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Impact of rocuronium bromide on muscular relaxation and inflammatory response in laparoscopic radical cystectomy

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Abstract: **Objective** To compare the muscle relaxant effects of rocuronium bromide and cisatracurium besylate in laparoscopic radical cystectomy for bladder cancer, as well as their impacts on pulmonary ventilation function and body's inflammatory response. **Methods** A total of 112 patients scheduled for laparoscopic radical cystectomy at the Inner Mongolia People's Hospital between January 2022 and June 2024 were randomly divided into the RB group (n=56, receiving rocuronium bromide as the muscle relaxant)and the CB group (n=56, receiving cisatracurium besylate as the muscle relaxant). The muscle relaxant effects, tracheal intubation condition ratings, and adverse reaction were compared between the two groups. Mean arterial pressure (MAP), heart rate, saturation of peripheral oxygen (SpO_2), and pulmonary ventilation function indicators[percentage area of center of ventilation (CoV), dependent silent spaces (DSS), and non-dependent silent spaces (NSS)]were recorded and compared immediately before anesthesia induction (T_0), immediately after tracheal intubation (T_1), immediately after tumor resection (T_2), and immediately after surgery (T_3). The levels of inflammatory markers[high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor- α (TNF-α), and white blood cell count (WBC)]were compared between the two groups before surgery and 2 hours after surgery. **Results** The onset time of muscle relaxation in the RB group was shorter than that in the CB group (P< 0.05), while the duration of muscle relaxation, recovery index, and extubation time in the RB group were longer than those in the CB group (P<0.05). The excellent rate of tracheal intubation conditions in the RB group was higher than that in the CB group[94.64% (53/56)*vs* 81.14% (46/56), χ^2=4.264, P=0.039]. At T_1, MAP and heart rate in the RB group were significantly lower than those in the CB group (P<0.05). SpO_2 in the RB group was significantly higher than that in the CB group at T_1 and T_2 (P<0.05). Compared with T_0, CoV significantly decreased at T_1, T_2, and T_3 in both groups (P<0.05), while DSS significantly increased (P<0.05). Two hours after surgery, serum hs-CRP, TNF-α, and WBC levels in CB group were higher than those in RB group (P<0.05). There was no significant difference in the incidence of adverse reactions between RB group and CB group[14.29% (8/56)*vs* 19.64% (11/56), χ^2=0.571, P= 0.450]. **Conclusion** The use of rocuronium bromide in laparoscopic radical cystectomy for bladder cancer provides better muscle relaxation compared to cisatracurium besylate, and can alleviate surgery-induced inflammatory responses. However, both have similar effects on pulmonary ventilation function.

Keywords: Rocuronium bromide; Laparoscopic; Cisatracurium besylate; Radical cystectomy; Muscular relaxation; Pulmonary ventilation function; Inflammatory response

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Bladder cancer is one of the common malignant tumors of the urinary system [1]. According to GLOBOCAN data, there were 86,000 new cases and 39,000 deaths from bladder cancer in China in 2020 [2]. Based on the depth of invasion, bladder cancer can be classified into two types: muscle-invasive bladder carcinoma (MIBC) and non-muscle-invasive bladder carcinoma (NMIBC) [1]. Radical cystectomy is the preferred clinical treatment for MIBC and high-risk NMIBC [3]. However, this surgical procedure is invasive and technically complex, and is prone to inducing significant intraoperative stress responses [4]. The administration of muscle relaxants can alleviate intubation discomfort, facilitate mechanical ventilation, and optimize the surgical field [5]. Rocuronium and cisatracurium besilate are currently the two most commonly used muscle relaxants, but there are relatively few comparative studies on their application in laparoscopic radical cystectomy [6-7]. This study aimed to analyze the clinical efficacy of these two muscle relaxants in laparoscopic radical cystectomy. The results are reported as follows.

1 Materials and Methods

1.1 General Information

A prospective study was conducted on patients with bladder cancer who were treated at the Inner Mongolia Autonomous Region People's Hospital from January 2022 to June 2024. This study was approved by the Ethics Committee of the Inner Mongolia Autonomous Region People's Hospital (No. 202503603L). Inclusion criteria: (1) Confirmed diagnosis of MIBC or high-risk NMIBC by pathological biopsy; (2) Aged 50–80 years; (3) Meeting the indications for radical cystectomy and scheduled to undergo laparoscopic radical cystectomy; (4) No contraindications to anesthesia; (5) American Society of Anesthesiologists (ASA) physical status classification I–III; (6) Voluntary signing of the informed consent form. Exclusion criteria: (1) Presence of distant metastasis; (2)

Complicated with pulmonary diseases or recent history of lung injury; (3) Impaired function of vital organs such as heart, kidney, and liver; (4) Presence of other primary malignant tumors; (5) Previous history of abdominal surgery. Dropout criteria: (1) Patient request for withdrawal from the study; (2) Conversion to open surgery during the operation.

A total of 112 eligible patients were randomly divided into the rocuronium bromide group (RB group) and the cisatracurium besilate group (CB group) using a random number table, with 56 patients in each group. There were no statistically significant differences in gender, age, body mass index (BMI), maximum tumor diameter, pathological type, T stage, or ASA classification between the two groups (P>0.05). See **Table 1**.

