

Original Article

Effects of dezocine combined with propofol on cognitive function and complement levels of patients with hysteromyoma undergoing laparoscopic surgery

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Abstract: Objective: To determine the influence of dezocine combined with propofol on the cognitive function and complement levels of patients with hysteromyoma undergoing laparoscopic surgery. Methods: Altogether 125 patients with hysteromyoma in our hospital between March 2015 and July 2019 were enrolled, of which 67 patients were treated with dezocine combined with propofol as an observation group, while others were treated with propofol combined with remifentanyl as a control group. The anesthesia indexes of the two groups were compared, and the blood pressure and heart rate (HR) of them were evaluated. Additionally, the visual analog scale (VAS) was adopted to evaluate the pain degree of patients in different time periods after operation, and the Mini-Mental State Examination (MMSE) was performed to evaluate the cognitive function of the patients. The expressions of complement C3 and C4 and inflammatory factors in patients from the two groups were quantified, and the adverse reactions of them were evaluated and recorded. Results: The improvement of anesthesia indexes, blood pressure, and heart rate in the observation group was significantly better than that in the control group, and the VAS score of the observation group was lower than that of the control group at 6, 12, and 24 h after operation. Additionally, the MMSE score and C3 and C4 levels of the observation group were all significantly higher than those of the control group, and the levels of inflammatory factors and total incidence of adverse reactions in the observation group were significantly lower than those in the control group. Conclusion: For patients undergoing laparoscopic hysteromyomectomy, infusion anesthesia with both dezocine and propofol can effectively alleviate their inflammatory response, reduce their postoperative pain and postoperative complications, and improve the postoperative cognitive function and complement levels.

Keywords: Dezocine, propofol, laparoscopic surgery, hysteromyoma, cognitive function, complement

Introduction

Hysteromyoma is the most common female pelvic tumor, which is caused by the proliferation of uterine smooth muscle cells [1, 2]. Hysteromyoma usually has no obvious clinical symptoms, but sometimes it is manifested by increased menstrual blood volume, abdominal constriction, or dysmenorrhea [3, 4]. With the progression of hysteromyoma, the tumor volume in the body keeps increasing, causing difficulty in urination and defecation [5]. At present, hysteromyoma is mostly removed by surgery, among which laparoscopic surgery causes less trauma and pain, and can accelerate postoperative recovery and provide better curative effect [6, 7]. However, during the surgery, it is

required to carry out general anesthesia and establish pneumoperitoneum. Under the stimulation of such sudden stimulation factors, the body will release inflammatory medium, resulting in low immunity of patients and compromising postoperative recovery [8-10]. Therefore, it is extremely important to select effective anesthesia measures to ensure the safety of surgery.

Dezocine is a novel synthetic opioid analgesic with a powerful activity of κ receptor agonist and μ -opioid antagonist. Research shows that dezocine has been widely adopted to treat postoperative and cancerous pain because of its unique analgesic ability [11]. One study by Zhang and others has pointed out that dezocine

can reduce the incidence and severity of post-operative catheter-related bladder discomfort, without causing related adverse reactions in clinical practice [12], and one other study by Zhou and others has revealed that for patients undergoing laparoscopic cholecystectomy, administration of dezocine contributes to better postoperative pain control with less side effects and can reduce the consumption of patient-controlled analgesia [13]. Propofol is an intravenous drug widely used to induce and maintain anesthesia. It is currently widely used for patients in intensive care units (ICU) and anesthesia maintenance because of its anti-inflammatory and antioxidant activities [14, 15]. One study by Bhakta and others has shown that compared with conventional anesthesia, anesthesia with propofol can accelerate the postoperative recovery of patients undergoing gynecologic laparoscopic surgery [16]. However, since propofol is a short-acting intravenous anesthetic with mediocre analgesic effect and cannot alleviate the pain caused by operation, dezocine is used along with propofol for anesthesia induction in this study. One study by Li and others has demonstrated that for patients undergoing gastroscopy or colonoscopy, dezocine combined with propofol not only requires less propofol, but also can lower the risk of causing inhibitory effect on cardiovascular and respiratory systems, enhance the analgesic effect, shorten the anesthesia wake-up time, and improve the anesthesia wake-up quality [17].

At present, there are few studies on dezocine combined with propofol in patients with hystero myoma undergoing laparoscopic surgery. This study analyzed the effects of dezocine combined with propofol on the cognitive function and complement levels of patients with hystero myoma undergoing laparoscopic surgery and anesthetic efficacy, with the goal of providing better reference basis for the treatment of such patients.

