EFFECT OF DEXMEDETOMIDINE COMBINED WITH PROPOFOL ANESTHESIA ON HEPATECTOMY FOR LIVER CANCER

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ABSTRACT

Objective: *To explore the effect of dexmedetomidine combined with propofol anesthesia on perioperative stress response and hemodynamics of patients with hepatectomy for liver cancer.*

Methods: *120 cases with hepatectomy for liver cancer admitted in our hospital from August 2017 to August 2019 were selected as the research objects, and randomly divided into group A (n=60) and group B (n=60).Both groups of patients were treated with propofol and other anesthetic drugs for anesthesia induction and anesthesia maintenance.Patients in group A were given intravenous infusion of dexmedetomidine before anesthesia induction, while those in group B were given equivalent normal saline. The surgical indexes, hemodynamic indexes and stress response indexes were compared between the two groups.*

Results: *There was no significant difference in surgical indexes between the two groups (P>0.05), but the heart rate and mean arterial pressure in group A were significantly lower than those in group B duringliver cutting, after liver cutting and at the end of the surgery (P<0.001), which showed that the hemodynamic indexes in group A were more stable. There was no significant difference in the levels of perioperative lactic acid and cortisol between the two groups, but the blood glucose level at the end of the surgery in group A was significantly lower than that in group B (P<0.001), which showed that the stress response of group A was relatively lighter.*

Conclusion: *Dexmedetomidine combined with propofol anesthesia can effectively improve the hemodynamic indexes and reduce the perioperative stress response of the patientswith hepatectomy for liver cancer, which should be further promoted in clinical practice.*

Keywords: *Dexmedetomidine, propofol, hepatectomy.*

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Introduction

According to the WHO data, there are more than one million new cases of liver cancer in the world every year, and this disease has become a common clinical disease and seriously affects human life and health. Surgery is the main treatment for liver cancer, but large incision and frequent intraoperative traction of hepatectomy for liver cancer will increase theischemia-reperfusion injury to the liver to certain extent, resulting in patients' severe stress response and obvious fluctuation of hemodynamic indexes,which greatly increases the surgical risk and affects the prognosis of patients(1-3). Reducing intraoperative stress response and stabilizing hemodynamic situation are the keys to ensuring the smooth surgery of patients. In recent years, studies have shown that dexmedetomidine can reduce the ischemia-reperfusion injury to the liver of patients, and the mechanism of action of the drug is similar to that of natural sleep. Rational use of dexmedetomidine in hepatectomy can play an ideal sedative and analgesiceffect(4-7). Based on this, this article was to explore the effect of dexmedetomidine combined with propofol anesthesia on perioperative stress response and hemodynamics of patients with hepatectomy for liver cancer. 120 cases with hepatectomy for liver cancer admitted in our hospital from August 2017 to August 2019 were selected for the research, with summary as follows.

Materials and methods

General data

120 cases with hepatectomy for liver cancer admitted in our hospital from August 2017 to August 2019 were selected as the research objects, and randomly divided into group A (n=60) and group B (n=60). There was no significant statistical difference in general data between the two groups (P>0.05), see Table 1. This study was approved by the hospital ethics committee.

Group	Group A (n=60)	Group B (n=60)	X^2/t	P
Gender			0.039	0.843
Male	42	41		
Female	18	19		
Age (years)				
Range	18-74	19-74		
Average age	51.21±6.20	51.23±6.21	0.018	0.986
Weight (kg)				
Range	47-78	48-77		
Average weight	58.62±6.11	58.76±6.52	0.121	0.904
ASA grade			0.034	0.853
I	35	34		
II	25	26		
Liver function classification			0.035	0.852
A	36	37		
B	24	23		

Table 1: Comparison of general data of patients.

Inclusion criteria

The inclusion criteria of this study were as follows:

• The patients or their family members were fully aware of the research process and signed the informed consent;

• The patients were diagnosed with liver cancer by examination and needed surgical treatment;

• The patients had no hyperthyroidism;

• The patients were not in pregnancy or lactation period.

