The Effect of Low-Flow Desflurane Anesthesia on Mucociliary Clearance

Mehmet Gamlı1, Hilal Zengin1, Dilşen Örnek1, Eyüp Horasanlı1, Oya Kılçı1, Canan Ün1, Semih Başkan1, Bayazit Dikmen1

1Ankara Numune Training and Research Hospital, Department of Anesthesiology and Reanimation, Ankara, Turkey.

Abstract

Background: The study aims to compare the effect of low and high-flow desflurane anesthesia between genders and on mucociliary clearance changes. Methods: A total of 50 patients aged 18 – 61 years of risk group ASA I-II, with previously planned middle ear surgery under general anesthesia were included in the study. Approval was granted by the hospital ethics committee and written informed consent was obtained from all the patients. The patients were randomly assigned into two different groups: (Group I, n=25) for low flow anesthesia and (Group II, n=25) for standard flow anesthesia. The nasal mucociliary clearance was measured with Saccharin nasal transit time (SNTT). The first measurement was for control, before the anesthesia, and the second one was after waking from anesthesia and gaining orientation. Results: There was no statistical significance in terms of demographic features and operation duration between the patient groups. The average postoperative saccharin nasal transit time (SNTT) was significantly longer in both groups compared to the preoperative transit time (p<0.05). The average SNTT of Group I was statistically longer than that of Group II (p=0.002). There were no other differences between the groups. Conclusion: Administration of desflurane anesthesia in two different flows prolongs saccharin nasal transit time. However, this prolongation was found to be within the normal limits, whereas compared between genders it was significantly longer in the female group.

Key words: Anesthesia, Desflurane, Mucociliary Clearance.

Introduction

Respiratory pathways are lined with pseudostratified ciliated epithelium, which functions in mucociliary clearance and trapping particulate material. Mucociliary clearance serves as the most important defence mechanism of the respiratory system. Changes in the mucociliary transport lead to mucus retention, colonization of bacteria and infections.[1] Many techniques have been used to measure ciliary activity and beat frequency,[2] In vivo techniques, saccharin, dyes (vegetable charcoal powder, methylene blue), radiopaque teflon discs, aluminium discs and radioactive substances are used. The Saccharin test was first described by Andersen in 1974 and is a valuable and reliable measurement method of nasal mucociliary clearance.[3] Through in vivo human research, experimental animal models and tissue cultures it has been shown that volatile anesthetics inhibit mucociliary clearance.[4] As a result postoperative complications such as atelectasia, retention of secretions, sinusitis and respiratory infections occur.[5] Low-flow anesthesia is defined as an inhalation anesthetic technique via a rebreathing system in which the rebreathing factor amounts to at least 50%. In this way, the consumption of anesthetic gases and volatile agents is significantly reduced, providing cost savings and a reduction in operating room and atmospheric pollution. With the re-use of expiratory gases through this technique, humidity levels of gases increase and loss of heat is minimalized. Thus the physiology of the tracheobronchial environment is better preserved. Although there have been studies of the effect of high-flow desflurane anesthesia on mucociliary clearance,[1,5,6] to the best of our knowledge, there have been no studies of the effect of low-flow desflurane anesthesia. The aim of this study was to evaluate the effect of low-flow desflurane anesthesia on nasal mucociliary clearance.

Materials and Methods

Approval for the study was granted by the Local Ethics Committee and informed consent was obtained from the patients. The study comprised 50 patients aged 18-61 years, of ASA I-II risk group, with planned elective middle ear surgery under general anesthesia. Smokers, patients with respiratory symptoms or diseases, deviated septum, nasal polyps, nasal surgery, or a history of allergy to any medication used in the study, ischemic heart disease, heart failure, liver or kidney failure, pregnant women...
and patients with infection were not included in the study.

