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Effects of Thoracic Paravertebral Block on Inflammatory Response, Stress Response, Hemodynamics and Anesthesia Resuscitation in Gallbladder Carcinoma

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ABSTRACT

The study aimed to explore the effects of the ultrasound-guided thoracic paravertebral block (TPVB) on the inflammatory response, stress response, hemodynamics and anesthesia resuscitation in gallbladder carcinoma. Eighty gallbladder carcinoma patients undergoing open cholecystectomy in Heilongjiang Provincial Hospital from February 2016 to April 2019 were selected and divided into observation group (n=40) and control group (n=40) using a random number table. All patients underwent open cholecystectomy under general anesthesia and tracheal intubation. Patient-controlled intravenous analgesia was adopted after the operation in the control group, while right TPVB was performed before general anesthesia in the observation group. The changes in inflammatory factors and oxidative stress factors were compared between the two groups, the anesthesia resuscitation indexes, and the changes in the bispectral index (BIS) and Ramsay score during anesthesia resuscitation were recorded, and the changes in the hemodynamic indexes in perianesthesia and anesthesia resuscitation-related complications were analyzed. At 15 min after anesthesia, the observation group had lower levels of inflammatory factors high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) (p<0.05), malondialdehyde (MDA) (p<0.05) and a higher level of superoxide dismutase (SOD) (p<0.05) than the control group. The anesthesia resuscitation time was shorter in the observation group than that in the control group (p<0.05). At 10 min, 20 min and 30 min after anesthesia, both BIS and Ramsay scores were significantly higher in the observation group than those in the control group (p<0.05). Moreover, the proportion of circulatory function-related complications and anesthesia resuscitation-related complications were lower in the observation group than that in the control group (p<0.05). The NRS score in the observation group was lower than that in the control group after anesthesia (p<0.05). TPVB in perianesthesia for gallbladder carcinoma patients can effectively lower the body's inflammatory and stress responses, promote anesthesia resuscitation, reduce complications in perianesthesia, and relieve postoperative pain.

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Introduction

Gallbladder carcinoma is a kind of highly malignant gastrointestinal tumor, and most patients have been in the middle-advanced stage when diagnosed (1). Studies have shown that (2) the morbidity rate of primary gallbladder carcinoma is the highest among various biliary system-related malignant tumors and the top three digestive system malignant tumors. The early clinical manifestations of gallbladder carcinoma are similar to those of simple gallstones or gallbladder inflammation, so it is often ignored, delaying the diagnosis and treatment, and leading to poor prognosis (3). The prognosis and quality of life of gallbladder carcinoma patients are related to the disease stage at the time of diagnosis and whether radical surgery can be performed (4). Surgical treatment is considered as the most effective therapeutic method currently. The standard radical surgeries for gallbladder carcinoma include the total cholecystectomy and lymph node dissection in the gallbladder bed and hepatoduodenal ligament. It is recommended that the extended radical surgeries be performed for patients with middle-stage gallbladder carcinoma, including the partial hepatectomy, duodenectomy and partial pancreatectomy (5), but they have large trauma and strong stress response in patients (6).

In thoracic paravertebral block (TPVB), the local anesthetics are directly injected around the intervertebral foramen nerves in paravertebral space to block the motion, sensation and sympathetic nerves in the spinal nerve-dominated region at the injection site,

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thereby enhancing the anesthetic effect at the injection site and improving the local blood flow (7). However, TPVB is most commonly used for postoperative analgesia and pain treatment but rarely used for the treatment of perianesthesia (8). The present study aims to explore the effects of right TPVB on the inflammatory response, stress response, hemodynamics and anesthesia resuscitation in perianesthesia in patients undergoing open cholecystectomy. It is now reported as follows:

