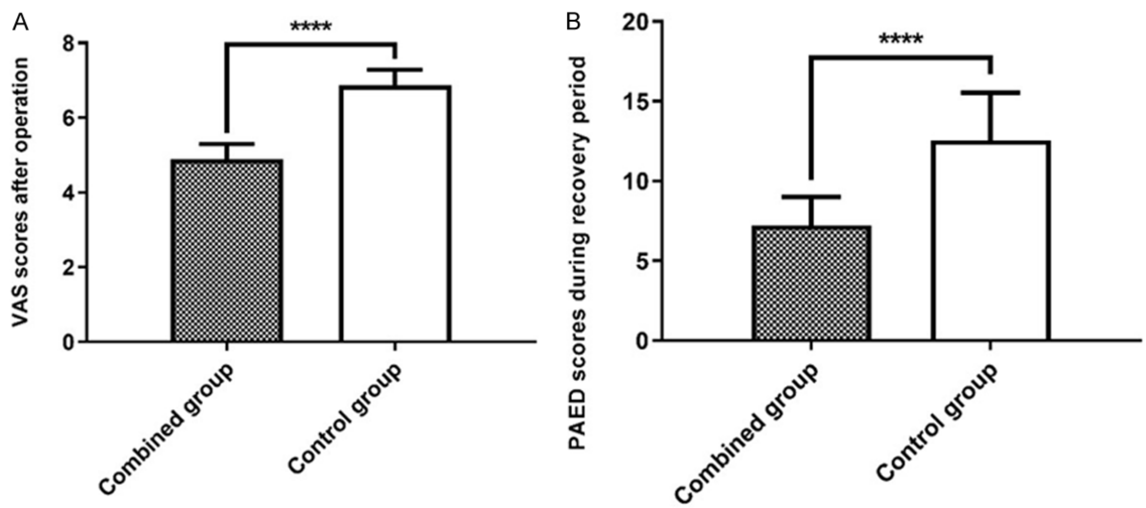

Figure 1. Comparison of postoperative pain between the EG and CG. A. By comparing the postoperative pain in the two groups, it was found that the VAS pain score in the EG was significantly lower than that in the CG (P < 0.05). Comparison of postoperative emergence agitation between the EG and CG. B. By comparing the emergence agitation in the two groups, it was found that the PAED score in the EG was significantly lower than that in the CG (P < 0.05).

Table 3. Comparison of expression levels of IL-8, IL-6 and TNF-α between the two groups after operation

Grouping	TNF-a	IL-6	IL-8
EG (n = 121)			
T_0	16.47±2.41	18.35±6.43	15.94±7.41
T_1	35.39±3.81*	68.77±12.70*	86.8±14.24*
T_2	37.39±3.66*	67.80±12.5*	89.71±15.86*
T_3	17.24±4.38	19.27±7.79	17.49±12.80
F value	1171.00	941.60	1228.00
P value	< 0.01	< 0.01	< 0.01
CG (n = 96)			
T_0	16.87±4.25	19.10±4.93	15.80±7.25
T_1	53.45±5.28*,#	85.97±17.46*,#	117.84±15.17*,#
T_2	62.44±6.39*,#	73.39±13.73*,#	123.78±17.67*,#
T_3	17.69±5.28	20.48±6.24	16.19±6.29
F value	1892.00	843.30	2220.00
P value	< 0.01	< 0.01	< 0.01

Note: *means the comparison with To, P < 0.05; #means the comparison with EG, P < 0.05.

was found that the PAED score of patients in the EG was significantly lower than that in the CG (P < 0.05) (**Figure 1**).

Comparison of expression levels of IL-8, IL-6 and TNF-α between the two groups after operation

The related inflammatory indexes were compared at different times. Compared with T_0, the expression levels of IL-8, IL-6 and TNF-α increased significantly at T_1 and T_2 (P < 0.05), and their expression levels returned to normal at T_3. The expression levels of IL-8, IL-6 and TNF-α in the EG were significantly lower than those in CG at T_1 and T_2 (P < 0.05) (**Table 3**).

