

Effect of supplemental dexmedetomidine in interventional embolism on cerebral oxygen metabolism in patients with intracranial aneurysms

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Abstract

Objective: To investigate the effect of supplemental dexmedetomidine in interventional embolism on cerebral oxygen metabolism in patients with intracranial aneurysms.

Methods: Ninety patients who underwent interventional embolism of intracranial aneurysms were equally divided into Group A and Group B. In Group A, dexmedetomidine was injected intravenously 10 minutes before inducing anesthesia, with a loading dose of 0.6 $\mu\text{g}/\text{kg}$ followed by 0.4 $\mu\text{g}/\text{kg}/\text{hour}$. Group B received the same amount of normal saline by the same injection method. Heart rate (HR), mean arterial pressure (MAP), arterial–jugular venous oxygen difference [D(a–jv) (O_2)], cerebral oxygen extraction [CE (O_2)], and intraoperative propofol use were recorded before inducing anesthesia (T_0) and at five time points thereafter.

Results: The amount of propofol in Group A was lower vs Group B. At all five time points after T_0 , HR, MAP, D(a–jv) (O_2), and CE (O_2) in Group A were significantly lower vs Group B, with significant differences for jugular venous oxygen saturation ($S_{jv}\text{O}_2$) and the oxygen content of the internal jugular vein ($C_{jv}\text{O}_2$) between the groups.

Conclusion: Dexmedetomidine resulted in less intraoperative propofol, lower D(a–jv) (O_2) and CE (O_2), and improved cerebral oxygen metabolism.

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Keywords

Dexmedetomidine, propofol, intracranial aneurysm, arterial–jugular venous oxygen difference [D(a-jv) (O_2)], cerebral extraction of oxygen [CE (O_2)], anesthesia, surgery

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Introduction

Intracranial aneurysm a common cerebrovascular disease and the main cause of spontaneous subarachnoid hemorrhage.¹ Neurosurgical clipping and interventional embolism are common treatments for intracranial aneurysms, and the latter has been increasingly popular owing to its minimal invasiveness.^{2,3} Strong stimuli, such as anesthesia and surgical operations, often lead to violent fluctuations within the circulatory system, and even aneurysm rupture and bleeding, which directly affect operation success and prognosis. Anesthesiologists must cooperate closely with surgeons intraoperatively to maintain the patient's hemodynamic stability as much as possible, reduce the stress response caused by perioperative noxious stimulation, and improve operation safety. Dexmedetomidine is a potent and highly selective α -2-adrenoceptor agonist with sympatholytic, sedative, amnesic, and analgesic properties.^{4,5} Arterial–jugular venous oxygen difference [D(a-jv) (O_2)] and cerebral extraction of oxygen [CE (O_2)], as important indicators reflecting the level of cerebral blood flow metabolism, can be used to evaluate brain injury.^{6,7} Studies have shown that a decrease in D(a-jv) (O_2) indicates sufficient craniocerebral oxygen supply, and a decrease in CE (O_2) indicates improved cerebral perfusion.^{8,9} To date, few reports have evaluated dexmedetomidine-assisted interventional embolism on cerebral oxygen metabolism in patients with intracranial aneurysms.

The aim of this study was to investigate the effect of supplemental dexmedetomidine in interventional embolism on cerebral oxygen metabolism in patients with intracranial aneurysms.

Methods

Study design, patients, and ethical approval

This study was conducted at the Department of Neurosurgery, Zhangzhou Affiliated Hospital of Fujian Medical University, Zhangzhou, China, from October 2018 to January 2020. The study was approved by the ethics committee of the Zhangzhou Affiliated Hospital of Fujian Medical University (approval number: 2020LWB061). Ninety patients with intracranial aneurysms who underwent interventional embolization were enrolled. Inclusion criteria were intracranial aneurysms diagnosed by magnetic resonance imaging (MRI) or whole-brain angiography and undergoing interventional embolization; American Society of Anesthesiologists (ASA) grade I–II; and written informed consent to participate. Exclusion criteria were dying patients or those having lost the opportunity for surgical treatment; patients with cardiac, lung, liver function, or kidney problems, or metabolic diseases; mental disorders preventing patients from cooperating; consciousness disorders, drowsiness, and coma before surgery and unable to complete the

examination in accordance with the instructions; a long history of sedative and analgesics use, or alcohol or psychotropic drug dependence; bradycardia or slow arrhythmia; shock, severe dehydration, or electrolyte disturbance; and heart rate (HR) less than 50 beats/minute and/or systolic blood pressure less than 90 mmHg (1 mmHg = 0.133 kPa). All patients were equally divided into Group A and Group B according to the different treatment methods (45 cases in each group).

