Effects of dexmedetomidine as an adjunct in transversus abdominis plane block during gynecological laparoscopy

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Abstract. Ultrasound-guided transversus abdominis plane (TAP) block for abdominal surgery has been widely studied in clinical settings. However, dexmedetomidine as an adjunctive analgesic combined with TAP block has been rarely reported. The present study evaluated the efficacy of TAP block combined with dexmedetomidine adjunct for gynecological laparoscopy. In brief, 90 patients were randomly divided into three groups: Group I, which received post-operative intravenous analgesia only after general anesthesia; Group II, which received a TAP block with 20 ml 0.375% ropivacaine; and Group III, which received a TAP block with 20 ml of 0.375% ropivacaine and 1 μg/kg dexmedetomidine after induction. In all groups, propofol was used for general anesthesia. The dosage of propofol, duration of the operation, and the time of awakening, spontaneous breathing and extubation were recorded. In addition, the Steward and visual analogue scale (VAS) scores were determined at 2, 4, 8, 12 and 24 h post-surgery. The occurrence of nausea and vomiting and/or respiratory depression was also recorded. Compared with those in Group I, the dosage of propofol, as well as the time of awakening, spontaneous breathing and extubation were significantly decreased in Group III ($P<0.01$ and $P<0.05$, respectively). In addition, the VAS score at 2 and 4 h in Group II (both $P<0.05$) and 2, 4 (both $P<0.01$) and 8 h ($P<0.05$) in Group III after the surgery were significantly lower compared with those in Group I. Furthermore, in Groups II and III, a lower number of cases experienced nausea and vomiting ($P<0.05$). In conclusion, the ultrasound-guided TAP block combined with dexmedetomidine adjunct may improve recovery from anesthesia and reduce post-operative pain (trial registration no. ChiCTR-IPR-15007398).

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Introduction

Gynecological laparoscopy is an effective, safe and well-tolerated approach characterized by short operation time, minimal trauma, fast turnover and rapid recovery from anesthesia. Possible adverse reactions after gynecological laparoscopy include incisional, visceral and shoulder pain, as well as nausea and vomiting stimulated by CO_2 pneumoperitoneum, which not only cause discomfort but also delay the patients' recovery, wound healing and time until discharge, as life-threatening complications may occur. In addition, these complications may reduce patient satisfaction. Therefore, it is important to improve the quality of anesthesia during surgery and reduce the incidence of post-operative complications in clinical practice (1,2).

With the use of ultrasound in anesthesiology, the application of all types of nerve blocks, particularly transversus abdominis plane (TAP) block, has become increasingly popular (3-7). TAP block decreases abdominal post-operative pain and in turn reduces the requirement for analgesics. However, limited studies are available on ultrasound-guided TAP block combined with dexmedetomidine for reducing post-operative nausea, vomiting and recovery from anesthesia (8).

Dexmedetomidine, a selective α2 adrenergic agonist, is an important adjuvant with analgesic and sedative properties for systemic anesthesia by intravenous infusion. Dexmedetomidine has been also applied in adjunction to peripheral nerve blocks (9,10). The aim of the present study was to investigate the recovery and analgesic effects of dexmedetomidine combined with TAP block for gynecological laparoscopy, and to provide guidance for its use in clinical practice.

Patients and methods

Patients. The present prospective, randomized, double-blinded study included 90 patients, and was performed between April and July 2014 in the First Affiliated Hospital of Wannan Medical College (Wuhu, China). Patients aged 20-50 years with American Society of Anesthesiologists grades (11) of I or II, who were scheduled for undergoing laparoscopic ovarian cyst resection under general anesthesia, were enrolled in the present study. The operations were performed by the same surgical group. The exclusion criteria were as follows:

A history of heart or respiratory disease, kidney or liver failure, coagulation disorders, morbid obesity, local infection at the site of block, mental disorder, allergy to the study drug and long-term use of painkillers or adrenergic receptor agonists or antagonists. During the pre-operative anesthesia assessment, the meaning of the visual analogue scale (VAS) (12) was explained to the patients in the context of pain assessment from 0 to 10, with 0 indicating no pain and 10 indicating the worst pain imaginable.

