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Original Article

Effect of dexmedetomidine on intracranial pressure in patients undergoing gynecological laparoscopic surgery in Trendelenburg position through ultrasonographic measurement of optic nerve sheath diameter

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Abstract: Objective: To evaluate the effect of dexmedetomidine on intracranial pressure (ICP) in patients undergoing gynecological laparoscopic surgery in Trendelenburg position through ultrasonographic measurement of optic nerve sheath diameter (ONSD). Methods: Ninety patients underwent total laparoscopic hysterectomy were selected as research subjects in this prospective study. These patients were divided into a dexmedetomidine group (n=45) and a control group (n=45) using a random number table. The dexmedetomidine group was pumped with 0.5 μg/kg dexmedetomidine (20041731, Yangtze River Pharmaceutical Group, China) 10 min before the anesthesia induction, followed by a continuous pump of 0.5 μg/(kg·h) until the end of the surgery, and the control group was pumped with 0.5 μg/(kg·h) 0.9% sodium chloride solution. Patients in both groups were assisted with mechanical ventilator after endotracheal intubation by rapid induction. Intraoperatively, the pneumoperitoneum pressure was maintained at 14 mmHg, and the bispectral index was maintained at 40 to 60. We recorded ONSD measured with ultrasonography in both groups at 5 min before induction of anesthesia in supine position (T1), 5 min after CO_2 pneumoperitoneum in Trendelenburg position (T2), 30 min after CO_2 pneumoperitoneum in Trendelenburg position (T3), 60 min after CO_2 pneumoperitoneum in Trendelenburg position (T4) and 5 min after the close of pneumoperitoneum in supine position (T5). The cerebral oxygen metabolism indicators of the two groups at different time periods were compared, including jugular venous oxygen saturation ($SjvO_2$), arterial content and arterial-to-internal jugular difference ($Da\text{-}jvO_2$), cerebral oxygen extraction rate ($CERO_2$). Heart rate (HR) and mean arterial pressure (MAP) were also recorded at T1-T5. Besides, American Society of Anesthesiologists (ASA) grade, time of endotracheal extubation, recovery time for orientation and postoperative adverse reactions were recorded in each group. Results: There were significant differences in ONSD at T2 ((4.77±0.14) mm vs. (4.98±0.13) mm), T3 ((5.19±0.15) mm vs. (5.53±0.14) mm), T4 ((5.10±0.11) mm vs. (5.27±0.13) mm) and T5 ((4.71±0.12) mm vs. (4.4±0.16) mm) between the two groups (all $P<0.05$), and obvious differences were also found within groups when comparing the ONSD at T2-T5 to that at T1 ($P<0.05$). There were also significant differences in $SjvO_2$, $Da\text{-}jvO_2$ and $CERO_2$ between the control group and the dexmedetomidine group at T2-T5 (all $P<0.05$), and obvious differences were found within groups when comparing the indices at T2-T5 to those at T1 ($P<0.05$). The incidences of postoperative dizziness (20.00%), nausea and vomiting (17.78%), and headache (13.33%) in the dexmedetomidine group and were significantly lower than those in the control group (55.56%, 48.89% and 42.22%, respectively; all $P<0.05$). At T2-T5, dexmedetomidine group had lower HR than control group ($P<0.05$), while no differences were found in MAP between the two groups ($P>0.05$). There were also no differences in ASA grade, time of endotracheal extubation, and recovery time for orientation between the two groups (both $P>0.05$). Conclusion: Dexmedetomidine can effectively decrease the occurence of increased ICP in patients undergoing gynecological laparoscopic surgery in Trendelenburg position, improve brain oxygen metabolism, and reduce the incidences of postoperative dizziness, nausea and vomiting as well as headache (China Clinical Trials Registration Center, registration number: ChiCTR2100052046, https://www.chictr.org.cn).

