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Original Research

Effects of dezocine and ropivacaine infiltration anesthesia on cellular immune function indicators, anesthesia recovery time and pain factors in patients with open liver resection

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Abstract: The current experiment was carried out to explore the effects of dezocine combined with ropivacaine infiltration anesthesia on the anesthesia recovery time and pain factors of patients with open hepatectomy. A prospective randomized controlled method was used to select 92 patients with open liver cancer resection in our hospital from August 2017 to November 2019. The patients were divided into a study group (n=46) and a control group (n=46) using a computer-generated random number table. Both groups underwent general anesthesia, based on this, the study group was treated with ropivacaine infiltration anesthesia 10 minutes before skin incision, and dezocine was given intravenously 0.5 h before surgery, the control group was anesthetized with ropivacaine 10 minutes before the incision, and was given a saline injection 0.5 h before the operation. Compared the recovery of anesthesia (recovery time of spontaneous breathing, time to open eyes, time to extubation), the incidence of adverse reactions, and cellular immune function indicators (peripheral blood $CD4^+$, $CD4^+/CD8^+$, NK cell levels), stress response indicators [serum blood glucose (Glu), norepinephrine (NE), adrenaline (E)], pain factors [serum dopamine (DA), neuropeptide Y (NPY), substance P (SP)] before induction of anesthesia (T_0), completion of surgery (T_1), 12 hours after surgery (T_2), and 24 hours after surgery (T_3) between the two groups, and the degree of pain (VAS score) at T_2 and T_3 were compared between the two groups. The levels of $CD4^+$, $CD4^+/CD8^+$, and NK cells in peripheral blood at T_1, T_2, and T_3 in the study group were higher than those in the control group ($P<0.05$); serum Glu, NE, and E levels in the study group at T_1, T_2, and T_3 were lower than those in the control group ($P<0.05$); serum DA, NPY, and SP levels in the study group at T_1, T_2, and T_3 were lower than those in the control group ($P<0.05$); the VAS scores of the study group at T_2 and T_3 were lower than those of the control group ($P<0.05$); the time of spontaneous breathing recovery, eyes opening and extubation in the study group were shorter than those in the control group ($P<0.05$); the incidence of restlessness (4.35%), transient hypertension (6.52%), and cough (2.17%) in the study group were lower than those in the control group ($P<0.05$). Dezocine and ropivacaine infiltration anesthesia can significantly shorten the recovery time of anesthesia and inhibit pain factor secretion in patients with open hepatectomy and can reduce the body's stress response after surgery, reduce immune function fluctuations, and can reduce the incidence of adverse reactions to anesthesia, and help promote patients' postoperative recovery.

Key words: Liver cancer; Open liver cancer resection; Dezocine; Ropivacaine; Infiltration anesthesia; Anesthesia recovery; Pain factor.

Introduction

Liver cancer means primary and metastatic malignant tumors in the liver, 85%~90% of which is primary liver cancer. With incidence rate ranking the third in malignant tumors of the digestive system, only second to gastric and esophageal cancers, it is one of the main diseases threatening human life safety (1). Surgery is an important approach for the treatment of liver cancer. Where, hepatectomy is more commonly used, but causes large surgical trauma, leading to postoperative immune stress response unconducive to postoperative recovery in patients (2). Literature reports show that postoperative pain is an important factor resulting in increased stress response and decreased immune function in patients (3). At present, analgesics or sedatives are mainly used in clinical practice to reduce postoperative stress response, which may easily cause adverse reactions such as respiratory depression or delayed wake-up. Ropivacaine, as amide local anesthetics, has dual effects of analgesia and anesthesia, which features low cardiotoxicity and neurotoxicity. Studies have shown that ropivacaine is safe and effective for postoperative analgesia (4). Dezocine as an opioid receptor agonist-antagonist can effectively overcome the abuse and body dependence caused by pure opioids, which has a good analgesic effect and exerts a small impact on the gastrointestinal tract and respiratory system (5). Based on this, this study analyzes for the first time the effects of dezocine and ropivacaine infiltration anesthesia on anesthesia recovery time and pain factors in patients with hepatectomy. The report is as follows.