Materials and methods

General data

Eighty gallbladder carcinoma patients undergoing open cholecystectomy in Heilongjiang Provincial Hospital from February 2016 to April 2019 were selected. They were all initially diagnosed via preoperative clinical manifestations combined with imaging findings and diagnosed through postoperative pathological biopsy. The patients and their families signed the informed consent before enrollment, and this study was approved by the Ethics Committee of Heilongjiang Provincial Hospitals. Inclusion criteria: patients aged 18-60 years old, and those with a normal mental condition, educational level of primary school and above, normal language and hearing ability. Exclusion criteria: patients with a systemic infection before the operation, cardiopulmonary insufficiency or renal insufficiency, those who used to undergo abdominal surgery, those with an abnormal mental condition, or those who were allergic to drugs used or had a stroke in the last 3 months. The patients enrolled were divided into observation group (n=40) and control group (n=40) using a random number table. In the observation group, there were 27 males and 13 females aged 18-60 years old with an average of (47.2±1.7) years old. The course of gallbladder carcinoma lasted for 3 days to 2 weeks with an average of (8.5±1.2) days. The anesthesia time was 180-230 min with an average of (205.5±10.0) min. The amount of intraoperative bleeding was 300-700 mL with an average of (500.0±20.0) mL. In the control group, there were 28 males and 12 females aged 18-60 years old with an average of (47.3±1.8) years old. The course of gallbladder carcinoma lasted for 3 days to 2 weeks with an average of (8.6±1.3) days. The anesthesia time was 180-230 min with an average of (205.0±10.5) min. The amount of intraoperative bleeding was 300-700 mL with an average of (500.5±20.5) mL. There were no statistically significant differences in the gender, age, course of gallbladder carcinoma, anesthesia time and amount of intraoperative bleeding between the two groups (p>0.05).

Methods

All patients underwent open cholecystectomy under general anesthesia and tracheal intubation. The venous fast induction tracheal intubation was performed for anesthesia induction. During operation, anesthesia was intravenously maintained, and the continuous arterial pressure, continuous venous pressure, end-tidal carbon dioxide partial pressure and bispectral index (BIS) of patients were monitored. In the control group, patient-controlled intravenous analgesia was adopted after operation using 100 mL of a mixture of 150 μg of sufentanil + 0.9% normal saline, and the flow rate of the analgesia pump was 2 mL/min (locking time: 15 min), with the single additional dose of 1.5 mL. In the observation group, right TPVB was performed before general anesthesia, in which ultrasound-guided nerve block was performed at the right T7-T9 using the 20G puncture needle, and 10 mL of 0.33% ropivacaine was administered.

Observation indexes

The changes in inflammatory factors and oxidative stress factors were compared between the two groups 15 min after anesthesia, the anesthesia resuscitation indexes, and the changes in the BIS and Ramsay score during anesthesia resuscitation were recorded in both groups, and the changes in the hemodynamic indexes in perianesthesia and anesthesia resuscitation-related complications were analyzed in both groups, and the variation trend of the numeric pain rating scale (NRS) score was studied within 48 h after anesthesia in both groups.

Evaluation criteria

Inflammatory factors included high-sensitivity C-reactive protein (hs-CRP, <10 mg/L) and interleukin-6 (IL-6, 0.37-0.46 ηg/L). Antioxidant indexes included malondialdehyde (MDA, 3.52-4.78 mol/L) and superoxide dismutase (SOD, 0.242-0.620 μU/mL). The objective indexes of anesthesia resuscitation were evaluated using the BIS: The score ≥90 points:

waking state, <40 points: too deep anesthesia, 40-60 points: anesthetic status, and 60-90 points: anesthesia resuscitation. The subjective indexes of anesthesia resuscitation were evaluated using the Ramsay score (1-6 points): 6 points: The patient is fully awake and quiet, and can cooperate normally with normal orientation, 5 points: The patient can act as directed, 4 points: The patient has a certain sense of drowsiness but has a response to the glabellar tapping or loud shout, 3 points: There is a state of anxiety and agitation, 2 points: The patient has a sense of drowsiness and has no or slow response to the glabellar tapping or loud shout, 1 point: There is a state of drowsiness or anesthesia, as well as no response to a stimulus. Hemodynamic indexes mainly included hypertension, hypotension, tachycardia and bradycardia, and anesthesia resuscitation-related complications mainly included agitation, nausea and vomiting, bucking and respiratory depression. The NRS score (0-10 points) indicates the pain degree: 0-3 points: mild pain, 4-7 points: moderate pain, and 8-10 points: severe pain. The score is positively related to the degree of pain.

Statistical processing

SPSS 20.0 software was used for statistical processing. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$). *t*-test was performed for the comparison of means between two groups, and χ^2 test for the comparison of rates between two groups. $p<0.05$ suggested the statistically significant differences.