General materials

Materials and methods

Altogether 125 patients with hystero myoma in our hospital from March 2015 to July 2019 were enrolled, and assigned to an observation group (obs group, n=67) and a control group (con group, n=58) according to anesthesia

methods. Patients in the obs group received target controlled infusion (TCI) of dezocine combined with propofol, while those in the con group received TCI of propofol combined with remifentanyl. This study was approved by the ethics committee of our hospital, and all participants were informed of the study in detail, and signed complete informed consent forms. The inclusion criteria of the study: patients diagnosed with hystero myoma [18], patients without contraindications to laparoscopic surgery, patients without an allergic history to drugs used in this study, and those with detailed general clinical data. The exclusion criteria of the study: Patients who dropped out from the study midway, patients with cognitive dysfunction, patients unable to complete the scoring of the cognitions scale, patients with other comorbid organ dysfunctions or hemorrhagic diseases, patients with a history of infection before surgery, patients who had taken drugs that had a impact on the indexes of this study, and those lost to follow up.

Anesthesia methods

Each patient in the two groups fasted for 8 h before surgery, and a venous channel was established for the patient after he/she entered the operating room. Then the electrocardiogram, blood pressure, as well as pulse blood oxygen saturation of the patient were monitored. During this process, the patient was in a lithotomy position. The patient was intramuscularly injected with 0.01 mg/kg penethyclidine hydrochloride (XY-100931, Xiyuan Biotechnology Co., Ltd., Shanghai, China) to prepare for tracheal intubation. Anesthesia induction was carried out as follows: The patient was given 4 mg midazolam (H10980025, Nhwa Pharmaceutical Co., Ltd., Jiangsu, China), 2 mg/kg propofol (CY19852, Chreagen Biotechnology Co., Ltd., Beijing, China), as well as 0.6 mg/kg rocuronium bromide (H20103495, North China Pharmaceutical Co., Ltd., Shijiazhuang, China). After satisfactory anesthesia induction, tracheal intubation was carried out. In addition, each patient in the con group received TCI of propofol combined with remifentanyl: The patient was continuously infused with 0.1 µg/kg-min remifentanyl (H20143315, Nhwa Pharmaceutical Co., Ltd., Jiangsu, China), and 2 min later, the patient was injected intravenously with 1.5 mg/kg propofol. In contrast, each patient in the

obs group received TCI of dezocine (H2008-0328, Yangtze River Pharmaceutical Group, Tianjin, China) combined with propofol: First, the patient was injected intravenously with 0.1 mg/kg dezocine, and 2 min later, the patient was injected intravenously with 1.5 mg/kg propofol. When the patient lost his/her consciousness, abdominal surgery was performed. During the operation, close attention was paid to the respiration, blood pressure, as well as heart rate (HR) of each patient in the two groups to prevent hypotension, bradycardia, and respiratory depression. Patients with respiratory depression were given oxygen inhalation via mask or pressure treatment, and patients with reduced blood pressure were given fluid infusion and blood pressure boosting treatment. Patients with bradycardia were given atropine.

Outcome measures

Comparison of anesthesia indexes: The operation time, postoperative consciousness recovery time, postoperative awakening time, spontaneous breathing recovery time, and orientation recovery time experienced by the two groups were evaluated.

Recording of blood pressure and HR: The systolic blood pressure (SBP), HR, and diastolic blood pressure (DBP) of the two groups before induction, before intubation, and after intubation were recorded.

Pain scoring in different time periods: The pain of each patient in the two groups at 6, 12, and 24 h after operation was scored using the visual analog scale (VAS) [19]. The scoring criteria: a movable 10 cm scale was adopted, which was divided into 10 scales. The scale of 0 point indicated painless, and a scale closer to the scale of 10 points indicated more severe pain.

Scoring with the Mini-Mental State Examination (MMSE) [20]: MMSE was adopted to evaluate the cognitive function of each patient in the two groups before and after operation. MMSE has a full score of 30 points, and a lower score indicates more severe cognitive dysfunction.

