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Clinical effects and safety evaluation of dexmedetomidine hydrochloride combined with etomidate fat emulsion in patients undergoing interventional treatment of stroke during anesthesia

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Abstract. – OBJECTIVE: Stroke patients are often elderly and afflicted with comorbidities that can make them more susceptible to surgical complications during anesthesia, such as respiratory depression. This study examined the clinical effects of dexmedetomidine hydrochloride combined with etomidate fat emulsion in patients undergoing interventional treatment of stroke during anesthesia.

PATIENTS AND METHODS: 90 patients with stroke admitted at the Second Hospital of Dalian Medical University between February 2015 and March 2016 were selected for interventional treatment in the study. The patients were randomly divided into three different treatment groups, with 30 patients in each group. Group A patients were treated with dexmedetomidine hydrochloride, group B patients were treated with etomidate fat emulsion, and group C patients were treated with dexmedetomidine hydrochloride combined with etomidate fat emulsion. Mean arterial blood pressure (MAP), heart rate (HR), wake-up time, and extubation time were compared and analyzed for the patients of each group at different time points.

RESULTS: MAP and HR of patients in group C were notably decreased after anesthesia, and were significantly lower than patients in groups A and B ($p<0.05$). MAP and HR of the patients in groups A and B did not significantly change over the different time points. The three groups also did not show dramatic changes when patients were extubated after 3 min ($p>0.05$). Further data on wake-up time, extubation, and spontaneous breathing recovery time among the patients did not show any significant differences in the three groups ($p>0.05$). However, the prevalence of complications in group C was lower than in groups A and B ($p<0.05$).

CONCLUSIONS: Dexmedetomidine hydrochloride combined with etomidate fat emulsion in patients undergoing interventional treatment of stroke during anesthesia has potential value in clinical applications, through the maintenance of ideal hemodynamics and a reduction in complications.

Key Words:
Dexmedetomidine hydrochloride, Etomidate fat emulsion, Stroke, Anesthesia.

Introduction

Stroke is a type of cerebral blood circulation disorder which starts suddenly and most commonly affects the elderly. Its clinical manifestations generally include permanent or transient ischemic attack. In the stroke treatment, interventions performed during anesthesia can improve clinical outcomes[1,2]. Therefore, it is important for the success of cerebral revascularization surgery to maintain the stability of anesthesia during the interventional treatment.

Dexmedetomidine hydrochloride (DEX) is an α2-adrenergic receptor agonist commonly used in clinical anesthesia, which plays a role in sedation, analgesia, and anti-sympathetic hormonal signaling[3-5]. During surgery, it has effects on sedation, pain relief, and stabilization of cerebrovascular circulation for patients. In addition, DEX has a minor impact on the inhibition of breathing[6,7].

Etomidate is able to inhibit the metabolism of the brain and decrease intracranial pressure. In the interventional treatment of stroke, it can protect brain tissue[8,9]. In our study, we combined

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DEX and etomidate during anesthesia in the interventional treatment of stroke, and discussed their effects on stroke patients for improving the safety and efficiency of interventional surgery.

Patients and Methods

Patients

All the patients enrolled signed and gave the informed consent. The investigation was approved by the Ethics Committee of the Second Hospital of Dalian Medical University. 90 patients with stroke admitted at the Second Hospital of Dalian Medical University between February 2015 and March 2016 were selected for interventional treatment in the study. These patients were randomly divided into group A, group B, and group C, each group with 30 patients and a distinct anesthesia administration plan. In the group A, there were 18 male patients and 12 female patients and their ages ranged from 55 to 79 years (mean 68.9 ±17.7). In the group B, there were 20 male patients and 10 female patients and their ages ranged from 56 to 82 years (mean 67.5 ±18.1). In the group C, there were 21 male patients and 9 female patients, and their ages ranged from 54 to 78 years (mean 67.9 ±18.5). There were no significant differences in demographics between the three groups and data from patients within each group was comparable.

Methods

Patients in the three groups did not take any medication before surgery. After the patients were brought into the operating room, a peripheral vein was accessed and mean arterial blood pressure (MAP) and heart rate (HR) were measured. Patients were injected with 0.3 mg hyoscine hydrobromide, 10 mg dexamethasone, 8 mg ondansetron, and 1 mg midazolam. At 30 min before anesthesia induction, patients in group A and group C received 0.5 μg/kg DEX by intravenous injection, while patients in group B were injected with the same amount of saline. For anesthesia induction, the patients were injected intravenously with 1 mg midazolam, 2 μg/kg fentanyl, and 0.2 mg/kg cisatracurium. Along with this anesthetic induction, patients in groups B and C were also injected with 0.15 mg/kg etomidate. Intubation was performed after complete muscle relaxation and intermittent positive mechanical ventilation was applied. The oxygen concentration was 100% and the flow rate was 2 l/min. The tidal volume was 8 ml/kg and the frequency was 12 breaths/min.