Anesthesia method

No pre-anesthetic medication was given, and venous access was established after entering the operation room. Both groups were pre-infused with 5 mL/kg compound sodium lactate solution, followed by continuous infusion of 8 to 10 mL/kg/hour. In Group A, a 0.6- μ g/kg loading dose of dexmedetomidine (4 μ g/mL dissolved in normal saline) was injected intravenously using an infusion pump 10 minutes before inducing anesthesia, followed by continuous infusion of 0.4 μ g/kg/hour. Normal saline of equal volume to the dexmedetomidine was injected intravenously in Group B 10 minutes before inducing anesthesia.

Anesthetic induction was achieved with the Marsh pharmacokinetic model for propofol in both groups: the initial plasma propofol target-controlled infusion (TCI) target concentration was 2 μ g/mL. When the target concentration of the effect chamber reached the set target concentration for 1 minute, the target concentration was increased at a concentration gradient of 0.5 μ g/mL. When the electroencephalogram (EEG) bispectral index (BIS) value dropped to 60, 3 μ g/kg of fentanyl and 0.6 mg/kg of rocuronium bromide were injected intravenously, and the laryngeal mask was placed 2 minutes later. After that, the anesthetic machine was used for mechanical ventilation. Tidal volume (TV) was set at 6 to 8 mL/kg, respiratory

rate (RR) at 10 to 12 times/minute, inhalation/exhalation ratio at 1:2, oxygen flow rate at 1.5 L/minute, and end-tidal carbon dioxide (PETCO₂) at 35 to 45 mmHg. After inducing anesthesia, 0.05 μ g/kg/minute remifentanyl continuous infusion was given to maintain anesthesia. After the operation, the infusion of propofol and remifentanyl was stopped. Interventional embolization was performed by the same group of surgeons in both groups.

Data collection

The patient's sociodemographic characteristics and the following surgical indicators were measured and recorded: operation time, infusion volume, intraoperative blood loss, and urine volume.

HR, mean arterial pressure (MAP), hemoglobin (Hb), arterial oxygen saturation (S_aO₂), jugular venous oxygen saturation (S_{jv}O₂), arterial oxygen content (CaO₂), partial arterial oxygen pressure (P_aO₂), partial jugular vein oxygen pressure (P_{jv}O₂), oxygen content of the internal jugular vein (C_{jv}O₂), and intraoperative propofol use were recorded before inducing anesthesia (T₀), 3 minutes post-laryngeal mask insertion (T₁), 5 minutes after the skin incision (T₂), 1 hour after the start of surgery (T₃), 2 hours after the start of surgery (T₄), and immediately after surgery (T₅). The D(a-jv) (O₂) and CE (O₂) were calculated according to the Fick formula;¹⁰ namely, $CaO_2 = Hb \times 1.36 \times S_aO_2 + P_aO_2 \times 0.0031$; $C_{jv}O_2 = Hb \times 1.36 \times S_{jv}O_2 + P_{jv}O_2 \times 0.0031$; $D(a-jv) (O_2) = CaO_2 - C_{jv}O_2$; and $CE (O_2) = D(a-jv) (O_2) / CaO_2$.

Statistical analysis

SPSS 25.0 statistical software (IBM Corp., Armonk, NY, USA) was used for the statistical analyses. Qualitative data were expressed as numbers and percentages, and the Shapiro–Wilk's test was used to

evaluate the normality of the quantitative data. Quantitative data with normal distribution were expressed as mean \pm standard deviation (SD), and the independent samples t-test was used for between-group comparisons. One-way repeated measures analysis of variance (ANOVA) was used for intra-group comparisons, and $P < 0.05$ was considered statistically significant.

