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ORIGINAL ARTICLE

Application value of opioid-free anesthesia in renal cyst decompression by laparoscopy

Valor de la aplicación de anestesia sin opiáceos en la descompresión de quiste renal por laparoscopia

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Abstract

Objective: *The objective of the study was to analyze the application value of opioid-free anesthesia (OFA) in renal cyst decompression by laparoscopy.* **Method:** *A total of 124 patients undergoing renal cyst decompression by laparoscopy in our hospital were selected and divided into opioid anesthesia (OA) and OFA groups (n = 62). Fentanyl and remifentanil were used for anesthesia induction in the OA group, while lidocaine and dexmedetomidine were employed for anesthesia induction in the OFA group. The homeostasis indicators (cortisol [Cor], adrenocorticotropic hormone [ACTH], C-reactive protein [CRP], and interleukin-6 [IL-6]) were also compared 10 min before anesthesia (T_a), at the end of operation (T_b), and 24 h after operation (T_c).* **Results:** *At T_1-T_3, heart rate, mean arterial pressure, mean airway pressure, and partial pressure of end-tidal carbon dioxide were all lower in OFA group than those in OA group ($p < 0.05$). At T_b-T_c, the levels of Cor, ACTH, CRP, and IL-6 were all higher in both groups than those at T_a ($p < 0.05$), while they were lower in OFA group than those in OA group ($p < 0.05$).* **Conclusion:** *OFA is more beneficial to the respiratory and circulatory system and homeostasis of patients, and has higher anesthetic safety.*

Keywords: Renal cyst decompression. Laparoscopy. Opioid-free. Anesthesia. Respiratory circulatory system.

Resumen

Objetivo: *Analizar el valor de la aplicación de anestesia libre de opiáceos (ALO) en la descompresión de quiste renal por laparoscopia.* **Método:** *Se seleccionaron 124 pacientes sometidos a descompresión de quiste renal por laparoscopia en nuestro hospital, que se dividieron en grupos de anestesia con opiáceos (AO) y ALO (n = 62). El fentanilo y el remifentanilo se utilizaron para la inducción de la anestesia en el grupo AO, mientras que la lidocaína y la dexmedetomidina se emplearon para la inducción de la anestesia en el grupo ALO. También se compararon los indicadores de homeostasis (cortisol, hormona adrenocorticotropa [ACTH], proteína C reactiva [PCR] e interleucina 6 [IL-6]) 10 minutos antes de la anestesia (T_a), al final de la operación (T_b) y 24 h después de esta (T_c).* **Resultados:** *En T_1-T_3, la frecuencia cardíaca, la presión arterial media, la presión media de las vías respiratorias y la presión parcial de dióxido de carbono al final de la espiración fueron todas más bajas en el grupo ALO que en el grupo AO ($p < 0,05$). En T_b-T_c, los niveles de Cor ACTH, PCR e IL-6 fueron más altos en ambos grupos que en T_a ($p < 0.05$), mientras que fueron más bajos en el grupo ALO que en el grupo OA ($p < 0.05$).* **Conclusión:** *La ALO es más beneficiosa para los sistemas respiratorio y circulatorio, y para la homeostasis, de los pacientes, y tiene mayor seguridad anestésica.*

Palabras clave: Descompresión de quiste renal. Laparoscopia. Anestesia libre de opiáceos. Sistema circulatorio. Sistema respiratorio.

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Introduction

Renal cyst is an asymptomatic benign disease with an incidence rate of about 50%. At present, this disease is mainly treated by surgeries, such as renal cyst decompression by laparoscopy that locates and resects renal cysts to relieve clinical symptoms. However, this surgical method poses high requirements to anesthetists. Improper anesthesia leads to intraoperative hemodynamic instability, post-operative pain, and other adverse events. Therefore, reasonable and effective anesthesia modes are particularly important for patients undergoing renal cyst decompression by laparoscopy[1]. General anesthesia can meet the requirements of anesthesia in this surgery, in which opioids are indispensable. With the use of opioid anesthetics, the pain problem has been overcome. However, opioid anesthetics can lead to adverse events such as respiratory depression, urinary retention, and hyperalgesia, which not only delay post-operative recovery but also increase the medical cost[2,3]. To solve the above problems, opioid-free anesthesia (OFA) has been put forward, which is a multi-mode anesthesia combining non-steroidal anti-inflammatory drugs, local anesthetics, and sedatives and primarily used to reduce adverse events caused by opioid anesthetics[4,5]. In this study, the application value of OFA in renal cyst decompression by laparoscopy was explored, thereby providing references for the selection of anesthesia mode.