Results and discussion

Comparisons of inflammatory factors and oxidative stress factors between the two groups at 15 min after anesthesia

At 15 min after anesthesia, the observation group had lower levels of inflammatory factors hs-CRP and IL-6 ($p<0.05$), a lower level of MDA and a higher level of SOD ($p<0.05$) than the control group (Table 1).

Comparisons of anesthesia resuscitation indexes between the two groups

In the observation group, the time of eye-opening, mechanical ventilation, extubation and anesthesia resuscitation was all shorter than that in the control group ($p<0.05$) (Table 2).

Changes in BIS during anesthesia resuscitation

There was no statistically significant difference in the BIS between the two groups when anesthesia was terminated ($p>0.05$). At 10 min, 20 min and 30 min after anesthesia, the BIS was increased markedly in the observation group compared with that in the control group ($p<0.05$) (Table 3).

Changes in Ramsay score in the two groups during anesthesia resuscitation

The Ramsay score had no statistically significant difference between the two groups when anesthesia was terminated ($p>0.05$), while at 10 min, 20 min and 30 min after anesthesia, the Ramsay score was significantly higher in the observation group than that in the control group ($p<0.05$) (Table 4).

Table 1. Comparisons of inflammatory factors and oxidative stress factors between the two groups at 15 min after anesthesia ($\bar{x} \pm s$)

	Hs-CRP (mg/L)	IL-6 (ηg/L)	MDA (mol/L)	SOD (U/L)
Observation group	7.2±1.3	0.4±0.1	3.7±0.4	0.7±0.2
Control group	16.1±2.5	1.1±0.2	6.5±0.5	0.4±0.1
t	19.976	19.799	27.656	8.485
p	0.000	0.000	0.000	0.000

Table 2. Comparisons of anesthesia resuscitation indexes between the two groups (min, $\bar{x} \pm s$)

	Time of eye-opening	Time of mechanical ventilation	Time of extubation	Time of anesthesia resuscitation
Observation group	20.2±2.5	21.8±2.9	23.3±2.1	25.5±3.2
Control group	33.9±3.5	36.9±3.8	38.5±4.3	41.4±4.7
t	20.145	19.979	20.089	17.686
p	0.000	0.000	0.000	0.000

Table 3. Changes in BIS during anesthesia resuscitation ($\bar{x} \pm s$)

	When anesthesia was terminated	10 min after anesthesia	20 min after anesthesia	30 min after anesthesia
Observation group	50.3±1.5	59.3±2.3	76.9±3.3	92.3±4.3
Control group	50.4±1.5	54.8±2.9	65.7±3.1	78.9±4.1
t	0.298	7.689	15.645	14.264
p	0.766	0.000	0.000	0.000

Table 4. Changes in Ramsay score in the two groups during anesthesia resuscitation (points, $\bar{x} \pm s$)

	When anesthesia was terminated	10 min after anesthesia	20 min after anesthesia	30 min after anesthesia
Observation group	0.4±0.1	1.5±0.2	3.3±0.5	5.6±0.3
Control group	0.4±0.1	1.3±0.1	2.4±0.3	4.3±0.4
t	0.000	5.657	9.762	16.444
p	1.000	0.000	0.000	0.000

Comparisons of hemodynamic indexes in perianesthesia between the two groups

In perianesthesia, there was 1 case of hypertension, 1 case of hypotension, 2 cases of tachycardia and 1 case of bradycardia in the observation group, and 11 cases of hypertension, 12 cases of hypotension, 14 cases of tachycardia and 9 cases of bradycardia in the control group. It can be seen that the observation group exhibited notably lower proportions of hypertension, hypotension, tachycardia and bradycardia than the control group (χ^2=7.941, 9.185, 11.815 and 5.600, p<0.05) (Figure 1).