The mucociliary clearance of the 50 patients included in the study was measured one day preoperatively by saccharin nasal transit time (SNTT). The preoperative saccharin test was performed at the same hour of the day and under the same climate conditions (23°C, room temperature and 60% humidity). Saccharin administration was performed by the same ENT specialist who was blinded to the study. The patients were told to blow their nose as strongly as possible. A saccharin granule of 1mm diameter was placed on the lower chonca with forceps. Patients were seated and told not to sneeze, eat or drink anything or lean their head backwards. Once every 30 seconds they were asked whether they had taste perception and the time until they felt any taste was calculated as the time of mucociliary clearance. The moment of perception of taste showed the transport of the saccharin to the oropharynx. Patients sneezing, sniffing or coughing during the test, or not feeling anything after 30 minutes were excluded from the study. Patients were taken to the operating room without premedication and through IV lines with 18 G or 20 G cannula were administered Ringer Lactate solution at 5ml/kg/hour. After standard anesthesia monitoring (ECG, heart rate (HR), non-invasive blood pressure, peripheral oxygen saturation and end tidal carbon dioxide (EtCO2) measurement) anesthesia induction was carried out. After 3 minutes of preoxygenation with 6 L/min 100% O2, induction began with 1-2 μg/kg fentanyl, 0.03-0.05 mg/kg midazolam, 5-7 mg/kg thiopenthal sodium. Endotracheal intubation was performed after administration of 0.1 mg/kg IV vecuronium bromide. Patients were randomly assigned to the standard flow group (Group II, n=25) or the low flow group (Group I, n=25). To patients undergoing high flow general anesthesia (Group II), 50% N2O+O2 4 L/min and 4-6% of desflurane was administered. To patients undergoing low flow general anesthesia (Group I), for the first 10 minutes 65% N2O+35% O2 4 L/min, 4-6% of desflurane were administered after which 50% N2O+O2 1 L/min was given and desflurane was increased by 0.5-1%. Anesthesia maintenance was administered at 0.5 L/min more than the calculated minute ventilation (MV). Muscle relaxation was antagonized with 0.05 mg/kg of neostigmine and 0.01 mg/kg of atropine, and then the patient was extubated. After the end of surgery, the patients were transferred to the post-op unit. After full anesthesia recovery, the postoperative saccharin test was performed and SNTT was evaluated. A Julian (Drager, Lubeck, Germany) machine was used for anesthesia and Soda-lime for CO2. At the end of each day the CO2 absorbant (soda-lime) was changed. The power analysis of the study was based on the study of Kesimci et al.10 The SNTT of this study was found to be 7.1±3.1 minutes under desflurane anesthesia. Under low flow anesthesia with desflurane, 3 minutes variance was considered significant and sample size was noted as 17 patients ($\alpha=0.05$, $\beta=0.80$). Therefore, 25 patients were included in each group.

Data analysis was performed with SPSS 12.0 program. The distribution of numerical values was examined with the Shapiro Wilk test, descriptive values were given as mean ± standard deviation or median (minimum-maximum), and categorical variables were given as number of patients and percentage. The difference between the two groups was determined with Student’s t-test for normal distribution, and with the Mann-Whitney U test for abnormal distribution. Repeated measures analysis of variance showed that time was significant in HR, SAP, DAP, MAP, and SpO2, therefore, groups including these data were compared with the Posthoc Bonferroni test. The Paired P test was used to compare the SNTT data within groups with the first measurements. For categorical comparison Chi-Square or Fisher’s exact test was used. A value of $p<0.05$ was considered statistically significant.

**Results**

There was no statistical significance in terms of demographic features and operation duration between the patients groups [Table 1]. The average of postoperative saccharin nasal transit time (SNTT) was significantly longer in both groups compared to the preoperative transit time (p<0.05). The average SNTT of Group I was statistically longer than that of Group II (p=0.002) [Table 2]. The average SNTT test between males and females in Group I was similar in terms of gender [Table 3]. The postoperative measurement compared to the first measurement for both genders was found to be significantly longer (p=0.001, p=0.015). The saccharin test average of Group II was found to be similar for both genders. In females, the postoperative measurement was found to be longer when compared to the first measurement (p=0.034). There were no differences between the groups in terms of average HR, mean arterial pressure (MAP), or changes in SpO2 measurements [Figure 1-3].

**Discussion**

Nasal mucociliary clearance is the first defence mechanism of the respiratory ciliary epithelium against inhaled particles. In this system, which is composed of ciliary and mucus-producing cells, the particles attached to the mucus are carried to the nasopharynx from the anterior part of the nose with wave-like motions. Primary or secondary nasal mucociliary dysfunctions may lead to long-term respiratory diseases. The measurement of nasal mucociliary clearance is a reliable index of upper and lower respiratory pathways clearance functions. SNTT is a widely-used method in the evaluation of mucociliary functions as it is cheap and easy to apply. A period of 30 minutes is considered to be normal. The major disadvantage of the method is the
impairment in the postoperative period, the rate of nasal mucociliary rates vary at different times of the day. Furthermore, smokers were excluded from the study due to impaired nasal mucociliary clearance. Special attention was paid to perform the tests where radioactive substances were used because it has been shown that smoking affects nasal functions returned to normal after septoplasty or preoperative SNTT values were found to be 3.0-12.6 minutes. In the current study, despite studies showing that nasal mucociliary transport.

Although studies of the volatile anesthetics, in vivo and in vitro studies of the volatile anesthetics, pentothal have shown them to be responsible for the decrease in mucociliary clearance.

In a study by Kesici et al., they found that volatile anesthetics had a direct effect on the tracheal epithelium cell cultures of the rats and inhibited the ciliary beat frequency. These findings show that volatile anesthetics have negative effects on mucociliary functions. In contrast, in a study with radioactive substances, Konrad et al showed no difference of the pre and postoperative bronchial mucus transport under general anesthesia with propofol, fentanyl, vecuronium, 1.5 MAC of isoflurane and O2:N2O.