Materials and Methods

General information

92 patients receiving hepatectomy in our hospital from August 2017 to November 2019 were selected by prospective randomized controlled trials, who were divided into a study group (n=46) and control group (n=46) based on computer-generated random number table. There are no significant differences in Child-Pugh classification of liver function (6), age, American

Table 1. Comparison of two groups of general information.

Project		Study group(n=46)	Control group(n=46)	t/χ^2	*P*
Gender (female/male)		18/28	20/26	0.179	0.672
Age (years)		48~72(59.35±5.66)	47~70(58.41±5.48)	0.809	0.421
Body mass(kg)		47~83(64.19±8.59)	45~80(63.50±8.24)	0.393	0.695
Clinical stage (cases)					
	PhaseIb	9(19.57)	10(21.75)		
	Phase II	21(45.65)	23(50.00)	0.554	0.290
	PhaseIIIa	16(34.78)	13(28.26)		
ASA grading (cases)					
	Grade I	21(45.65)	23(50.00)	0.174	0.676
	Grade II	25(54.35)	23(50.00)		
Child-Pugh classification of liver function (cases)					
	GradeA	27(58.70)	30(65.22)	0.415	0.519
	Grade B	19(41.30)	16(34.78)		

Society of Anesthesiologists (ASA) grading (7), body mass, clinical stage and gender between the two groups (P> 0.05), as shown in Table 1.

Selection criteria

Inclusion: (A) Meet the diagnostic criteria for liver cancer (8), and is confirmed by postoperative pathological diagnosis; (B) Clinical stage: stage Ib~IIIa; (C) Child-Pugh classification of liver function: grade A~B; (D) ASA grading: grade I~II; (E) first surgical treatment; (F) no contraindications to the drugs in this study; (G) no cognitive impairment; (H) elective surgical treatment, surgical tolerance; (I) patients and family members are aware of this study and have signed a consent form.

Exclusion: (A) patients with other malignant tumors and distant metastases of focus; (B) patients with hematological diseases; (C) patients with serious lesions in other organs such as heart, lung, brain, kidney, etc.; (D) patients with diabetes; (E) patients with communicable diseases or infectious diseases; (F) patients undergoing emergency surgery; (G) those who cannot cooperate with the researcher.

Methods

Both groups underwent hepatectomy by the same group of surgeons. The perioperative anesthesia was performed by the same group of anesthesiologists. The venous access opening was routinely performed to detect vital signs, and general anesthesia was given. Based on this, the study group was treated with 20 ml of 0.5% ropivacaine (Guangdong Jiabo Pharmaceutical Co., Ltd. H20173194) for infiltration anesthesia 10 min before the surgical incision, and was given an intravenous injection of 10 ml dezocine (Yangzijiang Pharmaceutical Group Co., Ltd. National Medicine Permission Number H20080329) 0.5 h before the surgery ended. The control group received ropivacaine infiltration anesthesia 10 min before skin incision, with the same usage and dosage as the study group. 10 ml of saline was injected intravenously 0.5 h before the surgery ended.

Observation indicators

The observation indicators were as the following.

(A) Cellular immune function indicators before anesthesia induction (T_0), at the end of surgery (T_1), 12 h after surgery (T_2) and 24 h after surgery (T_3) include peripheral blood $CD4^+$, $CD4^+/CD8^+$, NK cells. By collecting 2 ml peripheral venous blood from patients, the levels of $CD4^+$, $CD8^+$, NK cells were detected by NovoCyte D2061R type flow cytometer produced by ACEA Bio (Hangzhou) Co., Ltd., based on which $CD4^+/CD8^+$ level was calculated. (B) Stress response indicators at T_0, T_1, T_2 and T_3 in the two groups include serum glucose (Glu), norepinephrine (NE) and epinephrine (E) levels. 5 ml venous blood was collected from patients, centrifuged at 3000 r/min for 10 min to collect serum samples. Serum NE and E levels were measured by enzyme-linked immunosorbent assay, and serum Glu levels were measured by radioimmunoassay. The kits were purchased from Getein Biotech, Inc. (C) Pain factors at T_0, T_1, T_2 and T_3 in the two groups, including serum dopamine (DA), neuropeptide Y (NPY), substance P (SP) levels, were detected simultaneously with stress response indicators. Levels of the above indicators were measured by enzyme-linked immunosorbent assay. The kits were purchased from Getein Biotech, Inc. (D) The pain degree at T_2 and T_3 of the two groups were assessed using Visual Analogue Scales (VAS). The score ranges from 0 to 10 points, with 0 indicating no pain and 10 indicating the most severe pain. Higher values suggest more severe pain. (E) Anesthesia recovery in the two groups involves spontaneous breathing recovery time, eye-opening time and extubation time. (F) The incidence of adverse reactions (nausea, vomiting, restlessness, transient hypertension and cough) in the two groups was calculated.