Keywords: Dexmedetomidine, intracranial pressure, Trendelenburg position, optic nerve sheath diameter

Introduction

Laparoscopic gynecological surgery is a minimally invasive approach. However, due to the establishment of pneumoperitoneum, special positions of patients and surgical stimulation, patients still have surgical stress response [1]. The establishment of CO_2 pneumoperitoneum

and Trendelenburg position lead to elevated intra-abdominal pressure, intrathoracic pressure and airway pressure, which directly or indirectly result in increased intraoperative intracranial pressure (ICP) and intraocular pressure in patients [2]. Therefore, patients have a traumatic brain/eye injury may develop serious complications after this surgery. For patients who may have high ICP, surgery should be suspended first, and pneumoperitoneum should be closed. The patients should be put in a head-high position to accelerate cerebral venous reflux and reduce cerebral blood volume, so as to reduce ICP. Ali et al. pointed out that ICP can be significantly reduced after intraoperative conversion from the Trendelenburg position to the head-high position [3]. Second, patients should be given appropriate hyperventilation to reduce the $PaCO_2$, thereby reducing cerebral blood flow and decreasing ICP. If necessary, patients can be given drug intervention. The intravenous anesthetics propofol and the osmotic diuretic mannitol are the most commonly used drugs for reducing ICP in clinical practice. Ultrasonographic measurement of optic nerve sheath diameter (ONSD) has been recognized as a reliable, repeatable and noninvasive method for monitoring ICP [4]. Using ultrasound measurement of ONSD to assess ICP has been widely applied in patients with preeclampsia and traumatic brain injury [5]. However, there are few studies using this method to assess changes in ICP in patients during laparoscopic surgery in head-low position, and the conclusions are not consistent. Chin et al. used ultrasound to observe the changes in intraoperative ONSD in 21 patients undergoing laparoscopic radical resection of prostate cancer in head-low position [6]. They found that patients' ONSD was significantly widened 3 min after changing from supine to low-head position and after 3 min of head-low position combined with CO_2 pneumoperitoneum. After the operation, the CO_2 pneumoperitoneum was closed, and the patients' ONSD basically returned to a normal level after they were put to a supine position. Nevertheless, Philip observed intraoperative ONSD changes in 26 patients who underwent the same surgery but found no significant changes throughout the surgery [7]. Dexmedetomidine, an α_2 receptor agonist, inhibits catecholamine secretion and stabilizes intraoperative hemodynamics [8]. It has been reported that dexmedetomidine is often used to control ICP in cranial surgery and vascular interventional surgery or in special surgical positions, which may be related its function to reduce cerebral metabolic rate, maintain the balance of supply and demand of cerebral oxygen, and contract cerebral vessels [9]. The objective of this study was to evaluate the effect of dexmedetomidine on ICP in patients undergoing laparoscopic gynecological surgery by ultrasonographic measurement of ONSD.

Materials and methods

General data

This prospective randomized controlled blinded trial was approved by the Ethics Committee of Suzhou Municipal Hospital (No. SZSLYY20-2005011). All the patients and their family members have signed the informed consent. Ninety patients (35≤ age ≤65 years old) underwent total laparoscopic hysterectomy from May 2020 to February 2021 were selected as research subjects. They were divided into a dexmedetomidine group (n=45) and a control group (n=45) using a random number table.

Inclusion criteria: (1) Patients aged from 35 to 65 years old. (2) Patients had a body mass index between 18.5 to 28.0 kg/m^2. (3) Patients had conditions classified as I-II according to the American Society of Anesthesiologists. (4) Patients suffered from uterine fibroids, adenomyosis, uterine fibroids with adenomyosis, or refractory dysfunctional uterine bleeding.

Exclusion criteria: (1) Patients who had eye diseases, central nervous system diseases, cardiovascular diseases, cerebrovascular diseases or diabetes. (2) Patients whose ultrasound scans or measurements failed to clearly show the structure of ONSD. (3) Patients whose surgical time was less than 1 h. (4) Patients whose CO_2 pneumoperitoneum and Trendelenburg position was interrupted. (5) Patients who were sent to receive open cholecystectomy. (6) Patients who had a history of allergy to α_2 agonists.

Anesthesia methods

Patients were visited 1 day before surgery. The general data and related medical history of patients were recorded in detail. Patients were carefully evaluated according to the above

inclusion criteria and exclusion criteria, and those who did not meet the requirements were excluded.

