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ABDULKADİR İSKENDER

MELİH ENGİN ERKAN

MESUT ERBAŞ

DAMLA GÜÇLÜ GÜVEN

GÜLBİN SEZEN

See next page for additional authors

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Evaluation of the effects of desflurane and sevoflurane anesthesia on alveolar epithelial permeability by Tc-99m DTPA inhalation scintigraphy

Abdülkadir İSKENDER[1], Melih Engin ERKAN[2], Mesut ERBAŞ[1], Damla GÜÇLÜ GÜVEN[3], Gülbin SEZEN[1], Muhammet AŞIK[2], Yavuz DEMİRARAN[1], Mustafa YILDIRIM[4,*]

[1]Department of Anesthesiology, Faculty of Medicine, Düzce University, Düzce, Turkey
[2]Department of Nuclear Medicine, Faculty of Medicine, Düzce University, Düzce, Turkey
[3]Department of Otorhinolaryngology, Faculty of Medicine, Düzce University, Düzce, Turkey
[4]Department of Nuclear Medicine, Faculty of Medicine, Fatih University, Ankara, Turkey

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Aim: Recently studies showed that volatile anesthetics affect the ciliary beat frequency in vitro. We know that impairment of ciliary beat frequency is related to a risk of pulmonary complications with general anesthesia. Other studies have also shown that exposure to a volatile anesthetic can increase the permeability of the alveolar–capillary barrier. The present study aimed to determine the effects of desflurane and sevoflurane anesthesia on the technetium-labeled diethylene triamine penta-acetic acid (Tc-99m DTPA) clearance rate of the alveolar epithelium.

Materials and methods: A total of 40 patients who underwent elective tympanoplasty with general anesthesia were included in this study. Patients having any systemic disease or infection, or with any property that affected lung functions, were excluded from the study. Patients were randomized into 2 groups (20 patients in each) as receiving sevoflurane and desflurane. A Tc-99m DTPA aerosol inhalation lung imaging method was used to assess lung functions.

Results: Demographic properties were similar in both groups. There were no significant differences between basal and postoperative lung clearance of inhaled Tc-99m DTPA in either group.

Conclusion: We propose that neither sevoflurane nor desflurane induces pulmonary alveolar capillary injury in the acute period of general anesthesia based on Tc-99m DTPA scan results.

Key words: Sevoflurane, desflurane, alveolar epithelial permeability, Tc-99m DTPA, scintigraphy

1. Introduction

Volatile anesthetics currently use halogenated compounds for the maintenance of general anesthesia in patients (1). The pharmacodynamics of desflurane are similar to those of isoflurane. That volatile anesthetics affect the respiratory system has been well documented in previous studies (2–4); for example, they reduce the ciliary beat frequency (CBF) in vitro (5,6) and increase the permeability of the alveolar–capillary barrier (7,8).

Technetium-labeled diethylene triamine penta-acetic acid (Tc-99m DTPA) aerosol clearance from the lungs is a sensitive, noninvasive test of bronchoalveolar epithelial permeability (9). It has been generally assumed that Tc-99m DTPA clearance follows a simple first-order process with solute clearance through the respiratory epithelium (10).

The present study aimed to determine the effects of desflurane and sevoflurane anesthesia on the Tc-99m DTPA clearance rate of the alveolar epithelium in patients undergoing tympanoplasty surgery.

2. Materials and methods

2.1. Patients

The study was approved by the local ethics committee, and written informed consent was obtained from all subjects. This prospective study included 40 patients with an American Society of Anesthesiology physical status of I–II, aged 18–55 years, who were scheduled for elective tympanoplasty under general anesthesia. This was a randomized, double-blind, sectional study. There were 2 groups: patients receiving desflurane and patients receiving sevoflurane. None of the patients had a history of smoking or substance abuse,

