Early postoperative recovery after intracranial surgical procedures. Comparison of the effects of sevoflurane and desflurane[1]

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ABSTRACT

PURPOSE: To compared the effects of sevoflurane and desflurane on early anesthesia recovery in patients undergoing to craniotomy for intracranial lesions.

METHODS: After IRB approval, the study included 50 patients aged 18–70 years who had ASA physical statuses of I–II and were scheduled for intracranial surgery. Patients were randomly divided into two groups: sevoflurane and desflurane. Anaesthesia was routinely induced in all patients followed by desflurane 5%–6% or sevoflurane 1%–2%. Moreover remifentanil infusion (0.05-0.2 mcg/kg/min) was adjusted to maintain mean arterial pressure (MAP) within 20% baseline and heart rate <90 bpm. Postoperatively, patients were evaluated over time for responses to painful stimulus, eye opening, hand squeezing, extubation, orientation and time required to achieve a Modified Aldrete Score of 9–10. Parametric and non-parametric data were assessed using Student's *t*- and Mann–Whitney U tests, respectively. A $p<0.05$ was taken as statistically significant.

RESULTS: The times to responses to painful stimuli (7.7±2.7 *vs*. 4.8±1.7 min.; $p<0.001$), emergence (9.5±2.81 *vs.* 6.3±2.2 min.; $p<0.001$), hand-squeezing (12.1±2.9 *vs*. 8.2±2.3 min.; $p<0.001$), extubation (10.1±2.87 *vs*. 7.1±1.6 min.; $p<0.001$), orientation (15.3±3.2 *vs*. 10.3±2.7 min.; $p<0.001$) and Aldrete score of 9–10 (23.3±6.1 *vs*. 15.8±3.8 min.; $p<0.001$) were significantly lower with desflurane-based anaesthesia *vs*. sevoflurane-based anaesthesia.

CONCLUSION: Desflurane yields early recovery functions and facilitates early postoperative neurologic examinations of intracranial surgery patients.

Key words: Sevoflurane. Desflurane. Anesthesia. Postoperative Period.

Introduction

Ideally, neuroanaesthetic agents used in practice will yield the following outcomes with few side effects: reduction in cerebral metabolism, neuroprotection, haemodynamic stability, preservation of cerebral autoregulation, rapid onset of action and early postoperative recovery of neurologic functions[1,2]. Intracranial surgery remains associated with life-threatening postoperative complications, such as seizure, increased intracranial pressure, unexpected neurologic deficits and epidural, subdural or intracerebral haemorrhage[3]. Early neurologic evaluations help to avoid permanent injury by identifying these postoperative complications. Therefore, early recovery allows the best chance of a clinical assessment and neurological monitoring after most neurosurgical procedures[1].

Sevoflurane and desflurane are both widely used neuroanaesthetic agents and are characterized by low blood/gas partition coefficients that favour rapid recovery[4].The solubility coefficient is the main factor that determines the effect onset time and elimination time of an inhaled agent. Desflurane has a lower solubility coefficient than sevoflurane (blood/gas: 0.42/0.69, fat/blood: 27.2/47.5, brain/blood: 1.29/1.70). Despite many studies in which desflurane has been associated with a shorter emergence, early recovery time and early return of consciousness, particularly after long–duration surgeries because of low fat/blood and brain/blood solubility coefficients[5,6], a few reports from randomised clinical trials suggest that desflurane allows an earlier extubation time and shorter recovery time when compared with sevoflurane in patients undergoing intracranial surgery[7,8]. The different types of intravenous opioids affect postoperative recovery durations. Remifentanil, fentanyl and sufentanil are commonly used opioids for intracranial surgeries. Remifentanil has short duration of action which allows earlier emergence and recovery. Moreover remifentanil reduces mean arterial pressure and cerebral perfusion pressure[9].