Exclusion criteria

The exclusion criteria of patients of this study were as follows:

• Patients with mental problems or who were unable to communicate with others;

• Patients who were suffering from other organic diseases;

• Patients with sinus bradycardia;

• Patients who had taken analgesic and sedative drugs.

Methods

Both groups of patients were treated with propofol and other anesthetic drugs for anesthesia induction and anesthesia maintenance. Dexmedetomidine was intravenously pumped before anesthesia induction for patients in group A, while equivalent normal saline was given to patients in group B, with no difference in other steps.

The specific methods were as follows:

• All patients were given intravenous inhalational anesthesia and connected with monitoring instrument of physical sign data, and then their peripheral venous access was opened.0.02 mg·kg-1 of midazolam(Jiangsu Nhwa Pharmaceutical Co., Ltd.;NMPA approval No. H10980026) was intravenously injected at 0.5 h before anesthesia induction, and local anaesthesia was performed with 2% lidocaine (China Otsuka Pharmaceutical Co., Ltd.; NMPA approval No. H20065388), and then the radial artery and right internal jugular vein were punctured and catheterized, with routine infusion given to the patients as the last step;

• Before anesthesia induction, patients in group A were intravenously pumped with 0.4 µg·kg-1of dexmedetomidine (Cisen Pharmaceutical Co., Ltd.; NMPA approval No.H20130027) within 10 minutes, and then pumped with the rate of 0.2 µg.(kg.h)-1until the abdominal cavity was closed, while patients in the control group were given equivalent normal saline;

• Anesthesia induction.

0.3-0.5 µg·kg-1 of sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd.; NMPA approval No. H20054171), 0.2-0.3 mg·kg-1 of etomidate (No. H20090131, B.Braun Melsungen AG) were successively infused for all patients, and then 0.15 mg·kg-1 of cisatracurium (Jiangsu Heng Rui Pharmaceutical Co., Ltd.; NMPA approval No. H20060869)was intravenously injected after patients were unconscious;

• Anesthesia maintenance.

3-6 mg/kg/h of propofol, 0.2-0.4ug/kg/min of remifentanil (Jiangsu Nhwa Pharmaceutical Co., Ltd.; NMPA approval No. H20143314) were given by continuosin travenousn infusion, 0.05-0.1mg/kg of cisatracurium was given by intravenous injections intermittently, and meanwhile 1.5% of sevoflurane (Jiangsu Suncadia Pharmaceutical Co.,Ltd.; NMPA approval No. H20040771) was inhaled by patients, with BIS value at around 50. 0.3-0.4μg·kg-1of sufentanil was intravenously injected at 10 minutes before the surgery, and then sevoflurane and propofol were separately stopped at 0.5 h and 10 min before the surgery was ended. At last, 0.2 μg·kg-1of sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd.; NMPA approval No. H20054171) was intravenously injected during skin suturing.

Observation criteria

Surgical indexes.Anesthesia time, intraoperative blood loss,surgery time and infusion volume were included.

• Hemodynamic indexes.The heart rate (HR) and mean arterial pressure (MAP) were compared before anesthesia induction (T_0), after anesthesia induction (T_1), during skin incision (T_2),during liver cutting (T_3), after liver cutting (T_4) and at the end of the surgery(T_5)[8-11];

• Stress response indexes. The levels of lactic acid (LD), cortisol (COR) and blood glucose (GLU) were compared before anesthesia induction (T_0), during skin incision (T_2) and at the end of the surgery(T_5).

Statistic treatment

In this study, the data processing software selected was SPSS20.0 and the selected drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA). This study included count data and measurement data, and used X^2 test and t-test. P<0.05 indicated that the difference had a statistical significance.

Result

Comparison of surgical indexes of patients

There was no significant difference in surgical indexes between the two groups (P>0.05), see Table 2.