Results

Sociodemographic characteristics

Among the 90 patients, 49 (54.44%) were men, and 41 (45.56%) were women, aged 43 to 72 (62.55 ± 2.31) years. The patients' body mass index (BMI) ranged from 19 to 27 (23.74 ± 3.18) kg/m^2 . Thirty-three cases (36.67%) were complicated with hypertension, 25 cases (27.78%) with diabetes, and 14 cases (15.56%) with hyperlipidemia. Forty-eight cases (53.33%) were ASA grade I, and 42 cases (46.67%) were ASA grade II. Fifty-two cases (57.78%) had primary- and junior high school education levels, and 38 cases (42.22%) had high school and above levels of education (Table 1). A study flowchart is shown in Figure 1.

Comparison of surgical indicators

There were no significant differences in operation time, infusion volume, intraoperative blood loss, and urine volume between Group A and Group B (Table 2); the amount of intraoperative propofol in Group A was lower than that in Group B ($P < 0.001$; Table 2).

Comparison of HR and MAP

Compared with T_0 in the same group, HR and MAP in Group A and Group B were significantly different at T_1 , T_2 , T_3 , T_4 , and T_5 (all $P < 0.05$; Table 3).

There were no significant differences in HR and MAP between Group A and Group B at T_0 (Table 3). However, HR and MAP in Group A were significantly lower than those in Group B at T_1 , T_2 , T_3 , T_4 , and T_5 (all $P < 0.001$; Table 3).

Comparison of blood gas analysis indices

S_aO_2 was 100.00% at each time point in both groups. Compared with T_0 in the same group, P_aO_{2j} , $P_{jv}O_2$, $S_{jv}O_2$, $C_{jv}O_2$, $D(a-jv)(O_2)$, and $CE(O_2)$ in Group A and Group B were significantly different at T_1 , T_2 , T_3 , T_4 , and T_5 (all $P < 0.001$; Table 4).

Table 1. Patient demographic features.

Variable	Category	Frequency (%)
Sex	Male	49 (54.44)
	Female	41 (45.56)
Age	43–59 years	33 (36.67)
	60–72 years	57 (63.33)
BMI	19–22 kg/m^2	35 (38.89)
	23–27 kg/m^2	55 (61.11)
Complicated with illness	Hypertension	33 (36.67)
	Diabetes	25 (27.78)
	Hyperlipidemia	14 (15.56)
ASA	Grade I	48 (53.33)
	Grade II	42 (46.67)
Level of education	Primary and junior high school	52 (57.78)
	High school and above	38 (42.22)

BMI, body mass index; ASA, American Society of Anesthesiologists.

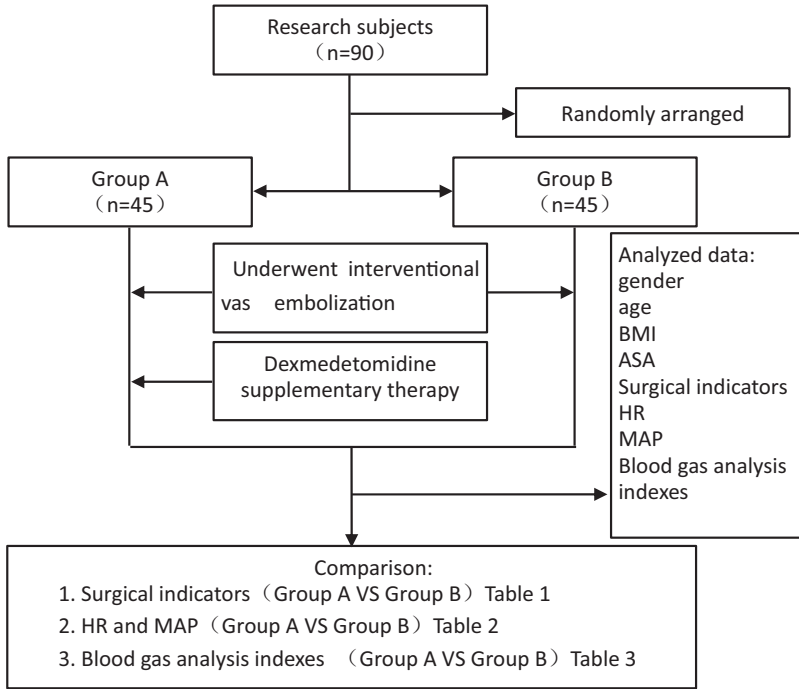


Figure 1. Flowchart of patients participating in the study.

