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Retrospective Study

Effect of Transversus Abdominis Plane Block with Remimazolam on Postoperative Recovery and Stress Response in Patients Undergoing Gastrointestinal Tumor Surgery

Impact of anesthesia on Gastrointestinal tumor surgery

Abstract

BACKGROUND

Transversus abdominis plane block is a block of the abdominal afferent nerve fibers between the internal oblique muscle and the transverse abdominal muscle achieved with local anesthetics. It can effectively block the conduction of the anterior nerve of the abdominal wall and exert a good analgesic effect. However, the effect of combining the block with remazolam on anesthesia in patients undergoing gastrointestinal tumor surgery is still unclear.

AIM

The aim of this study was to examine the effects of combining transversus abdominis plane block (TAPB) with remimazolam on the stress response and postoperative recovery of gastrointestinal tumor surgery patients.

METHODS

A retrospective analysis was conducted on the clinical data of 102 individuals diagnosed with gastrointestinal malignancies who underwent laparoscopic surgery under general anesthesia between April 2020 and June 2023. The patients were
categorized into a control group \((n = 51)\), receiving remimazolam for general anesthesia, and an observation group \((n = 51)\), receiving TAPB combined with remimazolam for general anesthesia. A comparison was made between both groups in terms of hemodynamic parameters, stress markers, pain levels, recovery quality, analgesic effects, and adverse reactions during the perioperative period.

RESULTS
The observation group had significantly higher heart rates (HRs) at time points T1 and T3 than the control group \((P<0.05)\). The mean arterial pressure (MAP) at time point T1 in the observation group was significantly higher than that in the control group \((P<0.05)\). Five minutes after extubation, the levels of the hormones adrenaline \((E)\) and noradrenaline \((NE)\) in the observation group were considerably lower than those in the control group \((P<0.05)\). At 12 h, 24 h, and 48 h following surgery, the VAS scores of the observation group were considerably lower than those of the control group \((P<0.05)\). The observation group had shorter awakening and extubation times and lower Riker sedation-agitation scale scores than the control group \((P<0.05)\). The observation group exhibited considerably fewer effective pump presses, lower fentanyl dosages, and lower incidences of rescue analgesia within 24 h following surgery than the control group \((P<0.05)\).

CONCLUSION
The combination of TAPB and remimazolam for general anesthesia has been found to offer enhanced anesthetic effects, facilitate better hemodynamic stability, reduce the occurrence of cardiovascular events, and promote faster postoperative recovery in individuals undergoing gastrointestinal tumor surgery. This approach is suitable for clinical promotion.

**Key Words:** Transversus abdominis plane block; Remimazolam; General anesthesia; Gastrointestinal tumor surgery; Stress response

**Core Tip:** Stress can lead to severe changes in hemodynamics during surgery and increase the risk of postoperative adverse events. In this study, the application value of transversus abdominis plane block (TAPB) combined with remazolam general anesthesia in patients undergoing gastrointestinal tumor surgery was observed. The results showed that the application of TAPB combined with remazolam general anesthesia had the advantages of stable anesthesia induction and small hemodynamic fluctuation, which was helpful to reduce the acute stress response of patients undergoing gastrointestinal tumor surgery and improve the quality of recovery.