Preoperative fasting (6 h) and no drinking (4 h) schemes were performed. After patients entered the operation room, routine monitoring of heart rate (HR), mean arterial pressure (MAP), oxygen saturation and electrocardiogram was carried out. Peripheral venous access to the right upper extremity was opened with a 18-gauge needle (BD Corporation, USA). During the surgery, a bispectral index (BIS)-Vista monitor (BIS Complete, Aspect, USA) was used to monitor the depth of anesthesia. The dexmedetomidine group was pumped with 0.5 μg/kg dexmedetomidine (20041731, Yangtze River Pharmaceutical Group, China) 10 min before the anesthesia induction, followed by a continuous pump of 0.5 μg/(kg·h) to the end of the surgery, and the control group was pumped with 0.5 μg/(kg·h) 0.9% sodium chloride solution (1G90A1, Otsuka Pharmaceutical, China). Anesthesia induction was based on intravenous administration of midazolam (MS200501, Jiangsu Enhua Pharmaceutical, China), propofol (20122331, Yangtze River Pharmaceutical Group, China), etomidate (20122331, Jiangsu Enhua Pharmaceutical, China), sufentanil (01A06191, Yichang Renfu Pharmaceutical, China) and vicuronium bromide (20042621, Jiangsu Hengrui Pharmaceutical, China). Besides, patients were given oxygen with mask for about 3 min. After the patient's muscles were completely relaxed, assisted mechanical ventilation was performed with endotracheal intubation. The respiratory parameters were set as 6-8 mL/kg of tidal volume, 12-16 times/min of respiratory rate, 1:2 of suction-to-exhalation ratio, 2.5 L/min of oxygen flow, and 60% of inhaled oxygen concentration. Intraoperatively, the respiratory parameters were adjusted to maintain end-tidal carbon dioxide partial pressure at 35-45 mmHg. An injection pump of propofol combined with remifentanil was applied for anesthesia. Intermittent bolus dosing of 1/3 to 1/2 of the initial dose of vicuronium bromide (00A06271, Yichang Renfu Pharmaceutical, China) was administered. The pneumoperitoneum pressure was maintained at 14 mmHg, and the BIS was maintained at 40 to 60. MAP was maintained ±20% based on the preoperative level. When MAP <60 mmHg, intravenous bolus of 6 mg ephedrine (200402, Shenyang No.1 Pharmaceutical, China) was administered, and the infusion was speeded up. When HR <50 beats/min, intravenous bolus of 0.5 mg atropine (201224, Broad Pharmaceutical, China) was applied. After the CO_2 pneumoperitoneum was established, the patient was put at 25-30 degrees in the head-down position. After the pneumoperitoneum was closed, the patient was placed in supine position.

Measurement methods for ONSD

Eye scans were performed for patients using portable color ultrasounds (Sonosite, USA). The patient's closed eyelids were covered with a sterile transparent dressing. The high-frequency linear array probe was evenly applied with a conductive gel to scan the cross-sectional and sagittal surfaces of one side of the eyeball. The ultrasound probe was placed horizontally or vertically on the patient's eyeball. The probe angle and depth during operation was slightly adjusted to obtain a clear optic nerve sheath (ONS) image without pressing the eyeball. The ONSD was measured with an electronic caliper at 3 mm behind the eyeball (see **Figure 1**). The ONSD of cross-sectional and sagittal surfaces of both eyes were measured. The final ONSD value was the average of the four measurements, accurate to 0.01 mm [6].

Outcome measures

Main outcome measures: We recorded ONSD in both groups at 5 min before induction of anesthesia in supine position (T1), 5 min after CO_2 pneumoperitoneum in Trendelenburg position (T2), 30 min after CO_2 pneumoperitoneum in Trendelenburg position (T3), 60 min after CO_2 pneumoperitoneum in Trendelenburg position (T4) and 5 min after the close of pneumoperitoneum in supine position (T5).

The cerebral oxygen metabolism indicators were recorded. Jugular bulbar blood (3 ml) and radial artery blood (3 ml) were collected from both groups at T1-T5 to detect jugular venous oxygen saturation ($SjvO_2$), arterial content and arterial-to-internal jugular difference ($Da\text{-}jvO_2$) and cerebral oxygen extraction rate ($CERO_2$).

Secondary outcome measures: ASA grades were recorded. ASA classify patients into five levels before anesthesia based on their physical condition and surgical risk. Grade 1: People have healthy physique, good development and

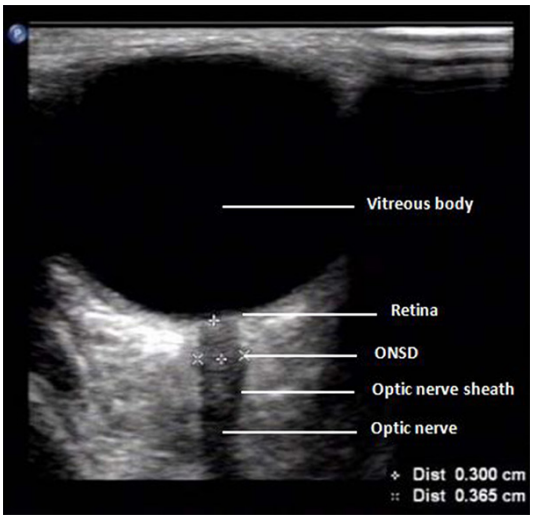

Figure 1. Optic nerve sheath diameter measured with ultrasonography.