Method

Subjects

A total of 124 patients undergoing renal cyst decompression by laparoscopy in our hospital from February 2021 to February 2022 were selected and divided into opioid anesthesia (OA) group (n = 62) and OFA group (n = 62) using a random number table. In the OA group, there were 38 males and 24 females aged 35-63 years, with a body mass index (BMI) of 22-28 kg/m^2. In the OFA group, there were 35 males and 27 females aged 35-65 years, with a BMI of 22-28.5 kg/m^2. The general data were comparable between the two groups (Table 1). Inclusion criteria were as follows: (1) patients with renal cysts diagnosed by imaging examinations, (2) those with unilateral cysts, (3) those undergoing renal cyst decompression by laparoscopy, meeting the surgical indications and without contraindications to surgery and anesthesia, (4) those in American Society of Anesthesiologists Grade I-III, (5) those not pregnant or lactating, and (6) those who voluntarily participated in this study. Exclusion criteria were as follows: (1) patients with local or systemic infection, (2) those with drug allergy, (3) those with a history of renal cyst decompression by laparoscopy, (4) those with abnormal pain sensitivity or unable to perceive pain, (5) those with coagulation dysfunction, (6) those with dysfunction of vital organs, such as the heart, liver and kidney, (7) those with cognitive or communication disorders, or (8) those with mental disorders.

Anesthesia methods

The patients in both groups were routinely deprived of food and water before the operation. After they entered the operating room, the venous access was opened, and the vital signs were routinely monitored. Fentanyl (intravenous [IV], 3 μg/kg) and remifentanil (IV pumping, 15.0 μg/kg·h) were used for anesthesia induction in OA group. In the OFA group, dexmedetomidine was intravenously pumped at 0.5 μg/kg within 10 min and then maintained at 0.5 μg/kg·h, and lidocaine was intravenously injected at 1.0 mg/kg and then maintained at 2.0 mg/kg·h. Other anesthetics were the same in both groups, including propofol (IV, 2 mg/kg), midazolam (IV, 0.03 mg/kg), and vecuronium (IV, 0.15 mg/kg). After anesthesia induction, the laryngeal mask was inserted and the bispectral index (BIS) monitor was connected. Based on the BIS, the dosage of propofol was adjusted and kept at 40-60. If the patient's heart rate (HR) was lower than 50 beats/min during operation, 0.5 mg of atropine would be intramuscularly injected. If the patient's blood pressure greatly fluctuated (>30% of the baseline value) during the operation, vasoactive drugs would be used. Extubation was performed after the recovery of consciousness. Routine analgesia, anti-inflammation, and anti-infection were all performed after the operation.

Surgical methods

After anesthesia, the patient in the lateral decubitus position was elevated at the waist on the affected side. A 15-mm transverse incision was made at the lower border of the 12th rib of the midaxillary line. Then the lumbar fascia and muscle layer were separated, and the peritoneum was pushed open, into which laparoscope (Tekno-Medical Optik-Chirurgie GmbH,

Germany; Registration Certificate for Medical Device: 20163061348) and laparoscopic surgical instruments (Olympus Winter and Ibe GmbH, Japan; Registration Certificate for Medical Device: 20173016482) were placed. Carbon dioxide was infused, and the pneumoperitoneum pressure was maintained at 14 mmHg. The extraperitoneal fat was removed, and three approximately avascular planes of the retroperitoneal cavity were dissected. The fat sac and perirenal fascia were separated to fully expose the renal cyst. The hernia sac wall was excised with an ultrasonic scalpel (Soering GmbH, Germany; Registration Certificate for Medical Device: 20163012365) at a distance of 00 cm from the renal parenchyma, and subjected to pathological examination. After hemostasis, the surgery was routinely completed when there was no active bleeding.

Evaluation of respiratory and circulatory system indicators

The stability of the respiratory and circulatory system was monitored and assessed by the HR, mean arterial pressure (MAP), partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$), and mean airway pressure (P_{mean}) at 10 min before anesthesia (T_0), at the time of anesthesia induction (T_1), 10 min after anesthesia (T_2), and 30 min after anesthesia (T_3).

Assessment of homeostasis

The homeostasis of patients was assessed by cortisol (Cor), adrenocorticotropic hormone (ACTH), C-reactive protein (CRP), and interleukin-6 (IL-6). At 10 min before anesthesia (T_a), at the end of operation (T_b), and 24 h after operation (T_c), 2 mL of venous blood was drawn, and the serum was separated. Then, the levels of Cor and ACTH were measured by radioimmunoassay, and the levels of CRP and IL-6 were measured using a DK-3506 automatic multifunctional microplate reader.

