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Original Article

Effect of general anesthesia combined with epidural anesthesia on circulation and stress response of patients undergoing hysterectomy

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Abstract: Objective: To investigate the effect of general anesthesia combined with epidural anesthesia on circulation and stress response of patients undergoing hysterectomy. Methods: A total of 97 patients undergoing hysterectomy in our hospital from December 2017 to December 2019 were recruited as the research participants, of whom 44 patients (general anesthesia group) received general anesthesia and 53 patients (joint group) received general anesthesia combined with epidural anesthesia during operation. The hemodynamic indexes, anesthetic effect, anesthetic recovery effect, cognitive function, and stress substance levels of the two groups were compared. Results: Compared with the general anesthesia group, the SBP and HR of the patients in the joint group were more stable, and the anesthesia effect and recovery effect in the joint group were better. The MMSE score of the joint group at 6 h and 12 h after anesthesia was significantly higher than that of the general anesthesia group ($P < 0.001$). There was no significant difference in the levels of adrenaline and norepinephrine between the two groups before operation ($P > 0.05$). The levels of stress substances in the two groups increased at 30 min after operation ($P < 0.001$), and those in the joint group were significantly lower than those in the control group ($P < 0.001$). Conclusion: Compared with general anesthesia, general anesthesia combined with epidural anesthesia produces better anesthetic effect in hysterectomy, has less influence on patients' circulatory response and can reduce stress response.

Keywords: General anesthesia, epidural anesthesia, hysterectomy, circulatory function, stress reaction

Introduction

Benign uterine disease is common in gynecology, and it will lead to the decline of female health-related quality of life. Hysterectomy is often used for patients with no fertility demand or patients with severe diseases, and it is one of the most common surgical operations in America [1]. Among the hysterectomies, laparoscopic hysterectomy accounts for 81.5% [2]. Laparoscopic surgery has less trauma, short hospital stay and quick recovery, which greatly reduces the severity of the disease and economic burden of patients, and can be widely used in clinical practice [3]. Although it has great benefits, there will still be strong pain stimulation during the operation. The level of surgical anesthesia will affect the immune system and health-related quality of life of patients [4], so it is particularly important to choose appropriate anesthesia methods.

Surgery under local anesthesia brings more benefits to patients, but laparoscopic hysterectomy is usually performed under general anesthesia [5]. Studies have shown that application of different anesthesia methods during surgery will have different effects on hemodynamics, stress response and cognitive function recovery of patients [6-8]. Combined anesthesia is the recommended choice for surgical anesthesia, which makes drugs have synergistic effect, has better anesthetic effect and better results in patients' waking [9]. Therefore, this study seeks a combined anesthesia method to reduce the influence of surgery on patients' circulatory response and minimize stress reaction. Epidural anesthesia and general anesthe-

sia are commonly used in clinic [10, 11]. At present, combined epidural anesthesia has been widely used in obstetrics in China because of its high safety [12, 13]. However, there have been few studies on the application of general anesthesia combined with epidural anesthesia in hysterectomy, and the influence of this combination on patients' circulation and stress response is still unclear. Therefore, this study explored the effect of general anesthesia combined with epidural anesthesia.

Materials and methods

Clinical data collection

A total of 97 patients undergoing hysterectomy in Yiwu Central Hospital from December 2017 to December 2019 were recruited as the research participants, of whom 44 patients (general anesthesia group) received general anesthesia and 53 patients (joint group) received general anesthesia combined with epidural anesthesia during operation. Inclusion criteria: the treatment were in line with the indications of laparoscopic hysterectomy; patients had complete clinical data; patients with ASA less than grade II [14]; patients had no obvious problems in cognition, language, and vision; patients and their families signed informed consent. Exclusion criteria: patients with malignant tumor; patients had deficiency of heart, liver or lung function; patients with infection; patients had insufficient coagulation function; patients were unable to complete the test independently; patients with poor compliance. This study was approved by the medical ethics committee of our hospital.

Anesthesia method

Patients in both groups were fasted for 12 hours before operation, and venous access was established 30 minutes before entering the operating room.