Determination of complement and inflammatory factors: Venous blood (5 mL) was sampled from each patient in the two groups before and after operation, centrifuged at 1500×g and 4°C for 10 min, and stored in a refrigerator at -70°C

for later analysis. The serum complement C3 and C4 in both groups before and after operation were quantified using the immunity transmission turbidity, and the C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor- α (TNF- α) in patients from the two groups before and after operation were quantified using a enzyme-linked immuno-sorbent assay (ELISA) with a CRP kit (EY-D9154, Yiyao Biotechnology Co. Ltd., Shanghai, China), IL-6 kit (70-EK106/2, MultiSciences (Lianke) Biotech Co., Ltd., Hangzhou, China), IL-10 kit (ant-112-0.5 mg, Jingke Chemical Technology Co., Ltd., Shanghai, China), and TNF- α kit (AT23561S/M, Sciben Biotech Co., Ltd., Nanjing, China), respectively, according to the kit instructions [21].

Adverse reactions: The incidence of adverse reactions in both groups after operation was recorded.

Statistical analyses

In this study, data were analyzed statistically using SPSS21.0 (EASYSO Company, China). Enumeration data were expressed as the number of cases/percentage (n/%), and inter-group comparison of them was carried out using the chi-square test. Data with theoretical frequency in chi-square test less than 5 were analyzed using the continuity correction chi square test. Measurement data were expressed as the mean \pm standard deviation (mean \pm SD), compared between groups using the independent-samples T test, and compared within groups before and after one time point using the paired t test. Expression at multiple time points was analyzed using the repeated measures analysis of variance, and expressed by F. $P < 0.05$ implies a significant difference.

Results

General materials

There was no significant difference between the obs group and the con group in clinical baseline data including age, body mass index, place of residence, nationality, educational background, myoma type, myoma size (cm), American Society of Anesthesiologists (ASA) classification, smoking history, drinking history, and number of uterine leiomyomas (all $P > 0.05$). See **Table 1**.

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Table 1. Comparison of general data between two groups [n (%)]/(mean \pm SD)

Item	The observation group (n=67)	The control group (n=58)	t/ χ^2 value	P-value
Age (Y)	38.94 \pm 4.23	38.85 \pm 4.21	0.118	0.905
BMI (kg/m ²)	22.68 \pm 3.45	23.01 \pm 3.56	0.525	0.600
Place of residence			1.471	0.225
Urban area	35 (52.24)	24 (41.38)		
Rural area	32 (47.76)	34 (58.62)		
Nationality			0.691	0.405
Han nationality	43 (64.18)	33 (56.90)		
Minority nationality	24 (35.82)	25 (43.10)		
Education background			1.618	0.203
\geq senior high school	34 (50.75)	36 (62.07)		
< senior high school	33 (49.25)	22 (37.93)		
Smoking history			0.039	0.842
Yes	37 (55.22)	31 (53.45)		
No	30 (44.78)	27 (46.55)		
Drinking history			3.231	0.072
Yes	32 (47.76)	37 (63.79)		
No	35 (52.24)	21 (36.21)		
Myoma type			3.622	0.057
Subserous myomas	29 (43.28)	35 (60.34)		
Intramural hysteromyoma	38 (56.72)	23 (39.66)		
Myoma size (cm)	4.53 \pm 1.02	4.61 \pm 1.05	0.431	0.666
ASA classification			0.180	0.671
Level I	45 (67.16)	41 (70.69)		
Level II	22 (32.84)	17 (29.31)		
Number of uterine leiomyomas	2.14 \pm 0.24	2.21 \pm 0.31	1.421	0.157

Table 2. Comparison of anesthesia indexes between the two groups (mean \pm SD)

Group	The number of patients	Operation time/min	Postoperative consciousness recovery time/min	Postoperative awakening time/min	Spontaneous breathing recovery time/min	Orientation recovery time/min
The observation group	67	94.24 \pm 6.35	7.73 \pm 1.68	10.08 \pm 2.04	4.78 \pm 0.68	21.17 \pm 3.21
The control group	58	96.89 \pm 6.36	11.46 \pm 1.94	18.67 \pm 2.14	7.31 \pm 0.73	27.36 \pm 3.43
t	-	2.325	11.520	22.950	20.050	10.420
P-value	-	0.021	<0.001	<0.001	<0.001	<0.001

Comparison of anesthesia indexes between the two groups

The operation time of the obs group was significantly shorter than that of the con group ($P<0.05$), and the postoperative consciousness recovery time, postoperative awakening time, spontaneous breathing recovery time, and orientation recovery time experienced by the obs group were greatly shorter than those experienced by the con group (all $P<0.05$). See **Table 2**.

