

Original Article

Sevoflurane, Laryngeal Mask Airway and Single-Dose Dexmedetomidine: A Better Choice for Patients Undergoing Endovascular Coil Embolization

Wen-Fei Tan, Yan-Hua Jiang, Hong Ma, and Jun-Ke Wang

ABSTRACT

Background: Patients diagnosed with intracranial aneurysms who undergo endovascular coil embolization (ECE), require sufficient dose of anesthesia to prevent rupture of the aneurysms. However, surgeons often prefer "fast-channel" anesthesia techniques in order to evaluate the effects of the treatment. We designed a double-blind, randomized placebo-controlled study to determine the effects of dexmedetomidine (DEX) on the recovery characteristics of patients who were scheduled to undergo ECE.

Methods: After intravenous anesthesia induction with propofol, fentanyl and cisatracurium, and laryngeal mask airway insertion, patients were randomly assigned to receive saline (Group C, N=33), 0.5 $\mu\text{g}/\text{kg}$ DEX (Group DEX1, N=34), or 1 $\mu\text{g}/\text{kg}$ DEX (Group DEX2, N=34). Maintenance of anesthesia was performed using 2 minimum alveolar concentration (MAC) of end-tidal sevoflurane. The length of time for the eyes to open and characteristics of emergence in patients were recorded after the anesthesia was discontinued.

Results: The incidence of intraoperative bradycardia in Group DEX2 (26.4%) was significantly higher than that in the other groups (15.1% in Group C and 11.8% in Group DEX1). Four patients (12.1%) in Group C exhibited emergence agitation, but it was not observed in any of the patients in the other groups. The length of time for the eyes to open in Group DEX2 was nearly 10 minutes longer than that in the other two groups.

Conclusions: We concluded that a single-dose of 0.5 $\mu\text{g}/\text{kg}$ DEX administered after induction of anesthesia reduced post-sevoflurane agitation in patients undergoing ECE with no adverse effects.

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Citation: Wen-Fei Tan, Yan-Hua Jiang, Hong Ma, Jun-Ke Wang. Sevoflurane, laryngeal mask airway and single-dose dexmedetomidine: a better choice for patients undergoing endovascular coil embolization. *J Anesth Perioper Med* 2015; 2: 153-7.

Sevoflurane is a popular anesthetic for patients undergoing neurosurgery because it has advantages of rapid onset, neuroprotective effects and quick patients recovery (1). However, it is associated with a higher incidence of emergence agitation (EA) than other anesthetics (2). An anesthetic technique that improves the quality of recovery without increasing the incidence of unintended events is desirable. Dexmedetomidine (DEX), a specific α_2 -receptor agonist, may be a useful adjuvant during general anesthesia by promoting hemodynamic stability and decreasing the dose of anesthetics and analgesics (3). Two investigations have examined the use of DEX in patients undergoing intracranial surgery (4, 5). Both of the studies concluded that the addition of DEX improved perioperative hemodynamic control. However, these reports did not include patients undergoing endovascular coil embolization (ECE) treatment for intracranial aneurysms. We designed a double-blind, randomized placebo-controlled study to determine whether the addition of a single dose of DEX would provide improved perioperative hemodynamic stability and better quality of recovery in patients undergoing ECE procedures.

METHODS

Study Design

The trial was approved by the ethics committee of the First Hospital of China Medical University (protocol 20121009) and registered with the Clinical Trials Registry (NCT01722409). All participants provided written informed consent in accordance with the Declaration of Helsinki. A randomised, double-blinded, controlled study was designed to examine whether the addition of a single dose of DEX would provide hemodynamic stability and better quality of recovery in patients undergoing ECE procedures. Major assessments were made during the surgery, immediately and 24 hours after the surgery. Consolidated Standards of Reporting Trials (CONSORT) recommendations were followed in designing and reporting the findings of the study.