General anesthesia group: general anesthesia was applied for patients. Midazolam (Jiangsu Ehwa Pharmaceutical Co., Ltd., SFDA Approval No. H20143222) with the dosage of 0.06 mg/kg, sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., SFDA Approval No. H20054171) with the dosage of 0.5 μg/kg, propofol (Hebei Yipin Pharmaceutical Co., Ltd., SFDA Approval No. H20093542) with the dosage of 1.5-2.0 mg/kg were injected intravenously for anesthesia guidance. Endotracheal intubation and anesthesia machine were used to control breathing 3 minutes after completion. Intravenous infusion of remifentanil (Jiangsu Ehwa Pharmaceutical Co., Ltd., SFDA Approval No. H20143314) with the dosage of 0.1-0.5 μg/(kg·min) and propofol with the dosage of 5 mg/(kg·h) was performed during operation to maintain anesthesia.

Joint group: patients were required to take the left lateral position, puncture and catheterization were performed through L1-2 space, 4 ml of 1.5% lidocaine (Beijing Yookon Pharmaceutical Co., Ltd., SFDA Approval No. H11020558) was injected, and 6 ml of 0.4% ropivacaine (Hebei Yipin Pharmaceutical Co., Ltd., SFDA Approval No. H20173027) was injected after 5 minutes of observation, and the anesthetic tissue plane was controlled below T6. The methods and drugs of induction and maintenance of intravenous anesthesia in the joint group were the same as those of general anesthesia group.

ELISA detection

A 5 ml of venous blood was collected from two groups of patients, added with heparin solution to prepare plasma, and then the contents of epinephrine and norepinephrine in plasma were determined by ELISA (adrenaline/norepinephrine ELISA detection kit, IBL, Germany, item number: RE59242). Blank well, standard well and sample well to be tested were set. SO standard with concentration of 0 was added into the blank well, standard solution was added into the standard well, and the sample to be tested was added into the sample well. Sample diluent and horseradish peroxidase (HRP)-labeled detection antibody were added to other micro-wells except the sample well. The wells were completely washed to remove unbound biotinylated antibody, then the HRP labeled avidin was added, and the wells were washed again and added with TMB substrate for developing. TMB turned blue under catalysis and turned yellow under the action of acid. The absorbance (OD value) was measured with a microplate reader at 450 nm, and the corresponding concentration was observed by using the standard curve.

Outcome measures

Main outcome measures: The changes of hemodynamic indexes before anesthesia (T0),

Table 1. Baseline data

Group	General anesthesia group (n=44)	Joint group (n=53)	χ^2/t	P
Age (years)	45.6 ± 8.2	47.2 ± 8.7	0.925	0.357
BMI (kg/m^2)	21.63 ± 2.21	22.14 ± 2.15	1.148	0.254
ASA grading				
I	35 (43.18)	24 (54.72)	1.280	0.258
II	21 (56.82)	26 (45.28)		
Education level				
< junior high school	17 (38.64)	23 (43.40)	0.635	0.225
≥ junior high school	27 (61.36)	30 (56.60)		
Residence				
Urban	23 (52.27)	21 (39.62)	1.552	0.213
Rural	21 (47.73)	32 (60.38)		
Smoking history				
Yes	13 (29.55)	20 (37.74)	0.719	0.397
No	31 (70.45)	33 (62.26)		
Drinking history				
Yes	20 (45.45)	31 (58.49)	1.639	0.201
No	24 (54.55)	22 (41.51)		
Dietary preference				
Light	18 (40.91)	28 (52.83)	1.370	0.242
Spicy	26 (59.09)	25 (47.17)		

5 min after anesthesia (T1), immediately after anesthesia (T2) and 24 h after anesthesia (T3) were observed. The anesthetic effects of the two groups were observed. The levels of epinephrine and norepinephrine were observed before and 30 min after operation.