Comparison of T cell subsets between the two groups after operation

T cell subsets were compared at different times. Compared with T_0, the levels of CD3+, CD4+ and the ratio of CD4+/CD8+ at T_1, T_2 and T_3 were significantly reduced in the two groups (P < 0.05). At T_1, T_2 and T_3, the levels of CD3+, CD4+ and the ratio of CD4+/CD8+ in the EG were higher than those in the CG (P < 0.05) (**Table 4**).

Comparison of postoperative lung related indexes between the two groups

The lung related indicators were compared at different times. Compared with T0, the OI, RI, PaO_2/PAO_2 changed in the two groups at T1 and T2, and returned to normal at T3. The lung func-

Table 4. Comparison of T cell subsets between the two groups after operation

Grouping	CD3+	CD4+	CD8+	CD4+/CD8+
EG (n = 121)				
T_0	62.87±13.55	35.57±7.89	28.19±6.43	1.31±0.46
T_1	53.80±12.28*	26.78±5.36*	27.84±4.46	1.27±0.72*
T_2	52.59±13.54*	26.51±8.56*	27.18±8.6	1.13±0.51*
T_3	51.29±9.85*	21.95±5.66*	26.95±6.39	0.82±0.37*
F value	21.75	79.94	0.91	21.20
P value	< 0.01	< 0.01	0.44	< 0.01
CG (n = 96)				
T_0	63.15±9.83	36.05±6.19	25.75±6.93	1.09±0.61
T_1	47.44±8.32*,#	21.94±4.13*,#	26.84±6.90	0.87±0.34*,#
T_2	46.43±11.54*,#	20.41±4.07*,#	26.96±5.58	1.07±0.28*,#
T_3	45.15±9.94*,#	18.18±5.77*,#	25.77±8.80	0.80±0.47*,#
F value	69.04	238.60	0.82	10.19
P value	< 0.01	< 0.01	0.48	< 0.01

Note: *means the comparison with To, P < 0.05; #means the comparison with EG, P < 0.05.

Table 5. Comparison of postoperative lung related indexes between the two groups

Grouping	RI	OI	PaO_2/PAO_2
EG (n = 121)			
T_0	0.27±0.14	472.21±48.76	0.76±0.08
T_1	0.64±0.21*	302.40±53.92*	0.63±0.06*
T_2	0.87±0.24*	216.36±71.97*	0.59±0.04*
T_3	0.29±0.13	475.84±42.33	0.75±0.15
F value	294.5	655.3	103.5
P value	< 0.01	< 0.01	< 0.01
CG (n = 96)			
T_0	0.25±0.17	468.12±44.57	0.77±0.09
T_1	0.84±0.22*,#	252.59±51.36*,#	0.52±0.05*,#
T_2	1.18±0.32*,#	171.97±42.76*,#	0.48±0.05*,#
T_3	0.28±0.08	474.5±53.24	0.78±0.03
F value	421.800	969.800	699.200
P value	< 0.01	< 0.01	< 0.01

Note: *means the comparison with To, P < 0.05; #means the comparison with EG, P < 0.05.

tion indexes in EG at T1 and T2 were significantly better than those in CG (P < 0.05) (**Table 5**).

Comparison of postoperative quality of life scores between the two groups

The SF-36 scores of all dimensions in EG were significantly higher than those in CG after operation for 3 months (P < 0.05) (**Table 6**).

Discussion

The etiology of LC has not been completely clear up to now. A large amount of data show that long-term smoking is closely related to the development of LC. The incidence of LC in urban residents is higher than that in rural residents, which may be correlated with air pollution and carcinogens in smoke dust [14, 15]. There are many surgical methods for LC. With the development of thoracoscopic technology, thoracoscopic surgery is the first choice for most LC operations. However, one-lung ventilation is a commonly used respiratory tract management method in thoracic surgery anesthesia. One-lung ventilation will cause mechanical ventilation-related injuries to the lungs, and surgical operations will stimulate the body and cause injuries, resulting in neuroendocrine reactions and cardiovascular effects or visceral vasoconstriction [16, 17].