**INTRODUCTION**

The gastrointestinal tract includes the stomach, duodenum, jejunum, ileum, cecum, colon, and rectum. Gastrointestinal tumors are the most common digestive tract tumors worldwide. Based on statistical data [1], gastric cancer (GC) is the second most prominent cause of cancer death in China, following lung cancer. Recently, there has been a notable increase in the occurrence of colorectal cancer (CRC), resulting in its inclusion among the five most prevalent forms of cancer. Since most gastrointestinal tumor patients have subtle symptoms in the early stages of the disease and are usually diagnosed at an intermediate or advanced stage, timely surgical intervention is necessary to control disease progression [2] before distant metastasis. Due to its minimal invasiveness, reduced pain, and faster recovery, laparoscopic surgery has been widely used in treating gastrointestinal tumors. However, carbon dioxide (CO₂) pneumoperitoneum is established during laparoscopic surgery, increasing intra-abdominal pressure. When the intra-abdominal pressure drops suddenly, it can lead to
ischemia–reperfusion injury and a stress response, and the change in surgical position will also affect the body's homeostasis, causing severe postoperative pain and adversely affecting the patient's recovery \(^3\). Prior research has demonstrated that stress conditions can potentially augment the production and release of cortisol, epinephrine, norepinephrine, and blood glucose in individuals. The drastic changes in hemodynamics can increase the risk of adverse events postoperatively, significantly affecting the effectiveness of surgical treatment and postoperative recovery \(^4\). Therefore, a reasonable anesthesia approach reduces stress responses during laparoscopic surgery and promotes faster postoperative recovery.

Transverse abdominis plane block (TAPB) provides regional anesthesia by effectively blocking the sensory nerve fibers within the abdominal cavity, explicitly targeting the area between the internal oblique and transverse abdominis muscles. It can effectively block the transmission of the anterior abdominal wall nerves, thus providing analgesic effects \(^5\). The relevant literature has shown that remimazolam can be safely and effectively used in outpatient gastrointestinal endoscopy and bronchoscopy. Its successful sedation rate is similar to that of propofol, but it is significantly safer. It can be used for anesthesia induction and maintenance \(^6\). There are few reports on the use of TAPB combined with remimazolam in laparoscopic surgery for the treatment of gastrointestinal tumors. The primary objective of this study was to examine the effects of the combination of TAPB and remimazolam for anesthesia on the stress responses and postoperative recovery of individuals undergoing gastrointestinal tumor surgery. The findings of this study can be used to establish a theoretical foundation for the prevention or reduction of stress responses in patients, as well as to provide evidence-based choices for clinical anesthesia.

**MATERIALS AND METHODS**

2 Subjects and Methods

2.1 Study subjects
Medical information from a cohort of 104 patients diagnosed with gastrointestinal malignancies and who underwent laparoscopic surgery under general anesthesia at our institution from April 2021 to June 2023 was retrospectively acquired. The criteria for inclusion are outlined below: confirmed diagnosis of gastrointestinal tumors; being suitable for laparoscopic surgery; American Society of Anesthesiologists (ASA) classification II-III; 18-65 years old; and complete medical records. Patients who suffered severe drug allergies during the perioperative period, cancelled the surgery due to factors not associated with anesthesia, decided to withdraw from the study voluntarily, or were withdrawn from the study by the anesthesiologist based on medical considerations were excluded. In this study, the clinical data of 104 patients with gastrointestinal tumors who underwent laparoscopic surgery under general anesthesia were reviewed, including 52 patients in the observation group and 52 patients in the control group. In the observation group, 1 patient without gastrointestinal tumors was excluded; in the control group, 1 patient was excluded due to missing intraoperative hemodynamic data. Finally, 51 patients in the observation group and 51 patients in the control group were included in the statistical analysis. All participants submitted informed consent forms, and the study methodology followed the Helsinki Declaration.

2.2 Anesthesia Methods

2.2.1 Preanesthetic Preparation

All patients underwent relevant examinations preoperatively and were advised to fast for 6-8 h before surgery. Upon arrival to the operating room, peripheral intravenous access was established, and routine monitoring of the heart rate (HR), bispectral index (BIS), respiratory rate (RR), oxygen saturation (SpO2), mean arterial pressure (MAP), and electrocardiography (ECG) was commenced.