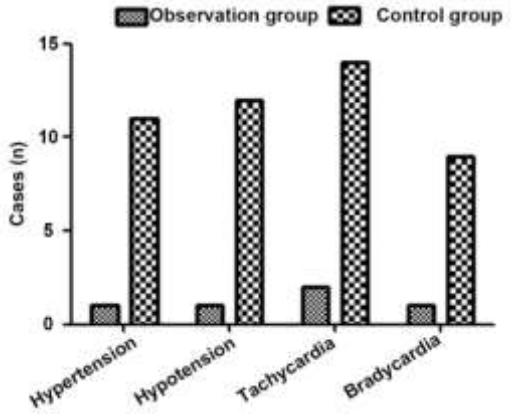

Figure 1. Comparisons of hemodynamic indexes in perianesthesia between the two groups. The observation group exhibits notably lower proportions of hypertension, hypotension, tachycardia and bradycardia than the control group (p<0.05)

Comparisons of anesthesia resuscitation-related complications between the two groups

During anesthesia resuscitation, 1 case of agitation, 1 case of nausea and vomiting, 1 case of bucking and 1 case of respiratory depression occurred in the observation group, and the total proportion of complications was 10.0%. In the control group, 9 cases of agitation, 4 cases of nausea and vomiting, 3 cases of bucking and 2 cases of respiratory depression occurred, and the total proportion of complications was 45.0%. It can be seen that the overall proportion of the above complications was lower in the observation group than that in the control group (χ^2=10.596, p=0.001<0.05) (Figure 2).

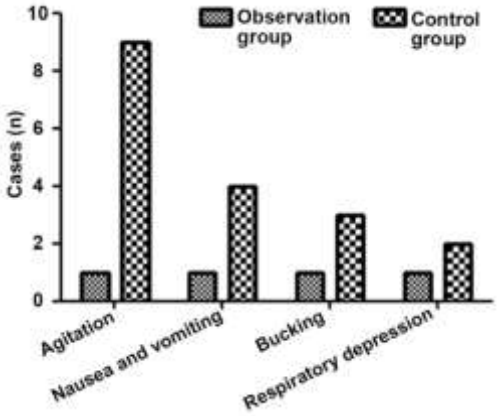

Figure 2. Comparisons of anesthesia resuscitation-related complications between the two groups. The overall proportion of agitation, nausea and vomiting, bucking and respiratory depression is lower in the observation group than that in the control group (p<0.05)

Changes in the NRS score between the two groups within 48 h after anesthesia

The NRS score in the observation group was remarkably decreased in comparison with that in the control group at 2 h, 8 h, 12 h, 24 h and 48 h after anesthesia [(3.2±0.3) points vs. (5.6±0.5) points, (3.4±0.4) points vs. (5.3±0.4) points, (2.5±0.3) points vs. (4.7±0.3) points, (2.3±0.2) points vs. (4.3±0.2) points, (1.7±0.1) points vs. (3.6±0.2) points] (t=26.032, 21.243, 32.796, 44.721 and 53.740, p=0.000<0.05) (Figure 3).

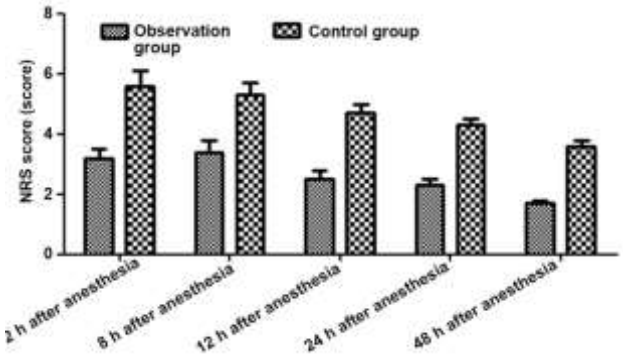

Figure 3. Changes in the NRS score between the two groups within 48 h after anesthesia. The NRS score in the observation group is remarkably decreased in comparison with that in the control group at 2 h, 8 h, 12 h, 24 h and 48 h after anesthesia (p<0.05)

Gallbladder carcinoma is the most common malignant tumor of the biliary system, and its morbidity rate is increasing year by year in the world (9). A study showed that (10) ever since the 21st century, the morbidity rate of gallbladder carcinoma is among the top three biliary diseases, and its mortality rate ranks the 1st in China. Clinically, gallbladder carcinoma is characterized by insidious onset and early metastasis, so more than 80% of patients have been in the middle-advanced stage when diagnosed (11). The median survival time of gallbladder carcinoma is less than 6 months, and its 5-year survival rate is lower than 5%, so gallbladder carcinoma is the most malignant gastrointestinal tumor with the poorest prognosis (12). Radical surgery is the most effective treatment means for gallbladder carcinoma, but only 25% of early diagnosed cases possess the opportunity of radical surgery (13). In radical surgery, however, intervention needs to be made in the gallbladder, liver, duodenum and even pancreas, resulting in large trauma and obvious postoperative pain (14). TPVB has been applied in clinical practice since the 1950s, mainly characterized by anatomical positioning and blind operation, and there are certain risks of pneumothorax, total spinal anesthesia and hematoma, thus limiting its clinical popularization. With the clinical application and popularization of the ultrasound technique in recent years, the visualized nerve block has been realized, and ultrasound-guided TPVB greatly improves the safety of operation, which is more beneficial to the clinical application and popularization (15).