Secondary outcome measures: The recovery effect of anesthesia in two groups was observed. The mini-mental state examination (MMSE) [15] was used to score the cognitive function of patients in the two groups at 6 h, 12 h and 24 h after anesthesia, with a total score of 30 points. Patients with less than 27 points showed cognitive impairment, and the lower score indicates the higher degree of impairment.

Statistical analysis

SPSS22 was used for statistical analysis of the collected data. Prism 7 (Shenzhen Softhead Software Technology Co., Ltd., China) was used for visualizing the figures, and the counting data were represented by rate (%) and analyzed by Chi-square test, which was expressed as χ^2. Measurement data were expressed by mean ± SD, independent sample t test was used for comparison between two groups, and paired t test was used for comparison within groups, which was expressed by T. When $P < 0.05$, there was a statistical difference between the two groups.

Results

Comparison of baseline data between the two groups

By comparing the baseline data of two groups of patients, it was found that there was no statistical difference in age, body mass index (BMI), ASA grade, educational level, residence, smoking history, drinking history and dietary preference between the two groups, which is comparable, as shown in **Table 1**.

Comparison of hemodynamic indexes

At T1, SBP and HR in both groups were significantly lower than those at T0, while at T2, SBP and HR in general anesthesia group were still significantly different from those at T0. SBP and HR in joint group were significantly lower than those in general anesthesia group at T2, SBP and HR in joint group at T3 were not significantly different from those at T0, but SBP in general anesthesia group was significantly higher than that at T0, indicating that there were significant differences between the two groups, as shown in **Figure 1**.

Comparison of anesthetic effects

By comparing the anesthetic effects of the two groups, it was found that there was no significant difference in anesthetic duration between the two groups ($P > 0.05$), but the onset time of anesthesia and extubation time in the joint group were significantly shorter than those in the general anesthesia group ($P < 0.001$), as shown in **Table 2**.

The awake time, language recovery time and respiratory recovery time of patients in the joint group were significantly shorter than those in the general anesthesia group ($P < 0.001$), as shown in **Table 2**.

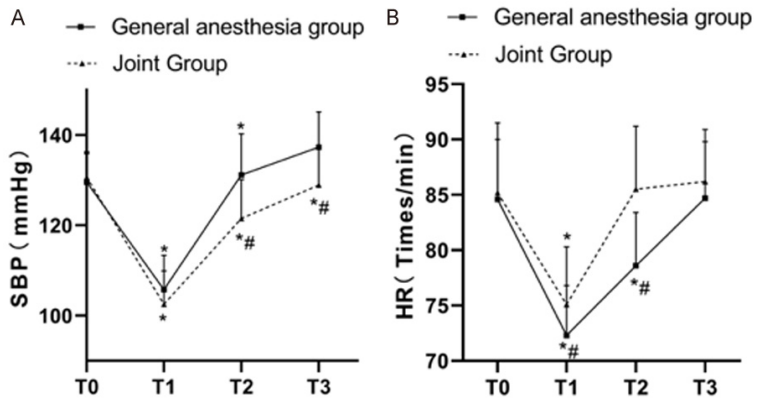

Figure 1. Comparison of hemodynamic indexes. A. SBP changes in two groups. SBP levels in the joint group at T2 and T3 were significantly lower than those in the general anesthesia group. B. Changes of HR in the two groups. HR in the joint group was significantly higher than that in the general anesthesia group at T1 and T2. * indicates a statistical difference compared with T0; # indicates a statistical difference compared with another group.

Comparison of MMSE scores

The cognitive function of the two groups was evaluated by MMSE scores. The results showed that the MMSE scores of the joint group at 6 h and 12 h after anesthesia were significantly higher than those of the general anesthesia group ($P < 0.001$), and there was no significant difference between the two groups 24 h after anesthesia ($P > 0.05$), as shown in **Table 3**.

Comparison of stress substance levels

The results of ELISA showed that there was no significant difference in the levels of adrenaline and norepinephrine between the two groups before operation ($P > 0.05$), but the stress substance levels of the two groups increased 30 min after operation ($P < 0.001$), and those of the joint group were significantly lower than those of the control group ($P < 0.001$), as shown in **Figure 2**.