Efficacy evaluation

The anesthetic efficacy (excellent, good, and poor) was evaluated. The efficacy was excellent if no pain or discomfort occurred during the operation and the effect of muscle relaxation was good. The efficacy was good if mild pain or discomfort occurred during the operation, and drug-assisted sedation was needed. The efficacy was poor if unbearable severe pain occurred, and the anesthesia mode needed to be changed. Excellent/good rate of anesthesia = ([excellent cases + good cases]/total cases) ×100%.

Safety evaluation

The incidence of anesthesia-related adverse reactions, including nausea and vomiting, bucking, dysphoria, respiratory depression, and urinary retention, was recorded in the two groups.

Evaluation of post-operative recovery time

The recovery time of spontaneous breathing, awakening time, and observation time was compared between the two groups.

Analysis of incidence of post-operative cognitive impairment

The patient's cognitive status was assessed using the mini-mental state examination at 12 h, 24 h, and 48 h after operation. The total score < 17 points for illiteracy, < 20 points for primary school, < 22 points for technical secondary school and senior high school, and < 23 points for junior college and above indicated cognitive impairment.

Statistical analysis

SPSS22.0 software was used for statistical analysis. Measurement data were described by ($\bar{x} \pm s$) and compared by the independent-samples *t*-test between two groups and at each time point within the same group by repeated measures analysis of variance. Count data were described by percentage and compared between two groups by the χ^2 test. The rank sum test was conducted on ranked data. $p < 0.05$ was considered statistically significant.

Results

General data

There were no significant differences in the general data between OA and OFA groups ($p > 0.05$) (Table 1).

Levels of respiratory and circulatory system indicators

The respiratory and circulatory system indicators (HR, MAP, P_{mean} and $P_{ET}CO_2$) had no statistically

Table 1. General data

Indicator	OA group (n = 62)	OFA group (n = 62)	χ^2/t	p
Gender				
Male	38 (61.29)	35 (56.45)	0.300	0.584
Female	24 (38.71)	27 (43.55)		
Age (years)	50.62 ± 3.41	50.29 ± 4.25	0.477	0.634
BMI (kg/m²)	25.63 ± 2.33	25.72 ± 2.34	0.215	0.830
ASA grade	11 (17.74)	14 (22.58)		
I	29 (46.77)	30 (48.39)	0.777	0.678
II	22 (35.48)	18 (29.03)		
III				
Type of surgery				
Lithotripsy of ureteral calculi	12 (19.35)	14 (22.58)	0.585	0.989
Urethroplasty	3 (4.84)	4 (6.45)		
Excision of renal cyst	10 (16.13)	9 (14.52)		
Removal of renal calculi	13 (20.97)	12 (19.35)		
Excision of renal tumor	15 (24.19)	13 (20.97)		
Excision of bladder tumor	9 (14.52)	10 (16.13)		

OA: opioid anesthesia; OFA: opioid-free anesthesia; BMI: body mass index; ASA: American Society of Anesthesiologists.

significant differences between OA group and OFA group at T_0 ($p > 0.05$). At T_1-T_3, HR, MAP, P_{mean}, and $P_{ET}CO_2$ all increased in OA group compared with those at T_0 ($p < 0.05$), and they also increased in OFA group compared with those at T_0, but there were no statistically significant differences ($p > 0.05$). At T_1-T_3, HR, MAP, P_{mean}, and $P_{ET}CO_2$ were all lower in OFA group than those in OA group ($p < 0.05$) (Table 2).

Perioperative homeostasis

The levels of homeostasis indicators (Cor, ACTH, CRP, and IL-6) had no statistically significant differences between OA group and OFA group at T_a ($p > 0.05$). At T_b-T_c, they were all higher in both groups than those at T_a ($p < 0.05$), while they were lower in OFA group than those in OA group ($p < 0.05$) (Table 3).

Anesthetic efficacy

The anesthetic efficacy had no statistically significant difference between OA group and OFA group ($p > 0.05$) (Table 4).

