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Study on the Clinical Anesthesia of Esketamine Combined with Propofol in Endoscopic Retrograde Cholangiopancreatography

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Abstract: *Objective: To observe the safety and effectiveness of the intravenous anesthesia of Esketamine and propofol in endoscopic retrograde cholangiopancreatography (ERCP). Method: 80 patients undergoing ERCP in our hospital were selected, aged 40-65 years old, the body mass index (BMI) 20-24, ASAI-II. They were divided into control group (40 cases) and observation group (40 cases) according to the random digital table. Patients in the control group received intravenous anesthesia by Dezocine combined with propofol, and patients in the observation group received intravenous anesthesia by Esketamine combined with Propofol. The patient's heart rate (HR), non-invasive systolic pressure (SBP), diastolic blood pressure (DBP) and pulse oxygen saturation (SPO2) at pre-anesthesia induction time (T0), induction immediate time (T1), the gastroscope immediate time (T2), the before-end time (T3), recovery immediate time (T4); recovery time and total amount of propofol, adverse reactions; the satisfaction of patients, anesthesia doctors and surgeons for the whole process were recorded. Results: There was no significant difference in blood pressure and heart rate difference between the two groups. Compared with the control group, the respiratory inhibition, postoperative dizziness, nausea of patients in Esketamine group decreased (P <0.01), the total use of propofol was less than the control group (P <0.05). The satisfaction of patients, anesthesia doctors and surgeons were superior to the control group (P <0.01). Conclusion: Esketamine combined with propofol for intravenous anesthesia can be safely and efficiently applied to ERCP. In the operation, the patients' breathing is stable and controllability is good with less postoperative adverse reactions. The satisfaction of patients and physicians is high. Thus, it has high clinical promotion value.*

Keywords: *ERCP, Esketamine, Intravenous anesthesia*

1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) as the gold standard for the diagnosis of extrahepatic bile duct stones, with an accuracy of more than 90%, has become an important method for the diagnosis and treatment of cholangiopancreatic diseases. However, invasive stimulation in the process of operation can bring discomfort to patients and even cause serious cardiovascular complications [1]. Therefore, intravenous general anesthesia for patients undergoing ERCP can greatly reduce the adverse reactions of patients during the operation, make patients comfortable through the perioperative period, and improve the success rate of operation. Studies have shown that opioids combined with propofol for painless endoscopy can reduce drug dosage and reduce the incidence of adverse reactions [2]. Esmketamine is a chiral cyclohexanone with strong analgesic effect, and it is also a separation anesthetic. Clinical dose of esmketamine can excite the sympathetic nervous system, increase blood pressure and pulse, and its sympathetic like characteristics can offset the inhibition of propofol on hemodynamics, so as to reduce the risk of cardiovascular and respiratory system [3]. Studies have shown that the anesthetic dose of esmketamine can produce good sedative and analgesic effects, do not inhibit the patient's respiratory center, but also maintain the tension of respiratory muscles and ensure the stability of patients' respiratory function during operation. It is more suitable for total intravenous anesthesia than opioids [4] [5]. The purpose of this study is to explore the anesthetic effect and safety of ketamine combined with propofol in ERCP, and to seek a more rational anesthetic

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method to guide clinical medication.

2. Data and Methods

2.1. General Data

The trial was approved by the ethics committee of Jingzhou central hospital. Before the trial, all participants were informed of the relevant test contents and possible risks in the research process. The patients in the experimental group and the control group and their families signed the informed consent form. Eighty patients aged between 40 and 65 who underwent ERCP surgery (ASA grade I-II) were included in this prospective randomized controlled single-blind study. They were divided into control group (40 cases) and observation group (40 cases). The control group was treated with dizocine combined with propofol intravenous anesthesia, and the observation group was treated with esmketamine combined with propofol intravenous anesthesia. Exclusion criteria: ASA III or above; Severe cardiopulmonary impairment; Severe impairment of liver and kidney function; Previous mental history or personality abnormality; Patients who can't clearly express their meaning or don't cooperate and can't communicate well; Severe chronic obstructive pulmonary disease; Reject the test; Have a long-term history of sedative or narcotic analgesics or alcohol abuse; Basal peripheral oxygen saturation < 90%, age > 65 years.