Comparison of blood pressure and HR between the two groups in different time periods

There was no significant difference between the two groups in SBP, DBP, and HR before induction (all $P<0.05$), and SBP, DBP, and HR of both groups before and after intubation were lower than those before induction (all $P<0.05$). Additionally, after intubation, SBP, DBP, as well as HR of both groups decreased (all $P>0.05$), and the levels of them in the obs group were significantly lower than those in the con group

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Table 3. Comparison of blood pressure and HR between the two groups in different time periods (mean \pm SD)

Group	The number of patients	SBP (mmHg)			DBP (mmHg)			HR (times/min)		
		Before induction	Before intubation	After intubation	Before induction	Before intubation	After intubation	Before induction	Before intubation	After intubation
The observation group	67	131.37 \pm 6.52	94.68 \pm 3.29	101.45 \pm 3.04	89.14 \pm 3.27	63.45 \pm 4.07	70.47 \pm 3.48	86.47 \pm 3.21	66.45 \pm 3.79	80.38 \pm 3.06
The control group	58	130.21 \pm 6.54	98.47 \pm 3.35	104.53 \pm 3.37	88.45 \pm 3.25	67.75 \pm 3.68	80.87 \pm 3.74	86.05 \pm 3.53	73.58 \pm 3.47	84.68 \pm 3.22
t	-	0.990	6.369	5.371	1.180	6.157	16.090	0.696	10.910	7.647
P-value	-	0.323	<0.001	<0.001	0.240	<0.001	<0.001	0.487	<0.001	<0.001

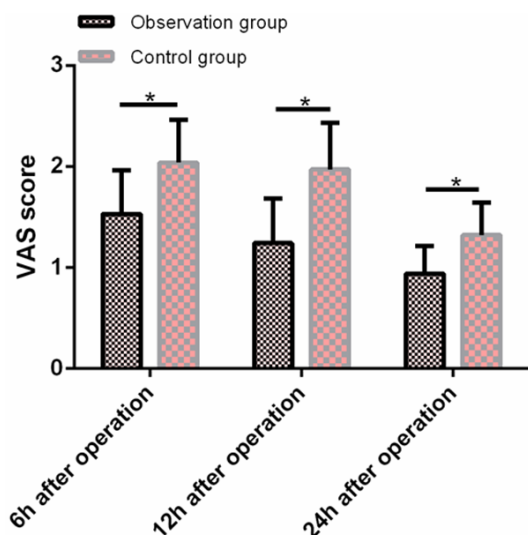


Figure 1. Comparison of VAS score between the two groups of patients in different time periods after operation. Comparison of VAS score between the two groups at 6 h, 12 h and 24 h after operation. Note: * indicates $P<0.05$.

before and after intubation (all $P<0.05$). See **Table 3**.

Comparison of VAS score between the two groups in different time periods after operation

The VAS score of both groups decreased significantly with time ($P<0.05$), and the score of the obs group was significantly lower than that of the con group at 6, 12, and 24 h after operation (all $P<0.05$). See **Figure 1**.

Comparison of MMSE score between the two groups before and after operation

There was no significant difference between the two groups in MMSE score before operation ($P>0.05$). After operation, the MMSE score of the obs group did not change significantly ($P>0.05$), but the score of the con group decreased significantly ($P<0.05$), and the MMSE score of the con group was significantly lower than that of the obs group ($P<0.05$). See **Figure 2**.

Comparison of complement levels between the two groups before and after operation

There was no significant difference between the two groups in the levels of C3 and C4 before

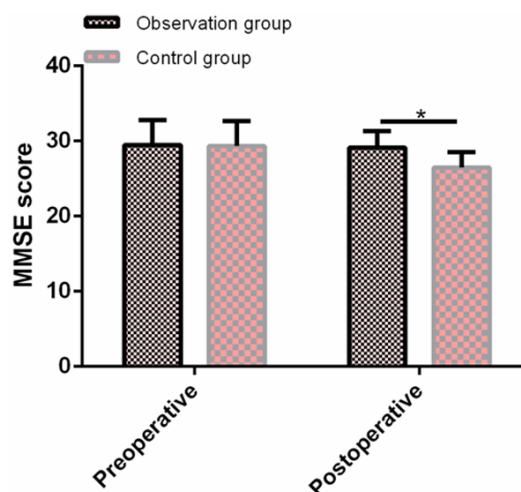


Figure 2. Comparison of MMSE score between the two groups before and after operation. Comparison of MMSE score between the two groups before and after operation. Note: * indicates $P<0.05$.

operation (both $P>0.05$), while the levels of them in both groups decreased greatly after operation (both $P<0.05$), and the degree of decrease in the con group was higher than that in the obs group ($P<0.05$). See **Table 4**.