nutrition, and normal function of each organ. Grade 2: In addition to surgical diseases, patients have other mild diseases, with sound function compensation. Grade 3: Patients have additional severe illness and limited physical activity, but are still able to cope with daily activities. Grade 4: Patients have additional severe diseases, lose daily activity, and often face life threats. Grade 5: Patients are dying probably in 24 hours whether the operation is performed or not.

The HR and MAP at T1-T5, as well as the time of endotracheal extubation and recovery time for orientation were recorded in both groups.

Postoperative adverse reactions

The incidence of adverse reactions, such as dizziness, postoperative nausea and vomiting (PONV) and postoperative headache (POHA) within 3 hours after surgery was recorded in both groups.

Statistical analysis

As shown in the pretest, the ONSD value was 5.18±0.13 mm at T3 in dexmedetomidine group, and 5.31±0.14 mm at T3 in control group. With a two-tailed α of 0.05, a confidence coefficient of 95%, a loss to follow-up rate of 20%, we predicted that 45 patients are needed in each group, so 90 patients were included in this study.

SPSS 26.0 software was adopted for statistical analyses. Measurement data with normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± sd). The pairwise comparisons between groups were carried out using group t-test, and comparisons within group were analyzed by repeated measures analysis of variance. Count data were tested by Pearson's chi-square test. Differences of *P*-values <0.05 were considered statistically significant.

Results

Comparison of general data

In this experiment, a total of 94 patients receiving gynecological laparoscopic surgery were selected. Two patients who refused to participate in the experiment were excluded. The rest were randomly divided into two groups, with 46 cases in each group. There was 1 case with surgery time less than 1 h in the dexmedetomidine group, and 1 case was sent for open cholecystectomy in the control group. In the end, 90 eligible cases were included for the analysis, with 45 cases in each group. No patient was loss to follow up in both groups. In dexmedetomidine, there were 19 cases of uterine fibroids, 16 cases of adenomyosis, 7 cases of uterine fibroids with adenomyosis, and 3 cases of refractory dysfunctional uterine bleeding group, while in control group, there were 20, 15, 6 and 4 cases of the above types of diseases, respectively.

There were no statistically significant differences in terms of general data and intraoperative indicators between the two groups (all P>0.05). See **Table 1**.

Comparison of ONSD

Statistically significant differences in ONSD at T2-T5 were found between the control group and the dexmedetomidine group (P<0.05), while there was no significant difference at T1 between the two groups (P>0.05). The ONSD at T2-T5 in dexmedetomidine group was obviously shorter than that in control group (P<0.05). In addition, the ONSD at T2-T5 was longer than that at T1 in both groups (P<0.05). See **Table 2** and **Figure 2**.

Comparison of cerebral oxygen metabolism indicators

There were significant differences in $SjvO_2$, $Da\text{-}jvO_2$ and $CERO_2$ between the control group

Table 1. Comparison of general data ($\bar{x} \pm sd$)

Case (n)	Dexmedetomidine group (n=45)	Control group (n=45)	t/χ^2	P
Types of diseases				
Uterine fibroids	19	20	0.045	0.832
Adenomyosis	16	15	0.049	0.824
Uterine fibroids with adenomyosis	7	6	0.089	0.764
Refractory dysfunctional uterine bleeding	3	4	0.155	0.694
ASA I/II	24/21	22/23	0.178	0.673
Age (years)	46.5±7.1	47.6±8.3	0.676	0.501
BMI (kg /m^2)	22.83±2.21	23.61±2.45	1.586	0.116
Pneumoperitoneum time (min)	112.36±10.63	109.09±11.31	1.413	0.161
Amount of bleeding (mL)	135.32±22.73	129.54±20.36	1.271	0.207
Amount of rehydration (L)	1.08±0.41	1.12±0.39	0.474	0.637

Note: t: data from t-test; χ^2: data from Chi-squared test. BMI: body mass index. ASA, American Society of Anesthesiologists.