2.2. Anesthesia Method

All patients fasted the night before operation and did not receive preoperative medication. 20G venous indwelling needle was placed in the left or right anterior elbow area of the patient. During the operation, Ringer solution was continuously injected at the speed of 5ml /min until the recovery room was observed after the operation. 10 minutes before anesthesia, the patient took orally 10 ml of dacronin hydrochloride mucus (production batch No.: 20211350, Yangzi Pharmaceutical Group) to remove bubbles in the upper gastrointestinal cavity, so as to obtain a clear field of vision in endoscopic surgery. All patients were placed in prone position and inhaled oxygen through nasal catheter (4 L / min).

Anesthesia induction: the control group was given 5 mg of dizocine (production batch No.: 211105b, Yangzijiang Pharmaceutical Group), and the observation group was given 0.4 mg / kg of esmketamine (production batch No.: 202125bl, Jiangsu Hengrui Pharmaceutical Co., Ltd.). After 2 minutes, both groups were given 1 mg / kg of propofol (production batch No.: 21pl8667). After the patient's consciousness and eyelash reflex disappeared, the dose was maintained by anesthesia. The control group was given 60 UG / kg / h of dizocine combined with 3 mg / kg / h of propofol, The observation group was treated with esmketamine 0.5mg/kg/h combined with propofol 3mg / kg / h.

Both groups maintained the BIS value at 50-55, and propofol was stopped at the time of withdrawal. During the operation, if bis > 55, propofol 0.08-0.1mg/kg will be added appropriately according to the needs and patient conditions. If bis < 50 points, the infusion speed of propofol will be slowed down. During the operation, if the blood pressure is 30% lower than the basic value, give ephedrine 5mg, heart rate < 50 times / min, give atropine 0.2mg, SpO2 < 90% give mask assisted ventilation, and halve the infusion speed in the above cases.

2.3. Observation Index

The heart rate (HR), non-invasive systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse oxygen saturation (SpO2) were recorded before anesthesia induction (T0), immediately after induction (T1), immediately after gastroscopy passing through the throat (T2), immediately before the end (T3) and immediately after awakening (T4); Record the anesthesia time (the total time from the beginning of giving dezocine or esmketamine to the patient's recovery room), the recovery time and the total dosage of propofol; The occurrence of adverse reactions such as respiratory depression, nausea, vomiting and dizziness were recorded; Patients, anesthesiologists and surgeons use the visual analog scoring method to subjectively score the satisfaction of the whole examination process (10 scorse system, > 6 scores indicate satisfaction, > 8 scores indicate very satisfaction, < 4 scores indicate dissatisfaction, and < 2scores indicate very dissatisfaction).

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2.4. Statistical Analysis

SPSS 22.0 was used to analyze the data. The measurement data of normal distribution are expressed as mean ± standard deviation (SD) ($\bar{x} \pm s$). The comparison between groups adopts independent sample t-test, and the counting data is expressed as n (person time) percentage (%). The comparison between groups adopts x2 test, and the probability value $p < 0.05$ is considered to be statistically significant.

3. Result

3.1. General Information of Two Groups of Patients

There was no significant difference in age, sex ratio, BMI, ASA grade and operation time between the two groups ($P > 0.05$, see table 1).

Table 1: Age, sex ratio, BMI and ASA grade of patients in the two groups

Group	Number of Cases	Age(year, $\bar{x} \pm s$)	Sex Ratio(Male / Female)	BMI(kg/m2, $\bar{x} \pm s$)	ASA(I/II)
Control Group	40	56±7	27/13	23.5±1.5	5/35
Observation Group	40	56±7	28/12	23.0±1.2	7/33

3.2. Comparison of SBP, DBP, HR and SpO2 between the Two Groups at Each Time Point

There was no significant difference in SBP, DBP, HR and SpO2 between the two groups at each time point ($P > 0.05$, see table 2).

Table 2: Comparison of blood pressure, heart rate and SpO2 between the two groups at each time point

Index	Group	Number of Cases	T0	T1	T2	T3	T4
SBP (mmHg, $\bar{x} \pm s$)	Control Group	40	142±12	106±10	145±16	124±9	139±7
	Observation Group	40	137±13	109±11	139±15	130±10	138±8
DBP (mmHg, $\bar{x} \pm s$)	Control Group	40	80±11	68±7	85±6	73±10	79±9
	Observation Group	40	82±10	71±9	83±9	75±11	80±10
HR (times/min, $\bar{x} \pm s$)	Control Group	40	75±6	62±5	80±6	70±6	73±9
	Observation Group	40	73±7	65±6	82±7	71±8	75±8
SPO2 (%, $\bar{x} \pm s$)	Control Group	40	99±1	97±5	96±5	98±5	99±1
	Observation Group	40	99±2	97±2	97±2	99±2	99±1

3.3. Comparison of Adverse Reaction Rates between the Two Groups

The incidence of respiratory depression, dizziness, nausea and vomiting in the observation group was significantly lower than that in the control group ($P < 0.01$). See Table 3.

