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Original Article

The effect of dexmedetomidine combined with sevoflurane for controlled hypotension on renalfunction during shoulder arthroscopy

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Abstract: Objective: To investigate the effect of dexmedetomidine (DMED) and sevoflurane (SEV) for controlled hypotension (CH) on patients' renal function during shoulder arthroscopy. Methods: One hundred patients undergoing shoulder arthroscopy were equally assigned to five groups. The patients in group A (control) received SEV, while the patients in groups B, C, D, and E received DMED and SEV (DMED 0.2, 0.4, 0.6, 0.8 μg/kg respectively). We measured the following: mean arterial pressure (MAP) and heart rate (HR) before anesthesia (T1), 10 min after anesthesia induction (T2), 5 min after initiating CH (T3), 1 h after initiating CH (T4), and 10 min after stopping CH (T5); the erythrocyte sedimentation rate (ESR), whole blood specific viscosity, creatinine, blood urea nitrogen (BUN), cystatin C, and glomerular filtration rate (GFR) at 2 h and 24 h post-operation. Results: No intergroup differences were observed in the MAP and HR at T1, T2, or T5 (all $P>0.05$). At T3 and T4, the two markers were reduced in the four groups (reduction level: group E>D>C>B, all $P<0.05$). Moreover, no intergroup differences were found in preoperative levels of creatinine, BUN, cystatin C, and GFR (all $P>0.05$). At 2 h and 24 h post-operation, group A had higher creatinine, BUN, cystatin C and lower GFR levels (creatinine, BUN, cystatin C levels: group A>B>C>D, group E>D, GFR level: group A<B<C<D, group E<D, all $P<0.05$); ESR and whole blood specific viscosity levels were similar among the groups. Conclusions: DMED combined with SEV during shoulder arthroscopy can achieve good hypotension results. DMED at a dose of 0.6 μg/kg has a minimal impact on renal function and exhibits protective effects on the kidneys.

Keywords: Dexmedetomidine, sevoflurane, controlled hypotension, shoulder arthroscopy, renal function

Introduction

The shoulder joint is the joint that has the greatest range of motion in the human body. As a major joint connecting the upper limb to the trunk, the shoulder joint plays a critical role in maintaining the normal function of the upper limbs, and injury to this joint can severely affect one's quality of life [1, 2]. Due to the rapid advancement in technologies for treating shoulder joint diseases, the medical specialty of shoulder surgery is quite advanced in developed countries [3, 4]. In recent years, the techniques of shoulder arthroscopy have been improved in China, and since the diagnosis and treatment of shoulder joint conditions have been advancing, the number of surgeon mastering arthroscopy has been rising [5, 6]. Studies have revealed that under the preconditions of adequate blood and oxygen supply to brain, controlled hypotension (CH) during shoulder arthroscopy can help provide a clear surgical field, shorten the duration of surgery, improve the surgical quality, and significantly reduce the incidence of various complications caused by large amounts of infusion in surgery. Thus, applying CH in shoulder arthroscopy is quite essential [7, 8].

CH refers to a technique that uses antihypertensive agents and methods to deliberately reduce the systolic blood pressure or mean arterial pressure (MAP) to a certain level during surgery. The technique will not lead to any hypoxic-ischemic injury to the essential organs, and after it is ceased, the blood pressure quick-

ly returns to its normal level without causing any permanent organ damage [9]. However, current drugs used for CH can bring about a high incidence of renal function damage [10]. It has been reported that dexmedetomidine (DEMD), which has sedative and analgesic properties, can reduce the stress reaction during the perioperative period and protect renal blood perfusion and renal function [11]. Therefore, our study aimed to investigate the optimal concentration of DMED for CH and the effect of DMED combined with SEV on the renal function of patients undergoing CH during shoulder arthroscopy.

Materials and methods

The patients' characteristics

A total of 100 patients who received shoulder arthroscopy under general anesthesia in Affiliated Cixi Hospital, Wenzhou Medical University between July 2015 and June 2018 were chosen for this study (65 males, 35 females; age: 40-60; American Society of Anesthesiologists (ASA) classes: I-II). According to a random number table, the patients were assigned to either a control group (20 patients) or the study groups (80 patients). The study groups consisted of four groups based on the concentration of DMED used in the surgery, which were groups B (0.2 μg/kg), C (0.4 μg/kg), D (0.6 μg/kg), and E (0.8 μg/kg), with 20 patients each. The patients in the study groups were given different levels of DMED in addition to sevoflurane (SEV) for CH, but those in the control group received SEV only. The study was approved by the Ethics Committee of the Affiliated Cixi Hospital, Wenzhou Medical University, and informed consent was obtained from the patients.