Grouping. All patients (n=90) were randomly allocated to one of the following three groups at a 1:1:1 ratio (n=30 in each): Control group (Group I), ropivacaine group (Group II), and dexmedetomidine combined with ropivacaine group (Group III). This randomized, double-blind study was approved by the First Affiliated Hospital of Wannan Medical College Ethics Committee. Additionally, written informed consent was obtained prior to the surgery we obtained. The randomization was performed using simple random sampling. The randomization scheme was generated using the table of random sampling numbers. Patients were blinded to the treatment allocation, and the recorder was blinded to the study groups. Patients in Group I received post-operative intravenous analgesia only after the surgery; Group II received a TAP block with 20 ml 0.375% ropivacaine prior to the surgery, following the induction of anesthesia; and Group III received a TAP block with 20 ml 0.375% ropivacaine and 1 μg/kg dexmedetomidine prior to the surgery, following the induction of anesthesia.

Anesthesia, surgery and analgesia. All patients fasted for 8 h prior to the operation and took no medications during this time. Peripheral venous access was obtained after the patient had entered the operating room. Standard monitoring included continuous electrocardiography, non-invasive determination of the blood pressure (BP), pulse oximetry to measure oxygen saturation and capnography to measure end-tidal CO_2 ($P_{ET}CO_2$). In addition, the depth of anesthesia and sedation were simultaneously determined by detecting brain waves with a Narcotrend monitor (version 3.1; MonitorTechnik, Bad Bramstedt, Germany). Prior to the induction of anesthesia, 10 ml/kg lactated Ringer's solution was rapidly infused. During the surgery, 6% hydroxyethyl starch was infused at a rate of 6 ml/kg/h based on the amount of bleeding and urine output.

Induction of anesthesia was performed as follows: General anesthesia was induced with midazolam (0.05 mg/kg), fentanyl (4 μg/kg), propofol (2 mg/kg) and vecuronium (0.08-0.12 mg/kg). A laryngeal mask airway (LMA) was inserted when loss of the eyelash reflex was confirmed. The Aestiva/5 anesthesia machine (Datex-Ohmeda Inc.; GE Healthcare, Little Chalfont, UK) was used for mechanical ventilation, with the following settings: Tidal volume, 8-10 ml/kg; ventilation frequency, 12 times per min; inspiratory-to-expiratory ratio, 1:2; fractional inspired O_2, 100%; and oxygen flow, 2 l/min. Anesthesia was maintained with remifentanil using micropump injection at a speed of 0.2 μg/kg/min. Vecuronium was used to maintain muscle relaxation through intermittent intravenous boluses. The rate of the propofol pump was adjusted based on Narcotrend monitoring to maintain the Narcotrend index value at 37-46, intraoperative BP and HR fluctuations <20%, an urine output of >1 ml/kg/h and a $P_{ET}CO_2$ of 35-45 mmHg with mechanical ventilation. After completion of the operation, the administration of anesthetics was stopped. Only Group I was treated with disposable intravenous analgesia pumps (non-electric-drive) with the following analgesic formula: Sufentanil (100 μg) + butorphanol (4 mg) + granisetron (3 mg), dissolved in normal saline and diluted to 100 ml; analgesia pump parameters were set to infusion at 3 ml/h. After the patients had recovered from anesthesia and were spontaneously breathing, the LMAs were removed. Patients were returned to the ward after the vital signs were stable. The patients from the three groups did not receive any additional analgesics for 24-36 h after the operation.