Table 3: Comparison of adverse reaction rates between the two groups

Group	Number of Cases	Respiratory Depression [case/(%)]	Nausea [case/(%)]	Vomiting [case/(%)]	Dizziness [case/(%)]
Control Group	40	20/50	8/20	6/15	25/62.5
Observation Group	40	5/12.5△	2/5△	1/2.5△	2/5△

Note: compared with the control group, △ $P<0.01$

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3.4. Comparison of Anesthesia Time (The Total Time from the Beginning of Giving Dezocine or Esmketamine to the Time When the Patients Can Return to the Recovery Room Safely), Recovery Time, Total Dosage of Propofol and Doctor-Patient Satisfaction between the Two Groups

There was no significant difference in anesthesia time and recovery time between the two groups ($P > 0.05$). The total amount of propofol used in the observation group was significantly less than that in the control group ($P < 0.01$), and the satisfaction of doctors and patients in the observation group was better than that in the control group ($P < 0.01$). See Table 4.

Table 4: Comparison of anesthesia, recovery time, total dosage of propofol and doctor-patient satisfaction between the two groups

Group	Number of Cases	Anesthesia time(min, $\bar{x} \pm s$)	recovery time(min, $\bar{x} \pm s$)	total amount of propofol(mg, $\bar{x} \pm s$)	satisfaction of patients (score)	Satisfaction of Anesthesiologists(score)	satisfaction of doctor(score)
Control Group	40	48±13	8±3	158±16	6±1.2	7±1	7±1.4
Observation Group	40	50±12	5±2	100±13△	9±2△	10±1△	9±2△

Note: compared with the control group, △$P<0.01$

4. Discussion

In ECPR surgery, while the patients are in prone position and take anesthesia, sedation and analgesia, we have been looking for ideal general anesthetics with slight or even no respiratory inhibition and less adverse reactions. However, at present, there is no one drug that can be met, and most of them are used in combination with several drugs.

In recent years, the combined application of propofol and opioids has become the standard of outpatient intravenous anesthesia. Propofol inhibits the cardiovascular system by inhibiting sympathetic nerve. A large dose can affect the patient's circulatory function and increase the risk of respiratory depression [6], but because it is mainly sedative and has weak analgesic effect [7], it needs to be combined with opioids for compatible anesthesia. Opioids, It has a certain inhibitory effect on respiration, and there are many adverse reactions. At present, the concept advocated in the perioperative period of accelerated rehabilitation surgery is weak opioid anesthesia or opioid analgesia. Esmketamine is a dextral isomer isolated from ketamine. Its pharmacological characteristics are similar to ketamine. It produces general anesthesia and analgesia by blocking NMDA receptor conduction. Esmketamine has strong analgesic effect, fast onset, slight impact on respiration, does not inhibit the protective reflex of throat, has excitatory effect on circulatory system, and the incidence of adverse reactions is low [8] [9]. Studies have shown that esmketamine combined with propofol is used in the treatment of painless induced abortion and gastroenteroscopy. It is found that compared with propofol alone, the hemodynamics is more stable and the dosage of propofol is reduced; Compared with fentanyl, adverse reactions such as nausea, vomiting and respiratory depression were reduced [10].

The feasibility of ERCP combined with propofol and ketamine was compared. The results showed that esmketamine combined with propofol anesthesia had stable hemodynamics, mild respiratory inhibition, and less postoperative adverse reactions such as nausea, vomiting and dizziness. The satisfaction scores of patients, anesthesiologists and surgeons in the observation group were very satisfactory, which was significantly higher than that in the control group.

To sum up, the application of esmketamine combined with propofol in ERCP intravenous anesthesia has stable hemodynamics, small respiratory impact, less postoperative adverse reactions and good doctor-patient experience, which is worthy of clinical promotion.

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