Choosing appropriate anesthesia methods and drugs not only provides better surgical conditions, but also maintains the hemodynamic stability of perioperative patients, which is extremely important for patient health and recovery [18]. Dexmedetomidine for postoperative analgesia can reduce the dosage of opioids, improve the analgesic effect and reduce the incidence of adverse reactions of opi-

Table 6. Comparison of postoperative quality of life scores between the two groups

Categories	Physiological quality	Role quality	Psychological quality	Social quality
EG (n = 121)	75.62±8.57	78.92±9.97	83.43±7.59	77.77±6.21
CG (n = 96)	69.36±9.32	71.53±6.34	72.31±6.15	67.16±5.77
t value	5.141	6.318	11.64	12.9
P value	< 0.01	< 0.01	< 0.01	< 0.01

oids. Currently, it is widely used in clinical practice [7, 19, 20]. In this study, dexmedetomidine was used for postoperative intravenous analgesia. The results showed that the VAS pain score and PAED score of patients in the EG were obviously lower than those in the CG after operation ($P < 0.05$). It showed that dexmedetomidine can effectively reduce postoperative pain and inhibit agitation in patients undergoing thoracoscopic radical resection of LC. This might be due to the analgesic and sedative effects of dexmedetomidine on central and peripheral α2AR. Dexmedetomidine can reduce the degree of lung injury in hemorrhagic shock and sepsis by inhibiting the release of inflammatory cytokines [21, 22]. During one-lung ventilation in thoracoscopic LC surgery, the unventilated lung will be in a contracted state, and the blood perfusion will be relatively insufficient, resulting in local hypoxia. During one-lung ventilation, the number of alveolar macrophages and neutrophils in the lung will increase, which will increase the synthesis and release of pro-inflammatory cytokines and intercellular adhesion molecules. At the same time, alveolar epithelial cells can produce and release chemokines and cytokines, which will aggravate the inflammatory reaction of lung tissue [23]. In this study, the concentration of serum TNF-α, IL-6 and IL-8 in the EG were lower than those in the CG at T1-T3, suggesting that dexmedetomidine can alleviate the inflammatory reaction after one-lung ventilation. The OI, RI and PaO_2/PAO_2 is generally used to evaluate lung oxygenation function in patients undergoing radical resection of LC. The results of this study revealed that the lung function of patients decreased in the two groups at T1 and T2, and it returned to normal level at T3. However, the above indexes in the EG were better than those in the CG at T1 and T2, suggesting that dexmedetomidine can alleviate the decline of lung function caused by hypoxia and ischemia of lung tissue during one-lung ventilation. During one-lung ventilation, the collapse of the non-ventilated side will lead to the decrease of oxygen free radical scavenging function of the lung. After full expansion of the lung, the collapsed part will be re-perfused, and a large amount of oxygen free radicals will be produced and accumulate, which will mediate reperfusion injury. Studies by Zeng et al. [24] have revealed that dexmedetomidine can inhibit oxidative stress and further reduce ischemia-reperfusion injury, so as to have a certain protective effect. When the immune function of tumor patients is suppressed, the helper lymphocyte subsets CD4+T lymphocytes decrease, and the inhibitory lymphocyte subsets CD8+T lymphocytes increase relatively. It is of great significance to detect of T lymphocyte subsets in peripheral blood for evaluating patients' cellular immune function and diagnosing diseases. The results of this study revealed that compared with T0, the immune function of patients was inhibited to a certain extent in both groups at T1 and T2, showing that CD3+ and CD4+T, CD4+/CD8+ lymphocytes decreased significantly, which suggests that surgical trauma may cause the decrease of cellular immune function in patients undergoing radical resection for LC. This indicated that dexmedetomidine can effectively control the immune function and reduce the stress response of patients undergoing radical resection of LC during perioperative period. At the end of the research, we compared the scores of quality of life in both groups, and found that the SF-36 scores of all dimensions in the EG were significantly higher than those in the CG after operation for 3 months ($P < 0.05$), indicating that dexmedetomidine can effectively reduce postoperative pain and systemic stress levels, and ameliorate the quality of life of patients.

In conclusion, we validated the conventional anesthesia combined with dexmedetomidine can improve the immune function, reduce stress response and emergence agitation, and ameliorate the postoperative quality of life of patients undergoing thoracoscopic radical resection of LC, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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