A single-injection ultrasound-guided left-sided unilateral TAP block was performed in Groups II and III. After induction of anesthesia, a linear array ultrasound probe (5-10 MHz) was applied with the patient in the supine position. The ultrasound probe was placed in the midaxillary line, in a transverse plane to the lateral abdominal wall. Subsequently, the needle was inserted into the plane under ultrasound guidance and advanced until it reached the plane between the internal oblique and transversus abdominis muscles; a local anesthetic was not used. The needle continued until it reached the plane, leading to TAP expansion, which appeared as a hypoechoic space. Careful aspiration was performed to exclude the possibility of vascular puncture. After negative aspiration, Group II received 0.375% ropivacaine (20 ml) and Group III received 0.375% ropivacaine (20 ml) + dexmedetomidine (1 μg/kg). The nerve block and ultrasound analysis were performed by the same anesthesiologist.

Endpoints. The operative time, propofol dosage, time to awakening (the time from the cessation of propofol administration until the patients can open eyes after calling the their name), time to spontaneous breathing (measured from the cessation of propofol administration), extubation time (the time from the cessation of propofol administration to the remove the laryngeal mask airway) were recorded. Furthermore, the Steward score (13) was determined 5 min after extubation as follows: i) The level of consciousness was scored as 2 for full recovery; 1 for responsiveness to stimulation and 0 for no responsiveness to stimulation; ii) the degree of unobstructed respiratory tract was scored as 2, patient is able to cough on request; 1, the respiratory tract is unobstructed and may be maintained without support; 0, requirement for respiratory support; iii) physical activity was scored as 2, moving of limbs purposefully; 1, non-purposeful moving of limbs; 0, no motoric activity of limbs. In addition, the VAS score (0 points, no pain; <3 points, slight pain that is endurable; 4-6 points, pain affecting sleep that may still be endured; 7-10 points, increasingly strong pain that cannot be endured) was determined when the patients were in a quiet and inactive state at 2, 4, 8, 12 and 24 h post-operation as the patient's self-reported their level of pain. Nausea and vomiting, as well as respiratory depression ($Spo_2 \leq 93\%$ following extubation) were also recorded. All data were recorded continuously by anesthesiologists, who were blinded to the treatment.

Statistical analysis. Continuous variables were expressed as the mean ± standard deviation. Normally distributed continuous variables were compared between multiple groups using one-way analysis of variance for inter-group comparisons. Categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. All analyses were two-tailed, and P<0.05 was considered to indicate a statistically significant difference.

Results

Characteristics of patients. No significant differences were present among the groups regarding general characteristics, including age, body mass index and operation type (Table I).

Table I. Demographic data and surgical characteristics of the patients of the three groups (n=30 in each).

Parameter	Group I	Group II	Group III
Age (years)	37.4±9.82	34.4±8.15	35.6±7.35
BMI (kg/m^2)	22.22±2.40	21.75±2.44	21.73±1.53
Duration of surgery (h)	1.49±0.41	1.41±0.53	1.48±0.47

Values are expressed as the mean ± standard deviation. BMI, body mass index.

Dosage of propofol and recovery parameters. Compared with those in Group 1, the dose of propofol, as well as the time of awakening, spontaneous breathing and extubation were significantly decreased in Group III (P<0.01 and P<0.05, respectively). In addition, there was no significant difference in the Steward score between groups (Table II).

Adverse event. The incidence of nausea and vomiting in Groups II and III was significantly decreased compared with that in Group I (P<0.05; Table III). No respiratory depression was observed in the three groups.

VAS score. In addition, the VAS score at 2 and 4 h in Group II (both P<0.05) and 2, 4 (P<0.01) and 8 h (P<0.05) in Group III after the surgery were significantly lower compared with those in Group I. No significant differences were observed 12 and 24 h after the surgery (Table IV).

Discussion

The present study demonstrated that combination of dexmedetomidine with a TAP block by ropivacaine significantly reduces the propofol dosage. According to previous studies (14-16), the dosage of dexmedetomidine for nerve block ranged from 0.75 to 1 μg/kg. In the present study, 1 μg/kg dexmedetomidine was selected as the experimental dose.