In this study, we compared the effects of sevoflurane and desflurane on early anesthesia recovery in patients undergoing to craniotomy for intracranial lesions.

Methods

After receiving approval from the institutional review board and ethics committees, our study was performed by medical faculty at the İstanbul University neurosurgery clinics between February and May 2011. A total of 50 patients (age range,18–70 years; American Society of Anaesthesiology (ASA) class I–II; Glasgow Coma Scale (GCS), 15) scheduled to undergo intracranial operation were enrolled in this prospective, double blinded, randomised study after providing written informed consent. Patients were divided into two groups via computer-generated randomisation: sevoflurane group (Group S; 25 patients) and desflurane group (Group D, 25 patients). Patients were blinded to phase. Anesthesiologists were blinded to the study drug used until a patient randomized on the study. The study coordinator that collected data was blinded to groups throughout the study. On the day of surgery, the anesthesologist opened the envelopes that stored randomized sequence numbers in the operating room in order to not change patients' allocation. Patients younger than 18 years or older than 70 years, those with an ASA class >III–IV status, a known renal, hepatic, chronic lung (chronic obstructive pulmonary disease, asthma), or cardiac disease (e.g.coronary heart disease, decompensated heart failure, experienced myocardial infarction within the previous 6 months), obesity (body mass index >30), or a known hypersensitivity to any anaesthetic agent, and those from whom informed consent had not been obtained were not included in the study.

Preoperatively, all patients received an infusion of an isotonic crystalloid solution (8–10 ml/kg ideal body weight (IBW)) through a peripheric intravenous catheter. Patients did not receive any pharmacological premedication. For all patients, an electrocardiogram (ECG), peripheral oxygen saturation (SpO_2) monitoring, non-invasive blood pressure (NIBP) monitoring, train of four (TOF watch; Organon Teknika, Durham, NC, USA) for neuromuscular monitoring, and bladder catheter for body temperature monitoring were used. Intraoperative normothermia was maintained with a heated blanket. The adductor pollicis and ulnar nerve were used for neuromuscular monitoring, and the hand temperature was maintained above 33ºC.

All patients were preoxygenated with 100% oxygen for 2 minutes, and anaesthesia was induced using midazolam (0.05–0.2mg/kg IBW), fentanyl (1–2 mcg/kg IBW), propofol (2–3 mcg/kg IBW) and vecuronium (0.1 mg/kg). After orotracheal intubation, mechanical ventilation was adjusted to maintain atidal volume of 8 ml/kg, partial carbon dioxide pressure (PaCO2) of 35–40 mmHg, and positive end-expiratory pressure (PEEP) of 5 in the pressure control ventilation (PCV) mode (Datex Ohmeda; S/5 Avance Healthcare, Helsinki, Finland). Anaesthesia was maintained witha 60%/40% air/oxygen mixture to maintain a partial oxygen pressure (PaO2) of 100–200 mmHg. Both anaesthetic agents were

adjusted to maintain a minimum alveolar concentration (MAC) of 1%–2% for sevoflurane or 5%–6% for desflurane. For all patients, remifentanil was infused at a dosage of 0.05–0.2 mcg/kg/min during surgery. Repeated doses of vecuronium were administered according to TOF monitoring.

In all patients, a radial artery cannula connected to a Haemomed transducer (Siemens, Munich, Germany) and central venous catheter were applied after the anaesthesia induction period. Anaesthetic agents were adjusted to maintain a mean arterial pressure (MAP) within 20% of the baseline and heart rate of <90 bpm. A MAP >30% of the baseline value that persisted for>1 minute despite an adequate maximal anaesthetic concentration was treated with labetolol. Hypotension (MAP <20%ofbaseline) was treated first with adequate fluid replacement; if this was inadequate, the remifentanyl infusion dose was decreased, followed by ephedrine (5–10mg) treatment. Bradycardia was defined as a heart rate <45 bpm. This condition was treated with atropine (0.015 mg/kg) if clinically indicated. Blood gas measurements were evaluated every hour intraoperatively. The central venous pressure was also measured intraoperatively at 1-hour intervals.