Comparison of inflammatory factor levels between the two groups before and after operation

Before operation, there was no significant difference between the two groups in the levels of CRP, IL-6, IL-10, as well as TNF- α (all $P>0.05$), while after operation, the levels of them in both groups increased greatly (all $P<0.05$), and the degree of increase in the obs group was greatly lower than that in the con group ($P<0.05$). See **Table 5**.

Comparison of postoperative adverse reactions between the two groups

The total incidence of adverse reactions in the obs group was significantly lower than that in the con group (7.46% vs. 20.69%, $P<0.05$). See **Table 6**.

Discussion

Hysteromyoma is a hormone-dependent benign tumor [22]. With a relatively high prevalence rate, it has affected 20% to 60% of reproductive women and may bring about a negative impact on fertility and pregnancy outcome [23].

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Table 4. Comparison of complement levels between the two groups before and after operation (mean \pm SD)

Group	The number of patients	C3 (mg/L)		C4 (mg/L)	
		Before operation	After operation	Before operation	After operation
The observation group	67	1.34 \pm 0.32	1.16 \pm 0.34	0.26 \pm 0.05	0.18 \pm 0.06
The control group	58	1.29 \pm 0.29	0.92 \pm 0.14	0.24 \pm 0.08	0.12 \pm 0.04
t	-	0.909	5.018	1.699	6.470
P-value	-	0.364	<0.001	0.091	<0.001

Table 5. Comparison of inflammatory factor levels between the two groups before and after operation (mean \pm SD)

Group	The number of patients	CRP (mg/L)		IL-6 (pg/ml)		IL-10 (ng/L)		TNF- α (ng/mL)	
		Before operation	After operation	Before operation	After operation	Before operation	After operation	Before operation	After operation
The observation group	67	1.66 \pm 0.27	6.73 \pm 0.31	10.68 \pm 3.27	13.26 \pm 3.42	8.54 \pm 2.12	35.47 \pm 8.64	8.19 \pm 2.53	13.45 \pm 4.02
The control group	58	1.64 \pm 0.29	8.56 \pm 0.34	10.59 \pm 3.34	17.02 \pm 3.57	8.62 \pm 2.14	30.92 \pm 8.64	8.23 \pm 2.56	17.69 \pm 4.13
t	-	0.399	31.470	0.151	6.006	0.209	2.936	0.087	5.807
P-value	-	0.690	<0.001	0.879	<0.001	0.834	0.004	0.930	<0.001

Table 6. Total incidence of postoperative adverse reactions in the two groups [n (%)]

Group	The number of patients	Abdominal pain	Diarrhea	Nausea and vomiting	Restlessness	Shortness of breath	The total incidence
The observation group	67	1 (1.49)	1 (1.49)	2 (2.99)	1 (1.49)	0 (0.00)	5 (7.46)
The control group	58	2 (3.45)	1 (1.72)	4 (6.90)	3 (5.27)	2 (3.45)	12 (20.69)
χ^2	-	0.507	0.010	1.041	1.359	2.348	4.629
P-value	-	0.476	0.918	0.307	0.243	0.125	0.031

At present, surgery has become the main treatment method for hysteromyoma. In the past few years, as the female reproductive age gets older, the incidence rate of hysteromyoma is increasing annually, and laparoscopic minimally invasive surgery that only resects uterine fibroids to maintain fertility has been widely accepted [24]. However, laparoscopic surgery is prone to causing certain stress, and postoperative pain and cognitive dysfunction are still the main problems affecting the recovery of patients [25]. Therefore, it is of great significance to give reasonable anesthesia to patients during the surgery to improve the therapeutic effect on hysteromyoma after laparoscopic hysteromyomectomy.