The Steward score system is used to evaluate recovery of patients following general anesthesia by assessing respiration, consciousness and motor coordination (12). Currently, the system is used worldwide to evaluate the recovery of patients in post-anesthesia care units. Wang *et al* (17) used the Steward score to evaluate the recovery of patients from general anaesthesia following gynaecological laparoscopic surgery 5, 15, 30 min after extubation. In the current study, the Steward score was used to evaluate the recovery of patients 5 min after extubation.

Previous studies have indicated no difference between unilateral and bilateral TAP (5,18). Mukhtar and Singh (19) were the first to report on the use of ultrasound-guided bilateral TAP block for laparoscopic surgery. They performed a left-sided unilateral TAP block, which required no opioids in the immediate post-operative period. In the present study, a left-sided unilateral TAP block was also used.

In the present study, dexmedetomidine was administered as a TAP block rather than by intravenous injection. This technique has been demonstrated to produce similar sedation effects to those of intravenous injection. The phenomenon of sedation by a dexmedetomidine TAP block is consistent with studies investigating the use of dexmedetomidine for peripheral nerve block. Harsoor *et al* (20) reported that intravenous injection of dexmedetomidine is effective in reducing the stress response to surgical trauma and requirement of sevoflurane during entropy-guided general anesthesia. Furthermore, Fragen and Fitzgerald (21) indicated that dexmedetomidine at a plasma concentration of 0.7 ng/ml decreases the minimum alveolar concentration of sevoflurane in adults by 17%.

The administration of dexmedetomidine by different routes, e.g., intranasal or epidural, may produce a similar sedation to that achieved by intravenous injection. Savla *et al* (22) reported that intranasal dexmedetomidine pre-treatment significantly reduced the concentration of sevoflurane required to produce 50% of the maximal effect by LMA administration in children by 21%. In addition, Sheta *et al* (23) determined that intranasal 1 μg/kg dexmedetomidine is an effective and safe alternative for pre-medication in children, which results in superior sedation compared with 0.2 mg/kg intranasal midazolam. Kaur *et al* (24) investigated epidural anesthesia with 150 mg 0.75% ropivacaine with adjunct dexmedetomidine (1 μg/kg) and identified that the sedation score gradually increased during surgery compared with single ropivacaine therapy. Furthermore, Fares *et al* (25) identified a significantly prolonged duration of arousable sedation by using a combination of dexmedetomidine (1 μg/kg) and caudal bupivacaine 0.25% (1 ml/kg) for pediatric major abdominal cancer surgeries. Also She *et al* (26) indicated that the mean duration of sedation is significantly prolonged by caudal dexmedetomidine, while Lin *et al* (27) observed that the addition of 1 μg/kg dexmedetomidine to ropivacaine for cervical plexus block extended the duration of analgesia, with the patients appearing sedated and arousable. Similar results have been obtained for brachial plexus blocks (28).

Regarding the Steward score 5 min after extubation, no significant difference was identified between the three groups of the present study. Dexmedetomidine increased the anesthetic potency of propofol, but the overall dosage was reduced. By contrast, the time to awakening, time to spontaneous breathing and extubation time in the dexmedetomidine group were lower than those in the control group.

Table II. Dosage of propofol and recovery parameters among the patients of the three groups (n=30 in each).

Parameter	Group I	Group II	Group III
Dosage of propofol (μg/kg/min)	94.3±24.1	81.7±26.2	60.8±13.5[a]
Time until awakening (min)	4.05±0.73	3.43±0.63	3.18±0.43[b]
Time until spontaneous breathing (min)	5.60±0.80	4.68±0.54	3.62±0.71[b]
Extubation time (min)	6.80±1.01	5.68±0.61	4.14±0.72[b]
Steward score 5 min after extubation	5.90±0.22	5.95±0.30	6.00±0.01

Values are expressed as the mean ± standard deviation. [a]P<0.01, [b]P<0.05 vs. Group I.

Table III. Incidence of nausea and vomiting in the three groups (n=30 in each) after the operation.