Tab.1 Comparison of general data between two groups (n=56)

Item	RB group	CB group	$\chi^2/t/Z$ value	P value
Gender (male/female, case)	45/11	47/9	0.243	0.622
Age (years, $\bar{x}\pm s$)	64.15±6.27	62.98±6.53	0.967	0.336
BMI (kg/m², $\bar{x}\pm s$)	23.75±2.38	23.43±2.26	0.730	0.467
Maximum tumor diameter (cm, $\bar{x}\pm s$)	4.02±1.13	3.96±1.09	0.286	0.775
Pathological type (case)				
Urothelial carcinoma	46	43		
Adenocarcinoma	5	6	0.525	0.769
Squamous cell carcinoma	5	7		
T stage (case)				
Ta-T2	41	43	0.190	0.663
T3-T4	15	13		
ASA classification (case)				
Grade I	18	20		
Grade II	30	29	0.433	0.699
Grade III	8	7		

1.2 Methods

Upon admission to the operating room, all patients underwent routine establishment of peripheral venous access, and were connected to a monitor (Mindray, BeneView T8, Shenzhen) and an electrical impedance tomography (EIT) device (C500 EIT System). Anesthesia induction: Intravenous injection of midazolam 0.04 mg/kg, propofol 2.5 mg/kg, and sufentanil 0.4 μg/kg. A muscle relaxation monitor (Model M206983, Zhongxi Yuanda, Beijing) was connected, and calibration of muscle relaxation monitoring was performed when the bispectral index (BIS) fell below 60, followed by intravenous administration of muscle relaxant. Specifically, the RB group received intravenous rocuronium bromide injection (Zhejiang Xianju Pharmaceutical Co., Ltd., National Medical Product Administration Approval No. H20093186) at a dose of 0.5 mg/kg; the CB group received intravenous cisatracurium besilate for injection (Jiangsu Hengrui Medicine Co., Ltd., National Medical Product Administration Approval No. H20060869) at a dose of 0.12 mg/kg. Tracheal intubation and mechanical ventilation were performed when the train-of-four (TOF) ratio was less than 5%. The ventilation parameters were set as follows: tidal volume 8–10 mL/kg, respiratory rate 10–12 breaths/min. After the establishment of CO_2 pneumoperitoneum, the tidal volume was adjusted to 6–8 mL/kg and the respiratory rate to 12–18 breaths/min. The end-tidal carbon dioxide partial pressure ($PETCO_2$) was maintained at 35–45 mmHg, and the saturation of peripheral oxygen (SpO_2) was maintained at ≥ 90%. TOF monitoring was initiated to assess the degree of muscle relaxation block. Anesthesia maintenance: Continuous intravenous pump infusion of propofol 2 mg/(kg·h) and remifentanil 0.2 μg/(kg·min). If the amplitude of the first twitch response in TOF recovered to 25% during the operation, an additional dose of muscle relaxant (1/4 of the initial dose) was administered, with the number of additional doses limited to ≤ 3 times. The administration of additional muscle relaxant was discontinued 15 minutes before the end of the operation. At the end of the operation, atropine 1 mg and neostigmine 2 mg were intravenously injected to antagonize residual muscle relaxation effects.

1.3 Observation Indicators

1.3.1 Muscle Relaxation Efficacy

The onset time of muscle relaxation (time from completion of muscle relaxant injection to maximum block of the first twitch response amplitude), duration of muscle relaxation (time from completion of muscle relaxant injection to recovery of the first twitch response amplitude to 25% of the baseline value), recovery index (time from recovery of the first twitch response amplitude from 25% to 75% of the baseline value), and extubation time (time from discontinuation of muscle relaxant to extubation) were compared between the two groups.

1.3.2 Hemodynamic Parameters

The mean arterial pressure (MAP), heart rate (HR), and SpO_2 were compared between the two groups at four time points: immediately before anesthesia induction (T0), immediately after tracheal intubation (T1), immediately after tumor tissue resection (T2), and immediately at the end of the operation (T3).

1.3.3 Tracheal Intubation Condition Rating

The tracheal intubation conditions of patients in both groups were evaluated using the Cooper tracheal intubation scoring system [8]. Grade I: Obvious mandibular muscle relaxation, fully open glottis, smooth intubation, no cough. Grade II: Relatively obvious mandibular muscle relaxation, slight adduction of vocal cords, relatively smooth intubation with mild cough. Grade III: Tense mandible, obvious adduction of vocal cords, obvious cough during intubation. Grade IV: Markedly tense mandible, closed glottis, intubation unable to be completed due to inadequate muscle relaxation. Grades I and II were defined as good tracheal intubation conditions.

1.3.4 Pulmonary Ventilation Function Indicators

EIT was used to monitor the percentage areas of the center of ventilation (CoV), dependent silent spaces (DSS), and non-dependent silent spaces (NSS) in both groups.

1.3.5 Inflammatory Indicators

Peripheral venous blood samples (5 mL each) were collected from patients in both groups before surgery (upon admission to the operating room) and 2 hours after surgery. Of each sample, 3 mL was centrifuged and stored

for subsequent analysis. The serum level of high-sensitivity C-reactive protein (hs-CRP) was determined by immunoturbidimetry, and the serum level of tumor necrosis factor-α (TNF-α) was measured by enzyme-linked immunosorbent assay (ELISA); all kits were purchased from Nanjing Jiancheng Bioengineering Institute. The remaining 2 mL of venous blood was used to determine the white blood cell count (WBC) using an XE-2100 hematology analyzer (Sysmex Corporation, Japan).

1.3.6 Adverse Reactions

The incidence of adverse reactions such as hypoxemia, regurgitation and aspiration, and nausea and vomiting was compared between the two groups.

1.4 Statistical Methods

Data analysis was performed using SPSS 28.0 statistical software. Measurement data conforming to a normal distribution were expressed as $\bar{x}\pm s$, and comparisons were conducted using independent-samples *t*-test or paired-samples *t*-test. Repeated measures data were analyzed by repeated measures analysis of variance (ANOVA), with pairwise comparisons performed using the Bonferroni method. Count data were expressed as cases (percentage) [n (%)], and comparisons between groups were conducted using the chi-square test. Ordinal data were compared using nonparametric tests. A *P* value<0.05 was considered statistically significant.

