Comparison of the synergistic effects of sevoflurane and desflurane on muscle relaxant vecuronium in laparoscopic colon cancer surgery

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Abstract
Sevoflurane and desflurane are commonly used inhalation anesthetics in clinical practice. This study compared the synergistic effects of sevoflurane and desflurane on the muscarinic agent vecuronium in laparoscopic colon cancer surgery. The aim of this study was to compare sevoflurane and desflurane in a synergistic effect on the muscle relaxant vecuronium in laparoscopic colon cancer surgery. Sixty patients undergoing elective laparoscopic radical resection of colon cancer were randomly divided into sevoflurane (n = 30) and desflurane (n = 30) groups. After anesthesia and successful tracheal intubation, patients in both groups were maintained with combined remifentanil. Muscle relaxant effects were monitored in both groups using a muscle relaxant monitor (train of stimuli-Watch), the onset time, T1 and T2 recovery time, and muscle relaxant dosage of vecuronium were observed. Hemodynamic changes were observed in both groups, and the dosage of vasoactive drugs was recorded. The quality of recovery of the patients was evaluated using the Mini-Mental State Examination (MMSE) and the discharge from the Aldrete score criteria. There was no significant difference in the onset time of vecuronium between the two groups (P > .05). The desflurane group’s T1 and T2 recovery times were later than that of the sevoflurane group. The dosage of vecuronium was statistically significantly less than that in the sevoflurane group (P < .05); the exhalation time in the desflurane group was statistically significantly longer than that in the sevoflurane group (P < .05). There were no significant differences in preoperative and intraoperative mean arterial pressure, heart rate, ephedrine and atropine dosage, MMSE score, and Aldrete score between the two groups (P > .05). Compared with sevoflurane, desflurane has a stronger synergistic effect on the muscle relaxant of vecuronium without increasing the incidence of cardiovascular adverse reactions and affecting patient recovery.

Abbreviations: BIS = bispectral index, HR = heart rate, MAP = mean arterial pressure, MMSE = Mini-Mental State Examination, PetCO2 = pressure of end-tidal carbon dioxide, TOF = train of stimuli.

Keywords: desflurane, radical resection of colon cancer, sevoflurane, synergistic effect of muscle relaxant, vecuronium

1. Introduction
Colon cancer is a common digestive system disease in clinical practice,[1] closely related to smoking, intestinal inflammation, poor dietary habits, genetic factors and age.[2] Based on the advantages of laparoscopic surgery, such as less trauma and rapid postoperative recovery, laparoscopic tumor resection has become the first choice for the treatment of colon cancer.[3] Endotracheal intubation combined with general anesthesia is a commonly used anesthesia method in clinical practice. Laparoscopic surgery requires a good muscle relaxant, and muscle relaxants are essential adjuvant drugs in general anesthesia, facilitating endotracheal intubation during general anesthesia and maintaining good muscle relaxants during surgery.[4] Vecuronium has no histamine-releasing effect and less adverse reactions, and is a commonly used non-depolarizing neuromuscular blocker in general anesthesia. Excessive use of intraoperative inotropes can lead to delayed postoperative recovery of patients. Inhaled anesthetics also have muscle relaxant effects up to a certain depth and can enhance the effect of muscle relaxants. Their synergistic effect on muscle relaxants also gradually increases with increasing inhalation concentration and time. Sevoflurane and desflurane are commonly used inhalation anesthetics in clinical practice. Both have low blood/gas partition coefficient[5] and are easy to operate.[6] At present, there is no relevant study on the comparison of the synergistic effect of sevoflurane and desflurane on muscle relaxant vecuronium, so we selected 60 patients undergoing elective laparoscopic radical resection of colon cancer in our hospital as the study subjects to observe the difference in the synergistic effect.
of 1.3 MAC sevoflurane and desflurane on vecuronium muscle relaxant.