2.2.2 Anesthesia methods

Anesthesia Induction: The following drugs were sequentially administered intravenously for anesthesia induction: remimazolam (0.2 mg/kg), cisatracurium (0.2-0.4 mg/kg), and sufentanil (0.4-0.6 μg/kg). After the BIS value fell below 60 and
appropriate conditions for endotracheal intubation were ascertained, tracheal intubation was executed. Subsequently, the anesthetic device was attached to facilitate controlled respiration. The tidal volume was set at 8-10 mL/kg, the respiratory rate at 12-14 breaths per min, and the inspiratory-expiratory ratio at 1:2. During the surgery, respiratory parameters were adjusted to maintain the PETCO₂ between 30-40 mmHg. In the observation group, bilateral TAPB was performed 5 min after anesthesia induction by the side entry method. A linear ultrasound probe guided the needle into the transversus abdominis plane. The ultrasonic probe was positioned at a right angle to the anterior axillary line, within the space bounded by the iliac crest and the costal edge on one side. The probe was then adjusted until the three distinct muscles of the transverse abdominal muscle group were discernible. When the needle tip reached the plane of the transverse fascia of the abdomen, it was drawn back to confirm that there was no blood or air. Ropivacaine (20 mL of 0.375%) was injected into the fascial sheath between the internal oblique and transverse abdominals muscles to obtain spindle-shaped hypoechoic images. The same procedure was repeated on the other side to complete the bilateral TAPB. The control group received only remimazolam.

Anesthesia maintenance: Intravenous remimazolam 0.4-1.2 mg/kg/h was administered, while cisatracurium was injected at a rate of 0.1 mg/kg/h. On the other hand, sufentanil 6-12 μg/kg/h was provided intravenously. The dosage of anesthetic drugs was adjusted based on the patient’s BIS, MAP, and HR. The BIS value was maintained between 40-60. Atropine (0.3-0.5 mg) was administered if the patient's HR dropped below 50 beats per min, and esmolol (0.5 mg/kg) was administered if the HR exceeded 100 beats per min. Drugs were readministered if necessary.

Flurbiprofen (50 mg) was administered for postoperative analgesia during skin closure, and all patients received patient-controlled intravenous analgesia (PCIA) after surgery. The PCIA scheme consisted of sufentanil 100 μg, flurbiprofen 200 mg, and ondansetron hydrochloride 32 mg, mixed in a total volume of 100 mL. The initial infusion rate was set at 2 mL/h, followed by a self-controlled infusion rate of 1.5 mL/h. The maximum self-controlled infusion rate allowed was 8 mL/h, with a lockout period
of 20 minutes. After the surgical procedure, the individuals were sent to the postanesthesia care unit (PACU) for observation and recovery. Tracheal extubation was successfully performed in all patients, and they were then moved back to the ward.

2.3 Observational Parameters

(1) Hemodynamics Comparison: Mean arterial pressure (MAP) and heart rate (HR) were compared at different time points, including upon leaving the operating room (T3), immediately after tracheal intubation (T2), 1 min after induction (T1), and before anesthesia induction (T0). (2) Stress response: Blood samples were obtained from the radial artery of patients at two specific time points: 10 minutes before the introduction of anesthesia and 5 minutes following extubation. The concentrations of plasma NE and epinephrine (E) were measured using an enzyme-linked immunosorbent assay (ELISA). (3) Pain intensity: Pain intensity in both groups was evaluated at 4, 12, 24, and 48 h post surgery using the visual analog scale (VAS). The scores ranged from 0 to 10, with higher values denoting greater pain intensity. (4) Recovery quality: Recorded parameters included time to eye-opening, time to extubation, PACU stay duration, and Riker sedation-agitation score assessed at extubation. A Riker score ≥5 indicated agitation at extubation. (5) Safety: The examiners monitored the number of successful activations of the PCA pump, the amount of sufentanil administered, and the frequency of rescue analgesic administrations during the 24 h following the surgical procedure. The occurrence rates of vomiting, nausea, pruritus, and respiratory depression were compared between the two groups within 48 h after surgery.