2 Results

2.1 Comparison of Muscle Relaxation Efficacy Between the Two Groups

The onset time of muscle relaxation in the RB group was significantly shorter than that in the CB group ($P<0.05$), while the duration of muscle relaxation, recovery index, and extubation time were significantly longer than those in the CB group ($P<0.05$). See **Table 2.**

2.2 Comparison of Hemodynamic Parameters and SpO_2 Between the Two Groups

There were statistically significant differences in MAP, HR, and SpO_2 between the two groups in terms of intergroup effect, time effect, and interaction effect ($P<0.05$). Compared with the baseline (T0) within the same group, the MAP and HR in the RB group were significantly decreased at T2 and T3, and SpO_2 was significantly decreased at T2 ($P<0.05$). In the CB group, MAP and HR were significantly increased at T1, significantly decreased at T2 and T3, and SpO_2 was significantly decreased at T1 and T2 ($P<0.05$). At T1, the MAP and HR in the RB group were significantly lower than those in the CB group at the same time point ($P<0.05$). At T1 and T2, the SpO_2 in the RB group was significantly higher than that in the CB group at the same time points ($P<0.05$). See **Table 3**.

2.3 Comparison of Tracheal Intubation Condition Ratings Between the Two Groups

In the RB group, 46 cases were rated as Grade I, 7 cases as Grade II, and 3 cases as Grade III. In the CB group, 37 cases were rated as Grade I, 9 cases as Grade II, 9 cases as Grade III, and 1 case as Grade IV. The tracheal intubation condition rating in the RB group was significantly better than that in the CB group ($Z=2.085$, $P=0.039$). The rate of good tracheal intubation conditions in the RB group was significantly higher than that in the CB group [94.64% (53/56) vs. 81.14% (46/56), $\chi^2= 4.264$, $P=0.039$].

2.4 Comparison of Pulmonary Ventilation Function Indicators Between the Two Groups

There were statistically significant time effects on CoV and DSS in both groups ($F=302.355$, 371.384, $P<0.05$). However, there was no significant intergroup effects or interaction effects on CoV and DSS between the two groups ($P>0.05$). Compared with T0, CoV was significantly decreased and DSS was significantly increased in both groups at T1, T2, and T3 ($P<0.05$). See **Table 4**.

2.5 Comparison of Inflammatory Indicators Before and After Surgery Between the Two Groups

At 2 hours after surgery, the serum levels of hs-CRP, TNF-α, and WBC in both groups were significantly higher than those before surgery ($P<0.05$), and the levels in the CB group were significantly higher than those in the RB group ($P<0.01$). See **Table 5**.

2.6 Comparison of Adverse Reactions Between the Two Groups

In the RB group, 1 case of hypoxemia, 3 cases of nausea and vomiting, and 4 cases of fatigue were observed. In the CB group, 3 cases of hypoxemia, 1 case of regurgitation and aspiration, 5 cases of nausea and vomiting, and 2 cases of fatigue were observed. There was no statistically significant difference in the incidence of adverse reactions between the RB group and the CB group [14.29% (8/56) vs. 19.64% (11/56), $\chi^2= 0.571$, $P=0.450$].

Tab.2 Comparison of muscular relaxation effects between two groups (n=56, min, $\bar{x}\pm s$)

Group	Onset time of muscle relaxation	Duration of muscle relaxation	Recovery index	Extubation time
RB group	1.62±0.23	45.81±5.87	18.35±2.72	35.32±2.58
CB group	1.85±0.27	40.15±5.24	14.48±2.56	28.25±2.39
***t* value**	4.853	5.383	7.753	15.044
***P* value**	<0.001	<0.001	<0.001	<0.001

Tab.3 Comparison of MAP, heart rate and SpO2 between two groups (n=56, $\bar{x}\pm s$)

Time Point	MAP (mmHg)		HR (beats/min)		SpO_2 (%)	
	RB group	CB group	RB group	CB group	RB group	CB group
T_0	87.24±8.32	88.33±8.76	78.45±8.26	77.94±8.73	98.18±0.97	98.22±1.04
T_1	86.30±9.15[a]	93.55±10.08[b]	77.83±8.61[a]	82.56±9.22[b]	97.85±0.95[a]	97.09±0.92[b]
T_2	79.25±8.72[b]	80.38±9.21[b]	71.46±7.96[b]	72.23±8.89[b]	97.21±0.90[ab]	96.74±0.93[b]
T_3	82.59±8.34[b]	83.54±9.52[b]	73.57±8.28[b]	74.19±9.05[b]	98.03±0.91	97.94±0.96
$F_{group}/F_{time}/F_{interaction}$ value	5.053/32.942/3.174		3.720/25.155/2.785		6.526/43.571/3.493	
$P_{group}/P_{time}/P_{interaction}$ value	0.002/<0.001/0.025		0.012/<0.001/0.042		<0.001/<0.001/0.017	

Note: Compared with CB Group at the same time point,[a]P<0.05; Compared with T_0 in the same group, [b]P<0.05.

Tab.4 Comparison of indexes of pulmonary ventilation function between two groups (n=56, %, $\bar{x}\pm s$)

Time Point	CoV		DSS		NSS	
	RB group	CB group	RB group	CB group	RB group	CB group
T_0	56.82±2.16	57.24±2.09	2.37±0.38	2.34±0.41	4.17±0.54	4.20±0.56
T_1	51.63±2.57[a]	51.18±2.60[a]	3.61±0.52[a]	3.76±0.58[a]	4.25±0.59	4.23±0.64
T_2	47.15±2.33[a]	46.97±2.45[a]	5.43±0.85[a]	5.65±0.79[a]	4.28±0.67	4.24±0.69
T_3	48.65±2.26[a]	48.25±2.39[a]	4.62±0.78[a]	4.84±0.81[a]	4.31±0.68	4.32±0.73
$F_{group}/F_{time}/F_{interaction}$ value	1.685/302.355/2.012		1.982/371.384/2.303		0.436/0.663/0.251	
$P_{group}/P_{time}/P_{interaction}$ value	0.172/<0.001/0.113		0.117/<0.001/0.079		0.724/0.576/0.864	

Note: Compared with T_0 in the same group,[a]P<0.05.

