Comparison of the effects of desflurane and sevoflurane in awakening and cognitive function after a general anaesthesia

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Abstract

Introduction The pharmacokinetics of desflurane and sevoflurane favour improved intraoperative control of anaesthesia and led to faster postoperative recovery. These anaesthetics have a lower blood/gas coefficient than isoflurane and halothane. (1) The low fat/gas coefficient and low brain/blood coefficient of desflurane lead to faster elimination of and faster awakening from anaesthesia. This leads to a quicker return of cognitive functions and speedier discharge from the Post Anaesthesia Care Unit (PACU). **Objectives** The purpose of this study is to compare the emergence time and time of return of cognitive functions in patients with general inhalation anaesthesia (general anaesthesia) maintained with inhalant anaesthetics desflurane and sevoflurane, respectively, under standardized conditions. **Material and methods** This study included ASA I and II patients undergoing colorectal abdominal surgery who were randomly assigned into two groups: the first group received the inhalation anaesthetic desflurane in combination with the analgesic remifentanil for anaesthesia maintenance, while the second group was kept under using sevoflurane in combination with fentanyl. We used standard hemodynamic monitoring, the Train of Four (TOF) and the Bispectral Index System (BIS) to determine the depth of the anaesthesia. We recorded the time required for extubation, the opening of the eyes, verbal response, the modified Aldrete score of 9, the Mini Mental State Examination (MMSE) of 25 and the Short Orientation-Memory-Concentration Test (OMCT). **Results** The results, expressed in minutes and obtained in both patient groups, demonstrate a significantly shorter time for regaining cognitive functions in the patients who received a desflurane inhalation anaesthetic with remifentanil compared to the patients who received a sevoflurane inhalation anaesthetic with fentanyl. This is thought to be due to the faster pharmacokinetic profile of desflurane, leading to an accelerated elimination in the patients. Desflurane, in combination with remifentanil, a short-acting opioid, further shortens the recovery time of cognitive functions. **Conclusion** This study underscores that the time required for early recovery from anaesthesia is markedly shorter in patients receiving desflurane compared with patients given sevoflurane when administering general anaesthesia. This finding emphasizes the potential benefits of desflurane in optimizing perioperative outcomes, including faster emergence from anaesthesia and cognitive recovery. **Keywords**: desflurane, sevoflurane, inhalational anaesthetics, opioids, cognitive function**.**

INTRODUCTION

As developed countries push to save hospital resources, doctors are under increasing pressure to develop targeted strategies for a faster postoperative recovery of patients and, thus, a shorter hospital stay. Desflurane and sevoflurane are inhalant anaesthetics with clinical and pharmacological profiles that make them ideal for the rapid recovery of patients. (2) The development of minimally invasive surgical techniques has led to an increased need for rapid awakening of patients from general anaesthesia after surgical procedures. An anaesthesiologist can make a difference through physiological mechanisms that relieve pain and shorten the time it takes to recover protective reflexes, especially those related to the airways, and regain cognitive functions. As a result, there is an increasing need for anaesthetics that induce sufficiently deep anaesthesia while making the emergence from it quick, i.e. quickly restoring vital functions without any side effects. (3)

Inhalation anaesthetic agents are used to induce and maintain general anaesthesia, and they are delivered to the patient through a mixture of carrying gases, most commonly air/oxygen. They exert their effect on the CNS to cause loss of consciousness, the establishment of anaesthetic sleep and the loss of the response to harmful stimuli, while the depth of anaesthesia is proportional to the partial pressure of the anaesthetic in the lungs and brain. Since the concentration of the inhalation aesthetic in these two organs cannot be measured (except in a computer simulation), the alveolar end-tidal partial pressure of the inhalation anaesthetic is used as a replacement for the concentration of the inhalation anaesthetic at the site of action. (4) Desflurane is a volatile anaesthetic that is the latest to enter anaesthetic practice and is used to maintain general anaesthesia. It is desirable for surgical techniques that require rapid induction and rapid awakening from anaesthesia, such as major and long head and neck surgeries. Its low solubility (blood/gas coefficient of 0.42) and low distribution volume are useful for patients undergoing long surgery and bariatric surgery, in which the distribution volume of drugs soluble in lipids is higher. Desflurane's pharmacological profile makes it even more suitable for general anaesthesia. (5) Compared to other inhalation anaesthetics, its low solubility makes it easier to reach an equilibrium between alveolar and inspired concentration. Therefore, we have a rapid induction of general anaesthesia and rapid awakening from anaesthesia. Only a small percentage of desflurane, 0.02%, is metabolized in the body, while 99.98% of it is exhaled unchanged through the lungs.