Postoperative management

Upon completion of surgery, the neuromuscular block was reversed using neostigmin (0.05 mg/kg) and atropine sulphate (0.015 mg/kg) if the patients failed to maintain a sustained contraction according to TOF. The emergence time (elapsed time between the end of anaesthesia and eye opening), extubation time (elapsed time from anaesthetic discontinuation to extubation), hand squeezing time and time from eye opening to verbal commands were evaluated. Spatial, temporal and personal orientation were evaluated by inquiring about the patient's own and father's names and place and date of birth at 30, 45 and 60 second intervals (e.g.'how are you?', 'what is your name?','what is your father's name?', 'where are we now?', 'which day is today?'); the time required to achieve a modified Aldrete score[10] (Table 1) of 9–10 was determined by an observer who was blinded to the anaesthesia strategy. All patients were followed at a post-anaesthesia care unit (PACU) for 2 hours. Postoperative nausea and vomiting were prevented by administering 4–6 mg. ondansetron before extubation. Haemodynamic instabilities (e.g.hypotension, hypertension, bradycardia, tachycardia) were treated. Tramadol (0.8–1 mg/kg) infusion was administered postoperatively to all patients for pain management.

TABLE 1 - Modified Aldrete Scoring System[1].

Activity: able to move, voluntarily or on command	
Four extremities:	2
Two extremities:	1
No extremities:	0
Respiration:	
Able to breathe deeply and cough freely	2
Dyspnea, shallow or limited breathing	1
Apnea	0
Circulation:	
Blood pressure within 20 mmHg of preoperative level	2
Blood pressure within 20-50 mmHg of preoperative level	1
Blood pressure within ± 50 mmHg of preoperative level	0
Conciousness:	
Fully awake	2
Arousable on calling	1
Unresponsive	0
Oxygen Saturation:	
Saturation > % 92	2
Needs oxygen to maintain saturation % 90	1
Saturation < %90 with oxygen	0

[1]Nine or more points are required for recovery to be confirmed.

Statistical analysis

We aimed in this study to obtain a power of 90% and confidence interval %95 to detect 25% decrease in extubation time with standard deviation of 3.5. The sample size of the study was based on mean extubation time of 11.3 minutes with desflurane 15.2 minutes with sevoflurane in study of Magni et al..(7) 17 person was calculated per group as sample size. We increased sample size to 25 patients for each grour to have adequate power. Statistical Package for the Social Sciences (SPSS) 15(SPSS, Inc.,Chicago, IL, USA) was used for the statistical data analysis. For both groups, continuous data are presented as means ± standard deviations, whereas categorical variables are presented as frequencies and percentages. Student's *t*-test and the Mann–Whitney U test were used to assess parametric and nonparametric data, respectively. A *p* level of <0.05 was considered statistically significant.

Results

All 50 recruited patients completed the study. All patients were extubated while on the operating table, and none required

intensive care unit admission or mechanical ventilation. The sevoflurane and desflurane groups did not differ significantly with regard to the mean age, sex distribution, weight, ASA (American society of Anesthesiologists) status or anaesthesia and surgery duration (Table 2).

TABLE 2 - Demographic data of the patients.

Characteristic	Sevoflurane	Desflurane	*p*
Age (years)	45,3±13,4	47,5±12,1	0,74
Gender(F/M)	13/12	14/11	0.65
weight(kg)	67.1±12	74.4±13.9	0.56
Anesthesia time (min)	338.2±63.1	360.1±98.4	0.09
Total	25	25	

Mean ± standard deviation; n: Patient number; Differences between groups in all variables are not statistically significant; F: female; M: male.

A distribution of the operations by group is shown in Table 3. This study included frontal, temporal and occipital lesions, meningiomas, suprasellar lesions, trigeminal neuralgia and cranial aneurysms.