Table 2. Levels of respiratory and circulatory system indicators ($\bar{x} \pm s$)

Indicator	Time point	OA group (n = 62)	OFA group (n = 62)	t	p
HR (beat/min)	T_0	76.89 ± 10.73	76.93 ± 10.32	0.022	0.983
	T_1	86.67 ± 7.93	77.89 ± 7.09	6.499	< 0.001
	T_2	96.76 ± 10.15	79.43 ± 9.22	9.951	< 0.001
	T_3	84.52 ± 8.93	80.92 ± 8.15	2.345	0.021
MAP (mmHg)	T_0	85.42 ± 9.91	85.53 ± 9.98	0.062	0.951
	T_1	94.62 ± 8.93	87.71 ± 9.42	4.192	< 0.001
	T_2	104.53 ± 10.32	88.92 ± 9.87	8.607	< 0.001
	T_3	96.78 ± 10.34	87.45 ± 7.93	5.638	< 0.001
P_{mean} (cmH_2O)	T_0	32.15 ± 2.19	32.18 ± 2.22	0.076	0.740
	T_1	36.74 ± 3.33	33.42 ± 3.89	5.105	< 0.001
	T_2	39.09 ± 3.12	35.71 ± 3.51	5.667	< 0.001
	T_3	36.18 ± 3.52	34.29 ± 3.20	3.128	< 0.001
$P_{ET}CO_2$ (mmHg)	T_0	3.10 ± 0.24	3.12 ± 0.23	0.474	0.637
	T_1	4.12 ± 0.20	3.67 ± 0.21	12.220	< 0.001
	T_2	5.89 ± 0.42	3.98 ± 0.16	33.460	< 0.001
	T_3	4.32 ± 0.14	3.71 ± 0.13	25.140	< 0.001

OA: opioid anesthesia; OFA: opioid-free anesthesia; T_0: 10 min before anesthesia; T_1: at the time of anesthesia induction; T_2: 10 min after anesthesia; T_3: 30 min after anesthesia; HR: heart rate; MAP: mean arterial pressure; P_{mean}: mean airway pressure, $P_{ET}CO_2$: partial pressure of end-tidal carbon dioxide.

Table 3. Perioperative homeostasis ($\bar{x} \pm s$)

Indicator	Time point	OA group (n = 62)	OFA group (n = 62)	t	p
Cor (ng/mL)	T_a	123.42 ± 10.79	123.51 ± 10.86	0.046	0.963
	T_b	165.82 ± 18.93	143.44 ± 11.73	7.913	< 0.001
	T_c	150.92 ± 13.54	130.92 ± 10.02	9.349	< 0.001
ACTH (pg/mL)	T_a	24.53 ± 2.06	24.56 ± 2.13	0.080	0.937
	T_b	48.07 ± 6.89	33.19 ± 2.34	16.100	< 0.001
	T_c	30.42 ± 3.41	27.80 ± 2.31	5.009	< 0.001
CRP (ng/mL)	T_a	334.52 ± 48.91	334.61 ± 47.93	0.010	0.992
	T_b	469.08 ± 55.03	389.09 ± 41.28	9.156	< 0.001
	T_c	400.01 ± 45.81	352.01 ± 28.93	6.976	< 0.001
IL-6 (pg/mL)	T_a	10.32 ± 1.17	10.54 ± 1.09	1.083	0.281
	T_b	23.51 ± 1.23	18.90 ± 3.29	10.330	< 0.001
	T_c	18.98 ± 1.28	14.28 ± 2.13	14.890	< 0.001

OA: opioid anesthesia; OFA: opioid-free anesthesia; T_a: 10 min before anesthesia; T_b: at the end of operation; T_c: 24 h after operation; Cor: cortisol; ACTH: adrenocorticotropic hormone; CRP: C-reactive protein; IL-6: interleukin-6.

Table 4. Anesthetic efficacy (n [%])

Anesthetic efficacy	OA group (n = 62)	OFA group (n = 62)	χ^2	p
Excellent	45	43		
Good	12	15		
Poor	5	4		
Excellent/good rate	57 (91.34)	58 (93.55)	0.120	0.729

OA: opioid anesthesia; OFA: opioid-free anesthesia.

Table 5. Anesthetic safety (n [%])

Adverse reaction	OA group (n = 62)	OFA group (n = 62)	χ^2	p
Nausea and vomiting	3	2		
Bucking	1	0		
Dysphoria	2	1		
Respiratory depression	3	0		
Urinary retention	3	0		
Total incidence rate	12 (19.35)	3 (4.84)	6.143	0.013

OA: opioid anesthesia; OFA: opioid-free anesthesia.

Anesthetic safety

In OFA group, the anesthetic safety was higher, that is, the incidence of anesthesia-related adverse reactions was lower, than that in OA group ($p < 0.05$) (Table 5).

Post-operative recovery time

There was no significant difference in the recovery time of spontaneous breathing ([10.43 ± 1.29] vs. [10.47 ± 1.33] min), awakening time ([6.78 ± 0.89] vs. [6.90 ± 0.81] min) or observation time ([54.63 ± 4.51] vs. [54.89 ± 4.82] min) between OA and OFA groups ($p > 0.05$).