Comparison of hemodynamic indexes of patients

The HR and MAP at T3, T4 and T5 in group

Group	Anesthesia time (min)	Intraoperative blood loss(ml)	Surgery time (min)	Infusion volume (ml)
Group A	210.56±50.54	328.67±157.56	198.56±51.23	2256.54±620.51
Group B	205.56±64.78	355.45±165.89	204.54±55.56	2315.56±741.51
t	0.471	0.907	0.613	0.473
P	0.638	0.366	0.541	0.637

Table 2: Comparison of surgical indexes of patients ($\bar{x}\pm s$).

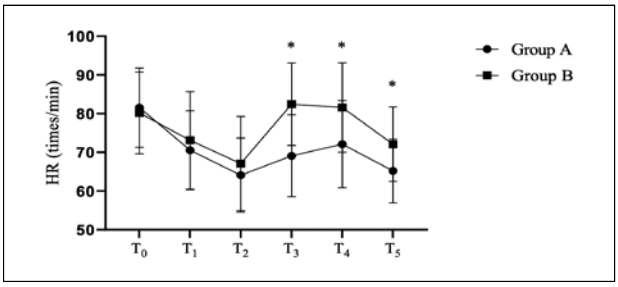

Figure 1: Comparison of the HR of patients at different time nodes ($\bar{x}\pm s$, times/min).

*Note: The horizontal axis of Figure 1 from left to right represented before anesthesia induction (T_0), after anesthesia induction (T_1), during skin incision (T_2), during liver cutting (T_3), after liver cutting (T_4) and at the end of the surgery (T_5). The vertical axis represented the HR (times/min). The line with dots represented group A and the line with squaresrepresented group B. The HR at $T_0$was (81.56±10.23) times/min in group A, and (80.20±10.54) times/min in group B; The HR at T_1 was (70.56±10.22) times/min in group A, and (73.12±12.58) times/min in group B; The HR at T_2 was (64.12±9.56) times/min in group A, and (67.12±12.14) times/min in group B ; The HR at T_3 was (69.11±10.56) times/min in group A, and (82.44±10.67) times/min in group B; The HR at T_4 was (72.11±11.23) times/min in group A, and (81.59±11.54) times/min group B; The HR at T_5 was (65.21±8.24) times/min in group A, and (72.12±9.62) times/min in group B. *meant P<0.001.*

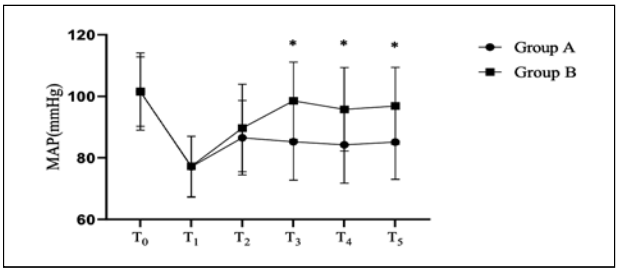

Figure 2: Comparison of the MAP of patients at different time nodes ($\bar{x}\pm s$, mmHg).

*Note: The horizontal axis of Figure 2 from left to right represented before anesthesia induction (T_0), after anesthesia induction (T_1), during skin incision (T_2), during liver cutting (T_3), after liver cutting (T_4) and at the end of the surgery (T_5). The vertical axis represented the MAP (mmHg). The line with dots represented group A and the line with squares represented group B. The MAP at T0 was (101.56±12.54) mmHg in group A, and (101.55±11.25) mmHg in group B; The MAP at T_1 was (77.10±9.89) mmHg in group A, and (77.23±9.80) mmHg in group B; The MAP at T_2 was (86.54±12.14) mmHg in group A, and (89.65±14.21) mmHg in group B; The MAP at T_3 was (85.23±12.44) mmHg in group A, and (98.57±12.52) mmHg in group B; The MAP at T_4 was (84.22±12.38) mmHg in group A, and (95.78±13.54) mmHg in group B; The MAP at T_5 was (85.12±12.10) mmHg in group A, and (96.87±12.50) mmHg in group B. *meant P<0.001.*

A were significantly lower than those in group B (P<0.001), see Figures 1-2.

