Effects of Dexmedetomidine on Perioperative Inflammation and Lung Function Protection in Patients Undergoing Radical Lung Cancer Surgery: Postprint

Authors: Guo Yuanbo, Xu Jindong, Ji Xuexia, Zhang Jianxing, Liang Jiexian, Zhou Guobin

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Abstract

Objective: To investigate the effect of dexmedetomidine on perioperative inflammation and lung function protection in patients undergoing radical lung cancer surgery. Methods: One hundred twenty-four patients undergoing radical lung cancer surgery in our hospital from May 2014 to May 2016 were enrolled and randomly divided into an experimental group and a control group (n=62 each). The control group received single-agent anesthesia, while the experimental group received dexmedetomidine in addition to the control regimen. Serum levels of IL-1β, IL-10, and tumor necrosis factor (TNF)-α were compared between the two groups at the beginning of surgery (T0), 30 min of one-lung ventilation (OLV) (T1), 60 min of OLV (T2), and at the end of surgery (T3). Enzyme-linked immunosorbent assay (ELISA) was used to measure the levels of malondialdehyde (MDA), myeloperoxidase (MPO), and xanthine oxidase (XOD) in lung tissue homogenates. Arterial partial pressure of oxygen (PaO2), oxygenation index (OI), airway plateau pressure (APP), and airway resistance (AR) were monitored in both groups. Results: In both groups, IL-1β, IL-10, TNF-α, MDA, MPO, and XOD were significantly elevated at T1 and T2. Moreover, the experimental group exhibited significantly lower levels of IL-1β, IL-10, TNF-α, and MDA, but significantly higher levels of MPO and XOD compared with the control group ($P<0.05$). In both groups, PaO2 and OI were significantly decreased while airway plateau pressure and airway resistance were significantly increased at T1 and T2. However, the experimental group showed significantly lower airway plateau pressure and airway resistance, and significantly higher PaO2 and OI compared with the control group ($P<0.05$). Conclusion: Dexmedetomidine anesthesia in patients undergoing radical lung cancer surgery can effectively attenuate pulmonary inflammatory response and exerts significant protective

effects on lung function.

Full Text

Abstract

Objective: To investigate the protective effects of dexmedetomidine against perioperative inflammation and on pulmonary function in patients undergoing radical lung cancer resection. **Methods:** From May 2014 to May 2016, 124 patients scheduled for radical lung cancer surgery were randomly assigned to either an experimental group (n=62) or a control group (n=62). The control group received standard anesthesia with a single agent, while the experimental group received additional dexmedetomidine. Serum levels of interleukin-1β (IL-1β), IL-10, and tumor necrosis factor-alpha (TNF-α) were measured before surgery (T0), at 30 minutes (T1) and 60 minutes (T2) during one-lung ventilation (OLV), and at the end of surgery (T3). Enzyme-linked immunosorbent assay (ELISA) was used to determine malondialdehyde (MDA), myeloperoxidase (MPO), and xanthine oxidase (XOD) levels in lung tissue homogenates. Arterial oxygen partial pressure (PaO_2), oxygenation index (OI), airway plateau pressure (APP), and airway resistance (AR) were also recorded. **Results:** At T1 and T2, IL-1β, IL-10, TNF-α, MDA, MPO, and XOD levels increased significantly in both groups. However, the experimental group exhibited significantly lower IL-1β, IL-10, TNF-α, and MDA levels, while MPO and XOD levels were significantly higher compared to the control group ($P<0.05$). In both groups, PaO_2 and OI decreased while APP and AR increased at T1 and T2, but the experimental group showed significantly lower APP and AR and higher PaO_2 and OI than the control group ($P<0.05$). **Conclusion:** Dexmedetomidine anesthesia in patients undergoing radical lung cancer surgery effectively attenuates pulmonary inflammatory responses and provides significant protection for lung function.