For anesthesia maintenance, the patients in each of the three groups were administered 1-2% sevoflurane by inhalation. Then, patients in group A were administered 0.2-0.4 μg/(kg·h) DEX; patients in group B were administered 0.5-1.0 mg/(kg·h) etomidate; and patients in group C were administered both DEX and etomidate, with the same groups A and B dosages. 30 min before the end of surgery, injection of DEX into patients was stopped, and the concentration of sevoflurane was reduced to 1%. When the surgery was completed, all anesthesia was immediately stopped.

Clinical Observation Indicators

The seven set time points were observed as follows: before anesthesia (T0), endotracheal intubation (T1), the beginning of surgery (T2), 30 min after surgery (T3), the end of surgery (T4), extubation (T5), and 3 min after extubation (T6). At each time point, MAP, HR, wake up time, extubation time, and spontaneous breathing recovery time were observed and recorded for each patient.

Statistical Analysis

SPSS 1.5 statistical software (SPSS, Inc., Chicago, IL, USA) was applied for all data analysis and statistical processing. A *t*-test was applied to assess differences between groups and to test for statistical significance. $p<0.05$ indicated that differences in the data were considered statistically significant.

Results

Anesthesia Analysis

Based on our data (Table I), we found that the wake-up time, the extubation time, and the spontaneous breathing recovery time of patients did not show any significant differences between the three groups ($p>0.05$)

Comparison of MAP and HR at Different Time Points

Compared with measures at T0, MAP and HR of patients in each of the three groups decreased over the subsequent time points. MAP and HR measures at the end of surgery (T4) and extubation (T5) were both lower than before anesthesia (T0) ($p<0.05$). However, MAP and HR of the three groups did not show significant differences ($p>0.05$) at 3 min after extubation (T6). In comparison between the groups, MAP and HR

Table I. Comparison of wake time, extubation time and spontaneous breathing recovery time among the three groups.

Group	n	Spontaneous breathing recovery time (min)	Extubation time (min)	Wake up time (min)
A	30	9.3±4.2	16.3±4.8	10.3±4.3
B	30	9.3±5.9	16.8±4.3	10.9±4.8
C	30	8.9±4.3	15.7±4.3	9.4±4.3

Data are presented as mean ± standard deviation. There were no statistically significant differences (p >0.05).

Table II. Comparison MAP and HR of patients between the three groups and at different time points.

Groups	N		T0	T1	T2	T3	T4	T5	T6
A	30	MAP	79.3±8.3	73.2±7.2	69.3±6.3	73.2±6.7	73.2±3.2[b]	74.3±6.1[b]	79.3±5.2
		HR	80.2±9.4	69.3±8.2	65.3±7.3	65.3±7.3	67.3±9.2[b]	71.2±7.3[b]	71.3±7.8
B	30	MAP	78.2±9.4	71.2±7.2	70.3±5.4	70.3±6.5	74.3±3.2[b]	75.3±5.4[b]	79.4±5.2
		HR	80.2±10.4	69.2±8.3	69.3±3.2	65.8±8.2	68.3±3.3[b]	70.3±7.8[b]	72.5±8.3
C	30	MAP	78.3±8.2	68.3±6.8[a]	66.8±8.3[a]	68.2±3.3[a]	72.3±4.9[ab]	75.5±4.2[b]	76.4±6.4
		HR	80.3±10.2	67.2±9.2[a]	64.3±2.3[a]	64.3±8.2[a]	68.3±9.2[ab]	72.3±8.3[b]	72.3±8.2

Data are presented as mean ± standard deviation. MAP is measured in mmHg and HR is measured in bpm. [a]p <0.05 for MAP and HR of group C vs. groups A and B. [b]p <0.05 for MAP and HR of each group at T4 and T5 compared with T0.

Table III. Comparison of clinical indicators after surgery and the prevalence of complications among patients of the three groups.

Group	n	Complications Muscle fibrillation	Injection pain	Postoperative restlessness	Incidence (%)
A	30	2	3	1	20
B	30	0	4	1	16.7
C	30	0	0	0	0[a]

Prevalence of complications was significantly lower among group C compared to groups A and B ([a]p <0.05).

showed minimal overall differences among the three groups (p>0.05). At the final time points, MAP and HR from groups A and B did not have significant differences (p>0.05). However, MAP and HR from group C was lower than both groups A and B at T1, T2, T3, and T4 (p<0.05) (Table II; Figures 1 and 2).

Comparison of Complication Indicators after Surgery

There were no significant differences in the prevalence of postoperative complications between patients in group A and group B. The complication rate of group C was 0, which was notably lower than that of the other two groups (p<0.05) (Table III).

Discussion

The occurrence of stroke in patients is often associated with a variety of other conditions and complications. Many have complex diseases and treatment plans that affect their tolerance for interventions. Older stroke patients also have a weaker tolerance in general, which makes perioperative anesthesia a difficult challenge in patient care[10-12].