BMI, body mass index; ASA, American Society of Anesthesiologists; HR, heart rate; MAP, mean arterial pressure.

Table 2. Comparison of surgical indicators between the two groups.

Parameter	Group A (n = 45)	Group B (n = 45)	P value
Operation time (minutes)	150.11 ± 15.75	152.05 ± 15.96	0.563
Infusion volume (mL)	3076.05 ± 322.83	3100.72 ± 325.40	0.719
Intraoperative blood loss (mL)	785.13 ± 82.34	777.99 ± 81.61	0.680
Urine volume (mL)	911.99 ± 95.73	915.30 ± 96.06	0.870
Amount of intraoperative propofol (mg)	613.94 ± 64.45	798.60 ± 95.99	<0.001

CaO₂ in Group A and Group B were significantly different at T₁, T₂, T₃, and T₄ (all P < 0.001; Table 4).

There were no significant differences in P_aO₂, CaO₂, P_{jv}O₂, S_{jv}O₂, C_{jv}O₂, D(a-jv) (O₂), and CE (O₂) between Group A and Group B at T₀ (Table 4). However, there were significant differences in S_{jv}O₂, C_{jv}O₂, D(a-jv) (O₂), and CE (O₂) between Group A and Group B at T₁, T₂, T₃, T₄, and T₅ (all P < 0.001; Table 4).

Discussion

Violent fluctuations in perioperative hemodynamics cause cerebral ischemic injury in patients undergoing intracranial aneurysm surgery and increase perioperative risks, such as cerebral hypoxia. Increased HR reduces shear stress on the vessel walls and increases the risk of cerebrovascular rupture. Therefore, maintaining proper low-level MAP and HR during intracranial

Table 3. Comparison of HR and MAP at the different time points.

Index	Group	n	T ₀	T ₁	T ₂	T ₃	T ₄	T ₅
HR (beats/minute)	Group A	45	92.23 ± 7.94	87.14 ± 6.75 ^Δ	72.42 ± 5.61 ^Δ	73.39 ± 5.71 ^Δ	74.74 ± 6.01 ^Δ	75.58 ± 5.80 ^Δ
	Group B	45	91.20 ± 7.79	89.22 ± 7.13 ^Δ	87.22 ± 6.79 ^Δ	85.28 ± 6.63 ^Δ	87.93 ± 6.58 ^Δ	85.51 ± 6.38 ^Δ
P value			0.537	<0.001	<0.001	<0.001	<0.001	<0.001
MAP (mmHg)	Group A	45	108.77 ± 11.41	94.26 ± 9.87 ^Δ	80.14 ± 8.41 ^Δ	79.30 ± 8.32 ^Δ	77.57 ± 8.14 ^Δ	81.26 ± 8.54 ^Δ
	Group B	45	106.24 ± 12.77	103.11 ± 11.89 ^Δ	93.10 ± 11.19 ^Δ	91.12 ± 9.56 ^Δ	90.58 ± 9.52 ^Δ	95.24 ± 9.98 ^Δ
P value			0.324	<0.001	<0.001	<0.001	<0.001	<0.001

Note: compared with T₀ in the same group, ^Δ indicates P < 0.05.

T₀, before inducing anesthesia; T₁, 3 minutes post-laryngeal mask insertion; T₂, 5 minutes after the skin incision; T₃, 1 hour after the start of surgery; T₄, 2 hours after the start of surgery; T₅, immediately after surgery.

HR, heart rate; MAP, mean arterial pressure.

aneurysm surgery is conducive to perioperative safety and reduces the risk of intraoperative brain injury.