The inclusion criteria were as follows: 1) patients met the criteria for shoulder arthroscopy, including the presence of long head of biceps tendon (LHBT) injury, labral tear, cartilage damage, early degeneration, adhesive capsulitis, and shoulder joint instability; 2) patients aged between 40-60 years; 3) ASA class: I-II.

The exclusion criteria were: 1) patients who had infections at the surgical site; 2) patients who had renal function damage before the operation; 3) patients with cardiopulmonary insufficiency; 4) patients with coagulation disorders; 5) patients who had bradycardia, or atrioventricular block II-III as determined using electrocardiography, which disqualified patients for general anesthesia; 6) patients with ischemic peripheral vascular disease; 7) patients with hypovolemia or severe anemia; 8) patients allergic to DMED and SEV.

Grouping

According to a random number people, the 100 subjects were divided into five groups of 20 patients each. The patients in the control group (group A) received SEV only for CH, while those in the four study groups (groups B, C, D, and E) were given 0.2 μg/kg, 0.4 μg/kg, 0.6 μg/kg, and 0.8 μg/kg DMED respectively in addition to SEV for CH.

Anesthesia

After entering the operating room, all the patients underwent peripheral intravenous cannulation. Then multi-lead electrocardiography was performed, and the device for monitoring oxygen saturation was connected. The radial artery on the uninjured side was cannulated under local anesthesia for monitoring blood pressure.

The patients received oxygen for 2 min and were then injected intravenously with midazolam 0.05 mg/kg, propofol 2 mg/kg, atracurium 0.2 mg/kg, and fentanyl 0.01 mg/kg for smooth anesthesia induction.

During the surgery, the patients received target-controlled infusions of propofol and remifentanil. The levels of propofol and remifentanil in the plasma were kept at 1.5-3 μg/L, and 8 ng/L respectively. Meanwhile, the patients inhaled 2% SEV for the maintenance of combined anesthesia.

In the group A (the control group), CH was performed in the patients after the arthroscope was inserted into the shoulder joint. The SEV concentration was raised to 4%, and a continuous pumping of 0.9% normal saline was conducted. During the operation, if the MAP value was close to 50 mmHg, the drugs for CH would be stopped, and an intravenous injection of phenylephrine (3 mL, 20 μg/mL) was administered. The SEV concentration was adjusted to 2% after the removal of the arthroscope.

In group B (0.2 μg/kg DMED), the CH was performed after the arthroscope entered the shoulder joint. The SEV concentration was raised to 4%, and the target-controlled infusion of 0.2 μg/kg DMED was administered at a speed of 0.4 μg/kg/h with continuous pumping until the arthroscope was removed. During the operation, if the MAP value approached 50 mmHg, administration of SEV and DMED was stopped, and an intravenous injection of phenylephrine (3 mL, 20 μg/mL) was given.

In group C (0.4 μg/kg DMED), CH was performed after the arthroscope entered the shoulder joint. The SEV concentration was raised to 4%, and the DMED concentration for the target-controlled infusion was 0.4 μg/kg with a pumping speed of 0.4 μg/kg/h. After the removal of the arthroscope, the infusion of DMED was stopped.

In group D (0.6 μg/kg DMED), the CH was performed after the arthroscope entered the shoulder joint. The SEV concentration was raised to 4%, and the DMED concentration for the target-controlled infusion was 0.6 μg/kg with a pumping speed of 0.4 μg/kg/h. After the removal of the arthroscope, the infusion of DMED was ceased.

In group E (0.8 μg/kg DMED), CH was performed after the arthroscope entered the shoulder joint. The SEV concentration was raised to 4%, and the DMED concentration for the target-controlled infusion was 0.8 μg/kg with a pumping speed of 0.4 μg/kg/h. After the removal of the arthroscope, the infusion of DMED was ceased.

During CH, if a patient's heart rate (HR) decreased to 50 beats/min, atropine (0.2 mg) was administered to ensure MAP was controlled at 50-60 mmHg.

Outcome measures

After entering the operation room, the patients' MAP and HR before anesthesia (T1), 10 min after anesthesia induction (T2), 5 min after initiating CH (T3), 1 h after initiating CH (T4), and 10 min after ceasing CH (T5) were recorded and compared between the groups. Meanwhile, the markers indicating the patients' renal functions at 2 h and 24 h after surgery were also compared, including the levels of creatinine, blood urea nitrogen (BUN), cystatin C, and glomerular filtration rate (GRF).