The times to respond to a painful stimulus, interval from eye opening to verbal stimulus, and times to extubation, handgrip, orientation and achievement of a Modified Aldrete score of 9–10 were found to be significantly shorter in the desflurane group ($p<0.001$; Table 4). A postoperative comparison of the sevoflurane and desflurane groups found no neurosurgical complications requiring early reoperation.

TABLE 3 - Distibution of surgical operations according to groups.

	Sevoflurane	Desflurane
Frontal lesion	3	2
Suprasellar lesion	8	8
Temporal lesion	4	5
Trigeminal nevralgia	3	1
Aneurysm	4	5
Occipital lesion	1	2
Menengioma	2	2
Total	25	25

TABLE 4 - Comparison of groups according to recovery criteria and Modified Aldrete scores.

	Sevoflurane	Desflurane	*p*
Time to pull with painful stimulus (min)	7,7±2,7	4,8±1,7	<0,001
Emergence (min)	9,5±2,81	6,3±2,2	<0,001
Extubation (min)	10,1±2,87	7,1±1,6	<0,001
Handgripping (min)	12,1±2,9	8,2±2,3	<0,001
Orientation (min)	15,3±3,2	10,3±2,7	<0,001
Time to MAS 9-10 (min)	23,3±6,1	15,8±3,8	<0,001
Total	n=25	n=25	

MAS: Modified Aldrete Score; Min: minute.

There were 12 intraoperative hypertensive episodes mostly during pin application (5 in Group S, 7 in Group D) and 5 hypotensive episodes (3 in Group S, 2 in Group D). Postoperatively, hypertensive episodes were recorded in 10 of 50 patients (4 in Group S, 6 in Group D). Tachycardia was recorded in 14 of 50 patients. (6 in Group S, 8 in Group D). There was not any bradycardia seen during operations.

The mean total dose of remifentanil was (mcg h^{-1}): 650 +- 9,1 in group S and 689 +- 2,1 in Group D.

Discussion

In this study of early function recovery and the ability to conduct a post-intracranial surgery neurologic examination after general anaesthesia involving the volatile anaesthetics desflurane and sevoflurane, we demonstrated that the times to response to a painful stimulus, eye opening, extubation and handgrip were significantly shorter inthedesflurane group relative to the sevoflurane group. We also observed significantly shorter times required to achieve orientation and a Modified Aldrete score of 9–10 in the desflurane group.

Some parameters are particularly important in the context of neuroanaesthesia, including haemodynamic stability, avoiding damage to the cerebral perfusion pressure, early recovery, soft extubation, early control of airway opening and surgical complications. Desflurane has some potential advantages resulting from its uptake and recovery characteristics in neurosurgical patients, along with the desired early recognition of postoperative

sequelae. However, some previous studies limited the use of desflurane in neurosurgical patients because of a potential increase in intracranial pressure. Despite some animal studies in which desflurane[11] and sevoflurane[12,13] were found to increase intracranial pressure, this has not been observed in human studies[14].