2. Materials and methods

2.1. General information

This study has been approved by the medical ethics committee of the hospital [2021 Ethical Review No. KT-017], and all patients signed an informed consent form. The study was conducted on sixty patients who underwent elective laparoscopic radical resection of colon cancer in the Affiliated Hospital of Binzhou Medical College from June 2021 to April 2022. Inclusion criteria aged ≥18 years, ASA I-II, normal liver and kidney function, normal cardiopulmonary function. Exclusion criteria: malnutrition, suffering from neuromuscular system diseases, recent use of anti-sympathetic and sedatives, allergy to the selected anesthetic drugs. Methods: 60 patients were randomly divided into sevoflurane group and desflurane group, with 30 people in each group.

2.2. Methods

After the patients were admitted to the operating room, venous access was routinely established, electrocardiogram (ECG) was monitored, mean arterial pressure (MAP), heart rate (HR), saturation (SpO2), bispectral index (BIS) were measured by radial artery puncture, and muscle relaxant monitoring was performed. Anesthesia induction: intravenous injection of midazolam 2 mg, fentanyl 4 μg/kg, vecuronium 0.1 mg/kg, etomidate 20 mg, after the patient's consciousness completely disappeared, when the four train of stimuli (TOF) count was 0, tracheal intubation was performed, after successful intubation, continuous inhalation of 100% O2 2L/min. Maintenance of anesthesia: The concentration of inhalation anesthetics was adjusted to maintain the end-tidal concentration of sevoflurane and desflurane at 1.3 MAC. Remifentanil was continuously pumped in both groups, and the pumping rate was adjusted according to hemodynamic changes. When the muscle relaxant monitor showed T2 recovery, additional muscle relaxants were added in time, and each additional pumping rate was adjusted according to hemodynamic changes.

3. Results

3.1. General information

Eighty-eight patients undergoing elective laparoscopic radical resection of colon cancer were initially screened. Twenty-three patients with ASA physical status III and above and 23 patients who refused to participate in this study were excluded. Sixty-five patients were randomly divided into the sevoflurane group (n = 32) and the desflurane group (n = 33). Patients who underwent partial hepatectomy due to intraoperative liver metastases in the groups sevoflurane (n = 2) and desflurane (n = 3) were excluded. Finally, 30 patients in each group participated in this study (Fig. 1). There was no significant difference in gender composition, age, BMI, ASA grade composition, operation time, anesthesia time, atropine and ephedrine dosage, blood loss, urine volume, infusion volume and hospital stay between the two groups (P > .05); the extubation time in the sevoflurane group and remifentanil dosage in the sevoflurane group were less than that in the sevoflurane group, and the differences had statistical significance (P < .05, Table 1).

3.2. Comparison of HR and MAP between the two groups

The HR and MAP at t2, t3 and t4 in the two groups were statistically significantly lower than those at t1 (P < .05), but there was no significant difference between the two groups at the same time point (P > .05). More details are shown in Figure 2A and B.

3.3. Muscle relaxant comparison

T1 and T2 recovery times in desflurane group were later than that in sevoflurane group, and the difference had statistical significance (P < .05) (Fig. 3). There was no significant difference in the onset time of muscle relaxant between the two groups (P > .05) (Fig. 4A). The dosage of muscle relaxant in the desflurane group was statistically significantly less than that in the sevoflurane group (P < .05) (Fig. 4B).

4. Discussion

Vecuronium bromide is a medium-acting non-depolarizing muscle relaxant with a rapid onset of action, good muscle relaxant effect, and no significant effect on the body's circulatory function. Its pharmacological effects are mainly through competing...
Figure 1. Flow chart of patient's recruitment.

Table 1
Comparison of general and surgery information between the two groups of patients.