Tab.5 Comparison of inflammatory indicators before and after operation between two groups (n=56, $\bar{x}\pm s$)

Group	hs-CRP (mg/L)		TNF-α (ng/L)		WBC ($\times10^9$/L)	
	Pre-operation	2 h Post-operation	Pre-operation	2 h Post-operation	Pre-operation	2 h Post-operation
RB group	5.78±1.04	11.23±2.80[a]	8.79±1.53	26.34±4.98[a]	6.54±1.17	10.37±1.82[a]
CB group	5.52±0.96	15.31±3.06[a]	9.25±1.68	32.27±5.22[a]	6.29±1.23	12.51±1.95[a]
t value	1.375	7.361	1.515	6.151	1.102	6.004
P value	0.172	<0.001	0.133	<0.001	0.273	<0.001

Note: Compared with CB Group at the same time point,[a]P<0.05.

3 Discussion

Rocuronium and cisatracurium besilate are two of the most commonly used muscle relaxants in anesthesia practice. Rocuronium is characterized by rapid onset, minimal effects on the cardiovascular system, weak histamine release, no cumulative effect, and is mainly metabolized by the liver with a small portion excreted via the kidneys [9]. Cisatracurium besilate has no histamine-releasing effect, no significant vagolytic effect, minimal impact on the cardiovascular system, no cumulative effect, and is metabolized primarily through Hofmann elimination, independent of hepatic and renal function [10]. However, cisatracurium besilate has a relatively slow onset time [10]. The results of this study showed that compared with cisatracurium besilate, rocuronium had a shorter onset time of muscle relaxation and a longer duration of muscle relaxation.

In laparoscopic radical cystectomy, an optimal muscle relaxant is conducive to maintaining intraoperative hemodynamic stability. In this study, the MAP and HR in the RB group at T1 were significantly lower than those in the CB group, while the SpO_2 was significantly higher than that in the CB group. Tracheal intubation can significantly stimulate the pharynx, leading to abnormal hemodynamic fluctuations. However, the MAP and HR in the RB group did not change significantly at this time point, whereas those in the CB group decreased significantly, and the decrease in SpO_2 in the CB group was more pronounced. These findings suggest that rocuronium can more effectively maintain intraoperative hemodynamic stability compared with cisatracurium besilate. The underlying mechanism may be attributed to the faster onset and superior muscle relaxation effect of rocuronium, which can attenuate the stress response induced by tracheal intubation. Moreover, the onset speed and efficacy of muscle relaxants can directly affect tracheal intubation conditions [11]. In this study, the rate of good tracheal intubation conditions in the RB group reached 94.64%, which was significantly higher than that in the CB group.

The Trendelenburg position and increased intra-abdominal pressure caused by CO_2 pneumoperitoneum during laparoscopic radical cystectomy can lead to upward displacement of abdominal viscera and cephalad shift of the diaphragm, thereby reducing lung compliance and functional residual capacity, disturbing intrapulmonary gas distribution, and inducing or exacerbating ventilation-perfusion mismatch [12]. EIT is a novel non-invasive pulmonary ventilation monitoring technology. Unlike other pulmonary function testing techniques, EIT can quantify the regions of good and poor pulmonary ventilation, thus enabling effective assessment of regional pulmonary ventilation distribution [13]. The CoV value reflects the region of optimal pulmonary ventilation; silent spaces are defined as regions with impedance changes less than 10%, representing areas of hypoventilation. DSS and NSS reflect regions of lung collapse or atelectasis and regions of already or over-expanded lung, respectively. In this study, compared with T0, CoV was significantly decreased and DSS was significantly increased in both

groups at T1, T2, and T3, but there were no significant differences in CoV and DSS between the two groups at the same time points; furthermore, there were no significant changes in NSS at all time points in both groups. These results indicate that laparoscopic radical cystectomy can exert a certain impact on patients' pulmonary ventilation function, with the ventilation center shifting ventrally and the area of lung atelectasis expanding to a certain extent, while the area of over-ventilation does not change significantly. This phenomenon may be attributed to the use of low tidal volume ventilation.

Laparoscopic radical cystectomy is an invasive surgical procedure, and intraoperative surgical stimulation can induce a stress response in the body [4] and stimulate the release of various inflammatory factors. Studies have confirmed that different anesthetic regimens and drugs during surgery can directly affect the degree of perioperative inflammation and stress [14]. hs-CRP, TNF-α, and WBC are commonly used clinical markers reflecting the body's inflammatory response, and their levels can increase significantly in the presence of infection or tissue injury [15]. In this study, the serum levels of hs-CRP, TNF-α, and WBC in both groups were significantly higher at 2 hours after surgery than those before surgery, but the increase amplitude in the RB group was lower than that in the CB group. The possible reason is that rocuronium has a faster onset time and better muscle relaxation effect during anesthesia induction, which can alleviate the surgical stimulation to the body, reduce the release of inflammatory factors, and mitigate the degree of the body's inflammatory response. A study by Zhao Xianji [16] also demonstrated that the application of rocuronium in radical resection of colorectal cancer results in a milder stress response in patients compared with cisatracurium besilate.

In conclusion, compared with cisatracurium besilate, rocuronium bromide has a faster onset time and better muscle relaxation effect in laparoscopic radical cystectomy, which can achieve superior tracheal intubation conditions, thereby reducing the stress and inflammatory responses induced by intubation. However, there is no significant difference in the impact of the two muscle relaxants on intraoperative pulmonary ventilation function.