The patients with gallbladder carcinoma in the control group received radical surgery under general anesthesia, combined with postoperative patient-controlled intravenous analgesia, while those in the observation group underwent right TPVB at T7-T9 before anesthesia. The inflammatory factors and oxidative stress factors were compared between the two groups 15 min after anesthesia, and it was found that at 15 min after anesthesia, the observation group had lower levels of inflammatory factors (hs-CRP and IL-6) and MDA and a higher level of SOD than the control group, indicating that TPVB before anesthesia can effectively alleviate the inflammatory and stress responses in patients with gallbladder carcinoma. Moreover, the anesthesia resuscitation indexes were compared between the two groups. The results showed that the time of eye-opening, mechanical ventilation, extubation and anesthesia resuscitation in the observation group was all shorter than that in the control group, suggesting that TPVB in perianesthesia for gallbladder carcinoma patients can effectively shorten the anesthesia resuscitation time. At the same time, the changes in the BIS and Ramsay scores during anesthesia resuscitation were detected, and it was observed that at 10 min, 20 min and 30 min after anesthesia, both BIS and Ramsay scores were higher in the observation group than those in the control group, implying that TPVB in perianesthesia for gallbladder carcinoma patients can significantly promote the anesthesia resuscitation of patients. In addition, according to the comparisons of hemodynamic indexes and anesthesia resuscitation-related complications in perianesthesia between the two groups, the proportions of hypertension, hypotension, tachycardia and bradycardia in the observation group were all lower than those in the control group, and the overall proportion of agitation, nausea and vomiting, bucking and respiratory depression also declined in observation group compared that in the control group, demonstrating that TPVB in perianesthesia for gallbladder carcinoma patients can better maintain the hemodynamic stability, reduce the anesthesia resuscitation-related complications and raise the anesthesia safety. Finally, the changes in the NRS score were compared between the two groups within 48 h after anesthesia, and it was found that the observation group had remarkably lower NRS scores than the control group at 2 h, 8 h, 12 h, 24 h and 48 h after anesthesia, further indicating that TPVB in perianesthesia for gallbladder carcinoma patients is of important significance in reducing perioperative pain.

In TPVB, the local anesthetics are directly injected around the intervertebral foramen nerves in paravertebral space to block the motion, sensation and sympathetic nerves in the spinal nerve-dominated region at the injection site (16), which is widely used for analgesia after unilateral thoracic and abdominal surgery and pain treatment (17). After local anesthetics are injected into the proposed nerve root, the sympathetic chain and sensory nerve conduction pathway are directly blocked (18), the transduction of perioperative noxious signals to the central nervous

system is also effectively blocked, and the central sensitization is weakened. TPVB before anesthesia also exerts a preemptive analgesic effect, which effectively blocks the nerve impulse transmission caused by laparotomy trauma and other noxious stimuli in patients with gallbladder carcinoma (19), reduces the dose of sedative and analgesic drugs, alleviates the cardio-cerebrovascular stress and inflammatory responses, maintains the hemodynamic stability in perianesthesia, and ensures the analgesic effect (20).

In conclusion, TPVB in perianesthesia for gallbladder carcinoma patients can effectively lower the body's inflammatory and stress responses, promote anesthesia resuscitation, reduce the complications in perianesthesia, and relieve postoperative pain.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

DL wrote the manuscript. DL and HL collected and analyzed general data of patients. JW and BG were responsible for observation indexes analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the ethics committee of Heilongjiang Provincial Hospital and written informed consents were signed by the patients and/or guardians.

Consent for publication

Not applicable.

Conflict interest

The authors declare that they have no conflict of interest.

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