Adverse event	Group I	Group II	Group III
Nausea and vomiting	18 (60)	7 (23)[a]	4 (13)[a]

Values are expressed as n (%). [a]P<0.01 vs. Group I.

Table IV. Visual analogue scale scores in patients of the three groups (n=30 in each) at different time-points after the operation.

Time after operation (h)	Group I	Group II	Group III
2	1.75±0.20	0.76±0.19[a]	0.55±0.15[b]
4	1.75±0.23	0.81±0.17[a]	0.59±0.15[b]
8	1.45±0.24	0.86±0.18	0.73±0.13[a]
12	1.10±0.24	0.76±0.22	0.59±0.12
24	0.35±0.16	0.10±0.06	0.05±0.04

Values are expressed as the mean ± standard deviation. [a]P<0.05, [b]P<0.01 vs. Group I.

Gynecological laparoscopy has the advantages of small trauma, quick recovery and less pain when compared with traditional laparotomy. Although the total recovery and hospitalization time tend to be shorter, post-operative pain continues to be a notable problem in laparoscopic surgery. Post-operative pain is most severe during the first 24 h post-surgery. Analgesia is an important factor during this period (29). In the present study, Groups II and III exhibited good analgesic effects on post-operative pain. The analgesic effects of Group II were better than those of intravenous post-operative analgesia within the first 4 h, however 8 h after the surgery, the analgesic effects in Group II were not significantly different from those in Group I. Group III exhibited good analgesic effects within 8 h post-surgery. In conclusion, these results demonstrated the advantage of TAP in gynecological laparoscopy for post-operative analgesia.

As patients are placed in the Trendelenburg position during surgery, the pneumoperitoneal pressure is usually high and long-lasting, and due to the use of general anesthetics and post-operative intravenous analgesics as well as due to other factors, the incidence of post-operative nausea and vomiting is high (30). In the present study, fewer patients suffered from nausea and vomiting in the TAP block group and the dexmedetomidine group compared with those in the control group. This was slightly inconsistent with the study published by Aniskevich *et al* (31), which indicated that nausea and vomiting were not significantly different between the TAP block and control groups. These discrepancies may be due to differences in the method of anesthesia, patients and analgesic schemes. The mechanism by which TAP reduces the incidence of nausea and vomiting may be as follows: TAP block acts as a regional block method; local anesthetic is injected into the fascial plane between the internal oblique and transverse abdominis so as to block the dominant nerve of the abdominal front wall, thus blocking stimulation through the abdominal wall sensory nerve and effectively preventing the formation of peripheral and central sensitization to reduce abdominal incision pain (32,33). TAP reduces the number of post-operative narcotics and post-operative analgesics used.

The present results indicated that due to its convenient application, reliable post-operative analgesic effects and fewer adverse reactions, TAP block is of clinical importance. Compared with TAP block by ropivacaine alone, TAP block by ropivacaine combined with dexmedetomidine reduces the amount of anesthetic required. However, there are further advantages, including post-operative analgesia, as well as the reduction of nausea and vomiting. The present study only evaluated the consumption of anesthetics, recovery time, post-operative analgesia effect, and nausea and vomiting. Accordingly, it does not reflect all differences between the three groups encompassing all aspects of anesthesia and post-operative analgesia. Further comprehensive evaluation using a systematic research is therefore required.

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Availability of data and materials

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Authors' contributions

YC and YX designed the experiments. YX and HY performed the experiments and wrote the manuscript. YX, HY and YC analyzed the experimental data. YC revised the manuscript. The final version of the manuscript has been read and approved by all authors, and each author believes that the manuscript represents honest work.

Ethical approval and consent to participate

The present study was approved by the institutional review board in the First Affiliated Hospital of Wannan Medical College and written informed consent was obtained from all participants.

Patient consent for publication

The patients have provided written informed consent for the publication of any associated data.

Competing interests

The authors declare that they have no competing interests.

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