Conflict of interest None

Reference

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·论 著·

罗库溴铵在腹腔镜膀胱癌根治术中的肌肉松弛效果及对患者炎症反应的影响

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摘要：目的 对比腹腔镜膀胱癌根治术中应用罗库溴铵或苯磺顺阿曲库铵的肌肉松弛（肌松）效果，以及对患者肺通气功能和机体炎症反应的影响。**方法** 将2022年1月至2024年6月内蒙古自治区人民医院收治的拟行腹腔镜膀胱癌根治术治疗的112例患者随机分为RB组（n=56，使用罗库溴铵作为肌松药）与CB组（n=56，使用苯磺顺阿曲库铵作为肌松药）。比较两组肌松效果、气管插管条件评级以及不良反应，记录两组麻醉诱导前即刻（T_0）、气管插管后即刻（T_1）、肿瘤组织切除后即刻（T_2）以及术毕即刻（T_3）的平均动脉压（MAP）、心率、外周血氧饱和度（SpO_2）、肺通气功能指标[通气中心（CoV）、依赖静止区（DSS）以及非依赖静止区（NSS）面积百分比]并进行比较。比较术前、术后2 h两组患者的炎症指标水平[超敏C反应蛋白（hs-CRP）、肿瘤坏死因子-α（TNF-α）以及白细胞计数（WBC）]。**结果** RB组肌松起效时间短于CB组（P<0.05），肌松维持时间、恢复指数及拔管时间长于CB组（P<0.05）。RB组气管插管条件良好率高于CB组[94.64%（53/56）*vs* 81.14%（46/56），χ^2=4.264，P=0.039]。T_1时RB组的MAP、心率均显著低于CB组（P<0.05）。RB组在T_1、T_2的SpO_2均显著高于同期CB组（P<0.05）。与T_0相比，两组T_1、T_2、T_3时点CoV均显著降低（P<0.05），DSS均显著升高（P<0.05）。术后2 h，CB组hs-CRP、TNF-α及WBC高于RB组（P<0.05）。RB组和CB组不良反应发生率比较差异无统计学意义[14.29%（8/56）*vs* 19.64%（11/56），χ^2=0.571，P=0.450]。**结论** 将罗库溴铵应用于腹腔镜膀胱癌根治术中相对于苯磺顺阿曲库铵能起到更佳的肌松效果，并能减轻手术诱发的炎症反应，但二者对肺通气功能的影响相近。

关键词： 罗库溴铵；腹腔镜；苯磺顺阿曲库铵；膀胱癌根治术；肌肉松弛；肺通气功能；炎症反应
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Impact of rocuronium bromide on muscular relaxation and inflammatory response in laparoscopic radical cystectomy

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Abstract: Objective To compare the muscle relaxant effects of rocuronium bromide and cisatracurium besylate in laparoscopic radical cystectomy for bladder cancer, as well as their impacts on pulmonary ventilation function and body's inflammatory response. **Methods** A total of 112 patients scheduled for laparoscopic radical cystectomy at the Inner Mongolia People's Hospital between January 2022 and June 2024 were randomly divided into the RB group (n=56, receiving rocuronium bromide as the muscle relaxant) and the CB group (n=56, receiving cisatracurium besylate as the muscle relaxant). The muscle relaxant effects, tracheal intubation condition ratings, and adverse reaction were compared between the two groups. Mean arterial pressure (MAP), heart rate, saturation of peripheral oxygen (SpO_2), and pulmonary ventilation function indicators [percentage area of center of ventilation (CoV), dependent silent spaces (DSS), and non-dependent silent spaces (NSS)] were recorded and compared immediately before anesthesia induction (T_0), immediately after tracheal intubation (T_1), immediately after tumor resection (T_2), and immediately after

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surgery (T_3). The levels of inflammatory markers [high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-α (TNF-α), and white blood cell count (WBC)] were compared between the two groups before surgery and 2 hours after surgery. **Results** The onset time of muscle relaxation in the RB group was shorter than that in the CB group (P<0.05), while the duration of muscle relaxation, recovery index, and extubation time in the RB group were longer than those in the CB group (P<0.05). The excellent rate of tracheal intubation conditions in the RB group was higher than that in the CB group [94.64%(53/56) *vs* 81.14%(46/56), χ^2=4.264, P=0.039]. At T_1, MAP and heart rate in the RB group were significantly lower than those in the CB group (P<0.05). SpO_2 in the RB group was significantly higher than that in the CB group at T_1 and T_2 (P<0.05). Compared with T_0, CoV significantly decreased at T_1, T_2, and T_3 in both groups(P<0.05), while DSS significantly increased (P<0.05). Two hours after surgery, hs-CRP, TNF-α, and WBC levels in CB group were higher than those in RB group (P<0.05). There was no significant difference in the incidence of adverse reactions between RB group and CB group [14.29% (8/56) *vs* 19.64% (11/56), χ^2=0.571, P=0.450]. **Conclusion** The use of rocuronium bromide in laparoscopic radical cystectomy for bladder cancer provides better muscle relaxation compared to cisatracurium besylate, and can alleviate surgery-induced inflammatory responses. However, both have similar effects on pulmonary ventilation function.