* Correspondence: drmustafayildirim@yahoo.com

or ongoing viral and bacterial lung infections. Their chest X-rays were normal. Exclusion criteria were the presence of cardiopulmonary, renal, hepatic, and any other systemic diseases, and employment in any occupation that may affect the pulmonary system. Pregnant women were also excluded. The patients were randomly split into 2 groups. A computer-generated randomized list was used to assign patients to 1 of 2 groups. Neither patients nor the nuclear medicine physician were informed as to which volatile anesthetic was used. On arrival to the anesthetics room, a vein was cannulated, arterial blood pressure was measured with an automated oscillometer, and monitoring of arterial oxygen saturation and electrocardiogram commenced. Anesthesia was induced with 1–2 µg/kg fentanyl, 0.6 mg/kg rocuronium, and 1–3 mg/kg propofol and maintained with 66% nitrous oxide in oxygen; patients in the first group were given 2% sevoflurane, while the second group of patients received 6% desflurane.

2.2. Tc-99m DTPA aerosol inhalation lung imaging

Tc-99m DTPA radioaerosol inhalation lung scans were performed on all patients, 1 day before the operation and 24 h after the end of anesthesia. Tc-99m DTPA (MON. DTPA.KIT, MONROL, Turkey) solution of 1480 MBq (40 mCi) was placed into the reservoir of a nebulizer system (VENTI-SCAN BIODEX III, USA). The mass median aerodynamic diameter of the Tc-99m DTPA radioaerosol was smaller than 1 µm, with an oxygen air flow rate of 7 L/min. All of the subjects were studied in the supine position and inhaled for 2 min from the aerosol delivery unit until the total radioactivity was over 200,000 counts by normal tidal breathing. Immediately after the inhalation, scintigraphic data were recorded dynamically (1 frame/min) in a posterior projection on a 64 × 64 matrix for 30 min using a single-head gamma camera (Siemens E.CAM), which included a low-energy, high-resolution collimator. Regions of interest (ROIs) were drawn around the periphery of the right lung and on the major airways on the first-minute image. To obtain a pure alveolar ROI and to exclude the entire bronchial activity, the outer third of each lung was used as a peripheral lung region. The inner two-thirds of the lungs were defined as the central lung region. The brightness of the image was increased to visualize body background and the lung periphery to obtain the correct peripheral ROI. Time-activity curves were generated from the right lung of all subjects and percent clearance of radioaerosol in 30 min was obtained. Clearance half-time, T1/2, was calculated by placing a monoexponential fit on the curves (Figure 1). Penetration index (PI) was also calculated by dividing the peripheral total counts by the sum of the peripheral and central total counts on the first-minute image in order to quantify the distribution of the inhaled radioaerosol.

2.3. Statistical analysis

The α-value was set to 0.05 and power was accepted as 0.90. We used the clearance half-time of the Tc-99m DTPA of alveolar epithelial permeability for the primary end-point when calculating the sample size for our study. Standardized effect size was calculated as 0.90 by using the parameters of a previous report (11). Finally, the required sample size was calculated as 15 patients in each group. Statistical analyses were performed using SPSS 12 for Windows (SPSS Inc., Chicago, IL, USA) and a P-value of less than 0.05 was considered as statistically significant. Frequencies (%) of sex in each group were defined with a chi-square test. Normal distributions of continuous variables were analyzed with the Shapiro–Wilk test. The Mann–Whitney U test was used for comparing median ages among groups. Pre- and postoperative differences in clearance half-time (T1/2 min) and PI were analyzed using the Wilcoxon sign test in each group. Durations of anesthesia and operations within groups were analyzed with an independent samples t-test. Repeated-measures analysis of variance was used to evaluate mean arterial blood pressures changes in each group.