Table 2. Comparison of optic nerve sheath diameter (mm, $\bar{x} \pm sd$)

Group	T1	T2	T3	T4	T5
Dexmedetomidine group (n=45)	4.63±0.14	4.77±0.14[a,b]	5.19±0.15[a,b]	5.10±0.11[a,b]	4.71±0.12[a,b]
Control group (n=45)	4.61±0.11	4.98±0.13[a]	5.53±0.14[a]	5.27±0.13[a]	4.84±0.16[a]

Note: Compared with T1, [a]P<0.05; compared with control group, [b]P<0.05. T1: 5 min before induction of anesthesia in recumbent position, T2: 5 min after CO_2 pneumoperitoneum in Trendelenburg position, T3: 30 min after CO_2 pneumoperitoneum in Trendelenburg position, T4: 60 min after CO_2 pneumoperitoneum in Trendelenburg position, T5: 5 min after the close of pneumoperitoneum in recumbent position.

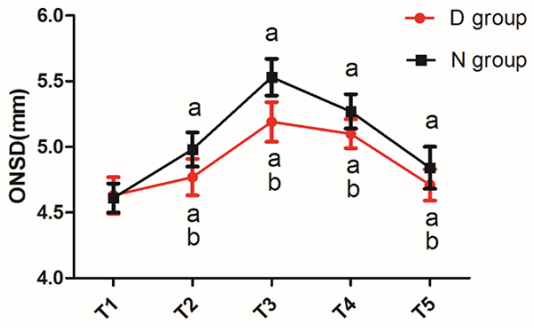

Figure 2. Comparison of ONSD at different time points. ONSD, optic nerve sheath diameter; D group, dexmedetomidine group; N group, control group. Compared with T1, [a]P<0.05; compared with control group, [b]P<0.05. T1: 5 min before induction of anesthesia in recumbent position, T2: 5 min after CO_2 pneumoperitoneum in Trendelenburg position, T3: 30 min after CO_2 pneumoperitoneum in Trendelenburg position, T4: 60 min after CO_2 pneumoperitoneum in Trendelenburg position, T5: 5 min after the close of pneumoperitoneum in recumbent position.

and the dexmedetomidine group at T2-T5 (all P<0.05), and obvious differences were also found within groups when comparing the indices at T2-T5 to those at T1 (P<0.05). See **Table 3**.

Comparison of HR and MAP

At T1, the difference in the HR between the two groups was not statistically significant (P>0.05). At T2-T5, dexmedetomidine group had lower HR than control group (P<0.05). As for MAP, there was no difference between the two groups at T1-T5 (P>0.05). See **Tables 4**, **5**.

Comparison of time of endotracheal extubation and recovery time for orientation, as well as PONV, POHA and dizziness within 3 hours after surgery

No difference was found in time of endotracheal extubation and recovery time for orientation between the two groups (both P>0.05). While the incidences of PONV, POHA and dizziness within 3 hours after surgery in dexmedetomidine group were significantly lower than that in control group (all P<0.05). See **Table 6**.

Discussion

Compared with traditional open surgery, laparoscopic surgery has been promoted in clinical practice in recent years due to less bleeding,

Table 3. Comparison of cerebral oxygen metabolism indicators ($\bar{x}$ ± sd)

Indicators	Group	T1	T2	T3	T4	T5
$SjvO_2$ (%)	Dexmedetomidine group (n=45)	61.23±8.32	56.56±8.92[a,b]	53.64±8.11[a,b]	57.72±9.05[a,b]	58.57±8.93[a,b]
	Control group (n=45)	60.57±9.03	55.15±8.44[a]	50.01±8.53[a]	53.30±8.81[a]	56.11±8.56[a]
Da-jvO_2 (mmol/L)	Dexmedetomidine group (n=45)	50.12±5.34	53.16±5.46[a,b]	56.94±5.04[a,b]	53.33±4.98[a,b]	52.62±5.23[a,b]
	Control group (n=45)	50.41±4.92	55.53±5.22[a]	63.60±5.71[a]	60.39±5.35[a]	56.84±4.99[a]
$CERO_2$ (%)	Dexmedetomidine group (n=45)	35.12±4.87	38.20±4.86[a,b]	41.25±4.87[a,b]	40.56±5.05[a,b]	37.52±4.96[a,b]
	Control group (n=45)	34.71±4.66	42.04±5.03[a]	48.67±5.31[a]	46±4.93[a]	42.61±5.19[a]

Note: $SjvO_2$, jugular venous oxygen saturation; Da-jvO_2, arterial content and arterial-to-internal jugular difference; $CERO_2$, cerebral oxygen extraction rate. T1: 5 min before induction of anesthesia in recumbent position, T2: 5 min after CO_2 pneumoperitoneum in Trendelenburg position, T3: 30 min after CO_2 pneumoperitoneum in Trendelenburg position, T4: 60 min after CO_2 pneumoperitoneum in Trendelenburg position, T5: 5 min after the close of pneumoperitoneum in recumbent position. Compared with T1, [a]P<0.05; compared with the control group, [b]P<0.05.