Keywords: Rocuronium bromide; Laparoscopic; Cisatracurium besylate; Radical cystectomy; Muscular relaxation; Pulmonary ventilation function; Inflammatory response

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膀胱癌是泌尿系统常见恶性肿瘤之一[1]。根据GLOBOCAN数据显示，2020年中国膀胱癌新发病例和死亡病例数分别为8.6万、3.9万[2]。膀胱癌根据浸润深度可划分为肌层浸润性膀胱癌(muscle invasive bladder carcinoma，MIBC)与非肌层浸润性膀胱癌(non-muscle invasive bladder carcinoma，NMIBC)两类[1]。其中，针对MIBC以及高危NMIBC临床首选治疗方法为根治性膀胱切除术[3]。但该术式属于侵入性手术，操作复杂，术中容易引起较为明显的应激反应[4]。肌肉松弛(肌松)药的使用可减少插管不适、便于实施机械通气、优化手术环境[5]。罗库溴铵和苯磺顺阿曲库铵是目前最常使用的两种肌松药，但关于二者在腹腔镜膀胱癌根治术中的对比研究较少[6-7]。本研究旨在分析这两种肌松药在腹腔镜膀胱癌根治术中的应用效果。现报道如下。

1　资料与方法

1.1　一般资料　前瞻性选择2022年1月至2024年6月内蒙古自治区人民医院接受治疗的膀胱癌患者。本研究已通过内蒙古自治区人民医院伦理委员会审核批准(202503603L)。纳入标准：(1) 经病理活检等确诊为MIBC或高危NMIBC；(2) 年龄50~80岁；(3) 符合根治性膀胱切除术适应证，并拟行腹腔镜膀胱癌根治术治疗；(4) 无麻醉禁忌证；(5) 美国麻醉医师协会(American Society of Anesthesiologists，ASA)分级Ⅰ~Ⅲ级；(6) 自愿签署知情同意书。排除标准：(1) 存在远处转移；(2) 合并肺部疾病或近期有肺损伤史；(3) 心、肾、肝等重要脏器功能不全；(4) 存在其他原发恶性肿瘤；(5) 既往有腹腔手术史。脱落标准：(1) 患者要求退出研究；(2) 术中转开放手术。将纳入的112例患者以随机数字表法分为RB组与CB组，每组56例。两组性别、年龄、身体质量指数(body mass index，BMI)、肿瘤最大直径、病理类型、T分期、ASA分级差异无统计学意义(P<0.05)。见表1。

表1　两组一般资料比较　(n=56)

Tab.1　Comparison of general data between two groups　(n=56)

项目	RB组	CB组	$\chi^2/t/Z$值	P值
性别(男/女，例)	45/11	47/9	0.243	0.622
年龄(岁，$\bar{x}\pm s$)	64.15±6.27	62.98±6.53	0.967	0.336
BMI(kg/m^2，$\bar{x}\pm s$)	23.75±2.38	23.43±2.26	0.730	0.467
肿瘤最大直径(cm，$\bar{x}\pm s$)	4.02±1.13	3.96±1.09	0.286	0.775
病理类型(例)				
尿路上皮癌	46	43		
鳞状细胞癌	5	6	0.525	0.769
腺癌	5	7		
T分期(例)				
Ta~T2	41	43	0.190	0.663
T3~T4	15	13		
ASA分级(例)				
Ⅰ级	18	20		
Ⅱ级	30	29	0.433	0.699
Ⅲ级	8	7		

1.2　方法　所有患者入室后常规建立外周静脉通路，连接监护仪(深圳迈瑞，BeneView T8)和阻抗断层成像仪(electrical impedance tomography，EIT)设备(C500 EIT系统)。麻醉诱导：静脉注射咪达唑仑

0.04 mg/kg+丙泊酚2.5 mg/kg+舒芬太尼0.4 μg/kg。连接肌松监测仪(M206983型,北京中西远大),待脑电双频指数(bispectral index,BIS)低于60对肌松监测进行定标,随后静脉注射肌松药。其中,RB组给予罗库溴铵注射液(浙江仙琚制药,国药准字H20093186)0.5 mg/kg静脉注射;CB组给予注射用苯磺顺阿曲库铵(江苏恒瑞医药,国药准字H20060869)0.12 mg/kg静脉注射。待四个成串刺激(train-of-four,TOF)比值<5%后,进行气管插管机械通气。设置潮气量8~10 mL/kg,通气频率10~12次/min,待建立CO_2人工气腹后将潮气量调至6~8 mL/kg,通气频率调至12~18次/min,呼气末二氧化碳分压(end-tidal carbon dioxide partial pressure,$P_{ET}CO_2$)维持在35~45 mmHg,外周血氧饱和度(saturation of peripheral oxygen,SpO_2)≥90%。启动TOF监测肌松阻滞程度。麻醉维持:持续静脉泵注丙泊酚2 mg/(kg·h)+瑞芬太尼0.2 μg/(kg·min)。若术中TOF第1个肌颤搐反应幅度恢复至25%时追加肌松药,追加剂量为基础剂量的1/4,追加次数≤3次。术毕前15 min停止追加肌松药。术毕给予阿托品1 mg+新斯的明2 mg静脉注射,以拮抗肌松残余作用。

1.3 观察指标

1.3.1 肌松效果 比较两组肌松起效时间(即肌松药注射完成至第1个肌颤搐反应幅度达最大阻滞的时间)、肌松维持时间(即肌松药注射完成至第1个肌颤搐反应幅度恢复至基础值的25%的时间)、恢复指数(即第1个肌颤搐反应幅度从基础值的25%恢复至75%的时间)及拔管时间(即停用肌松药至拔管的时间)。

1.3.2 血流动力学参数 比较两组麻醉诱导前即刻(T_0)、气管插管后即刻(T_1)、肿瘤组织切除后即刻(T_2)以及术毕即刻(T_3)的平均动脉压(mean arterial pressure,MAP)、心率、SpO_2。

1.3.3 气管插管条件评级标准 参照Cooper气管插管条件评分法[8]对两组患者进行气管插管条件评级。Ⅰ级:有明显的下颌肌松,声门开放,顺利插管,无呛咳发生;Ⅱ级:有较为明显的下颌肌松,声带略有内收,插管较顺利,但有轻度呛咳发生;Ⅲ级:下颌较紧张,有明显的声带内收,插管出现明显呛咳;Ⅳ级:下颌明显紧张,声门紧闭,气管插管因肌松不佳无法完成。以Ⅰ级和Ⅱ级为气管插管条件良好。