Cognitive status disorders in the postoperative period are common after major surgeries, and general anaesthesia is considered the main cause. Postoperative cognitive disorders can be classified into: postoperative delirium, postoperative cognitive dysfunction, and dementia. (6,7) Postoperative cognitive dysfunction is a mild neurological disorder characterized by impairments in memory, concentration, linguistic understanding, and social relationships. The diagnosis is formulated days after surgery and can result in a lifelong decrease to the patient's quality of life. The pathophysiological mechanism responsible for postoperative cognitive disorders in patients remains unclear. (8) Predisposing factors include age and degree of education, presence of a preoperative cognitive disorder, chronic use of opioids and benzodiazepines, the existence of comorbidities, cerebrovascular disorders, and the appearance of postoperative delirium. (9,10) Other factors that increase the risk of cognitive disorders are duration of anaesthesia, re-operation, infection, and postoperative pulmonary complications.

GOAL

The purpose of this scientific study is to examine the effects of volatile anaesthetics on patients' cognitive functions. Therefore, we compare the impact of two inhalation anaesthetics, desflurane and sevoflurane act, on the cognitive functions of patients who, due to the type of surgical intervention, had to be placed under general anaesthesia. Our second goal is to prove that the short-acting inhalation anaesthetic, desflurane, along with the short-acting opioid anaesthetic, remifentanil (not fentanyl), is among the best combinations for patients who need a long surgical intervention and general anaesthesia with no postoperative impact on cognitive functions. To achieve these two goals, we will evaluate and compare the time of the return of reflexes to the airways and regaining of cognitive functions after general anaesthesia with desflurane and sevoflurane, with the former being combined with remifentanil and the latter in a typical combination with fentanyl. All other factors affecting waking time from general anaesthesia will be the same for both groups of examinees.

MATERIAL AND METHODS

In this observational study conducted at the Clinic for Anaesthesia, Resuscitation and Intensive Treatment (KARIL), the University Clinic for Traumatology, Orthopaedic Diseases, Anaesthesia, Reanimation, Intensive Care and Emergency Centre (UC TOARILUK) over a period of 24 months included 60 respondents, 26 of whom received halogenated inhalational desflurane (MAC=0.7-1), while 34 respondents received halogenated inhalational sevoflurane (MAC=0.7-1) to administer general anaesthesia. In the desflurane group, thirteen subjects received fentanyl intraoperatively, while 13 subjects were maintained under anaesthesia by remifentanil, and in the sevoflurane group, 17 received fentanyl, while 17 were maintained under anaesthesia by remifentanil. Inclusion criteria for the study encompassed ASA 1.2 and 3 with BMI below 35 and an age limit of 18–65 years for both sexes. The subjects received elective general anaesthesia with an inhaled anaesthetic desflurane or sevoflurane for colorectal pathology during an elective surgery lasting between 2 and 3 hours. The depth of anaesthesia was monitored by the Bispectral Monitoring Index, which ranged from 45 to 55 in both groups, corresponding to stage 3 surgical anaesthesia. The awakening time from anaesthesia was measured from the cessation of the inhalation of the anaesthetic to the return of reflexes to the airways (laryngeal reflex). Then, the extubation time was measured, followed by the time of first opening of the eyes in response to a verbal command, the moment of holding the head raised for 5 seconds, and the orientation to person, place, and time, using a modified Aldrete score that needed to be above 9. Cognitive functions were evaluated according to the time required to complete the Mini Mental State Examination (MMSE) test and the Orientation-Memory-Concentration Test (OMCT), which were filled in for each patient 4 times: preoperatively, in the recovery room (PACU), and on the first and second postoperative days. The study's exclusion criteria were ASA over 3, age under 18 and over 65 years, morbid obesity, BMI over 35, existence of neuromuscular diseases, history of possible malignant hyperthermia, obstructive lung disease with regular use of bronchodilators and the presence of preoperative cognitive disorder, which originates from chronic opioid or benzodiazepine use, as well as cerebrovascular disorders.