Table 4. Comparison of heart rate ($\bar{x}$ ± sd)

Indicator	Group	T1	T2	T3	T4	T5
Heart rate (beat/min)	Dexmedetomidine group (n=45)	81.23±8.21	64.30±5.32[a,b]	55.37±4.68[a,b]	53.21±2.93[a,b]	62.28±8.34[a,b]
	Control group (n=45)	82.51±8.33	71.41±6.74[a]	69.33±6.82[a]	67.54±4.26[a]	73.36±6.81[a]

Note: Compared with T1, [a]P<0.05; compared with control group, [b]P<0.05. F_{time}=220.036, P_{time}=0.000; $F_{inter\text{-}group}$=3.389, $P_{inter\text{-}group}$=0.003; $F_{interaction}$=0.937, $P_{interaction}$=0.393. T1: 5 min before induction of anesthesia in recumbent position, T2: 5 min after CO_2 pneumoperitoneum in Trendelenburg position, T3: 30 min after CO_2 pneumoperitoneum in Trendelenburg position, T4: 60 min after CO_2 pneumoperitoneum in Trendelenburg position, T5: 5 min after the close of pneumoperitoneum in recumbent position.

Table 5. Comparison of mean arterial pressure ($\bar{x}$ ± sd)

Indicator	Group	T1	T2	T3	T4	T5
Mean arterial pressure (mmHg)	Dexmedetomidine group (n=45)	90.71±10.92	89.93±7.35	87.65±8.09	88.43±6.26	87.21±6.48
	Control group (n=45)	89.24±9.58	88.31±8.56	89.69±7.58	87.61±5.93	88.75±7.65
t		1.63	1.415	1.839	1.696	1.03
P		0.107	0.161	0.093	0.093	0.306

Note: t: data from t-test. T1: 5 min before induction of anesthesia in recumbent position, T2: 5 min after CO_2 pneumoperitoneum in Trendelenburg position, T3: 30 min after CO_2 pneumoperitoneum in Trendelenburg position, T4: 60 min after CO_2 pneumoperitoneum in Trendelenburg position, T5: 5 min after the close of pneumoperitoneum in recumbent position.

Table 6. Comparison of time of endotracheal extubation, recovery time for orientation, PONV, POHA and dizziness within 3 hours after surgery (n, %)

Group	Time of endotracheal extubation (min)	Recovery time for orientation (min)	PONA	POHA	Dizziness
Dexmedetomidine group (n=45)	8.21±3.42	15.23±5.18	8 (17.78%)[b]	6 (13.33%)[b]	9 (20.00%)[b]
Control group (n=45)	7.96±4.14	14.12±6.21	22 (48.89%)	19 (42.22%)	25 (55.56%)
t/χ^2	0.337	0.921	9.801	9.36	12.1
P	0.737	0.359	0.002	0.002	0.001

Note: t: data from t-test; χ^2: data from chi-square test. Compared with the control group, [b]P<0.05. PONV: postoperative nausea and vomiting; POHA: postoperative headache.

less trauma and faster recovery [10]. In order to obtain a good surgical field of view, apart from ensuring a certain amount of intra-abdominal actual pressure, patients should lay supine on the back with the feet elevated above the head, namely the Trendelenburg position, during the operation. Previous studies have revealed that Trendelenburg position and pneumoperitoneum can increase the ICP [11, 12], leading to higher incidence of POHA and nausea than open cholecystectomy [13]. Besides, severe neurological complications are found due to long-time steep head-down position and pneumoperitoneum [14, 15]. After pneumoperitoneal inflation, the abdominal pressure can be transmitted to the chest cavity, causing an increase in the pressure of the superior vena cava, resulting in intracranial venous return disorders. Meanwhile, the intracranial vein is easy to expand and congest in Trendelenburg posi-