Keywords: radical lung cancer resection; dexmedetomidine; inflammation; pulmonary function

Introduction

Lung cancer surgery typically employs general anesthesia combined with double-lumen endobronchial intubation for one-lung ventilation (OLV) to provide optimal surgical visualization. However, mechanical ventilation, OLV, and surgical trauma can trigger systemic immune responses, leading to the release of immune-related inflammatory mediators such as IL-1β, IL-10, and TNF-α, which cause pulmonary inflammatory reactions and subsequent lung injury. Appropriate selection of anesthetic agents during general anesthesia may help mitigate lung damage and protect pulmonary function. Dexmedetomidine (DEX), a novel sedative with high selectivity for α_2-adrenergic receptors, has been widely used in clinical anesthesia. Previous studies have reported that DEX stabilizes heart rate and blood pressure during anesthesia and improves oxygenation during

OLV in thoracic surgery. Animal experiments have further demonstrated that DEX can suppress the release of pro-inflammatory mediators, thereby inhibiting inflammatory responses and reducing lung injury. Additionally, DEX protects against sepsis-induced lung injury by attenuating oxidative stress, mitochondrial dysfunction, and mitochondria-mediated apoptosis. While most previous research has been limited to animal studies, clinical investigations remain relatively scarce and have yielded inconsistent results. The question of whether intraoperative intravenous DEX can similarly suppress inflammatory responses and provide lung protection during lung cancer radical surgery, where OLV and surgical trauma induce significant inflammation, has not been adequately addressed. This study aimed to investigate the effects of DEX on serum inflammatory factors, lung tissue inflammatory mediators, and pulmonary function in patients undergoing radical lung cancer surgery, thereby exploring its protective mechanisms against perioperative inflammation and lung injury.

Methods

Patient Selection

We enrolled 124 patients scheduled for radical lung cancer surgery at our hospital between May 2014 and May 2016. This study was approved by our institutional medical ethics committee, and all patients and their families provided written informed consent. Inclusion criteria were: (1) unilateral peripheral lung tumor with diameter <5 cm, and (2) no significant lymph node enlargement on chest CT examination. Exclusion criteria included: (1) psychiatric disorders requiring long-term medication, (2) concurrent respiratory or pulmonary infection, (3) history of asthma, and (4) poor preoperative pulmonary function test results.

Anesthesia Protocol

Patients were randomly assigned using a random number table to either the experimental group (n=62) or control group (n=62). The experimental group comprised 39 males and 23 females, aged 40-69 years (mean $55.3\$\pm10.2 years), while the control group included 38 males and 24 females, aged 41–70 years (mean 55.8±$10.9 years). There were no statistically significant differences between groups in gender, age, or other baseline characteristics (P>0.05), ensuring comparability.

All patients fasted for 6-8 hours and abstained from fluids for 4 hours before surgery. Upon entering the operating room, routine monitoring of pulse oximetry, blood pressure, and heart rate was established, and warming blankets were applied. Fifteen minutes before anesthesia induction, penehyclidine hydrochloride (0.01 mg/kg) was administered to reduce airway secretions. General anesthesia was induced with midazolam (0.05 mg/kg), sufentanil (3 g/kg), etomidate (0.25 mg/kg), and cisatracurium (0.2 mg/kg). All patients received a 37F left double-lumen endobronchial tube positioned under fiberoptic bronchoscopy guidance. Mechanical ventilation was initiated with 35% inspired oxygen con-

centration, and respiratory parameters were set according to established literature. In the experimental group, dexmedetomidine was administered as a 1 g/kg bolus over 10 minutes immediately after intubation, followed by a continuous infusion of 0.4 g/kg/h until 30 minutes before the end of surgery; the control group received no dexmedetomidine. Both groups received maintenance anesthesia with propofol (3-4 mg/kg/h), remifentanil (0.1-0.15 g/kg/min), and cisatracurium (3 g/kg/h). Anesthesia depth was maintained by adjusting propofol and remifentanil infusion rates and monitored using a German Narcotrend device. Cisatracurium infusion was discontinued 30 minutes before surgery completion, while propofol and remifentanil were stopped 10 minutes before the end, with additional sufentanil administered for analgesia.

OLV was initiated at the beginning of surgery. If persistent oxygen desaturation occurred, surgery was paused to reposition the tube, perform suctioning, and manually ventilate to correct the issue. After chest closure and air evacuation, double-lung ventilation was resumed. Patients were transferred to the post-anesthesia care unit and extubated when fully awake with recovered spontaneous breathing and stable vital signs.

Measurement of Inflammatory Mediators and Pulmonary Function

Inflammatory Mediators: Venous blood samples (15 mL) were collected at four time points: before surgery (T0), at 30 minutes of OLV (T1), at 60 minutes of OLV (T2), and at the end of surgery (T3). Samples were centrifuged at 3000 rpm for 10 minutes, and serum was stored for analysis. Serum IL-1β, IL-10, and TNF-α levels were measured using enzyme-linked immunosorbent assay (ELISA) with an AP-960 automatic analyzer (Kyowa Medex, Japan).