Statistical analysis

The statistical software SPSS 19.0 was applied for the data analysis. The count data are expressed as the frequency, and the comparisons between groups were performed using χ^2 tests. The measurement data are presented as the means ± standard deviation, and the groups were compared using analyses of variance (ANOVA) and Bonferroni post hoc tests; meanwhile, the data at different time points between the two groups were compared by repeated measures ANOVA and Bonferroni post hoc tests. $P<0.05$ was considered to indicate a statistically significant difference.

Results

The patients' characteristics

No intergroup differences were found among the five groups in terms of age, gender, protopathy, surgical duration, the volume of colloid infusion in the operation, or other basic information (all $P>0.05$). See **Table 1**.

MAP and HR

No intergroup differences were found among the five groups in MAP and HR at T1, T2, or T5 (all $P>0.05$). However, at T3 and T4, the two indices reduced significantly in groups B, C, D, and E (reduction level, E>D>C>B, all $P<0.05$). See **Figure 1**.

ESR (erythrocyte sedimentation rate) and whole blood specific viscosity

No intergroup differences were observed in the levels of ESR or whole blood specific viscosity before the operations, or at 2 h and 24 h after the operations (all $P>0.05$). See **Figure 2**.

Renal function

Creatinine level: No intergroup differences were observed in the creatinine level before the operations (all $P>0.05$). However, at 2 h and 24 h after the operations, the patients in group A had higher creatinine levels than the other groups (creatinine level: group A>B>C>D, group E>D, all $P<0.05$). See **Figure 3**.

BUN level: No intergroup differences were observed in the BUN level before the operations (all $P>0.05$). At 2 h and 24 h after the opera-

Table 1. Patients' characteristics

	Group A (n=20)	Group B (n=20)	Group C (n=20)	Group D (n=20)	Group E (n=20)	F/χ^2	P
Age (year)	45.6±5.1	43.3±4.8	44.3±4.4	46.3±2.5	45.6±3.4	1.678	0.066
Gender (male/female)	12/8	11/9	10/10	13/7	8/12	0.835	0.841
Protopathy						4.671	0.968
LHBT injury (n)	4	3	4	5	5		
Labral tear (n)	5	5	4	3	4		
Cartilage damage (n)	6	7	5	6	6		
Adhesive capsulitis (n)	8	7	8	5	7		
Shoulder joint instability (n)	2	3	4	6	5		
Intraoperative bleeding volume (mL)	58.3±8.5	59.3±7.8	58.7±6.4	60.4±6.6	57.4±3.5	1.582	0.062
Colloid infusion volume (mL)	859.3±123.1	856.5±130.8	854.3±128.8	857.3±127.7	854.3±103.2	0.594	0.094
Coexisting disease before operation						0.434	0.933
High blood pressure (n)	5	4	3	4	3		
Diabetes (n)	4	5	2	3	3		
Surgical duration (min)	88.3±5.5	85.3±5.7	85.3±4.9	85.8±5.8	85.9±5.0	1.288	0.051
Anesthesia duration (min)	65.4±4.7	64.8±5.0	65.6±4.4	66.8±5.2	64.8±4.3	1.734	0.054
SEV (mL)	18.3±2.3	19.2±2.8	18.6±2.2	17.4±2.7	18.4±2.5	2.335	0.074
CH duration (min)	35.6±7.2	36.7±8.1	35.9±7.8	36.8±7.1	36.2±6.3	1.458	0.070

Note: SEV, sevoflurane; LHBT, long head of biceps tendon; CH, controlled hypotension; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine.