WORK PROTOCOL

In the operating room, patients were connected to a monitor to observe the ECG, non-invasive blood pressure, pulse oximetry, and Bispectral Index. A peripheral neurostimulator was installed to monitor The Train of Four (TOF). Patients were reoxygenated with 100% oxygen within 3 minutes with a flow of fresh gases of 6 L/min and anaesthesia was induced with a standardized induction approach using sedative midazolam 0.03mg/kg i.v., fentanyl 1-2 mcg/kg, propofol 2mg/kg and muscle relaxant rocuronium 0.6mg/kg. The respiratory pathway is secured with an adequately-sized endotracheal tube and connected to an anaesthesiology ventilation machine with an inhaled anaesthetic desflurane (3–6%), (1–2%) to mas=0.7–1, with a flow of fresh gases of 2L/min, 50% air with 50% oxygen. Tidal capnography $etSO_2$, the inspiratory faction (Fi) of anaesthetic gases and the expiratory faction (FE) of volatile anaesthetics are monitored. Minute ventilation is set with a respiratory volume of 6–8ml/kg, a 12/min respiratory frequency and an inhale exhale ratio of 1:2 to maintain a 30–40mmHg CO_2 tidal. The dosage for maintenance of intravenous and inhaled anaesthetic agents is titrated to maintain BIS from 45–55. Additional bolus doses of fentanyl at a dose of 0.5mcg/kg were given as needed. Remifentanil was given at a dose of 0.125–0.25mcg/kg/min. Muscle relaxation was maintained with intermittent doses of rocuronium at a dose of 0.15mg/kg. The volatile anaesthetic was reduced 15 minutes before the surgery ended to MAS=0.5 and was interrupted after the last surgical stitch was placed. The flow of fresh gases was then increased to 6L/min with 100% oxygen. After achieving TOF≥3, a reversion of the neuromuscular block with Neostigmine 0.03mg/kg and Atropine 0.01mg/kg was administered. i.v.

STATISTICAL ANALYSIS

The data analysis was performed in statistics programs Statistics 7.1 for Windows and SPSS 23, in series of numerical variables (ASA, age, BMI, length of intervention), Description Statistics (Mean; Std. Deviation; ±95,00%CI; Median; Minimum; Maximum). The difference between the values of the parameters analysed in relation to the gender of the respondents was analysed by applying t-test, independent, by groups (t/p) depending on the distribution of the data. The correlation between two variables was derived with Pearson's correlation coefficient (r) and Spearman Rank Order R (R), depending on the distribution of the data. Significance was determined for $p<0.05$.

RESULTS

The results (expressed in minutes) obtained in the two patient study groups are significantly shorter in the group of patients who received a desflurane inhalation anaesthetic with the opioid remifentanil, compared to the group of patients who received a sevoflurane inhalation anaesthetic with fentanyl or remifentanil, when administering elective general anaesthesia.

Table.1 Demography and duration of surgical intervention

	Group D-f. (n=13)	Group D-r. (n=13)	Group S-f. (n=17)	Group S-r. (n=17)	p-value
Sex (m/f)	8/5	7/6	9/8	10/7	p<0.05*
ASA I/II/III	2/6/5	1/6/6	2/9/6	1/8/7	p<0.05*

Age	61±8.7	63±7	64±9.3	62±8.1	p<0.05*
BMI	22.23±.1	21±7 PM	23.5±4.0	22.2±3.1	p<0.05*
Length of intervention	149.4±11.2	151.1±9.3	157±8.5	156±7.7	p<0.05*

BMI=Body Mass Index, ASA=Physical Status Classification System, Group D-f=Fentanyl Desflurane, Group D-r=Remifentanil Desflurane, Group S-f=Fentanyl Sevoflurane, Group S-r=Sevoflurane with Remifentanil