Comparison of stress response indexes of patients

There was no significant difference in the levels of perioperative lactic acid and cortisol between the two groups.

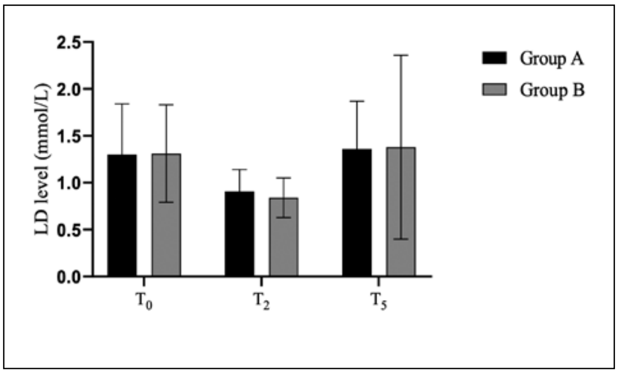

Figure 3: Comparison of the LD levels of patients ($\bar{x}\pm s$, mmol/L).

Note: The horizontal axis of Figure 3 from left to right represented before anesthesia induction (T_0), during skin incision (T_2) and at the end of the surgery (T_5). The vertical axis represented the LD level (mmol/L). The black area represented group A and the gray area represented group B. The LD level at T_0 was (1.30±0.54) mmol/L in group A , and (1.31±0.52) mmol/L in group B; The LD level at T_2 was (0.91±0.23) mmol/L in group A , and (0.84±0.21) mmol/L in group B; The LD level at T_5 was (1.36±0.51) mmol/L in group A, and (1.38±0.98) mmol/L in group B.

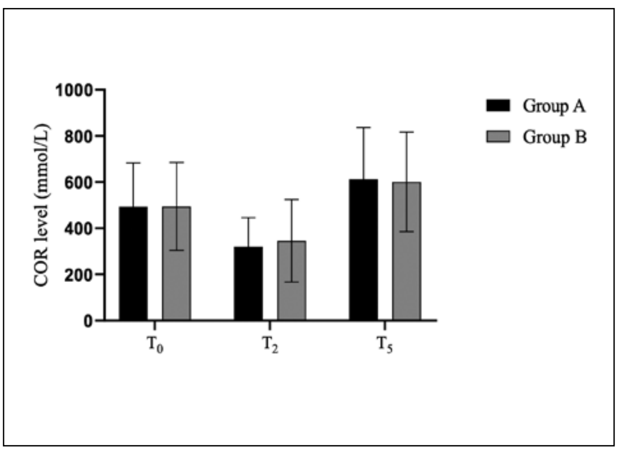

Figure 4: Comparison of the COR levels of patients ($\bar{x}\pm s$, mmol/L).

Note: The horizontal axis of Figure 4 from left to right represented before anesthesia induction (T_0), during skin incision (T_2) and at the end of the surgery (T_5). The vertical axis represented the COR level (mmol/L). The black area represented group A and the gray area represented group B. The COR level at T_0 was (493.56±189.51) mmol/L in group A, and (494.87±190.56) mmol/L in group B; The COR level at T_2 was (320.45±125.74) mmol/L in group A, and (345.74±178.52) mmol/L in group B; The COR level at T_5 was (612.54±223.52) mmol/L in group A, and (601.25±215.47) mmol/L in group B.