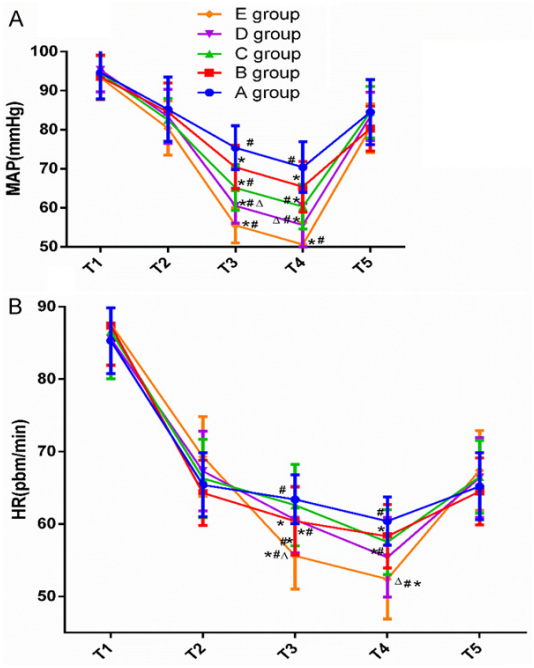

Figure 1. Changes in the MAP and HR values in the five groups. A: Changes in the MAP in the five groups; B: Changes in the HR in the five groups. MAP, mean arterial pressure; HR, heart rate; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine; T1, before anesthesia; T2, 10 min after anesthesia induction; T3, 5 min after initiating controlled hypotension; T4, 1 h after initiating controlled hypotension; T5, 10 min after ceasing controlled hypotension; *P<0.05 vs. group A; #P<0.05 vs. group B; ΔP<0.05 vs. group C.

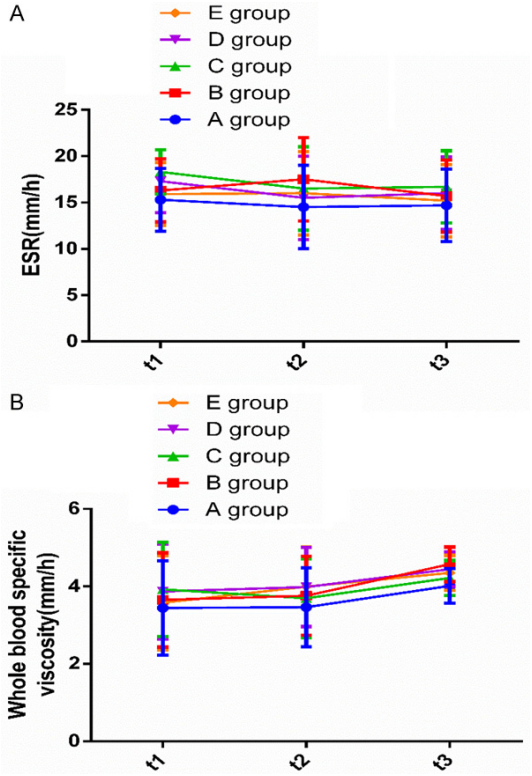

Figure 2. Changes in ESR and whole blood specific viscosity in patients. A: Changes in ESR in the five groups; B: Changes of whole blood specific viscosity in the five groups. ESR, erythrocyte sedimentation rate; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine; t1, before operation; t2, at 2 h after operation; t3, at 24 h after operation.

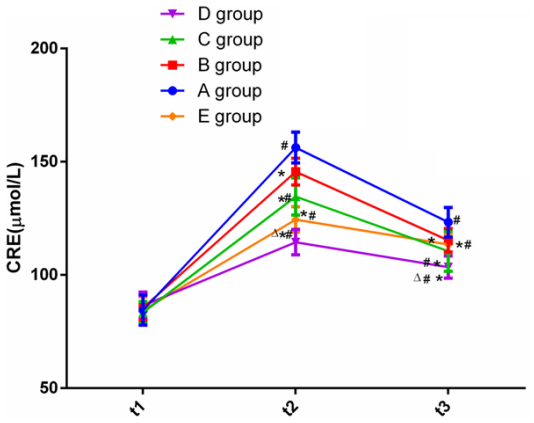

Figure 3. Changes in the creatinine levels in the five groups. Cre, creatinine; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine; t1, before operation; t2, at 2 h after operation; t3, at 24 h after operation; *P<0.05 vs. group A; #P<0.05 vs. group B; ΔP<0.05 vs. group C.

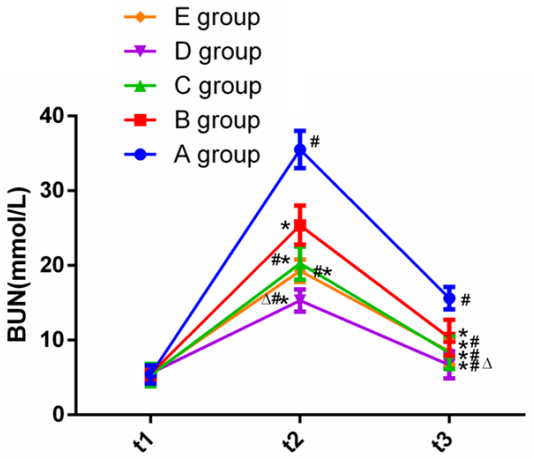

Figure 4. Changes in the blood urea nitrogen levels in the five groups. BUN, blood urea nitrogen; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine; t1, before operation; t2, at 2 h after operation; t3, at 24 h after operation; *P<0.05 vs. group A; #P<0.05 vs. group B; ΔP<0.05 vs. group C.

tions, the patients in group A had higher BUN levels than the other groups (BUN level: group A>B>C>D, and group E>D, all P<0.05). See **Figure 4**.