- The group maintained under anaesthesia by desflurane with remifentanil marks a shorter time of extubation, from the last surgical stitch of the operational operation, i.e., from discontinuation of the inhalation anaesthetic to extubation.
- The patients with desflurane-remifentanil anaesthesia mark shorter time of the opening of the eyes, the time from the last surgical stitch, from the cessation of the inhalation of anaesthetic to the opening of the eyes in response to a verbal command given by the examiner.
- Patients with desflurane-remifentanil mark shorter time of a verbal response after the last surgical stitch.
- The desflurane-remifentanil group marks shorter time from discontinuation of the inhalation anaesthetic to achieving Aldrete's score of 9.
- Cognitive function return more quickly to the desflurane group after the patient's awakening, i.e. the time from interruption of desflurane to time required to complete the Mini Mental State Examination (MMSE) in the recovery room with a score of more than 25 is shorter in the desflurane-remifentanil group.
- The Mini Mental State Examination (MMSE) test on the first postoperative day showed a higher score of cognitive function by patients who received desflurane-remifentanil.
- Patients who received desflurane-remifentanil achieved a better score on the Orientation-Memory-Concentration Test (OMST) when they were examined for the second time, i.e., in the recovery room.

Board.2 Time of emergence from anaesthesia

	Group D-f	Group D-r	Group C-f	Group S-r	r value
Extubation	7.2 ±1.6	7±8.3	8.9 ±2.0	8.4±1.1	p<0.05*
Eye opening	6.8 ±3.1	6.5±5.4	7.5 ±4.2	7.1± 3.4	p<0.05*
Verbal response	7.6 ±1.8	7.2±2.0	9.3 ±4.1	8.2±2.6	p<0.05*
Modified Aldrete score>9	13.3 ±5.0	13.1±1.2	16.7 ±3.9	15.5±4.4	p<0.05*
MMSE>25	60 ±7.2	57.8±1.8	64.3 ±3.3	61.3±3.4	p<0.05*
OMST<10	74±2	72±3.7	77.71±2.3	74.3±6.3	p<0.05*

MMSE=Mini Mental State Examination Test, Orientation-Memory-Concentration Test (OMCT) Group D-f=Fentanyl Desflurane, Group D-r=Remifentanil Desflurane, Group S-f=Fentanyl Sevoflurane, Group S-r=Remifentanil Sevoflurane

DISCUSSION

The purpose of this study was to compare the waking time and time of return of cognitive functions in patients after elective general anaesthesia maintained with inhalant desflurane in one group of patients and inhalant sevoflurane in another group of patients. The inhaled anaesthetics were combined with opioid anaesthetics, fentanyl or remifentanil.

The results showed that the waking time in all patients maintained under anaesthesia by a desflurane was shorter than that of patients maintained under anaesthesia by sevoflurane. The extubation time with desflurane anaesthesia was 7.2 ±1.6 minutes, which was significantly shorter than the time of extubation with sevoflurane, 8.9 ±2.0 minutes, while the verbal response time for desflurane anaesthesia was significantly smaller, 7.6 ±1.8 minutes, versus the time of verbal response to sevoflurane anaesthesia, which was 9.3 ±4.1 minutes. This is thought to be due to the faster kinetic profile of desflurane, which leads to a faster elimination from the patient.

We used the Bispectrality Monitoring Index, BIS, to ensure an adequate depth of anaesthesia, i.e., to achieve values between 40 - 60, correlated with loss of consciousness and surgical anaesthesia and independent between the two inhalation agents. The BIS value was compared at the introduction to anaesthesia and during waking up.

After the cessation of the inhalation anaesthetic and after the last stitch was made, in the early postoperative period, higher BIS values were observed in the desflurane group with opioid remifentanil, unlike the sevoflurane fentanyl group, where BIS values increased later.

Conclusion

The resulting values obtained from the cognitive function tests in the recovery room showed that in patients maintained under anaesthesia by desflurane and remifentanil, cognitive functions returned faster than in patients maintained under anaesthesia by desflurane-fentanyl. The same results were obtained in the sevoflurane-remifentanil group compared to the sevoflurane-fentanyl group.

This study contributed to an awareness of the differences in impact between the two inhalation anaesthetics on cognition and remembering after waking up from general anaesthesia. However, like any research, it can be extended through further studies with their own findings, be they positive or negative, from which we distance ourselves. This study did not measure the level of inhalation anaesthetics in the operating room, as gases are eliminated through an evacuation system in the external environment, nor has the concentration of the inhalation anaesthetic been measured in the external environment. Desflurane is known to damage the ozone hole, but it cannot affect as much as global warming affects the country's weather disasters. We leave this field of research to the specialties that deal with it.

