Effects of dexmedetomidine on the deformability of erythrocyte in patients with laparoscopic cholecystectomy

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Abstract: This study aims to study the impact of dexmedetomidine on the deformability of erythrocyte in patients with laparoscopic cholecystectomy. 40 patients scheduled for laparoscopic cholecystectomy were randomly divided into 2 groups: Dexmedetomidine group (0.5μg/kg loading within 10 min and 0.5μg·kg-1·h-1maintenance to the end of pneumoperitoneum, n=20, Group A) and control group (normal saline at the identical, n=20, Group B). The induction and maintenance of anesthesia of two groups were identical. Erythrocyte deformability index (EI) and haematocrit (Hct) were assayed before anesthesia and after the operation. Operation time, intraoperation blood loss and the amount of anesthetics were measured respectively. Compared with T0 (0.81±0.06), EI was significantly increased at T1 in-group B (P<0.05); Compared with T0 (0.82±0.07), EI was increased at T1 in-group A, but it showed no statistically significant difference (P>0.05). Compared with group B (1051±219) μg, (628±97) mg, the consumption of remifentanil and propofol were significantly reduced in-group A (874±167) μg, (410±77) mg (P<0.05). Dexmedetomidine can improve the deformability of erythrocyte of postoperative and reduce the amount of anesthetics.

Keywords: Dexmedetomidine; cholecystectomy; laparoscopic; erythrocyte deformability.

INTRODUCTION

Many changes in perioperative period can affect the stability of blood rheology such as surgical stress, anesthesia method and anesthetic drugs. The change in perioperative hemorheology is closely related with thrombosis after surgery, microcirculation stability, postoperative infection, etc (Connes *et al.,* 2013). All of that, the structure and function of erythrocytes are the most important factor affecting the blood fluidity and viscosity (Pytel *et al.,* 2012). Abnormal erythrocyte deformability causes blood viscosity increased, blood flow resistance increased, ability to transport oxygen reduced and microcirculation hypoperfusion (Jung *et al.,* 2011; Toksvang and Berg, 2013). According to a recent animal study of Arslan *et al*., prophylactic using of dexmedetomidine on hepatic ischemia reperfusion model in rats 30min before ischemia can improve erythrocyte deformability and reduce lipid peroxidation (Arslan *et al.,* 2012). Current study was to observe the impact of dexmedetomidine on the deformability of erythrocyte in patients with laparoscopic cholecystectomy.

MATERIALS AND METHODS

Inclusion and exclusion criteria

Selecting 40 patients in Air Force General Hospital, PLA for undergoing laparoscopic cholecystectomy from September 2012 to June 2013. Including 17 males and 23 females, ages of 18-60 yr, ASA I and II (American Society of Anesthesiology Classification), organ function and blood is normal, no blood system diseases. Exclusion criteria: Acute cholecystitis and cholangitis, acute pancreatitis, the other acute inflammation, thrombosis, BMI>30, using anticoagulant drugs recently, NSAIDs, steroid and other drugs affecting the indexes of blood rheology, conversion to open surgery patients. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Air Force General Hospital, PLA. Written informed consent was obtained from all participants.

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Grouping

The patients were randomly allocated in two groups: dexmedetomidine group (group A) and control group (group B), 20 cases of each group. Group A: Dexmedetomidine (batch number: 11122134, Jiangsu Hengrui medicine company Limited by Share, China) was diluted with 0.9% saline into 4μg/ml, administering 0.5 μg/kg of dexmedetomidine intravenously within 10 min before anesthesia induction, followed by pumping 0.5μg• kg^{-1}• H^{-1} of dexmedetomidine until pneumoperitoneum end. Group B: they were administered normal saline of the same amount intravenously at the corresponding time.