Cystatin C level: No intergroup differences were observed in the cystatin C levels in the five groups before the operations (all P>0.05). However, at 2 h and 24 h after the operations,

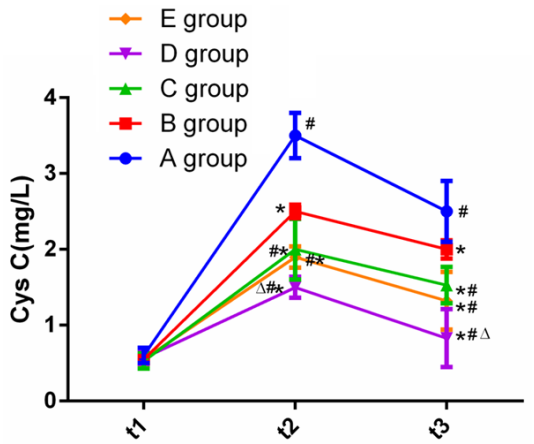

Figure 5. Changes in the cystatin C levels in the five groups. Cys C, Cystatin C; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine; t1, before operation; t2, at 2 h after operation; t3, at 24 h after operation; *P<0.05 vs. group A; #P<0.05 vs. group B; ΔP<0.05 vs. group C.

the patients in group A had higher cystatin C levels than the other groups (cystatin C level: group A>B>C>D, and group E>D, all P<0.05). See **Figure 5**.

GFR: No intergroup differences were observed in the GFR levels in the five groups before the operations (all P>0.05). However, at 2 h and 24 h after the operations, the patients in group A had lower GFR levels than the other groups (GFR value: group A<B<C<D, and group E<D, all P<0.05). See **Figure 6**.

Urine volumes during and 24 h after the operations: The patients in the study groups had much more urine volume during the operations and at 24 h after the operations compared with those in the control group. The results showed that the higher the concentration of DMED, the greater the increase in the urine volume in patients. However, when the concentration of DMEM exceeded 0.6 μg/kg, the urine volume decreased as the DMED level increased (**Table 2**).

Discussion

CH was first applied in clinical practice by Gardner in 1946. The main goal of this technique, under the precondition of adequate oxygen supply in important organs, is to reduce the intraoperative bleeding volume using antihy-

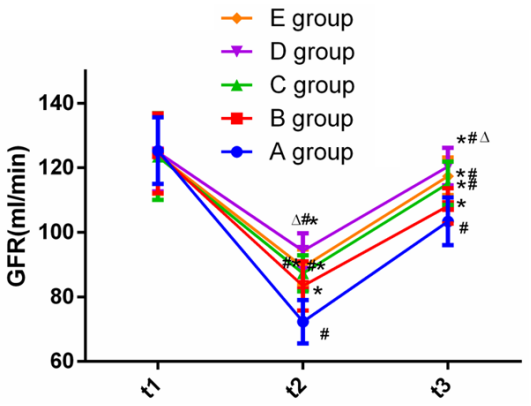

Figure 6. Changes in the glomerular filtration rate in the five groups. GFR, glomerular filtration rate; Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine; t1, before operation; t2, at 2 h after operation; t3, at 24 h after operation; *P<0.05 vs. group A; #P<0.05 vs. group B; ΔP<0.05 vs. group C.