References

1. Yasuda N, Targ AG, Eger EI 2nd, Johnson BH, Weiskopf RB. Pharmacokinetics of desflurane, sevoflurane, isoflurane, and halothane in pigs. Anesth Analg. 1990 Oct;71(4):340-8. doi: 10.1213/00000539-199010000-00004. PMID: 2400116.

2. Ergönenç J, Ergönenç T, İdin K, Uzun U, Dirik A, Gedikli G, Bican G. The recovery time of sevoflurane and desflurane and the effects of anesthesia on mental and psychomotor functions and pain. Anesth Essays Res. 2014 Sep-Dec;8(3):367-71. doi: 10.4103/0259-1162.143151. PMID: 25886337; PMCID: PMC4258961.
3. Prabhakar H, Singh GP, Mahajan C, Kapoor I, Kalaivani M, Anand V. Intravenous versus inhalational techniques for rapid emergence from anaesthesia in patients undergoing brain tumour surgery. Cochrane Database Syst Rev. 2016 Sep 9;9(9):CD010467. doi: 10.1002/14651858.CD010467.pub2. PMID: 27611234; PMCID: PMC6457852.
4. Miller AL, Theodore D, Widrich J. Inhalational Anesthetic. [Updated 2023 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554540/
5. Khan J, Liu M. Desflurane. [Updated 2022 Jun 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537106/
6. Daiello LA, Racine AM, Yun Gou R, Marcantonio ER, Xie Z, Kunze LJ, Vlassakov KV, Inouye SK, Jones RN, Alsop D, Travison T, Arnold S, Cooper Z, Dickerson B, Fong T, Metzger E, Pascual-Leone A, Schmitt EM, Shafi M, Cavallari M, Dai W, Dillon ST, McElhaney J, Guttmann C, Hshieh T, Kuchel G, Libermann T, Ngo L, Press D, Saczynski J, Vasunilashorn S, O'Connor M, Kimchi E, Strauss J, Wong B, Belkin M, Ayres D, Callery M, Pomposelli F, Wright J, Schermerhorn M, Abrantes T, Albuquerque A, Bertrand S, Brown A, Callahan A, D'Aquila M, Dowal S, Fox M, Gallagher J, Anna Gersten R, Hodara A, Helfand B, Inloes J, Kettell J, Kuczmarska A, Nee J, Nemeth E, Ochsner L, Palihnich K, Parisi K, Puelle M, Rastegar S, Vella M, Xu G, Bryan M, Guess J, Enghorn D, Gross A, Gou Y, Habtemariam D, Isaza I, Kosar C, Rockett C, Tommet D, Gruen T, Ross M, Tasker K, Gee J, Kolanowski A, Pisani M, de Rooij S, Rogers S, Studenski S, Stern Y, Whittemore A, Gottlieb G, Orav J, Sperling R; SAGES Study Group*. Postoperative Delirium and Postoperative Cognitive Dysfunction: Overlap and Divergence. Anesthesiology. 2019 Sep;131(3):477-491. doi: 10.1097/ALN.0000000000002729. PMID: 31166241; PMCID: PMC6692220.

7. Ntalouka MP, Arnaoutoglou E, Tzimas P. Postoperative cognitive disorders: an update. Hippokratia. 2018 Oct-Dec;22(4):147-154. PMID: 31695301; PMCID: PMC6825421.
8. Pappa M, Theodosiadis N, Tsounis A, Sarafis P. Pathogenesis and treatment of post-operative cognitive dysfunction. Electron Physician. 2017 Feb 25;9(2):3768-3775. doi: 10.19082/3768. PMID: 28465805; PMCID: PMC5410904.
9. Somnuke P, Srishewachart P, Jiraphorncharas C, Khempetch A, Weeranithan J, Suraarunsumrit P, Srinonprasert V, Siriussawakul A. Early postoperative neurocognitive complications in elderly patients: comparing those with and without preexisting mild cognitive impairment- a prospective study. BMC Geriatr. 2024 Jan 22;24(1):84. doi: 10.1186/s12877-024-04663-5. PMID: 38253999; PMCID: PMC10804619.
10. Tsai TL, Sands LP, Leung JM. An Update on Postoperative Cognitive Dysfunction. Adv Anesth. 2010;28(1):269-284. doi: 10.1016/j.aan.2010.09.003. PMID: 21151735; PMCID: PMC2998043.