2.4 Statistical Analysis

We used SPSS 22.0 software to analyze the data. The measured information is presented as the mean ± standard deviation (SD), and we compared them using t tests. Count data are expressed as numbers or percentages and were compared using chi-square tests. The chi-square value was corrected if the theoretical frequency was ≤5 5 but ≥1. Fisher's exact test was used if the theoretical frequency was <1. A p value less than 0.05 is indicative of a statistically significant difference.
RESULTS

3.1 A comparative analysis of the baseline characteristics between the two groups

Between the observation and control groups, there was no statistically significant variation in sex, age, or any other baseline characteristics (p>0.05, Table 1).

3.2 A Comparison of both groups' HRs at various time points

The two groups had no significant differences in HR at the T0 and T2 time points (p>0.05). Nevertheless, the observation group displayed substantially higher HRs at the T1 and T3 time points than the control group (p<0.05, Table 2 and Figure 1).

3.3 Comparison of MAP at Different Time Points between the Two Groups

No statistically significant variation was observed in the MAP between the two categories at the T0, T2, and T3 time points (p>0.05). Nevertheless, the MAP at the T1 time point exhibited a statistically significant elevation in the observation group compared to the control (p<0.05, Table 3 and Figure 2).

3.4 A comparative analysis of stress parameter levels at various time points between both groups

No statistically significant variations were observed in the levels of E and NE at 10 min prior to anesthesia induction between the two groups (p>0.05). Nevertheless, the E and NE levels 5 min after extubation exhibited a notable decrease in the observation group compared to the control (p<0.05, Table 4).

3.5 VAS scores at various intervals following surgery in both groups

No statistically significant differences were observed in the VAS score between the two groups at the 4-hour point following the surgical procedure (p>0.05). Nevertheless, the VAS scores recorded at 12, 24, and 48 h post surgery showed a statistically significant decrease in the observation group (p<0.05, Table 5 and Figure 3).

3.6 Comparison of Recovery Quality in both Groups

There were no statistically significant differences in the duration of PACU stay between the two groups, as indicated by a p value greater than 0.05. The observation group exhibited a significantly shorter eye-opening and time to extubation time than
the control group. Additionally, the observation group had a substantially lower Riker sedation-agitation score (p<0.05, Table 6).

3.7 Comparison of the postoperative analgesic situation within 24 h between the two groups

The observation group exhibited significantly lower effective PCA presses and sufentanil consumption within 24 h post surgery than the control group. Additionally, the observation group had a substantially lower number of cases requiring rescue analgesia (p<0.05, Table 7).

3.8 Comparative analysis of the postoperative adverse effect frequency in the two cohorts

No statistically significant disparity was observed in the occurrence of postoperative nausea, vomiting, itching, or other unpleasant responses when comparing the two groups (p>0.05, Table 8).

DISCUSSION

As the proportion of aging adults increases, the incidence of gastrointestinal tumors has been increasing yearly. Although laparoscopic surgery can prolong the survival time of patients, factors such as CO₂ pneumoperitoneum and positional changes during surgery can disturb the body's homeostasis, leading to stress responses and causing severe postoperative pain that significantly affects surgical outcomes and postoperative recovery. Research has shown that administering various anesthetic medications during the perioperative phase substantially influences the stress reactions exhibited by patients under general anesthesia. Propofol is currently the most widely used intravenous anesthetic drug worldwide. However, it has apparent inhibitory effects on circulatory and respiratory functions, which can lead to hemodynamic fluctuations during surgery. Long-term use of propofol has drawbacks, such as drug residue, especially in patients with poor cardiovascular function or the elderly [7-8]. Remimazolam, a new type of benzodiazepine sedative-hypnotic drug, has the advantages of rapid metabolism, no residual effects, and minimal impact on respiration
and circulation. It has been well applied in short and outpatient surgeries and is expected to be an anesthetic drug for reducing patient stress responses. Phase IIb/III trial results comparing propofol and remimazolam demonstrated that patients who received remimazolam had a lower incidence of adverse cardiovascular events such as bradycardia and hypotension than those who received propofol, confirming the safety and efficacy of remimazolam. However, the analgesic and sedative effects of remimazolam alone are similar to those of propofol. Thus, additional anesthetics must be combined with remimazolam to improve the analgesic and soothing effects, further reduce the intraoperative stress response, and stabilize hemodynamics during the perioperative period.