Studies have shown that dexmedetomidine can stabilize hemodynamics and protect brain tissues.^{11–13} This drug exerts analgesic and sedative effects by inhibiting the release of substance P and nociceptive peptides from the presynaptic membrane and inhibiting the transmission of nociceptive stimuli.¹⁴ The results of this study showed that compared with Group B, the hemodynamics were relatively stable, and MAP and HR intraoperatively were lower in the patients in Group A, which might be related to the effect of dexmedetomidine on the sympathetic nerves.¹⁵ However, it should be noted that the effect of dexmedetomidine on blood pressure is biphasic and dose-dependent. High-dose (1–2 μg/kg) rapid infusion directly stimulates vascular α-2 receptors and causes vasoconstriction, leading to a transient increase in blood pressure.¹⁶ Meanwhile, the risk of bradycardia also increases significantly at loading doses and high-concentration maintenance doses (>0.7 μg/kg/hour).¹⁷ Therefore, some scholars suggested that dexmedetomidine be administered slowly at low doses (loading dose: 0.3 μg/kg, maintenance dose: 0.2 to 0.3 μg/kg/hour) in clinical applications to avoid transient increases in blood pressure, bradycardia, and other adverse reactions.¹⁸ The dexmedetomidine loading dose used in this study was 0.6 μg/kg, and the maintenance dose was 0.4 μg/kg/hour; the above-mentioned adverse reactions were not observed.

As important indicators for cerebral oxygen metabolism, D(a-jv) (O₂) and CE (O₂) can effectively evaluate the entire cerebral blood flow and metabolism.¹⁹ Decreased D(a-jv) (O₂) and CE (O₂) may indicate sufficient cerebral oxygen supply or improved cerebral blood flow perfusion. The results of this study showed that patients receiving dexmedetomidine had

Table 4. Comparison of blood gas analysis indices at different time points.

Index	Group	n	T ₀	T ₁	T ₂	T ₃	T ₄	T ₅
P _a O ₂ (mmHg)	Group A	45	527.68 ± 31.75	515.84 ± 27.26 ^Δ	507.74 ± 31.35 ^Δ	500.57 ± 45.12 ^Δ	496.45 ± 39.16 ^Δ	503.84 ± 40.61 ^Δ
	Group B	45	526.93 ± 37.26 ^a	514.72 ± 22.65 ^{Δa}	508.86 ± 47.02 ^{Δa}	501.74 ± 34.37 ^{Δa}	498.52 ± 35.98 ^{Δa}	504.16 ± 47.53 ^{Δa}
CaO ₂ (mL/L)	Group A	45	135.67 ± 9.15	126.53 ± 7.06 ^Δ	163.05 ± 5.33 ^Δ	134.54 ± 9.04 ^Δ	133.63 ± 13.41 ^Δ	137.30 ± 11.65
	Group B	45	136.72 ± 7.38 ^a	125.00 ± 6.14 ^{Δa}	162.71 ± 8.25 ^{Δa}	134.42 ± 10.16 ^{Δa}	133.28 ± 15.39 ^{Δa}	136.98 ± 14.78 ^a
P _v O ₂ (mmHg)	Group A	45	40.76 ± 14.52	41.62 ± 9.81	40.35 ± 10.17	39.65 ± 16.09	39.27 ± 12.18	41.44 ± 17.61
	Group B	45	40.49 ± 13.31 ^a	41.33 ± 8.45 ^a	40.49 ± 9.04 ^a	39.41 ± 15.35 ^a	39.56 ± 10.13 ^a	41.22 ± 13.96 ^a
S _v O ₂ (%)	Group A	45	70.17 ± 6.95	65.64 ± 5.25 ^Δ	66.46 ± 10.81 ^Δ	65.81 ± 11.93 ^Δ	67.24 ± 9.02 ^Δ	67.64 ± 7.78 ^Δ
	Group B	45	70.25 ± 9.14 ^a	61.24 ± 7.03 ^{Δb}	61.37 ± 13.26 ^{Δb}	63.07 ± 12.15 ^{Δb}	60.19 ± 13.58 ^{Δb}	62.91 ± 10.43 ^{Δb}
C _v O ₂ (mL/L)	Group A	45	94.17 ± 10.56	82.13 ± 7.34 ^Δ	107.45 ± 13.29 ^Δ	87.64 ± 9.58 ^Δ	88.93 ± 6.26 ^Δ	92.10 ± 9.16 ^Δ
	Group B	45	95.02 ± 12.77 ^a	75.70 ± 9.18 ^{Δb}	99.01 ± 10.15 ^{Δb}	83.92 ± 7.11 ^{Δb}	79.41 ± 8.04 ^{Δb}	85.32 ± 8.79 ^{Δb}
D(a-i) (O ₂) (mL/L)	Group A	45	41.50 ± 0.33	44.40 ± 3.30 ^Δ	55.60 ± 4.30 ^Δ	46.90 ± 4.10 ^Δ	44.70 ± 3.50 ^Δ	45.20 ± 3.50 ^Δ
	Group B	45	41.70 ± 0.32 ^a	49.30 ± 3.80 ^{Δb}	63.70 ± 5.10 ^{Δb}	50.50 ± 4.50 ^{Δb}	53.87 ± 4.90 ^{Δb}	51.66 ± 4.70 ^{Δb}
CE (O ₂) (%)	Group A	45	30.59 ± 2.14	35.09 ± 2.73 ^Δ	34.10 ± 2.65 ^Δ	34.86 ± 2.71 ^Δ	33.45 ± 2.60 ^Δ	32.92 ± 2.56 ^Δ
	Group B	45	30.50 ± 2.15 ^a	39.44 ± 3.07 ^{Δb}	39.15 ± 3.00 ^{Δb}	37.57 ± 3.94 ^{Δb}	40.42 ± 2.99 ^{Δb}	37.71 ± 3.01 ^{Δb}