Patients

A total of 123 patients undergoing elective ECE

treatment for intracranial aneurysms were enrolled in this study from December 2012 to April 2014 at the First Hospital of China Medical University. Patients were included in the study if they were (1) ethnic Chinese; (2) aged 18 to 65 years old; (3) American Society of Anaesthesiologists (ASA) physical status I or II. Exclusion criteria were body mass index exceeding 30 kg/m^2 , surgery time longer than 3 hours, history of cardiovascular, neurological, or psychiatric disease which was diagnosed by doctors, taking beta blockers, and allergy to drugs used in the study.

Randomization and Masking

All patients undergoing ECE treatment for intracranial aneurysms were randomly assigned via a computer-generated sequence with sealed envelopes to one of three groups: sevoflurane and saline infusion (Group C), sevoflurane and $0.5 \mu\text{g/kg}$ DEX infusion (Group DEX1), and sevoflurane and $1 \mu\text{g/kg}$ DEX infusion (Group DEX2). Treatment allocation was revealed by opening the envelope on the morning of surgery. Patients and their anesthesiologists were all blind to the allocation. Anesthesiologists who participated in anaesthesia management were not allowed to report study details to the staff who collected data. Staff members involved in postoperative data collection and analysis were blind to group allocation. The trial was monitored by an independent data and safety monitoring organisation. Group allocation was not revealed until the final statistical analysis was completed.

General Anaesthesia Procedure and Intervention

General anesthesia was induced with $4 \mu\text{g/kg}$ fentanyl, $2\text{--}2.5 \text{ mg/kg}$ propofol, and 0.2 mg/kg cisatracurium. Muscle relaxant was used to facilitate laryngeal mask airway (LMA) insertion. The patient's lung was ventilated with intermittent positive pressure. Tidal volume was adjusted at $6\text{--}8 \text{ ml/kg}$, and the ventilator rate was adjusted to maintain end-tidal CO_2 (EtCO_2) at $35\text{--}45 \text{ mm Hg}$ and with an end-tidal sevoflurane concentration of 2 minimum alveolar concentration (MAC). After induction of general anesthesia, Group DEX1 and Group DEX2 received a single DEX dose of $0.5 \mu\text{g/kg}$ and $1 \mu\text{g/kg}$ over 10 minutes respectively, and a placebo infusion

of normal saline was given at identical rates for Group C. The mean arterial blood pressure (MAP) was measured every 5 minutes. Electrocardiogram, the EtCO₂, the end-tidal concentration of sevoflurane, and hemoglobin oxygen saturation were continuously monitored throughout the surgery. A decrease in the MAP of more than 30% below the preanesthetic baseline level was corrected with intravenous (IV) ephedrine (4-8 mg), and a heart rate (HR) below 50 beats per minute (bpm) was corrected with 0.5 mg IV atropine, and recorded as intraoperative hypotension and bradycardia, respectively. Tachycardia (HR > 90 bpm) and hypertension (MAP > 20% increase from baseline) were treated with esmolol (5 to 10 mg) and urapidil (10 to 25 mg), respectively.

Measures

At the end of surgery, sevoflurane was discontinued without tapering and the patient's lungs were ventilated with 100% oxygen. Patients were called by name every 30 seconds and, asked (in Chinese) "Are you awake? Open your eyes". We measured the time from termination of the general anesthesia to the time that the patient's eyes opened. Patients were awakened in the operating room and transferred to the post-anesthesia care unit after they could follow simple commands. Anesthesiologists and nurses who were unaware of the anesthetic technique managed the postoperative recovery of the patients in the study and collected information on EA, postoperative nausea and vomiting for 24 hours after the surgery. We used the Richmond Agitation and Sedation Scale (RASS) (6), a diagnostic tool validated for intensive care units use, from comatose (score of -5) to combative (score of +4). Patients with RASS scores of +2 to +4 were considered to have EA if such a RASS level was noted at any one time (or more frequently) during 24 hours after the surgery.

Study outcomes

Primary outcomes were quality of recovery and perioperative hemodynamic stability.

Statistical analysis

Sample size was calculated on the basis of the average (mean \pm standard deviation [SD]) of time

Table 1. Patient Demographic Data.