| Factor                      | Sevoflurane group (n = 30) | Desflurane group (n = 30) | P     |
|-----------------------------|----------------------------|---------------------------|-------|
| Age (years)                 | 64.43 ± 9.89               | 67.03 ± 7.55              | .257  |
| Gender (male/female)        | 22/8                       | 21/9                      | .774  |
| BMI (kg/m²)                 | 23.22 ± 2.73               | 24.37 ± 2.16              | .076  |
| ASA (I/II)                  | 20/10                      | 15/15                     | .190  |
| Operation time (min)        | 174.40 ± 5.08              | 175.63 ± 4.75             | .336  |
| Anesthesia time (min)       | 208.73 ± 4.32              | 210.07 ± 5.71             | .312  |
| Extubation time (min)       | 13.47 ± 2.11               | 11.13 ± 1.96              | <.001 |
| Atropine (mg)               | 0.33 ± 0.14                | 0.37 ± 0.12               | .610  |
| Ephedrine (mg)              | 4.33 ± 1.37                | 4.00 ± 1.26               | .670  |
| Remifentanil (ug)           | 761.00 ± 105.42            | 667.33 ± 113.41           | .002  |
| Blood loss (mL)             | 20 (20, 30)                | 30 (20, 40)               | .152  |
| Urine volume (mL)           | 200 (200, 300)             | 200 (200, 300)            | .500  |
| Infusion (mL)               | 1600 (1600, 2100)          | 1600 (1600, 2100)         | .934  |
| Hospitalization time (d)    | 16 (15, 17)                | 16 (14.75, 17)            | .651  |
| MMSE score                  | 28 (27, 29)                | 28 (27, 29)               | .994  |
| Aldrete score               | 9 (9, 9.25)                | 9 (9, 10)                 | .813  |

ASA = American Society of Anesthesiologists, BMI = Body Mass Index, MMSE = Mini-Mental State Examination;
P < .05.

Figure 2. Changes in heart rate (HR) and mean arterial pressure (MAP) at different time points. (A) HR and (B) MAP.
with acetylcholine for nicotinic receptors located on the motor endplate of striated muscle, thereby blocking the conduction between striated muscle and nerve endings. The difference from depolarizing muscle relaxants is that this drug will not cause fasciculation of muscle fibers, and has no histamine release effect[10] and less adverse reactions. Intraoperative use of vecuronium can reduce abdominal muscle tension and relax abdominal wall muscles,[11] It is conducive to a smooth operation.

Inhalation anesthetics can also produce muscle relaxants with increasing concentration, time, and synergistic effects on muscle relaxants. Its mechanisms of action may be: inhibition of presynaptic voltage-gated sodium channels and reduction of acetylcholine release; increased sensitivity of skeletal muscle to non-depolarizing myosinoids; and decreased sensitivity of post-synaptic acetylcholine receptors to acetylcholine;[12] indirectly promote muscle relaxant through central inhibitory effects; increase muscle and transport more myotonics to act at the nerve-muscle junction; increase the threshold of endplate potentials to produce action potentials and weaken the conduction of nerve excitation, thereby inhibiting muscle fiber contraction.[13]

Sevoflurane and desflurane are commonly used inhalation anesthetics in clinical practice.[14] Both are characterized by low blood/gas partition coefficient, good controllability, and rapid recovery.[15] Combined use of remifentanil with rapid metabolism can prolong intraoperative analgesic effect.[16] Xu et al[17] showed that 1.3 MAC sevoflurane could significantly shorten the onset time of rocuronium. At the same time, 1.0 MAC had no significant effect. The concentration of inhalation anesthetics selected in this study was 1.3 MAC.

Our study found that the T1 and T2 recovery time in the desflurane group was significantly longer than that in the sevoflurane group, and the amount of muscle relaxant was significantly less than that in the sevoflurane group, indicating that desflurane has a better muscle relaxant synergy effect on vecuronium than sevoflurane. Hemmerling et al[18] found that the requirement of cisatracurium was reduced by 41% and 60% at 1.3 MAC with sevoflurane and desflurane, respectively, compared with sevoflurane, which significantly reduced the amount of cisatracurium compared with sevoflurane, which is consistent with the conclusions of our study. However, a study by Kang et al[19] on elderly patients found that there was no significant difference in the myorelaxant enhancement effect between 1.3 MAC sevoflurane and desflurane p-rocuro-

Figure 3. T1 and T2 recovery time between in groups of sevoflurane and desflurane.

5. Conclusion
Compared with sevoflurane, desflurane has stronger synergistic effect on the muscle relaxant vecuronium without increasing the

Figure 4. The onset of muscle relaxant and dose of muscle relaxant in the two groups.
incidence of cardiovascular adverse reactions and affecting the quality of recovery of patients.

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