1.3.4 肺通气功能指标 通过EIT监测两组T_0、T_1、T_2、T_3时点通气中心(central of ventilation,CoV)、依赖静止区(dependent silent spaces,DSS)以及非依赖静止区(non-dependent silent spaces,NSS)面积百分比。

1.3.5 炎症指标 分别于术前(入手术室时)和术后2 h采集两组患者的外周静脉血5 mL,取3 mL离心后备用。使用免疫比浊法测定血清超敏C反应蛋白(high-sensitivity C-reactive protein,hs-CRP)水平,并以酶联免疫法检测血清肿瘤坏死因子(tumor necrosis factor,TNF)-α水平,试剂盒均购自南京建成生物。取剩余2 mL静脉血运用日本SYSMEX公司XE-2100血液分析仪测定白细胞计数(white blood cell count,WBC)。

1.3.6 不良反应 比较两组低氧血症、反流误吸、恶心呕吐等不良反应情况。

1.4 统计学方法 使用SPSS 28.0统计学软件进行数据分析。符合正态分布的计量资料以$\bar{x}\pm s$表示,比较采用独立样本或配对样本t检验。重复测量数据选用重复测量方差分析,两两比较采用Bonferroni法。计数资料以例(%)表示,组间比较行χ^2检验,等级资料比较采用非参数检验。P<0.05为差异有统计学意义。

2 结 果

2.1 两组肌松效果比较 RB组的肌松起效时间显著短于CB组(P<0.05),而肌松维持时间、恢复指数以及拔管时间均显著长于CB组(P<0.05)。见表2。

2.2 两组血流动力学参数及SpO_2比较 两组MAP、心率、SpO_2的组间、时间和交互效应均有统计学意义(P<0.05);与组内T_0时点相比,RB组T_2、T_3时点MAP、心率显著降低,T_2时点SpO_2显著降低(P<0.05)。CB组T_1时点MAP、心率显著升高,T_2、T_3时点MAP、心率显著降低,T_1、T_2时点SpO_2显著降低(P<0.05)。T_1时点,RB组MAP、心率显著低于同时点CB组(P<0.05)。T_1、T_2时点,RB组SpO_2显著高于同时点CB组(P<0.05)。见表3。

2.3 两组气管插管条件评级比较 气管插管条件评级中RB组Ⅰ级46例,Ⅱ级7例,Ⅲ级3例;CB组中Ⅰ级37例,Ⅱ级9例,Ⅲ级9例,Ⅳ级1例。RB组气管

表2 两组肌松效果比较 (n=56, min, $\bar{x}\pm s$)

Tab.2 Comparison of muscular relaxation effects between two groups (n=56, min, $\bar{x}\pm s$)

组别	肌松起效时间	肌松维持时间	恢复指数	拔管时间
RB组	1.62±0.23	45.81±5.87	18.35±2.72	35.32±2.58
CB组	1.85±0.27	40.15±5.24	14.48±2.56	28.25±2.39
t值	4.853	5.383	7.753	15.044
P值	<0.001	<0.001	<0.001	<0.001

插管条件评级优于CB组（Z=2.085，P=0.039）。RB组气管插管条件良好率显著高于CB组[94.64%（53/56）*vs* 81.14%（46/56），χ^2=4.264，P=0.039]。

2.4　两组肺通气功能指标比较　两组CoV、DSS的时间效应均有统计学意义（F=302.355、371.384，P<0.05）。两组CoV、DSS的组间及交互效应均无统计学意义（P>0.05）。与T_0相比，两组T_1、T_2、T_3时点CoV均显著降低，DSS均显著升高（P<0.05）。见表4。

2.5　两组手术前后炎症指标比较　术后2 h，两组患者血清hs-CRP、TNF-α以及WBC高于同组术前（P<0.05），且CB组高于RB组（P<0.01）。见表5。

2.6　两组不良反应比较　RB组发生低氧血症1例，恶心呕吐3例，乏力4例。CB组发生低氧血症3例，反流误吸1例，恶心呕吐5例，乏力2例。RB组和CB组不良反应发生率比较差异无统计学意义[14.29%（8/56）*vs* 19.64%（11/56），χ^2=0.571，P=0.450]。

表3　两组MAP、心率及SpO_2的比较　（n=56，$\bar{x}\pm s$）

Tab.3　Comparison of MAP, heart rate and SpO_2 between two groups　（n=56，$\bar{x}\pm s$）

时点	MAP（mmHg）		心率（次/min）		SpO_2（%）	
	RB组	CB组	RB组	CB组	RB组	CB组
T_0	87.24±8.32	88.33±8.76	78.45±8.26	77.94±8.73	98.18±0.97	98.22±1.04
T_1	86.30±9.15[a]	93.55±10.08[b]	77.83±8.61[a]	82.56±9.22[b]	97.85±0.95[a]	97.09±0.92[b]
T_2	79.25±8.72[b]	80.38±9.21[b]	71.46±7.96[b]	72.23±8.89[b]	97.21±0.90[ab]	96.74±0.93[b]
T_3	82.59±8.34[b]	83.54±9.52[b]	73.57±8.28[b]	74.19±9.05[b]	98.03±0.91	97.94±0.96
$F_{组间/时间/交互}$值	5.053/32.942/3.174		3.720/25.155/2.785		6.526/43.571/3.493	
$P_{组间/时间/交互}$值	0.002/<0.001/0.025		0.012/<0.001/0.042		<0.001/<0.001/0.017	

注：同时间点与CB组比较，[a]P<0.05；与同组T_0时间点比较，[b]P<0.05。

表4　两组肺通气功能指标比较　（n=56，%，$\bar{x}\pm s$）

Tab.4　Comparison of indexes of pulmonary ventilation function between two groups　（n=56，%，$\bar{x}\pm s$）