	Group C (N=33)	Group EX1 (N=34)	Group DEX2 (N=34)
Age (years)	54.2 \pm 10.2	53.4 \pm 9.9	56.1 \pm 8.8
Gender (male/female)	16/17	15/19	18/16
Body mass index (kg/m ²)	24.1 \pm 3.3	24.5 \pm 4.1	22.9 \pm 6.7

Values were mean \pm SD or number of patients. Differences were not significant between groups.

to open eyes at the end of surgery in the pilot study (group DEX2: 21.6 \pm 20.3, C: 11.0 \pm 9.9, and DEX1: 11.1 \pm 10.1). The formula for sample size (7) was $N = 15.7/ES^2 + 1$, where ES is the effect size, defined as the difference between groups divided by the mean of the SD between groups, with $\alpha = 0.05$ and power = 0.8. The study was adequately powered with $N = 34$ for each group. Forty-one patients per group were originally enrolled to compensate for an estimated 20% dropout rate.

Results for parametric data were reported as means \pm SD. One-way analysis of variance (ANOVA) and χ^2 were used for statistical analysis. Differences among the groups were determined by ANOVA followed by the Dunnett post hoc test. A $P < 0.05$ was considered significant. All analyses were conducted using SPSS version 18 for Macintosh (SPSS, Inc., Chicago, IL, USA).

RESULTS

There were no significant differences in the demographic data of the three groups (Table 1). Three patients refused to finish the trial on the morning of the operation, and three patients underwent a craniotomy based on the recommendation of the surgeon. There were a total of 102 patients who finished the trial (Figure). The patients ranged in age from 43 to 65 years old, and 48.5% (49) of the patients were male. The data regarding intraoperative bradycardia, postoperative EA and length of time to opening eyes differed significantly among the three groups (Table 2). The incidence of intraoperative bradycardia in Group DEX2 (26.4%) was significantly higher than that in the other two groups (15.1% in Group C and 11.8% in Group DEX1). Four patients (12.1%) in Group C exhibited EA, but it was not observed in any of the patients in the other groups. The length of time for eyes to open in Group DEX2 was nearly 10

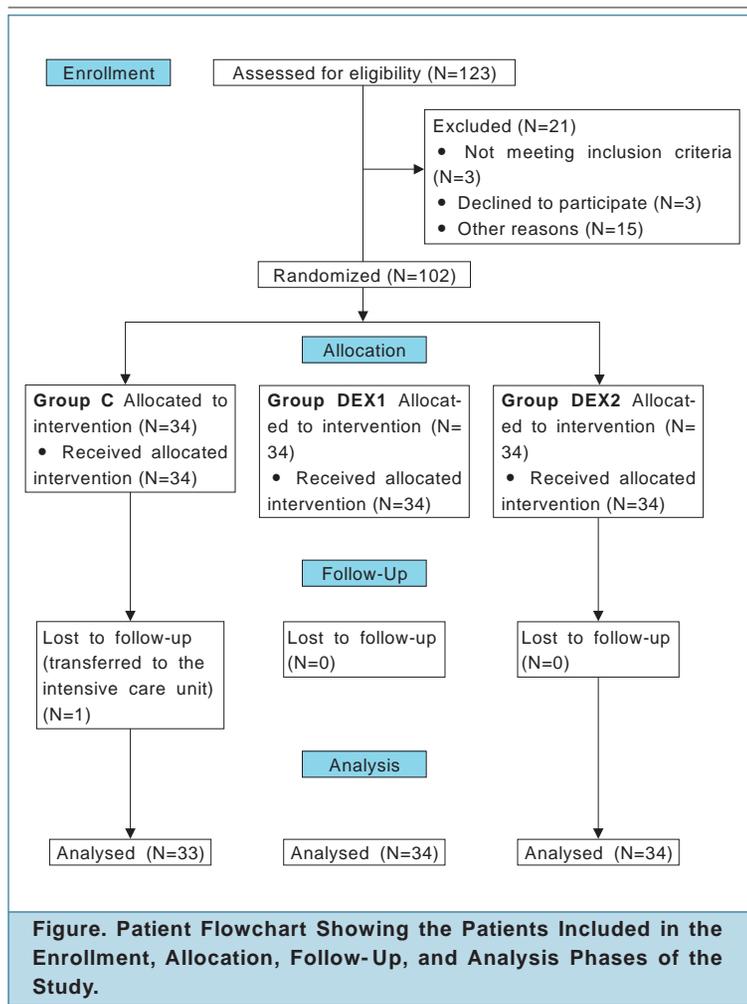


Table 2. Intraoperative and Postoperative Patient Characteristics.