Discussion

Hysterectomy is commonly applied for gynecological diseases. Laparoscopic hysterectomy is widely used in clinic because of its small incision, quick recovery and few complications. However, pain and stress will still occur during the operation, so it is particularly important to choose the appropriate anesthesia method to ensure the smoothness of the operation. At present, the clinical effect of general anesthesia combined with epidural anesthesia in hysterectomy on patients' circulation and stress response is unclear.

In this study, the hemodynamic indexes of patients during operation were detected, and it was found that the blood pressure of the two groups decreased significantly after anesthesia for five minutes, and then slowly increased. The blood pressure of patients under combined anesthesia was relatively stable, while the blood pressure of patients under general anesthesia was on the high side, and the HR of patients in joint group was relatively stable. These indicated that general anesthesia combined with epidural anesthesia had less influence on the hemodynamics of patients, and could better maintain the stability of patients' blood pressure, which had higher advantages for patients with hypertension. The research of Calvo-Soto and others [15] showed that compared with general anesthesia, epidural anesthesia combined with general anesthesia had better effect on reducing the hemodynamic response and adverse reaction of gallbladder cancer patients during operation, and on improving the postoperative cellular immunity and the quality of life of patients. Tangpaitoon and others [16] showed that the adverse reactions such as nausea and vomiting of patients under local epidural anesthesia were significantly less than those of patients under general anesthesia, and patients underwent epidural anesthesia had less postoperative pain, less use of analgesic drugs and higher satisfaction. Then, we compared the anesthetic effect and recovery effect between the two groups. The results showed that the anesthetic maintenance effect of the two groups was similar, while the anesthesia onset time and extubation time of the joint group were significantly shorter than those of the general anesthesia group. The postoperative awake time, language recovery time and respiratory recovery time in the joint group were significantly shorter than those in the general anesthesia group. This showed that the combined anesthesia and general anesthesia have

Table 2. Comparison of anesthetic effects

Group	General anesthesia group (n=44)	Joint group (n=53)	t	P
Anesthesia onset time	4.79 ± 1.18	3.02 ± 0.62	9.465	< 0.001
Withdrawal time	5.73 ± 2.14	8.91 ± 3.26	5.551	< 0.001
Duration of anesthesia	95.63 ± 14.52	98.64 ± 13.85	1.042	0.300
Awake time	7.92 ± 3.25	14.13 ± 4.15	8.078	< 0.001
Language recovery time	10.78 ± 4.37	15.86 ± 4.93	5.317	< 0.001
Respiratory recovery time	4.38 ± 2.04	7.61 ± 3.17	5.828	< 0.001

Table 3. Comparison of MMSE scores

Group	6 hours after anesthesia	12 hours after anesthesia	24 hours after anesthesia
General anesthesia group (n=44)	21.56 ± 2.43	26.31 ± 1.87	28.35 ± 1.25
Joint group (n=53)	24.28 ± 2.39	27.68 ± 1.53	28.73 ± 1.03
t	5.529	3.969	1.642
P	< 0.001	< 0.001	0.104