Anesthesia and operation informations

All patients were established intravenous access after they entered the operation room without using preoperative medication. Doctors monitored heart rate (HR), blood pressure (BP), pulse oxygen saturation (SpO2), electrocardiogram (ECG) end tidal carbon dioxide (PetCO2) and other vital signs. Pumping dexmedetomidine or physiological saline of the same amount intravenously for 10 min before anesthesia induction. Anesthesia was induced with midazolam (Jiangsu Enhua medicine company Limited by Share, China) 0.03-0.05 mg/kg, sufentanil (Yichang Renfu medicine company Limited by Share, China) 0.2-0.5 μg/kg, propofol (Xian Libang medicine company Limited by Share, China) 1.5-2.5mg/kg, cisatracurium (Jiangsu Dongyin medicine company Limited by Share, China) 0.15mg/kg, mechanical ventilation after tracheal intubation. Anesthesia was maintained with propofol 4-8 mg• kg^{-1}• H^{-1}, remifentanil (Yichang Renfu medicine company Limited by Share, China) 0.1-2μg• kg^{-1}• H^{-1}, every 40 min appended cisatracurium with the first dose of 1/3 to 1/2. Patients were only inputed lactated Ringer's solution (Anhui Shuanghe medicine company Limited by Share, China) without sugar during anesthesia and operation. Maintaining BP, HR as the initial value without deviating by 20% in operation by using cardioactive drug when necessary (When the mean arterial pressure is less than 20% of baseline or systolic blood pressure less than 90mmHg, diagnosed as hypotension, intravenous ephedrine 5-10mg; when the heart rate less than 60 beats / min, diagnosed as bradycardia, intravenous atropine 0.25-0.5mg), maintaining the PetCO2 at 35-45mmHg (1 mmHg=0.133kPa). Surgeries were completed by the same surgeons using three holes method and maintained pneumoperitoneum pressure on 12-14mmHg.

Data collection

Erythrocyte deformability index (EI) was assayed before anesthesia (T0) and after the operation time (T1), intraoperation blood loss, operation time and the amount of anesthetics were measured respectively. Sampling 5ml blood from the median cubital vein which side without intravenous infusion by using heparinized tubes at T0 and T1 point respectively to assay EI (first put 5ml heparin anticoagulant blood into Hemorrheology analyzer, and measure blood viscosity; secondly take out the remaining blood and put it into Blood Cell Analyzer to measure Hct; thirdly put the rest of the blood into the centrifuge at 3000 rpm for 10 min and measure plasma viscosity by using Hemorrheology analyzer; finally input the measured values into the computer to calculate the RBC deformability as EI. Hemorrheology analyzer: ZL9100c hemorrheology tester, Beijing Zhongchi Weiye, China; Blood Cell Analyzer: COULTER LH 780 ANALYZER).

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPSS16.0 statistical package. Measurement data were compared using mean ± standard deviation ($\bar{x}$±s). Count data were compared between groups using chi-square test. Difference between before and after surgery were compared using t-test. *P*<0.05 was considered statistically significant.

RESULTS

Basic data

The two groups were similar regarding gender structure, age, weight, ASA grade structure, anesthesia time and intraoperative blood loss (*P*>0.05, table 1).

Hemorheology

The Hct for patients at T0 and T1 points between two groups were not significance differences (*P*>0.05). It showed that Hct for patients were not obvious differences before and after operation. The EI for patients at T0 between two groups were not significance differences (*P*>0.05). It meant the patients between two groups had no significant differences in erythrocyte deformability. There were significant differences in EI between T1 (0.90±0.04) and T0 (0.81±0.06) in-group B (*P*<0.05), it indicated that laparoscopic cholecystectomy can change the erythrocyte deformability. There were no significant differences in EI between T1 (0.85±0.06) and T0 (0.82±0.07) in group A (*P*>0.05), it showed that dexmedetomidine can reduce the influence of anesthesia, operation and stress on erythrocytes deformability (table 2).

Drug dosage

Compared with group B, the dosage of remifentanil and propofol in-group A reduced (*P*<0.05). It meant that dexmedetomidine can reduce the amount of analgesics and sedatives during the surgery (table 3).

DISCUSSION

Erythrocyte deformability refers to the red blood cells can pass through micrangium which smaller than their own diameter freely (Xiang *et al.*, 2006). Normal erythrocyte deformability is the basis to ensure the adequate tissue oxygen supply, normal microcirculation and metabolic waste elimination (Berezniakova and Zhemela, 2013). In this study, EI was used to reflect the ability of erythrocyte deformability, it was influenced by Hct and measured by viscosity method, blood apparent viscosity was determined by erythrocyte deformability at high shear rate range, the value of EI measured bigger as the erythrocyte deformability got worse (Ye *et al.,* 2010; Dupire *et al.,* 2012). Previous research showed that the hemorheology of patients with laparoscopic cholecystectomy after pneumoperitoneum changed significantly compared with the preoperative (Beilin *et al.,* 2005), therefore this study used laparoscopic cholecystectomy patients as research subjects.

Dexmedetomidine is a highly selective α 2- adrenoceptor agonist, has the characteristics of analgesic, sedative, reducing the dosage of anesthetic drug, maintaining hemodynamic stability, easy to rouse and no respiratory depression (Wujtewicz *et al.,* 2013; Smithburger *et al.,*

Table 1: General information, anesthesia time and intraoperative blood loss between two groups ($\bar{x}$ ±s, n=20)

Group	Gender structure (cases, M/F)	Age (year)	Weight (kg)	ASA structure (cases, I/II)	Anesthesia time (min)	Blood loss (ml)
B	8/12	41±9	60.5±7.9	11/9	93±19	5±2
A	9/11	42±9	63.5±9.3	10/10	90±21	6±3

There was no statistical difference among the two groups.