时点	CoV		DSS		NSS	
	RB组	CB组	RB组	CB组	RB组	CB组
T_0	56.82±2.16	57.24±2.09	2.37±0.38	2.34±0.41	4.17±0.54	4.20±0.56
T_1	51.63±2.57[a]	51.18±2.60[a]	3.61±0.52[a]	3.76±0.58[a]	4.25±0.59	4.23±0.64
T_2	47.15±2.33[a]	46.97±2.45[a]	5.43±0.85[a]	5.65±0.79[a]	4.28±0.67	4.24±0.69
T_3	48.65±2.26[a]	48.25±2.39[a]	4.62±0.78[a]	4.84±0.81[a]	4.31±0.68	4.32±0.73
$F_{组间/时间/交互}$值	1.685/302.355/2.012		1.982/371.384/2.303		0.436/0.663/0.251	
$P_{组间/时间/交互}$值	0.172/<0.001/0.113		0.117/<0.001/0.079		0.724/0.576/0.864	

注：与同组T_0时间点比较，[a]P<0.05。

表5　两组手术前后炎症指标比较　（n=56，$\bar{x}\pm s$）

Tab.5　Comparison of inflammatory indicators before and after operation between two groups　（n=56，$\bar{x}\pm s$）

组别	hs-CRP（mg/L）		TNF-α（ng/L）		WBC（×10^9/L）	
	术前	术后2 h	术前	术后2 h	术前	术后2 h
RB组	5.78±1.04	11.23±2.80[a]	8.79±1.53	26.34±4.98[a]	6.54±1.17	10.37±1.82[a]
CB组	5.52±0.96	15.31±3.06[a]	9.25±1.68	32.27±5.22[a]	6.29±1.23	12.51±1.95[a]
t值	1.375	7.361	1.515	6.151	1.102	6.004
P值	0.172	<0.001	0.133	<0.001	0.273	<0.001

注：与同组术前比较，[a]P<0.05。

3　讨　论

罗库溴铵与苯磺顺阿曲库铵是麻醉过程中最常使用的两种肌松药。其中罗库溴铵起效快，对心血管系统影响较小，组胺释放弱，无蓄积作用，代谢主要经肝脏，少数经肾脏[9]。苯磺顺阿曲库铵无组胺释放作用，也无明显的迷走神经阻断作用，对心血管系统影响小，无蓄积作用，代谢主要经霍夫曼降解途径，不依赖肝肾[10]。但苯磺顺阿曲库铵起效时间较慢[10]。本研究结果显示，与苯磺顺阿曲库铵相比，罗库溴铵的肌松起效时间更短，肌松维持时间更长。

在腹腔镜膀胱癌根治术中，良好的肌松药有利于维持术中血流动力学的稳定。本研究中，RB组T_1时点MAP、心率显著低于CB组，SpO_2显著高于CB组。气管插管可明显刺激咽部，导致血流动力学异常波动，但RB组此时MAP、心率并无明显变化，CB

组则显著降低，且CB组SpO_2降幅更大。上述结果提示，罗库溴铵相对于苯磺顺阿曲库铵能更有效地维持术中血流动力学的稳定。其原因可能与罗库溴铵的肌松起效更快、肌松效果更好，从而能抑制气管插管造成的刺激有关。而肌松药的起效速度、肌松效果可直接影响气管插管条件[11]。本研究中RB组气管插管条件良好率达94.64%，显著高于CB组。

腹腔镜膀胱癌根治术中头低脚高体位以及CO_2气腹导致的腹内压升高可使腹腔脏器上移，膈肌向头侧移位，进而引起肺顺应性以及功能残气量降低，使肺内气体分布受到干扰，引发或加重通气血流比例失调[12]。EIT是一种新型无创肺通气监测技术，与其他肺功能检测技术不同的是，EIT可对肺部通气良好与不良区域进行量化，因此能有效了解肺局部通气分布情况[13]。CoV值反映的是肺通气良好区域；静止区是电阻抗变化小于10%的区域，反映的是低通气区域。DSS与NSS分别反映的是肺萎陷、肺不张区域以及已经或过度扩张区域。本研究中T_1、T_2、T_3时点，两组CoV较组内T_0时点显著降低，DSS较同组T_0时点显著升高，但两组同期CoV、DSS比较无差异；且两组各时点NSS亦无明显变化。该结果表明，腹腔镜膀胱癌根治术中可对患者肺通气功能产生一定的影响，通气中心向腹侧移动，肺不张区域可出现一定程度的扩大，但过度通气区域未发生明显增减变化，其原因考虑与小潮气量肺通气有关。

腹腔镜膀胱癌根治术属于侵袭性手术，手术刺激性操作会导致机体出现应激反应[4]，并刺激机体释放多种炎症因子。有研究证实，手术过程中麻醉方案和药物的不同可直接影响到围手术期炎症和应激程度[14]。hs-CRP、TNF-α、WBC都是临床常用的反映机体炎症反应的标志物，当机体出现感染或损伤时，其水平可明显升高[15]。本研究中两组术后2 h血清hs-CRP、TNF-α以及WBC都较术前显著升高，但观察组升高幅度不及对照组。其原因可能是罗库溴铵在麻醉诱导时起效更快，肌松效果更好，因此能减轻手术对机体产生的刺激，减少炎症因子释放，减轻机体炎症反应程度。赵贤姬[16]的研究也表明，在结直肠癌根治术中应用罗库溴铵相对于苯磺顺阿曲库铵，患者机体内应激反应更轻。

综上所述，在腹腔镜膀胱癌根治术中应用罗库溴铵相对于苯磺顺阿曲库铵的肌松起效更快，肌松效果更好，能获得更佳的气管插管条件，从而减轻患者因插管过程引起的应激反应和炎症反应，但二者对于术中肺通气功能的影响差异并不明显。

利益冲突　无

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