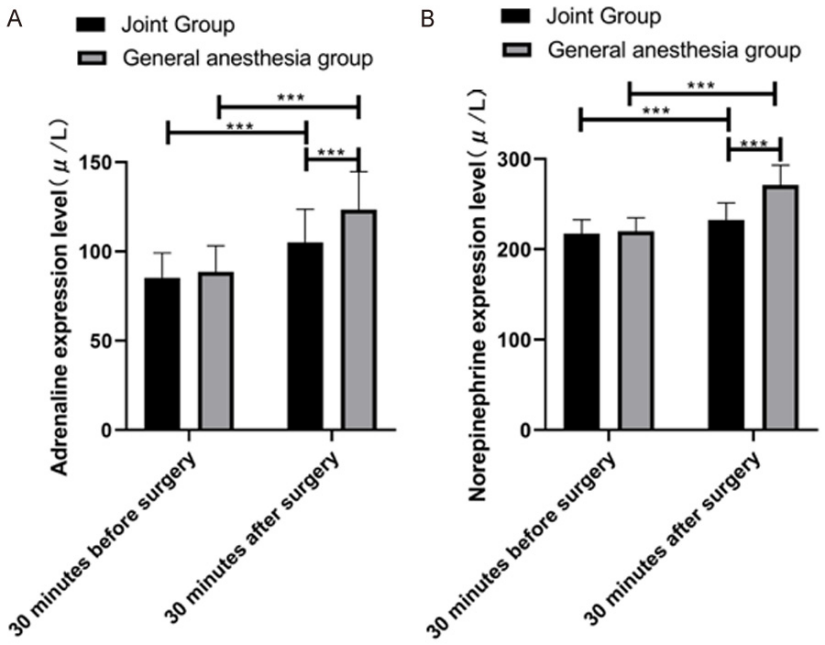

Figure 2. Comparison of stress substance levels. A. There was no significant difference in adrenalin levels between the two groups before operation. The adrenalin levels in the two groups 30 min after operation were higher than those before operation, and the adrenalin levels in the joint group were significantly lower than those in the control group. B. There was no significant difference in norepinephrine levels between the two groups before operation. The levels of norepinephrine in the two groups 30 min after operation were higher than those before operation, and the levels of norepinephrine in the joint group were significantly lower than those in the control group. *** indicates P < 0.001.

the same effect in anesthesia maintenance time, and have shorter onset time of anesthesia, so patients had better anesthesia recovery effect. The research results of Johnson and others [17] also indicated that the anesthetic effects of epidural anesthesia and general anesthesia were similar. However, during the operation under general anesthesia, the neurocognitive recovery of some patients is often delayed, which increases the incidence of cognitive dysfunction after operation [18, 19]. The research of Orhun and others [20] showed that compared with general anesthesia, epidural anesthesia combined with general anesthesia can effectively prevent cognitive dysfunction of the elderly. This is similar to our research.

Surgical treatments may have the risk of surgical incision infection, severe postoperative pain, stress response and various postoperative complications [21, 22]. Serious stress reaction will cause damage to tissues and organs, so reduction of the stress reaction of patients after anesthesia has become a topic of concern to clinical anesthesiologists in recent years. In this study, the cognitive function of patients was evaluated, and the results showed that compared with general anesthesia, the effect of combined anesthesia on cognitive function of patients was significantly reduced. At present, general anesthesia and epidural anesthesia are widely used in clinical surgery. General anesthesia can

make more drugs enter the central nervous system, while epidural anesthesia can block afferent nerves, thus reducing postoperative neuroendocrine stress substances and the impact on the center nervous system [23, 24]. Finally, we tested the changes of stress substance levels before and after operation. The results showed that there was no significant difference in adrenaline and norepinephrine levels between the two groups before operation, but they all increased significantly after operation. The stress substance levels in the joint group were significantly lower than those in the general anesthesia group, suggesting that all patients have a stress response after treatment due to surgical stimulation, while the stress response caused by combined anesthesia is light. The research by SULTAN and others [25] showed that general anesthesia played an inhibitory role in cerebral cortex and other parts of patients, but have little effect on blocking the peripheral nerve conduction block, thus resulting in the excitement of the sympathetic-adrenal medullary system of patients. At this time, the secretion of adrenaline and norepinephrine in patients increases, and the heart rate and average arterial pressure also increase after pneumoperitoneum, resulting in obvious stress reaction. Combined epidural anesthesia just makes up for this shortcoming.

Although this study confirmed that general anesthesia combined with epidural anesthesia in hysterectomy has a good anesthetic effect, there are still shortcomings. For instance, we did not follow up with the patients, and the impact of the two anesthesia methods on the quality of life of patients was not clear. Future research can supplement this content, and long-term follow-up survival conditions can be added to study the effect of anesthesia on the quality of life of patients.

To sum up, compared with general anesthesia, general anesthesia combined with epidural anesthesia has better anesthetic effect in hysterectomy and less influence on patients' circulatory response, and it can reduce stress response.

Disclosure of conflict of interest

None.

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