tion due to gravity. Obvious increased ICP is caused by pneumoperitoneal inflation and Trendelenburg position. There is hypercapnia due to carbon dioxide absorption, which further causes cerebral vasodilation. Elevated ICP of more than 20 mmHg has been detected in patients without neurological disease [16, 17]. Cerebral perfusion pressure is the difference between MAP and ICP. Elevated ICP may cause decreased cerebral perfusion pressure, which may result in serious consequences for the elderly with decreased cerebrovascular autoregulation or other patients at potential risk of cerebrovascular diseases. Therefore, for patients undergoing gynecological laparoscopic surgery, aggressive interventions are needed to reduce the elevation of ICP. The baseline ONSD of obese people is higher than that of normal weight people, and under pneumoperitoneum, the ONSD of obese people is also wider than that of normal weight people [16]. This may be related to the accumulation of pleural fat in heavy-weight patients, causing a relative decrease in volume. Besides, intrathoracic pressure is higher under CO_2 pneumoperitoneum, and the imbalance in the ventilation/blood flow ratio is severer. In addition, another study revealed that patients aged under 63 years old had larger baseline ONSD values and faster ONSD changes in Trendelenburg position during laparoscopic surgery than patients aged 63 years old or more [17]. This may be because the elderly have poor elasticity of ONS deteriorates, and younger people have faster compensatory compensation than the elderly when they have elevated ICP. The increase of ICP is determined by the widening of the ONS. ICP is the pressure of cranial cavity contents for the cranial cavity wall. Cranial cavity contents (brain tissue, cerebrospinal fluid, blood vessels) are responsible to maintain volume balance. Once the volume balance is broken, changes in ICP occur. In general, increased intracranial pressure is more common. The subarachnoid space in the optic nerve sheath and the subarachnoid space in the brain and spinal canal are continuous and communicative to each other, and the cerebrospinal fluid in it moves freely in the two spaces [18]. The pressure of the subarachnoid space of the brain increases with the rise of ICP. The cerebrospinal fluid moves to the subarachnoid space in the ONS through a common pathway. The ONS is elastic, which can be squeezed and deformed by the increased cerebrospinal fluid, then the ONSD becomes wider. The above information provides a theoretical basis that ultrasonographic measurement of ONSD indirectly reflects changes of ICP [19].

In this experiment, the ONSD value was measured with an ultrasound at 3 mm behind the eyeball to reflect ICP. A study including 516 healthy Chinese adults reported a normal ONSD value of 5.1 (4.7-5.4) mm [20]. In this study, there was no statistical difference in ONSD at T1 between the two groups, while the ONSD at T2-T5 in both groups were longer than that at T1. This indicates that the pneumoperitoneal compression and Trendelenburg position lead to the increase of ICP. In addition, the last measurement of ONSD before patients leaving the operation room did not return to the basal level, which suggested that after a long period of Trendelenburg position, the increase of ICP took time to recover. ROC analysis showed that when the ONSD exceeded 5.6 mm, the ICP may exceed 20 mmHg in Chinese adults [21]. Only one patient in this study had an ONSD >5.6 mm at two time points, and no significant associated complications were observed at postoperative follow-up.

Dexmedetomidine is a selective α_2 agonist with sedative, hypnotic, anxiolytic and analgesic effects, and its combination with opioids reduces the dose requirements for opioids [22]. However, the reported effect of dexmedetomidine on the ICP is controversial [23, 24]. Dexmedetomidine activates α2A receptors to show sedative, hypnotic, anti-vagal and neuroprotective effects, while activates α2B receptors to constrict cerebral blood vessels and reduce cerebral blood flow [25]. These receptor subtypes are all involved in inhibiting norepinephrine release. These mechanisms reduce brain metabolic rate, reduce brain oxygen consumption, and may reduce ICP by lowering cerebrospinal fluid pressure with no risk of cerebral ischemia [26]. Farag's investigation on the effect of dexmedetomidine on patients with acute nerve injury showed that in patients with traumatic brain injury, dexmedetomidine had no significant effect on the cerebral blood flow ratio, brain metabolic rate to cerebral blood volume [27]. In healthy adults, dexmedetomidine reduces brain metabolic rate in a dose-dependent manner. It can be seen that dexmedetomidine may have a neutral or even

beneficial effect on brain oxygen consumption, and the risk of inducing cerebral ischemia is small. Chi et al. revealed that under normal blood volume, dexmedetomidine might cause a proportional decrease in local cerebral blood flow and oxygen consumption [6]. When bleeding, local cerebral blood flow decreases more than oxygen consumption. Dexmedetomidine prevents an imbalance in the ratio of the two after bleeding, helping to provide the optimal oxygen supply and use ratio during bleeding. In addition, α_2 agonists are more effective venous constrictors in the cerebrovascular system than arteriolar vasoconstrictors, and the venous compartments account for the bulk of cerebral blood volume, so α_2 agonists can reduce intracranial pressure without significantly increasing arteriolar cerebrovascular resistance. We believe that intraoperative use of dexmedetomidine attenuates the elevation of ICP due to various factors during surgery.