Statistical methods

Data were processed using SPSS22.0 software. Measurement data were expressed as ($\bar{x} \pm s$) with a *t*-test conducted for comparison of difference, count data were expressed as n (%) with χ^2 test conducted for comparison of difference. P <0.05 suggests statistical significance.

Results

The level of cellular immune function indicators

The levels of peripheral blood $CD4^+$, $CD4^+/CD8^+$, NK cells at T_0 show no statistically significant difference between the two groups (P> 0.05); peripheral

blood $CD4^+$, $CD4^+/CD8^+$, NK cell levels are lower in T_1, T_2, T_3 than in T_0, but higher in the study group than in the control group (P <0.05), as shown in Table 2.

Levels of stress response indicators

Glu, NE and E levels at T_0 show no statistically significant difference between the two groups (P> 0.05); serum Glu, NE and E levels of both groups are higher at T_1, T_2, and T_3 than at T_0, but lower in the study group than in the control group (P <0.05), as shown in Table 3.

Serum pain factor level

Comparison of serum DA, NPY, and SP levels at T_0 between the two groups shows no statistically significant difference (P> 0.05). Serum DA, NPY and SP levels in both groups are higher at T_1, T_2 and T_3 than at T_0, but lower in the study group than in the control group (P <0.05), as shown in Table 4.

VAS score

At T_2 and T_3, the VAS score is lower in the study group than in the control group (P <0.05), as shown in Table 5.

Anesthesia recovery

The spontaneous breathing recovery time, eye-opening time and extubation time are shorter in the study group than in the control group (P <0.05), as shown in

Table 2. Comparison of cellular immune function indicators between the two groups($\bar{x}$ ±s).

Project	Group	No. cases	T_0	T_1	T_2	T_3
$CD4^+$(%)	Study group	46	36.84±6.61	28.95±5.39[a]	30.76±6.18[a]	32.39±6.97[a]
	Control group	46	37.16±7.24	22.61±6.08[a]	23.84±5.75[a]	25.92±6.24[a]
	t		0.221	5.292	5.560	4.691
	P		0.825	<0.001	<0.001	<0.001
$CD4^+/CD8^+$	Study group	46	1.24±0.26	1.08±0.21[a]	1.12±0.19[a]	1.14±0.24[a]
	Control group	46	1.30±0.22	0.85±0.18[a]	0.91±0.23[a]	0.96±0.26[a]
	t		1.195	5.640	4.774	3.450
	P		0.235	<0.001	<0.001	<0.001
NK cells(%)	Study group	46	22.06±5.39	18.25±4.60[a]	19.36±4.82[a]	20.17±5.05[a]
	Control group	46	21.47±6.16	14.74±4.26[a]	15.62±4.57[a]	16.94±5.28[a]
	t		0.489	3.797	3.819	2.998
	P		0.626	<0.001	<0.001	0.004

Table 3. Comparison of stress response indicators between the two groups($\bar{x}$ ±s).

Project	Group	Number of cases	T_0	T_1	T_2	T_3
Glu(mmol/L)	Study group	46	4.81±0.97	5.47±0.39[a]	6.02±0.54[a]	5.68±0.43[a]
	Control group	46	4.93±0.85	6.28±0.46[a]	6.97±0.69[a]	6.53±0.51[a]
	t		0.631	9.110	7.354	8.642
	P		0.530	<0.001	<0.001	<0.001
NE(pg/ml)	Study group	46	228.95±24.37	284.37±38.52[a]	346.72±46.65[a]	317.29±42.57[a]
	Control group	46	231.16±22.46	407.82±42.67[a]	539.04±54.83[a]	479.68±48.72[a]
	t		0.452	14.565	18.119	17.023
	P		0.652	<0.001	<0.001	<0.001
E(pg/ml)	Study group	46	69.71±12.46	76.74±13.64[a]	86.29±18.51[a]	81.95±15.27[a]
	Control group	46	70.63±11.50	104.37±17.93[a]	129.16±23.28[a]	114.62±20.85[a]
	t		0.368	8.318	9.776	8.574
	P		0.714	<0.001	<0.001	<0.001

Table 4. Comparison of serum pain factor levels between the two groups ($\bar{x}$ ±s).