The TAPB technique requires the administration of local anesthetics into the fascial gap across the transversus abdominis muscle and the internal oblique. This action effectively obstructs the abdominal wall nerves traversing this specific plane, hence inducing regional nerve block and analgesic effects on the anterior-lateral abdominal wall. The TAPB technique blocks pain signal transmission by acting on the peripheral nerves and nerve fibers in the transversus abdominis plane, reducing postoperative pain perception. Moreover, transversus abdominis plane block (TAPB) can impede the transmission of nerve signals within the transversus abdominis plane, encompassing the intercostal nerves, inguinal nerves, and rectus abdominis nerves, consequently leading to the mitigation of pain postoperatively. In recent years, with the continuous development of ultrasound-guided techniques, ultrasound-guided TAPB has been proven to effectively enhance the accuracy of needle insertion and enhance the analgesic and sedative effects of the blockade. Numerous studies have shown that TAPB can significantly alleviate postoperative pain and reduce opioid-related side effects, promoting postoperative recovery. The present study investigated the use of TAPB combined with remimazolam in individuals undergoing laparoscopic surgery for gastrointestinal malignancies. The study's findings indicate a statistically significant increase in heart rate (HR) at both T1 and T3 in the observation group compared to the control group. This suggests that the combination of transversus
abdominis plane block (TAPB) and remimazolam is effective in maintaining stable hemodynamics during surgery while exerting fewer inhibitory effects on the circulatory system than remimazolam alone.

The hypothalamic–pituitary–adrenal (HPA) axis is the primary mechanism mediating the acute stress response in the body. When sympathetic activation occurs during the perioperative period due to surgical trauma, fear and anxiety, or hypothermia, corticosteroid and catecholamine secretion, such as cortisol and E/NE, increases. The clinical manifestations include hemodynamic fluctuations, increased myocardial oxygen consumption, changes in respiratory rate, and increased metabolic rates. In severe cases, internal environment disturbances, acid–base imbalances, and even arrhythmias can occur. The outcomes of the present study demonstrated a significant decrease in E and NE levels 5 minutes following extubation in the observation group compared to the control group. This suggests that the combination of TAPB and remimazolam may be more effective in mitigating patient stress responses than remimazolam alone.

The Riker Sedation-Agitation Scale was proposed by Riker in 1999 and is mainly used to assess the level of agitation during the recovery phase in patients undergoing treatment under general anesthesia. It has higher reliability and authenticity in evaluating the awakening status of mechanically ventilated patients compared to the widely used Ramsay Sedation Scale. The present study’s findings indicate that the time to eye opening and extubation was significantly shorter in the observation group than in the control group. The Riker sedation agitation score was notably lower in the observation group. Additionally, the VAS scores at 12, 24, and 48 h after surgery were significantly lower in the observation group, indicating that TAPB combined with remimazolam provides good analgesic and sedative effects, improves patient comfort during anesthesia recovery, and has a positive impact on improving the quality of recovery. In addition, compared to the control group, the observation group exhibited fewer PCA pump pushes and less sufentanil intake during the 24 h following surgery. The number of patients requiring rescue analgesia was considerably lower in the
observation group, providing additional evidence to support the effective analgesic outcome of TAPB combined with remimazolam for postoperative pain control.

CONCLUSION
Combining TAPB and remimazolam provides better hemodynamic stability, a lower stress response, improved postoperative pain control, and enhanced recovery quality in gastrointestinal tumor surgery patients. This approach is promising for reducing stress and promoting optimal postoperative outcomes. The present study is subject to limitations, namely, a restricted sample size and an exclusive focus on patients undergoing gastrointestinal tumor surgery. The aim of the study is to increase the sample size to investigate the potential benefits of combining TAPB with remimazolam in a broader range of clinical scenarios.