Lung Tissue Indicators: At the same time points (T0, T1, T2, T3), small specimens of normal lung tissue were excised from the resected lobe at a distance >5 cm from the tumor. Lung tissue homogenate supernatants were analyzed for malondialdehyde (MDA), myeloperoxidase (MPO), and xanthine oxidase (XOD) using ELISA with the AP-960 analyzer.

Pulmonary Function Parameters: Arterial blood samples were collected from the radial artery at T0, T1, T2, and T3 to measure PaO_2 and OI. Airway plateau pressure and airway resistance were also recorded at identical time points to assess lung injury.

Statistical Analysis

Data were analyzed using SPSS 19.0 software. All data followed a normal distribution and are expressed as mean$\pm$standard deviation. Comparisons between groups were performed using t-tests. A P-value <0.05 was considered statistically significant.

Results

Serum Inflammatory Marker Levels

As shown in , IL-1β, IL-10, and TNF-α levels increased significantly at T1 and T2 in both groups. However, the experimental group exhibited significantly lower levels of these inflammatory markers compared to the control group ($P<0.05$).

Lung Tissue Oxidative Stress Markers

demonstrates that MDA, MPO, and XOD levels increased significantly at T1 and T2 in both groups. The experimental group showed significantly lower MDA levels but higher MPO and XOD levels compared to the control group ($P<0.05$).

Pulmonary Function Parameters

reveals that PaO_2 and OI decreased significantly while APP and AR increased at T1 and T2 in both groups. Notably, the experimental group had significantly lower APP and AR but higher PaO_2 and OI compared to the control group ($P<0.05$).

Discussion

Dexmedetomidine has been widely used as a novel sedative in surgical and intensive care settings. Beyond its sedative properties, accumulating evidence suggests that DEX possesses anti-inflammatory effects and organ-protective capabilities. Studies have shown that DEX attenuates inflammatory responses in toxin-induced shock models by suppressing the release of inflammatory mediators and cells, thereby reducing mortality and decreasing serum TNF-α and IL-6 levels. These mechanisms likely involve inhibition of inflammatory factor release and modulation of oxidative stress responses. In this study, we evaluated DEX' s anti-inflammatory effects during lung cancer surgery by measuring IL-1β, IL-10, and TNF-α. Our results demonstrate that patients receiving DEX anesthesia exhibited significantly reduced levels of these inflammatory markers at T1 and T2, confirming its anti-inflammatory properties and pulmonary protective effects. These findings align with previous research and suggest that DEX can be applied to various surgical procedures requiring general anesthesia and mechanical ventilation.

Oxidative stress represents another critical factor contributing to organ injury during surgery. We analyzed lung tissue levels of MDA, MPO, and XOD to assess oxidative stress responses. Our results indicate that DEX anesthesia reduces MDA content while increasing MPO and XOD levels, thereby exerting anti-oxidative effects. MDA can cause cross-linking and polymerization of vital macromolecules such as proteins and nucleic acids, exhibiting cytotoxicity and particularly severe damage to lung tissue. Myeloperoxidase (MPO), a

heme-containing protease, not only eliminates and engulfs intracellular microorganisms but also destroys various extracellular targets, including tumor cells, playing a crucial role in inflammatory mediators. Xanthine oxidase (XOD) oxidizes hypoxanthine, xanthine, and aldehydes, contributing to inflammatory response generation and regulation. Consequently, MPO and XOD serve protective functions in lung tissue, and continuous DEX administration during anesthesia increases their levels. Our findings demonstrate that DEX effectively modulates MDA, MPO, and XOD levels, thereby protecting the lungs from oxidative damage.

PaO_2, OI, APP, and AR are important indicators of pulmonary function that change significantly during OLV. While protective lung ventilation strategies can reduce acute lung injury, excessively low tidal volumes may compromise oxygenation and cause hypoxemia. Combining protective ventilation with DEX anesthesia can simultaneously inhibit pulmonary inflammatory responses and protect pulmonary function. In our study, patients receiving DEX showed significant changes in these parameters at T1 and T2, but with notably lower APP and AR and higher PaO_2 and OI compared to the control group, confirming pulmonary protection. Therefore, DEX anesthesia provides both anti-inflammatory effects and pulmonary function preservation, facilitating postoperative recovery and warranting broader application in various surgical procedures.

In summary, continuous dexmedetomidine administration during radical lung cancer surgery effectively attenuates pulmonary inflammatory responses and provides significant protection for lung function.

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