Table 2. Comparison of the urine volume during and 24 h after the operation in the five groups

	During the operation (mL)	24 h after the operation (mL)
Group A (n=20)	759.40±238.38	2242.10±572.38
Group B (n=20)	782.34±137.72	2452.34±527.32
Group C (n=20)	802.32±134.23	2534.38±348.27
Group D (n=20)	852.37±123.48	2634.28±438.91
Group E (n=20)	824.05±100.55	2452.42±354.02
F/χ^2	14.54	3.146
P	0.003	0.024

Note: Group A, control group; Group B, 0.2 μg/kg dexmedetomidine; Group C, 0.4 μg/kg dexmedetomidine; Group D, 0.6 μg/kg dexmedetomidine; Group E, 0.8 μg/kg dexmedetomidine.

pertensive drugs and methods and to make the blood pressure quickly return to the normal level after hypotension is ceased [12]. One essential part of this technique is that the tissue perfusion and organ protection should be ensured [13]. Currently, CH is primarily used in big, complicated surgeries or surgeries with a high bleeding risk and difficulty in hemostasis (e.g., neurosurgery, large orthopedic surgery including hip joint replacement and scoliosis surgery, aneurysmectomy, large tumor surgery, and vascular malformation surgery), surgery in confined and small areas (e.g., microsurgery that requires a clear surgical view and no bleeding), surgery with a limitation in blood transfusion (e.g., surgery in which there is a blood supply shortage or the patients are unwilling to receive allogeneic blood), and surgery in which the patients may experience secondary hypertension during anesthesia (e.g., pheochromocytoma surgery, or stress-induced hypertensive crisis caused by various reasons during surgery) [14, 15].

DMED is defined as an α_2-adrenergic receptor agonist, which can effectively inhibit the release of norepinephrine from the presynaptic membrane and that has anti-sympathetic, sedative, and analgesic properties [16, 17]. The mechanism of DMED in CH is that DMED can exert antisympathetic action through the activating of the locus coeruleus neuron α_{2A} receptor in the brainstem, thus the preventing sympathetic stimulation induced by CH. During CH, patients can have stable HR and blood pressure and will not experience reflex hypertension or tachycardia so that vital organs including the heart and brain during perioperative period can be protected to some extent [18, 19]. Goettel et al. have reported that when using DMED combined with propofol and remifentanil for CH, there can be an increase in blood stability and a reduction in the intraoperative bleeding volume [20]. In this study, we found that the combined use of SEV and DMED could also improve patients' hemodynamic stability, reduce the circulation function, and meet the surgical requirements on the premise of ensuring a normal blood flow and oxygen supply. The mechanism of SEV in CH is that the agent can expand peripheral vessels, reduce cardiac afterload, and barely inhibit myocardial contractility, hence having almost no impact on cardiac output. In the present study, SEV was used in the control group for CH, as it can achieve hypotension through expanding peripheral artery; meanwhile, the combined use of DMED, and SEV was applied in the study groups. The blood pressure in the four groups was controlled at 50-60 mmHg during the CH.

Renal function and high blood pressure are correlated with each other. Kidney disorders can elevate blood pressure, but a persistently high blood pressure in turn can damage the kidneys. DMED can stimulate the α_2 receptor, inhibit the release of norepinephrine, and suppress sympathetic activity, thus leading to the dilatation of the renal arteries and decreased blood pressure. During CH, DMED's protective effect on renal function is achieved not only through suppressing hemodynamic fluctuation caused by catecholamine, but also through the self-

adjustment function of renal blood flow; that is, GFR is reduced when systolic blood pressure goes down to 75 mmHg, leading to an adequate supply of oxygen and the dilation of renal blood vessels [21]. Qian et al. have reported transient reversible abnormalities in the urea nitrogen and creatinine levels two hours after the operation when using DMED for long CH during craniocerebral operations, and the abnormality can be eliminated gradually within 24 hours post-operation [22]. Huo et al. have documented that CH lasting for one hour is safe and effective during total hip replacement in senile patients; however, as the reduction in blood pressure increases, a transient glomerular filtration disorder may occur [23]. In a study by Onuigbo et al., it was demonstrated that when implementing intraoperative hypotension or CH, acute renal injury can happen when the blood pressure goes down to a certain level [24]. In this study, we found that DMED, when used for CH during shoulder arthroscopy, had little impact on the levels of creatinine, BUN, cystatin C, or GFR when MAP was controlled at 50-60 mmHg for a short period, which showed important protective effects on renal function.

A potential weakness of this study is the small number of outcome measures, so we will measure more indices relating to renal function in various surgical procedures in the future. Also, due to the small sample size and individual differences, more research with a larger sample size (optimally 200 subjects in each group) needs to be carried out so that the impact of DMED for CH on renal function can be further investigated.

In conclusion, the combined use of DMED and SEV can effectively reduce blood pressure during shoulder arthroscopy, and the impact of DMED at a concentration of 0.6 μg/kg on renal function is minimal, which shows its protective effects on the kidneys and indicates it can be recommended for clinical application.

Disclosure of conflict of interest

None.

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