Table 2: EI and Hct between two groups ($\bar{x}$ ±s, n=20)

Group	EI		Hct(L/L)	
	T0	T1	T0	T1
B	0.81±0.06	0.90±0.04***	0.37±0.03	0.36±0.04*
A	0.82±0.07**	0.85±0.06****	0.38±0.04	0.37±0.04*

*Versus Hct at T0 in the same group, *P*>0.05; **Versus EI at T0 in the group B, *P*>0.05; ***Versus EI at T0 in the group B, *P*<0.05; ****Versus EI at T0 in the same group, *P*>0.05.

Table 3: Dosage of remifentanil and propofol between two groups ($\bar{x}$ ±s, n=20)

Group	Remifentanil (μg)	Propofol (mg)
B	1051±219	628±97
A	874±167*	410±77*

*Versus group B, *P*<0.05.

2014). However, there is less research about effect of dexmedetomidine on blood rheology indices during the perioperation, especially erythrocyte deformation index. Observed in this clinical studies, compared with group B, the dosage of remifentanil and propofol in group A reduced significantly (*P*<0.05). It meant that dexmedetomidine can reduce the amount of analgesics and sedatives during the surgery. Two groups of patients before and after surgery Hct did not change significantly (*P*>0.05), meant that the two groups of patients before and after surgery Hct had no impact on EI; in group B, T1 compared with T0, EI was significantly higher in patients with statistical significance (*P*<0.05), described in patients after surgery decreased erythrocyte deformability; in group A, T1 compared with T0, EI has increased in patients but no significant difference (*P*>0.05), described perioperative using dexmedetomidine can improve erythrocyte deformability, which was impaired by surgery, anesthesia, stress and other adverse effects, and maintain perioperative blood rheology stability. Mustafa *et al*. animal studies showed that dexmedetomidine can improve erythrocyte deformability and consistent with the results of this study.

The specific mechanism of dexmedetomidine protect erythrocyte deformability is not clear, may have the following four reasons: 1) Dexmedetomidine can reduce the dosage of anesthetic and sedative drugs during the surgery (Sen *et al.,* 2013). It was reported that liposoluble anesthetic and sedative drugs can interact with rbc membrane *in vitro*, and cause erythrocyte deformability decreased *in vivo* (Reinhart and Felix, 2003). Reducing the use of anesthetic and sedative drugs in the perioperative period can reduce the effect of anesthesia and operation on erythrocyte deformability. 2) Dexmedetomidine can reduce the occurrence of operation stress and enhance antioxidant capacity (Cekic *et al.,* 2013; Nasr and Abdelhamid, 2013). Eser *et al*. research of focal cerebral ischemia-reperfusion injury in rats showed that dexmedetomidine can reduce the concentration of cortisol and increase enzyme activity of SOD and Na+-K+-ATP (Eser *et al.,* 2008), it meant dexmedetomidine can improve antioxidant capacity and reduce the stress response. 3) Dexmedetomidine can increase NOS (endothelial NO synthase) activity and the content of NO *in vivo* may by acting on endothelial cells and red blood cells (Snapir *et al.,* 2009). Researches show that NO in the red blood cells has an important role in maintaining the deformability of red blood cells and the NOS in the body is involved in the regulation of red cell deformability (Bor-Kucukatay *et al.,* 2003; Grau *et al.,* 2013). A study of healthy volunteers shows that clinical doses of dexmedetomidine can activate eNOS (endothelial NO synthase), makes the body having more NO (Snapir *et al.,* 2009). Kleinbongard *et al*. research reported that RBC membrane and cytoplasm have functional NOS (Kleinbongard *et al.,* 2006). 4) Dexmedetomidine can change the membrane permeability for ions to improve erythrocyte deformability may by acting on the erythrocyte membrane directly or working on the ion channel receptor in the cell membrane (Feng, 1994).

Erythrocyte deformability is closely related to perfusion of microcirculation and thrombosis in the perioperation period. The change of deformability can be used for the early detection of postoperative infection. These patients with hypertension, diabetes, aging, cancer or thrombosis should use dexmedetomidine to improve the erythrocyte deformability in the perioperation period. It may reduce intraoperative and postoperative complications, improve the long term prognosis of the patients.

This study shows that, perioperative use of dexmedetomidine, the amount of load to 0.5ug/kg 10 min after infusion, followed by 0.5ug/kg/h maintained until the end of pneumoperitoneum, can significantly improve the erythrocyte deformability of patients after laparoscopic cholecystectomy.

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