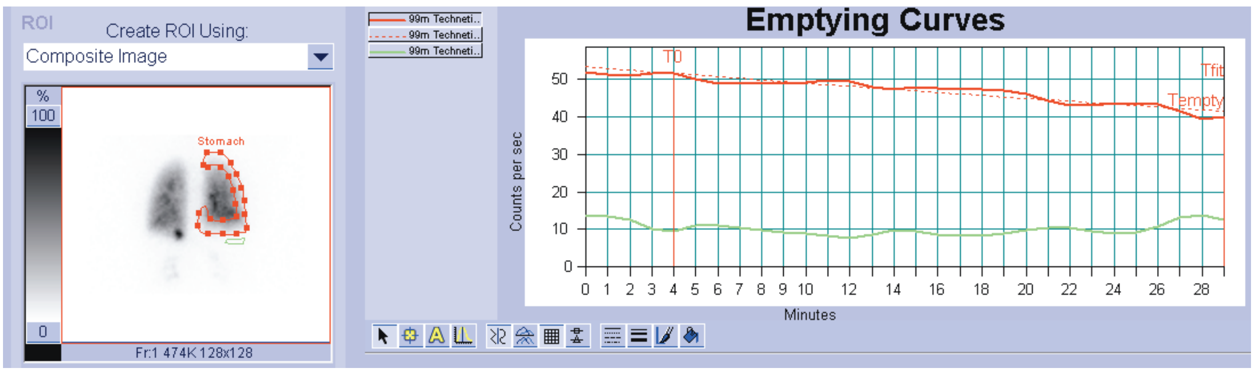

Figure 1. A) To obtain a pure alveolar ROI and to exclude the entire bronchial activity, the outer third of the right lung was used. B) Time-activity curves were generated and percentage clearance of radioaerosol in 30 min was obtained. Clearance half-time T1/2 (min) was calculated by placing a monoexponential fit (intermittent line) on the curves.

3. Results

There were 20 patients [5 females, 15 males, mean age of 30 (range: 20–62) years] in the sevoflurane group and 20 patients [9 females, 11 males, mean age of 32 (range: 19–42) years] in the desflurane group. The age range was similar in both groups. In sevoflurane patients, the median clearance half time (T1/2 min) of Tc-99m DTPA was 62 (range: 12.5–82) in the preoperative period and 60 (range: 28–156) in the postoperative period. The PI was 0.42 (range: 0.35–0.52) and 0.45 (range: 0.33–0.52), respectively. There were no significant differences between pre- and postoperative T1/2 (min) and PI in the sevoflurane group ($P > 0.05$). In the desflurane group, the median T1/2 (min) of Tc-99m DTPA was 70 (range: 30–123) in the preoperative period and 54 (range: 11–123) in the postoperative period. The PI was 0.48 (range: 0.39–0.55) and 0.48 (range: 0.41–0.60), respectively. There were also no significant differences between pre- and postoperative T1/2 (min) and PI in the desflurane group ($P > 0.05$) (Table). Although the mean arterial blood pressures of patients decreased during the operations and improved in the postoperative period ($P < 0.001$), there was no interaction between the groups (Figure 2).

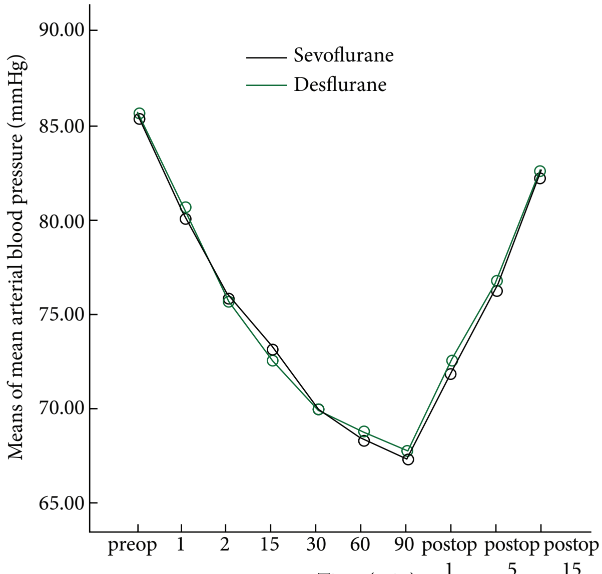

Figure 2. Mean arterial blood pressures of patients decreased during the operations and improved in postoperative period ($P < 0.001$). There was no interaction between groups.