In this study, we adopted dezocine combined with propofol to intervene with patients undergoing laparoscopic hysteromyomectomy, finding that combination of them effectively improved the prognosis of the patients. One study by Xu and others has revealed that for patients undergoing indolent colonoscopy,

dezocine combined with propofol can reduce the operation time and increase the blood flow of gastric mucosa and it exerts a regulating effect on gastrointestinal function [26]. One other study by Ma and others has demonstrated that anesthesia through dezocine combined with propofol for patients undergoing painless gastroscopy can reduce respiratory depression and body movement without interfering with hemodynamics [27]. In this study, the operation time of the obs group was significantly shorter than that of the con group, and the postoperative consciousness recovery time, postoperative awakening time, spontaneous breathing recovery time, as well as orientation recovery time experienced by the obs group were also greatly shorter than those experienced by the con group, which implied that dezocine combined with propofol poses little influence on the respiratory and circulatory system of patients, and contributes to rapid and stable awakening of the patients after operation. In addition, the mitogen-activated protein (MAP), central venous pressure (CVP), and HR

of patients decreased greatly during intubation, and after intubation, they recovered to the levels before intubation, which suggested that intervention through dezocine combined with propofol poses no significant impact on the physiological indexes of patients, and can relax the bronchial smooth muscle of the patients, resist airway constriction, and protect the lung tissue of patients from injury. One study has pointed out that most women suffer unexpected postoperative pain in nursing wards after anesthesia for laparoscopic surgery [28]. In our study, VAS was adopted to evaluate the pain degree of patients in the two groups during different time periods after operation. It came out that the VAS score of the obs group was significantly lower than that of the con group at 6, 12, and 24 h after operation, indicating that dezocine combined with propofol can better relieve the postoperative pain of patients, and the analgesic effect of the combination of the two is better than that of a separate one.

Postoperative cognitive dysfunction is one of the common complications of surgical patients, which is mainly manifested by the weakening of orientation ability, memory, attention, and behavior ability, and the weakening of them will compromise the postoperative recovery of patients and the therapeutic effect on them [29, 30]. The clinical pathogenesis of postoperative cognitive dysfunction has not yet been fully elucidated. It is believed that factors such as anesthetic drugs and patients themselves are involved [31]. According to one study, the complement system plays an essential role in many nervous system diseases [32]. For example, activating complement signal transduction in orthopedic surgery can alleviate neuroinflammation and cognitive impairment. Studies have revealed that serum complement can effectively reflect the immune pathological injury and acute reaction of the body, and changes in its levels can help to judge the prognosis of patients [33, 34]. In this study, the MMSE score of the obs group was significantly higher than that of the con group, implying that dezocine combined with propofol would not reduce the cognitive function of the patients after operation, and it can contribute to faster postoperative awakening and avoid memory decline and recall delay after awakening. The complement determination results in this study showed that the levels of C3 and C4 in patients from the two groups decreased significantly after operation,

and the levels of them in the obs group were significantly higher than those in the con group after operation, suggesting that the complement levels in the two groups declined to different degrees after operation, but dezocine combined with propofol had less influence on the complement and immune function of the patients, so it can better promote the recovery of the body and reduce postoperative cognitive impairment. We also determined the expression of inflammatory factors in the two groups before and after operation. Some studies have revealed that various stimuli during the perioperative period will make the body in an excessive stress state, which breaks the normal balance of cytokine levels and greatly affects the prognosis and outcome of patients after operation [35, 36]. In this study, the levels of CRP, IL-6, IL-10, as well as TNF- α in the two groups increased significantly after operation, while increase degree in the obs group was significantly lower than that in the con group, indicating that combination of dezocine and propofol can alleviate the inflammatory response of patients undergoing laparoscopic surgery by inhibiting the release of inflammatory factors. One study by Yin and others has revealed that opioid drugs combined with propofol cause few adverse reactions in gastroscopy and would not lead to respiratory depression and chest wall muscle stiffness [37]. Moreover, the results of this study showed that the total incidence of adverse reactions in the obs group was significantly lower than that in the con group, which indicated that dezocine combined with propofol is safe.

The study has verified that dezocine combined with propofol is a feasible anesthesia scheme in laparoscopic hysteromyomectomy, but it still has some shortcomings. The life quality of the patients has not been analyzed, and the factors affecting the prognosis have also not been explored, so the study has certain limitations. In the future, it is necessary to extend the research time and follow up the patients after surgery to further support the research results.

To sum up, for patients undergoing laparoscopic hysteromyomectomy, infusion anesthesia with dezocine combined with propofol can effectively alleviate their inflammatory response, reduce their postoperative pain and postoperative complications, and improve the

postoperative cognitive function and complement levels of them.

Disclosure of conflict of interest

None.

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