In this experiment, the ONSD at T2-T5 in dexmedetomidine group were obviously shorter than those in control group, suggesting that dexmedetomidine effectively controlled the increase of ONSD in pneumoperitoneal and Trendelenburg position. The central nervous system, sensitive to ischemia and hypoxia, plays an important role in maintaining the balance of supply and demand of brain oxygen, reducing brain oxygen metabolism for cerebral protection of patients with pneumoperitoneal in Trendelenburg position, and reducing postoperative neurological complications. Venous blood in the globules of the internal jugular vein mainly comes from the intracranial vein, so the blood of the globules of the internal jugular vein can be equivalent to the blood gas analysis of cerebral venous blood, and $SjvO_2$, Da-jvO_2 and $CERO_2$ can indirectly reflect the status of brain oxygen metabolism under stable oxygen supply. An increase in $SjvO_2$ and a decrease in Da-jvO_2 indicate adequate oxygen supply to the cranial brain, while a decrease in $CERO_2$ indicates an improvement in cerebral perfusion. Compared with those in the control group, there were significant differences in $SjvO_2$, Da-jvO_2 and $CERO_2$ in the dexmedetomidine group at T2-T5. It has been shown that dexmedetomidine has a cerebroprotective effect. Its mechanism may be related to its reduction of norepinephrine release from brain tissue, regulation of the balance of prepoptosis proteins and antiapoptotic proteins, reduction of the release of excitatory neurotransmitters such as glutamate, and inhibition of calcium ion inflow [28]. Dexmedetomidine acting on the α_2 receptor effectively inhibits catecholamine secretion, lowers heart rate, and stabilizes intraoperative hemodynamics [29].

In this study, there was no statistical difference in MAP at each time point between the two groups. The HR at T2-T5 in dexmedetomidine group were lower than those in control group. Only one patient was treated with atropine, and there were no related complications shown in postoperative follow-up. The partial pressure of arterial blood carbon dioxide has obvious effects on cerebrovascular vessels. To exclude this influencing factor, the respiratory parameters were adjusted in this experiment to ensure stable intraoperative end-expiratory carbon dioxide. Nausea, vomiting, and headache after general anesthesia are common in Trendelenburg position, and elevated ICP is another cause [30]. Recent research by Yilmaz et al. has found that an increase in intraoperative ONSD is significantly associated with the onset of PONV and POHA within 3 h after surgery [31]. In this study, the incidences of PONV and POHA within 3 h after surgery were lower in the dexmedetomidine group than in the control group. Dexmedetomidine may indirectly affect the occurrence of PONV and POHA by reducing elevated ICP. In this study, there were no differences in time of endotracheal extubation and recovery time for orientation between the two groups, indicating that dexmedetomidine not only had no effect on postoperative recovery but also reduced the occurrence of postoperative adverse reactions.

There are some limitations in this study. (1) The patients were not grouped based on the age. For younger patients, they can self-regulate the increased ICP better. (2) The sample size was small, and a future multi-center large sample study should be carried out. (3) In order to not affect the surgical operation, the effects of different angles and different pressure on ONSD were not measured. (4) ONSD only indirectly reflected the level of ICP but failed to reflect the real ICP.

In the future, to explore the relationship between Trendelenburg position and the increase of ICP, we can apply transcranial Dop-

pler for more accurate and intuitive monitoring of cerebral blood flow combined with cerebral oxygen saturation. At the same time, the incidence of complications such as PONV and POHA can be discussed to clarify the actual clinical significance of this change. Moreover, controlled studies can be conducted on changes of ONSD with different doses of dexmedetomidine.

To sum up, the application of dexmedetomidine effectively reduces the increased ICP of patients undergoing gynecological laparoscopic surgery in Trendelenburg position, improves brain oxygen metabolism, and decreases the incidence of postoperative dizziness, nausea and vomiting as well as headache.

Disclosure of conflict of interest

None.

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