4. Discussion

In the current study, we observed no significant differences between pre- and postoperative T1/2 (min) and PI in the sevoflurane group. There were also no significant differences between pre- and postoperative T1/2 (min) and PI index in the desflurane group. Various studies on the effects of volatile anesthetics on the lung have been published. The results of our study are consistent with the results of previous studies. Matsuura et al. (5) demonstrated that no CBF stimulatory effect of sevoflurane, halothane, or isoflurane was observed in purely isolated rat tracheal epithelial cells in vitro. In another study, Kesimci et al. (6) investigated the effects of sevoflurane and desflurane on nasal mucociliary clearance, as assessed by saccharin transit time (STT) following intravenous induction and tracheal intubation. They found that the STT values were delayed but were not significantly different from the preoperative STT values (6). Hu et al. (12) showed that isoflurane increased lung transendothelial albumin permeability in the isolated lung. It is well known that mucociliary clearance is affected by various factors, for example drugs (large doses of inhaled anesthetics), high oxygen concentrations, and smoking (13). A number of anesthesia-related factors, such as a drugs (cortisone, atropine) (14), large oxygen concentrations (11), and dry anesthetic gases (15) decrease mucociliary clearance (7). A study by Ledowski et al. (8) suggested that anesthesia with sevoflurane may lead to significantly impaired bronchociliary clearance. Raphael et al. (16) found that the volatile anesthetics halothane, isoflurane, and enflurane depressed ciliary function in vitro. This study's results were not compatible with our results. In an interesting study where the expression of human leukocyte antigen-DR (HLA-DR) was considered a meaningful indicator of immune response, the genetic effects of volatile anesthetics were investigated (17). Tuna et al. (17) did not find any difference in the levels of HLA-DR values in the early period. These results suggest that there is no harmful effect of volatile anesthetics on pulmonary epithelial tissue in the early period.

In a review of the literature, it was reported that inhalation of various substances (toluene, cigarette smoke, smoke by fire victims, etc.) (18) and systemic diseases such as Behçet's disease (19) have caused increased lung clearance of Tc-99m DTPA. Some researchers have found

Table. Pre- and postoperative alveolar epithelial clearance of Tc-99m DTPA and pulmonary index. AEP: Alveolar epithelial permeability.

		Preoperative (n = 20)	Postoperative (n = 20)	P-values
AEP (T1/2) (min)	Desflurane	70 (30–123)	54 (11–123)	0.594
	Sevoflurane	62 (12.5–82)	60 (28–156)	0.106
Pulmonary index	Desflurane	0.48 (0.39–0.55)	0.48 (0.41–0.60)	0.445
	Sevoflurane	0.42 (0.35–0.52)	0.45 (0.33–0.52)	0.401

significantly rapid pulmonary clearance of Tc-99m DTPA in rabbits under general anesthesia with high oxygen concentrations (79%) (20,21). Therefore, the more rapid pulmonary clearance of Tc-99m DTPA in patients who received desflurane and sevoflurane could be due to the effects of inhaler anesthetics rather than oxygen. Isoflurane has been found to destabilize the surfactant system (20). Hung et al. (22) studied the effects of volatile anesthetics on alveolar epithelial permeability, based on the findings of a DTPA lung scan, and reported no significant lung ventilation change or abnormality, while the Tc-99m DTPA clearance T1/2 (min) before and after anesthesia had no significant changes. These researchers found no significant change in alveolar epithelial permeability before surgery and after surgery (22). Wollmer et al. (21) showed that halothane, in combination with high oxygen concentrations, increases the permeability of the alveolar–capillary barrier. However, in our study, during the maintenance of anesthesia, all patients were mechanically ventilated with low oxygen (40% oxygen). The results of this study are consistent with our results.

Following onwards from these studies, this is a preliminary report regarding the effects of novel inhaler anesthetics, desflurane and sevoflurane, on the surfactant system. Results showed that there were no significant differences between basal and postoperative lung clearance of inhaled Tc-99m DTPA in both groups.

In conclusion, our study demonstrated that volatile anesthetics have no negative effect on lung permeability.

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