Incidence rate of post-operative cognitive impairment

The incidence rate of cognitive impairment in OFA group was lower than that in OA group at 12 h after the operation ($p < 0.05$), while it had no statistically significant difference between the two groups at 24 and 48 h after the operation ($p > 0.05$) (Table 6).

Table 6. Incidence rate of post-operative cognitive impairment (n [%])

Indicator	OA group (n = 62)	OFA group (n = 62)	χ^2	p
12 h after operation	14 (22.58)	4 (6.45)	6.499	0.011
24 h after operation	3 (4.84)	2 (3.23)	0.208	0.648
48 h after operation	1 (1.61)	0	1.008	0.315

OA: opioid anesthesia; OFA: opioid-free anesthesia.

Discussion

Opioid anesthetics have a good analgesic effect in traditional general anesthesia and solve many clinical problems. However, they have been gradually abused in clinical surgery due to the limitation of the quantitative evaluation method of pain, and the number of deaths due to opioids is increasing[6]. To solve the above problem, OFA has been gradually applied in general anesthesia. OFA combines a variety of non-opioid anesthetics, improving the safety of anesthetics, such as non-steroidal anti-inflammatory drugs, acetaminophen, sodium channel antagonists, and α_2-receptor agonists[7-9].

Studies have shown that lidocaine, a sodium channel antagonist, can reduce the dosage of analgesics during operation, effectively relieve the body stress response, and maintain hemodynamic stability[10,11]. Moreover, lidocaine intravenously injected can effectively relieve the internal environment disturbance caused by tracheal intubation and reduce the interference of tracheal intubation on the patient's autonomic nerve during the induction of general anesthesia[12,13]. Hanson et al.[14] found that as compared to ultrasound-guided unilateral single-injection TAP block, continuous infusion of lidocaine could achieve non-inferior post-operative analgesia without causing internal environment disturbance during the first 24 h after renal transplantation. Besides, dexmedetomidine is an α_2-receptor agonist and one of the most commonly used alternatives to opioids in OFA, which has a wide range of effects, such as sedation, analgesia, antianxiety, and anti-post-operative nausea and vomiting[15,16]. It has been found[17] that dexmedetomidine can activate α_2-receptors in the central nervous system to increase the vagus nerve activity, reduce the sympathetic outflow, and block peripheral ganglia, thereby exerting an anti-sympathetic effect. It has been reported[18,19] that dexmedetomidine inhibits the release of Cor through restraining the excitability of sympathetic nervous system, thus keeping homeostasis. Wang et al.[20] applied dexmedetomidine plus propofol IV

anesthesia in pediatric urological laparoscopic surgery and found that dexmedetomidine plus propofol IV anesthesia might help shorten the extubation time, recovery time, and residence time in anesthesia recovery room, improve the analgesic effect, and reduce the inflammatory response and expression of serum inflammatory cytokines, without increasing the risk of adverse reactions. In this study, OFA with lidocaine plus dexmedetomidine was used in renal cyst decompression by laparoscopy. The results showed that the anesthetic effect and post-operative recovery time were comparable between the two groups, but the incidence rate of adverse reactions was lower in OFA group, suggesting that OFA can reduce the incidence of anesthesia-related adverse reactions while ensuring the quality of anesthesia, which can be used for anesthesia in renal cyst decompression by laparoscopy.

According to studies[21-23], the patients are prone to respiratory and circulatory system disorders, and homeostasis changes under the stimulation of surgery and anesthesia, during which the expressions of Cor and ACTH will rise. With the increase in Cor, the secretion of CRP and IL-6 is enhanced. Therefore, the patient's homeostasis is often clinically assessed by Cor, ACTH, CRP, and IL-6. In this study, the influences of different anesthesia modes on the respiratory and circulatory system and homeostasis were analyzed. The results showed that compared with OA, OFA did not lead to respiratory and circulatory system disorders and homeostasis changes. In addition, the incidence of post-operative cognitive impairment was analyzed in the two groups. It was found that the incidence rate of cognitive impairment was lower in the OFA group than that in OA group at 12 h after the operation, but it had no significant difference between the two groups at 24 and 48 h after the operation. It can be inferred that OFA can lower the risk of post-operative short-term cognitive impairment and facilitate rapid post-operative cognitive recovery, further verifying the safety of OFA.

Conclusion

OFA and OA have comparable anesthetic effects on renal cyst decompression by laparoscopy. OFA is more beneficial to the respiratory and circulatory system and homeostasis of patients, has higher anesthetic safety, and contributes to rapid post-operative recovery, so it is potentially applicable to clinical practice.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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