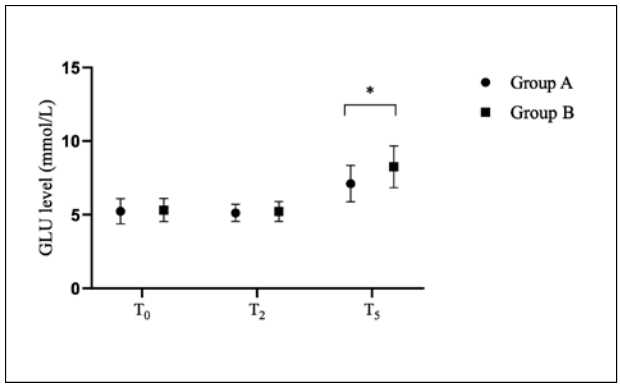

Figure 5: Comparison of the the GLU levels of patients ($\bar{x}\pm s$, mmol/L).

*Note: The horizontal axis of Figure 5 from left to right represented before anesthesia induction (T_0), during skin incision (T_2) and at the end of the surgery (T_5). The vertical axis represented the GLU level (mmol/L). The line with dots represented group A and the line with squares represented group B. The GLU level at T_0 was (5.23±0.85) mmol/L in group A, and (5.31±0.78) mmol/L in group B; The GLU level at T_2 was (5.12±0.58) mmol/L in group A, and (5.22±0.68) mmol/L in group B; The GLU level at T5 was (7.11±1.23) mmol/L in group A, and (8.25±1.42) mmol/L in group B. *meant P<0.001.*

The blood glucose levels at the end of the surgery in group A were significantly lower than those in group B (P<0.001), see Figures 3-5.

Discussion

The hepatectomy for liver cancer has the characteristics of large incision area and strong stimulation to the body . Some patients will show extremely severe stress response during the surgery, which will lead to a series of physiological changes such as obviously increasing release frequency of catecholamine, causing sharp fluctuation of the hemodynamic indexes, and seriously affecting the surgical outcomes and postoperative rehabilitation[12-15]. This study showed that the hemodynamic indexes of patients in both groups had a tendency to decrease after anesthesia, which was due to the pharmacological action[16-19].

However, the heart rate and mean arterial pressure during liver cutting,after liver cutting and at the end of the surgery in group A were significantly lower than those in group B (P<0.001), which showed that the hemodynamic indexes in group A were more stable, indicating that dexmedetomidine can weaken thesympathetic neurotransmission and inhibit the release frequency of catecholamine, with little effect on the blood vessels and better hemodynamics of patients[20-23]. Besides, this study also showed that there was no significant difference in the levels of perioperative lactic acid and cortisol between the two groups. Both lactic acid and cortisol are indicators of stress response, in which cortisol is the direct reflection of stress level. The cortisol concentration in the body will increase significantly when patients are under stress conditions, while it will decrease correspondingly after anesthesia, which means that anesthesia plays a sedative role and improves the conditions of stress response of patients(24). In the process of hepatectomy, the secretion rate of catecholamine and other hormones in the patients is accelerated, which reduces the insulin secretion. Therefore, the patients can not fully absorb glucose, and their blood glucose level will increase greatly. The blood glucose level at the end of the surgery in group A was significantly lower than that in group B ($P<0.001$), because dexmedetomidine could reduce the hypothalamus-pituitary excitability and the secretion of glucagon, so the lower blood glucose level can reflect less stress response in group A, indicating that dexmedetomidine had a good effect on inhibiting the stress response of patients.

In the study of scholar Okamura, the experimental group received dexmedetomidine in advance while the control group received equivalent normal saline, and both groups were given propofol and other drugs for anesthesia induction. The results showed that the GLU level of the experimental group was (5.21±0.74) mmol/L before anesthesia, (5.10±0.68) mmol/During skin incision and (7.08±1.15) mmol/L at the end of the surgery, which were significantly lower than those in the control group ($P<0.001$)(25), indicating that dexmedetomidine combined with propofol can effectively relieve the stress response of patients, with excellent application effect.

In conclusion, dexmedetomidine combined with propofol anesthesia can effectively improve the hemodynamic indexes and reduce the perioperative stress response of patients with hepatectomy for liver cancer, which has a high popularized value.

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