ARTICLE HIGHLIGHTS
Research background
CO2 pneumoperitoneum will be established in patients with gastrointestinal tumors during laparoscopic surgery, resulting in intra-abdominal hypertension, which is easy to cause stress response. At the same time, the change of posture will also aggravate the stress response, which will seriously affect the effect of surgical treatment and postoperative rehabilitation. Therefore, it is of great significance to adopt a reasonable anesthesia method to promote the postoperative recovery of patients. Transversus abdominis plane block (TAPB) can effectively block the conduction of the anterior nerve of the abdominal wall, resulting in analgesic effect. The success rate of remifentanil analgesia is similar to that of propofol, and the safety is significantly better than that of propofol. It can be used in the induction and maintenance of general anesthesia. The combination of TAPB and remazolam and remazolam can provide a basis for the anesthetic regimen to reduce the stress response of laparoscopic patients with gastrointestinal tumors.
Research motivation
The use of different anesthetics during the perioperative period of gastrointestinal tumors has an important impact on the stress response caused by general anesthesia. In the past, propofol was mostly used, but its obvious inhibition of circulatory and respiratory function can easily lead to intraoperative hemodynamic fluctuations. In addition, the change of intraoperative position can easily lead to stress response in patients, causing severe postoperative pain, which has a serious impact on the surgical effect and postoperative recovery. Remazolam has the advantages of fast metabolism, no residue and little influence on respiration and circulation. However, the analgesic and sedative effects of simple application of remifentanil general anesthesia are similar to those of propofol. Therefore, it is necessary to combine the application of transversus abdominis plane block on the basis of remifentanil general anesthesia to improve the analgesic effect. It is expected to become an important anesthetic and analgesic scheme for laparoscopic surgery of gastrointestinal tumors in the future.

Research objectives
This study mainly discussed the effect of transversus abdominis plane block combined with remazolam general anesthesia on stress response and postoperative recovery in patients undergoing gastrointestinal tumor surgery. The results showed that the application of TAPB combined with remazolam general anesthesia in gastrointestinal tumor surgery had the advantages of stable anesthesia induction, small hemodynamic fluctuation, low incidence of cardiovascular events, fast postoperative recovery and less agitation. It is helpful to reduce acute stress response, improve the quality of recovery, and the level of analgesia and sedation can meet the needs of surgery. In the future, it can be used as an anesthesia and analgesia program for patients undergoing laparoscopic surgery for gastrointestinal tumors.

Research methods
In this study, the clinical data of patients with gastrointestinal tumors who underwent laparoscopic surgery under general anesthesia were retrospectively analyzed. The patients were grouped according to different anesthesia schemes, and the hemodynamics, stress response and recovery quality of the observation group and the control group were compared. The data were analyzed by SPSS22.0 software to further clarify the application value of transversus abdominis plane block combined with remazolam general anesthesia in patients undergoing gastrointestinal tumor surgery.

**Research results**

This study further clarified that transversus abdominis plane block combined with remazolam general anesthesia can effectively alleviate the stress response of patients undergoing gastrointestinal tumor surgery. The level of analgesia and sedation is good, the intraoperative hemodynamic fluctuation is small, and the quality of recovery is good. However, this study is a retrospective analysis, and it is impossible to analyze the long-term effects of this anesthesia program and its application effect in other operations. In the future, the sample size will be further expanded to explore the application value of this anesthesia program.

**Research conclusions**

The application of transversus abdominis plane block combined with remifentanil general anesthesia in gastrointestinal tumor surgery has the advantages of stable anesthesia induction, small hemodynamic fluctuations, low incidence of cardiovascular events, rapid postoperative recovery and less agitation. It is helpful to reduce acute stress response, improve the quality of recovery, and the level of analgesia and sedation can meet the needs of surgery.

**Research perspectives**
In the future, the sample size will be expanded to explore the application value of transversus abdominis plane block combined with remifentanil general anesthesia in other types of laparoscopic surgery anesthesia.
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