Few studies have specifically compared sevoflurane and desflurane in the context of intracranial surgery. Magni *et al.*[7] divided 120 patients who underwent elective craniotomy into two groups of 60 patients. The authors measured extubation times after inhalation anaesthetic discontinuation of 15.2 ± 3.0 min and 11.3 ± 3.9 min. in the sevoflurane and desflurane groups, respectively; the observed times were significantly shorter in the desflurane group. Although we obtained similar results, the previously reported times were 4–5 min shorter than those in our study, and similar results were observed for the emergence time. These differences might be mainly attributed to the use of fentanyl for analgesia in the study by Magni *et al*.[15]; in contrast, we selected an ultra-short-acting opioid, remifentanyl, and our patients also had a younger mean age (by 15 years). Although an analysis of early cognitive functions by Magni *et al.*[15] found no differences in recovery functions between patients who received sevoflurane–fentanyl and propofol–remifentanil combinations while undergoing craniotomy for supratentorial intracranial surgery, the findings of many other studies agreed with our finding that anaesthesia with remifentanyl infusion provides an early recovery[16,17]. Kaye *et al.*[13] compared desflurane and isoflurane in the context of neurosurgery and achieved 50% decrease in early recovery and eye opening times in the desflurane group. However, the time required to obey orders was longer than that in our study (30 *vs.* 10 min). We attributed this discrepancy to our use of the very-short-acting opioid remifentanyl. Bilotta *et al.*[8] reported that in comparison to sevoflurane, desflurane was associated with shorter recovery and extubation times after anaesthesia for neurosurgery in overweight and obese patients. Compared with our study, Bilotta reported shorter times to recovery and achievement of an Aldrete score >9. This discrepancy might be attributed to a longer anaesthesia time relative to that reported in our study (260 min *vs*. 350 min).

Many studies have compared sevoflurane and desflurane in non-neurosurgical contexts. Most of these studies observed a more rapid recovery from desflurane than from sevoflurane[18-23], whereas others found no difference[24]; in addition, Tarazzi *et al.*[25] reported a marginally but not significantly better recovery with sevoflurane than with desflurane.

Eger *et al.*[18] applied sevoflurane and desflurane for 8 hours in a 2 L/min fresh gas flow to healthy volunteers; a comparison of the recovery properties revealed two-fold faster recovery in the desflurane group vs. the sevoflurane group. In our study, we observed a 30% reduction in the orientation time in the desflurane group. We attribute this difference to the influences of intracranial interventions on function recovery. Strum *et al.*[19] investigated the recovery times and capillary oxygen saturation with desflurane and sevoflurane in two groups of morbidly obese patients (n=25) subjected to elective open abdominal surgery. In that study, the recovery times were significantly lower in the desflurane group. The results from that study exceeded our recovery durations. However, we believe that these longer times are associated with obesity[26]. Baysalman *et al.*[27] did not detect a significant difference when comparing the effects of TIVA and desflurane anaesthesia on early postoperative recovery in different age groups. Relative to our study, the times reported by Baysalman *et al.*[27] were shorter. We might attribute this discrepancy toour study setting of neurosurgery and a longer operative duration (90 min *vs.* 350 min). Finally, in a modelling study, Dexter *et al.*[20] demonstrated that relative to sevoflurane, desflurane reduced the average extubation time by 20%–25%. This result was similar to the reduction observed in our study (~30%).

In this study, we concluded that remifantanil may provide earlier recovery properties. Remifentanil is a μ-opioid receptor agonist which has a short half life, commonly used in neuroanesthesia and neurointensive care units. The drug provides rapid recovery and neurologic evaluation, reducing extubation times[28,29] and ideal for selected pediatric neurological patients requiring serial neurological examinations[30]. Del Gaudio. reported earlier extubation times, obey commands orientation and faster Aldrete scores (8.6 min *vs*. 14.6 min, $p < 0.001$) with remifentanil in a study comparing remifentanil and fentanil in patients undergoing craniotomy[17]. Gerlach *et al*.[31] showed that remifentanil provided earlier extubation when comparing with sufentanil (6.4 min *vs*. 14.3 min; $P = 0.003$) (31) On the other hand, the NeuroMorfeo study reported no difference in time to reach Aldrete score ≥ 9 between remifentanil and fentanyl groups.

Conclusions

In the context of intracranial surgery, an earlier recovery and shorter extubation time could be achieved with desflurane vs. sevoflurane. Moreover, the ultra-short-acting opioid remifentanyl is beneficial with regard to the emergence time and post-anaesthesia recovery. We consider that desflurane with remifentanyl infusion might be preferable for neurosurgery interventions, as this

combination might enable the early recognition of potential postoperative complications and rapid treatment.

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