	Group C (N=33)	Group DEX1 (N=34)	Group DEX2 (N=34)	P
Intraoperative data				
Bradycardia (%)	15.1	11.8	26.4	0.031
Hypotension (%)	12.1	14.8	13.3	0.921
Postoperative data				
Emergence agitation (%)	12.1	0	0	0.001
Nausea and vomiting (%)	6.0	8.8	8.8	0.992
Duration of surgery (minute)	58.7±15.2	56.0±13.6	51.5±10.2	0.093
Duration of anesthesia (minute)	73.2±18.1	71.6±14.2	69.4±11.8	0.568
Time to open eyes (minute)	11.3±2.1	11.1±2.4	21.6±3.9	< 0.001

minutes longer than that in the other two groups, which represented a significant difference ($F_{(2,83)} = 163.217$, $P < 0.001$). The incidences of intraoperative hypotension, postoperative delirium and nausea and vomiting were not different between the three groups.

DISCUSSION

The present study confirmed that administration of a single-dose of 0.5 µg/kg DEX in patients undergoing ECE markedly decreased the incidence of EA, did not cause any major hemodynamic changes during the intraoperative periods and did not delay the length of time to open the eyes.

The sedative properties of the α2-agonists are well documented. The hypnotic and sedative actions of DEX are thought to be mediated primarily by postsynaptic α2- adrenergic receptors. These effects differ depending on the receptor location. In the locus ceruleus, stimulation of the receptors induces sedation (8). In healthy volunteers, 0.5 to 1 µg/kg IV DEX caused sedation within 5 minutes and achieved maximum effects at 15 minutes (9). In patients undergoing ECE in this research, 0.5 µg/kg IV DEX was sufficient to cause hypnotic and sedative effects and did not influence the recovery time.

In this study, we attempted to determine whether a single dose of DEX would provide improved perioperative hemodynamic stability and better quality of recovery. Patients diagnosed with intracranial aneurysms who undergo ECE require a sufficient dose of anesthesia to prevent rupture of the aneurysms, although surgeons often prefer "fast-channel" anesthesia techniques and effective quality of recovery in order to evaluate the effects of the treatment. The anesthesiologists stayed far away from the heads of the patients for most ECE operations. For all of the reasons listed, the patients were provided ventilation with LMA to avoid any chance of accidental bucking and disconnection of the endotracheal tube. With an end-tidal sevoflurane concentration of 2 MAC, all patients were able to tolerate the ECE procedure. However, EA is a frequent side effect of sevoflurane anesthesia (10). In this study, the results in Group C under the sevoflurane anesthesia were the same as the group without administration of DEX. Several studies have described the effects of DEX on EA after sevoflurane anesthesia (11, 12). The results of this study showed that administration of IV DEX at 0.5 µg/kg and 1 µg/kg after induction of anesthesia reduced the incidence of EA after sevoflurane anesthesia. However, IV administration of

1 $\mu\text{g}/\text{kg}$ caused intraoperative bradycardia and delayed the postoperative length of time to the opening of the eyes, which was similar to the results reported by Uyar and colleagues (13). The sedation effect of DEX is predictable based on the pharmacology of α_2 -receptor agonists and the bradycardic effect is presumably mediated by sympatholytic effect of DEX (14, 15).

There are several limitations in the present study that should be considered. The sample size was small, and the study was performed in patients with low ASA scores. More patients with cardiac disease who develop significant bra-

dycardia and hypotension and may need intervention when using DEX should be included.

CONCLUSIONS

In summary, we concluded that a single-dose of 0.5 $\mu\text{g}/\text{kg}$ DEX administered after induction of anesthesia reduced the post-sevoflurane agitation in patients undergoing ECE with no adverse effects.

There are no funding or research contracts or conflict of interest.

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