Note: compared with T₀ in the same group, ^Δ indicates P < 0.05; compared with group A, ^a indicates P > 0.05; compared with group A, ^b indicates P < 0.001. T₀, before inducing anesthesia; T₁, 3 minutes post-laryngeal mask insertion; T₂, 5 minutes after the skin incision; T₃, 1 hour after the start of surgery; T₄, 2 hours after the start of surgery; T₅, immediately after surgery.

P_aO₂, partial arterial oxygen pressure; CaO₂, arterial oxygen content; P_vO₂, partial jugular vein oxygen pressure; S_vO₂, jugular venous oxygen saturation; C_vO₂, oxygen content of the internal jugular vein; D(a-i) (O₂), arterial-jugular venous oxygen difference; CE (O₂), cerebral extraction of oxygen.

improved cerebral oxygen metabolism peri-operatively, and their brain tissues were more resistant to ischemia and hypoxia. The reasons for the decreases in D(a-jv) (O₂) and CE (O₂) owing to dexmedetomidine administration may be related to the following mechanisms: First, dexmedetomidine can bind to α -2 adrenoreceptors to inhibit sympathetic excitation, and, via activating the G protein-coupled inwardly rectifying potassium (IRK) current, to inhibit the paraventricular nucleus magnocellular neurons; thus, reducing cerebral oxygen consumption and improving S_{jv}O₂.^{20,21} Second, dexmedetomidine can protect D(a-jv) (O₂) by enhancing the expression of amino acids in cerebrospinal fluid.²² Third, dexmedetomidine can reduce the levels of inflammatory mediators, such as tumor necrosis factor- α (TNF- α) and interleukin (IL)-6, alleviating ischemic brain injury and reducing D(a-jv) (O₂).²³

This study revealed that using dexmedetomidine during anesthesia for intracranial aneurysm surgery could reduce the amount of intraoperative propofol. It should be noted that when using dexmedetomidine to protect the brain in clinical practice, doctors should also flexibly select the specific safe dose according to clinical experience and the individual patient. Further research in this area is needed to maximize patient safety.

Conclusion

Dexmedetomidine in patients with intracranial aneurysms before interventional embolization can reduce the amount of intraoperative propofol, lower D(a-jv) (O₂) and CE (O₂), and improve cerebral oxygen metabolism.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Author contributions

ZG acquired the data, drafted the manuscript, and contributed substantially to manuscript revision.

WW and DX acquired the data and drafted the manuscript.

RL drafted the manuscript, and read and approved the final manuscript.

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