Project	Group	Number of cases	T_0	T_1	T_2	T_3
DA(μmol/L)	Study group	46	42.79±5.48	69.07±8.41[a]	94.91±13.04[a]	78.52±11.60[a]
	Control group	46	43.42±5.71	102.13±14.27[a]	164.03±19.51[a]	136.68±17.92[a]
	t		0.540	13.537	19.977	18.479
	P		0.591	<0.001	<0.001	<0.001
NPY(pg/ml)	Study group	46	102.69±15.04	117.80±18.17[a]	142.62±21.93[a]	128.91±19.52[a]
	Control group	46	103.70±14.62	139.74±20.25[a]	175.36±26.14[a]	160.84±22.73[a]
	t		0.327	5.469	6.508	7.228
	P		0.745	<0.001	<0.001	<0.001
SP(μg/ml)	Study group	46	1.49±0.24	1.96±0.28[a]	2.38±0.36[a]	2.14±0.32[a]
	Control group	46	1.53±0.21	3.02±0.46[a]	4.76±0.58[a]	3.85±0.51[a]
	t		0.851	13.350	23.646	19.263
	P		0.397	<0.001	<0.001	<0.001

Table 5. Comparison of VAS scores between the two groups($\bar{x}$ ±s, score)

Group	Number of cases	T_2	T_3
Study group	46	3.37±1.29[a]	2.97±0.84[a]
Control group	46	5.06±1.42[a]	4.25±1.12[a]
t		5.975	6.201
P		<0.001	<0.001

Table 6.

Adverse reactions

The incidence of nausea and vomiting shows no statistically significant difference between the two groups (P> 0.05); the incidence of restlessness, transient hypertension, and cough is lower in the study group than in the control group (P <0.05), as shown in Table 7.

Discussion

Liver cancer is a highly malignant, strongly invasive and metastatic disease, whose long-term efficacy depends on whether it can be diagnosed and treated early (9). Recent years see more and more liver cancer patients detected in the early stage of onset. Hepatectomy has long been used for the treatment of liver cancer. The mature technology can effectively remove the lesion, so it is gradually used more in clinical application (10).

Hepatectomy is a traumatic stressor that demands long surgery time. The continuous surgical stimulation can cause a strong stress response in the body, which is the main factor affecting patients' prognosis and disease outcome (11). Studies have pointed out that the liver is an important metabolic organ of the human body, hepatocellular carcinoma patients already with liver cell damage, dysfunction of metabolism and biotransformation are less capable of resisting stress response (12). How to lower the stress response of liver cancer patients in surgery, has been a focus of clinical research. Anesthesia makes up an important part of the surgery, and the type of anesthetic drugs exerts an important effect on the degree of the perioperative stress response. Previously, the stress response is mainly suppressed by increasing anesthesia depth, which not only brings unobvious effect but also causes delayed postoperative anesthesia recovery. A large number of clinical reports have pointed out that pain is the main reason for stress response in patients with general anesthesia during the recovery period, and continuous and effective analgesia can help suppress stress response (13-14). Ropivacaine, one of the most commonly used anesthetic drugs in clinical practice, is often used for local anesthesia. It affects the transmission of nerve fiber impulses via reversible retardation, which demonstrates good analgesic effects with little damage to the heart and nerves (15). He Feng et al. [16] pointed out that infiltration anesthesia with 0.5% ropivacaine 10 min before skin incision could bring good analgesic effect. In addition, Liu Ying (17) found that intravenous injection of dezocine 0.5 h before the end of surgery could effectively reduce postoperative pain in patients receiving laparoscopic cholecystectomy under general anesthesia. Dezocine represents a new type of powerful opioid analgesic drug, which can directly act on μ receptors and K receptors after administration, exerting strong analgesic effects and slight sedative effects. With the analgesic effect comparable to morphine, it will not produce μ receptor dependence, showing high safety. In the meantime, it can effectively reduce the risk of gastrointestinal and respiratory dysfunction caused by the anesthetic drug. Some scholars have used dezocine in combination with sufentanil to relieve patient-controlled epidural analgesia after a total hysterectomy. It was found that not only postoperative pain was further reduced, but also the incidence of adverse reactions to anesthesia was lowered (18). Based on the above studies, this study applied dezocine in combination with ropivacaine infiltration anesthesia to hepatectomy patients in the study group. It was found that serum Glu, NE and E levels were significantly lower in the study group at the end of the surgery, 12 h after surgery, and 24 h after surgery. Moreover, the postoperative VAS score was lower in the study group, which was consistent with the above research conclusions. It fully demonstrates that dezocine combined with ropivacaine infiltration anesthesia can significantly reduce postoperative pain and stress response of hepatectomy patients. According to the results of this study, serum DA, NPY and SP levels were lower in the study group than in the control group at the end of surgery and after surgery. Where, DA as a monoamine neurotransmitter is mainly distributed in the striatum, substantia nigra, Pallidum, etc. of the central nervous system, reduced level of which can lead to lowered hyperalgesia and less inhibition of anesthetic effects. SP as a factor synthesized by spinal ganglia participates in the process of pain transmission. NPY widely distributed in the cen-