Stroke patients are more sensitive to pain. While neurointerventional treatment is a minimally invasive surgery, it requires patients to maintain relatively stable circulation to avoid a stress reaction[13-16]. Therefore, in choosing anesthetic options, anesthesiologists should select respiratory and sedative drugs which can pro-

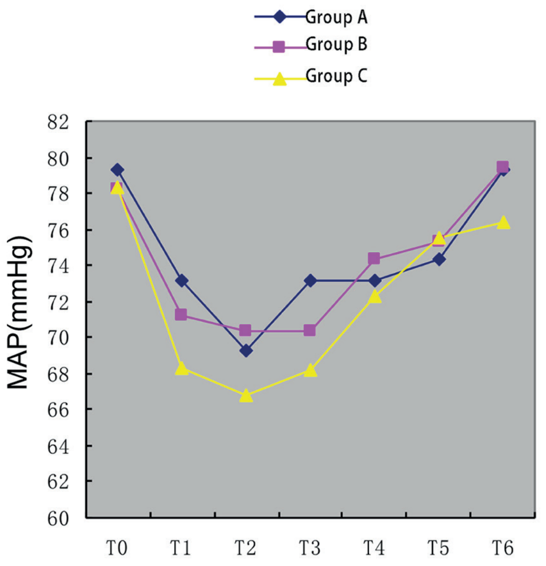

Figure 1. MAP (mmHg) trends of patients in different groups at different time points. Before anesthesia, MAP from three groups showed no differences (p>0.05). At the subsequent time points, MAP from groups A and B did not show significant differences (p>0.05), while MAP from group C (p<0.05) was lower than that of groups A and B at T1, T2, T3, and T4.

vide effective antihypertensive analgesia. During treatment, all aspects of the surgery must be carefully monitored to ensure precision, including stable circulation, no stress response, and no body movement. Anesthesia must also enable control of the patient's breathing, while still exerting sedative effects. To maintain respiratory stability, appropriate antihypertensive drugs should be given to prevent cerebral vasospasm[17,18]. In the selection of anesthesia, a moderate anesthetic drug has traditionally been used to avoid a negative impact on the patient's circulatory system. Previous studies have shown that adjuvant anesthesia with DEX can minimize the risk of a stress reaction during surgery. The use of DEX can reduce blood flow dynamic fluctuations[19], which reduces the risk of perioperative complications and improves the prognosis. However, during surgery, when anesthesia is administered, the patient's circulatory and respiratory function can be adversely impacted, such as with respiratory depression. Furthermore, excessive anesthesia administration can lead to serious complications.

Etomidate fat emulsion is a new type of narcotic drug which can effectively inhibit brain metabolism[20,21], reduce intracranial pressure, and protect brain tissue. In contrast, DEX is an adjuvant anesthetic drug. When it is combined with a general anesthetic drug, it can reduce the required use of anesthesia, thereby reducing the recovery period of chills, agitation, and other adverse reactions[22]. Furthermore, etomidate has a very minimal impact on the circulatory system, making it suitable for the anesthesia of elderly and frail patients, and patients with various complications[23,24]. However, it is not yet available for patients undergoing prolonged surgical anesthesia[25].

The combination of the two drugs plays an important role in stabilizing intraoperative circulation. In our study, patients in group B, who were anesthetized with etomidate, kept hemodynamic stability during surgery, and awoke and recovered in a reduced timeframe after surgery. Based on the use of etomidate, patients in group C, who were anesthetized with a combination of DEX and etomidate, kept hemodynamic stability during surgery and had reduced blood hemodynamic fluctuations during anesthesia induction, tracheal intubation and extubation. Compared with groups A and B, there were no differences in spontaneous breathing recovery time, wake-up time, or extubation for patients in group C.

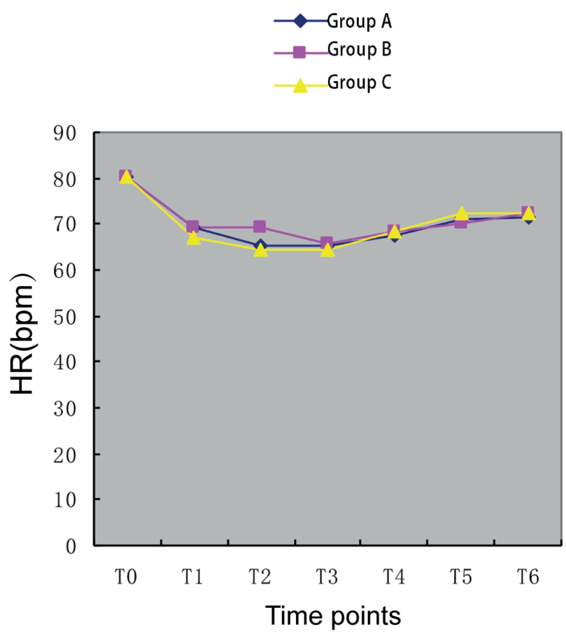

Figure 2. HR (bpm) trends of patients in different groups at different time points. Before anesthesia, HR from the three groups showed no differences (p>0.05). At the subsequent time points, HR from groups A and B did not show significant differences (p>0.05), while HR from group C (p<0.05) was lower than that of groups A and B at T1, T2, T3, and T4.

However, patients in the group C had the lowest prevalence of complications and, therefore, the highest degree of safety.

Conclusions

We found that the combination of DEX with etomidate in the treatment of stroke patients can maintain ideal hemodynamics and reduce complications, which supports its potential for wide usage in clinical applications.

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Conflict of Interest

The Authors declare that they have no conflict of interest.

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