Table 6. Comparison of anesthesia recovery between the two groups($\bar{x}$ ±s, min).

Group	No. cases	Spontaneous breathing recovery time	Eye-opening time	Extubation time
Study group	46	7.04±1.57	8.36±2.03	9.79±2.83
Control group	46	9.25±1.82	10.17±2.27	13.62±3.45
t		6.236	4.031	5.821
P		<0.001	<0.001	<0.001

Table 7. Comparison of the incidence of adverse reactions between the two groups n(%).

Group	No. cases	Feel sick and vomit	Restlessness	Transient hypertension	Cough
Study group	46	3 (6.52)	2 (4.35)	3 (6.52)	1 (2.17)
Control group	46	2 (4.35)	9 (19.57)	10 (21.74)	9 (19.57)
χ^2		0.000	5.059	4.390	7.181
P		1.000	0.025	0.036	0.007

tral and peripheral nervous system is one of the most abundant neuropeptides. Its increased levels can lead to hyperalgesia and weakened anesthetic effects (19). Intravenous injection of dezocine 0.5 h before the end of the surgery can further inhibit the expression of serum DA, NPY, SP in patients after surgery, thereby reducing pain and stress response. In addition, the incidence of restlessness, transient hypertension and cough was significantly lower in the study group than in the control group, which was related to the fact that dezocine intravenously administered 0.5 h before the end of surgery could effectively reduce the dosage of drugs used for anesthesia maintenance, thus effectively increasing anesthesia safety.

Studies of recent years have found that surgical operations can damage the body's immune system, thereby affecting patients' postoperative recovery (20). $CD4^+$, $CD4^+/CD8^+$ are common indicators reflecting the function of T lymphocytes. NK cells directly concern the body's antitumor immune regulation, which can directly kill tumor cells (21). This study found that hepatectomy patients had significantly reduced $CD4^+$, $CD4^+/CD8^+$, NK cells in the peripheral blood, which further verified that the surgical operation can aggravate immune function damage in liver cancer patients. However, postoperative indicator levels were higher in the study group than in the control group, suggesting that dezocine combined with ropivacaine infiltration anesthesia can help reduce postoperative immune function damage and promote postoperative recovery, which may be closely related to significantly reduced pain and stress response in the patients. Its specific mechanism of action has not yet been elucidated, demanding further investigations in the future. The spontaneous breathing recovery time, eye-opening time and extubation time were shorter in the study group than in the control group, further confirming the high effectiveness and safety of dezocine usage in combination with ropivacaine infiltration anesthesia.

In summary, it can be concluded that the use of dezocine in combination with ropivacaine infiltration anesthesia in hepatectomy shows significant effects in reducing postoperative stress response, alleviating immune function fluctuations and down-regulating pain factor expression, which can effectively reduce the incidence of adverse reactions of anesthesia, promote patients' postoperative wake-up and thus enjoys high clinical application value.

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