In vivo and in vitro studies of the volatile anesthetics, halothane, enflurane, isoflurane and desflurane, and of the IV anesthetic, pentothal have shown them to be responsible for the decrease in mucociliary transport. In a study by Raphael et al., it was shown that 3 MAC of halothane, enflurane and isoflurane reversely decreased the ciliary beat frequency. These findings show that volatile anesthetics have negative effects on mucociliary functions. In contrast, in a study with radioactive substances, Konrad et al showed no difference of the pre and postoperative bronchial mucus transport under general anesthesia with propofol, fentanyl, vecuronium, 1.5 MAC of isoflurane and O2:N2O. Matsuura et al. studied the in vitro effects of volatile anesthetics on tracheal epithelial cell cultures of rats. They found that volatile anesthetics had a direct effect on the tracheal epithelium cell cultures of the rats and inhibited the ciliary beat frequency. Sevoflurane had the lowest inhibition effect on ciliary beat frequency. Kesici et al. evaluated the effects of three different volatile anesthetics on nasal mucociliary clearance with the saccharin test. After induction with propofol and remifentanil the patients were intubated with cisatracurium and put on maintenance with remifentanil infusion (0.5 - 1 µg/kg/dk) and 1 MAC of isoflurane, desflurane and sevoflurane. It was reported that all three volatile anesthetics extended atelectasis and lower respiratory tract infections increases due to the retention of secretions.

Despite the subjectivity, the saccharin test was used in the current study because it was easy to apply, non-invasive, a widely-used test and compatible with the results of the tests where radioactive substances have been used. Patients with pathologies such as nasal septum deviation, allergic rhinitis, nasal polyposis and sinusitis were excluded from the study due to impaired nasal mucociliary clearance. Special attention was paid to perform the measurements at the same time of the day because nasal mucociliary rates vary at different times of the day. Despite studies showing that nasal mucociliary functions returned to normal after septoplasty or endoscopic sinus surgery, no patient with any kind of previous nasal surgery was included in the study. Furthermore, smokers were excluded from the study because it has been shown that smoking affects nasal mucociliary clearance and nasal ciliary beat frequency adversely.

In a study by Kesici et al., preoperative SNTT was found to be 3.3-12.6 minutes. In the current study, preoperative SNTT values were found to be 3.0-15.56 minutes and compatible with the previous studies mentioned. It has been shown that high oxygen concentrations, dry anesthetic gases, trauma due to aspiration procedures and the cuff of the endotracheal tube may lower mucociliary clearance. In addition, volatile anesthetics inhibit ciliary motility and impair bronchociliary clearance in a time and dose-dependent manner. As a result of mucociliary impairment in the postoperative period, the rate of saccharin test.
SNTT, although not to a statistically significant level.\[2\]
Due to the low blood/gas partition coefficient (0.42) of desflurane, the induction and recovery periods are short and in low flow anesthesia the anesthetic agent is quickly filled and emptied from the system. Clinical experience shows that induction and recovery periods are short and concentrations faster and easier adjusted.\[23\] However, desflurane has the greatest irritant effect on the airways compared to other volatile anesthetics.\[22\] As a result of the pungent smell of desflurane, signs such as an increase in secretion, coughing, breath-holding, and laryngospasm occur during induction, therefore its use is limited.\[24\]
Serwin and Lindberg evaluated the airway irritant effects of various volatile anesthetics including desflurane through the changes on mucociliary activity. The peak response of mucociliary activity was not apparent, although the area left under the curve was significantly high. It was emphasized that the peak response was late and biphasic.

In the current study, similar to the results of Kesimci et al, SNTT was found to be longer in patients under desflurane anesthesia. Kesimci et al. reported postoperative SNTT to be 7.1±3 mins in patients under desflurane, while in the current study, these values were 9.3±3.62 mins. The current study values were found to be different compared to the values of Kesimci et al. and significantly longer than the preoperative values.\[1\] These differences may be related to the induction agents used, the duration of the operation and anesthesia or the differences in the concentrations of desflurane. There has been gradually increasing interest in the use of low-flow anesthesia, which is defined as an inhalation anesthetic technique via a rebreathing system in which the rebreathing factor at least amounts to 50%.
The humidity and heat of anesthetic gases increases greatly in low-flow anesthesia techniques. Low-flow anesthesia, not only improves the environment, but also significantly reduces the consumption of anesthetic gases and volatile agents, thereby providing cost savings and a reduction in operating room and atmospheric pollution. Proper moistening and heating of anesthetic gases has great importance on the function of ciliary epithelium and mucociliary clearance.\[25\] The humidity levels are significantly higher when low flow gasses are used via rebreathable cycle systems compared to high flow anesthesia. While the humidity of the gases inhaled is usually affected by the flow, the heat is affected by the heat loss due to conductivity and the physical properties of the hose system.\[25-28\]

One group in the current study included patients who received low flow anesthesia because of better atmospheric conditions. To the best of our knowledge, there is no study in literature investigating the effects of low flow desflurane anesthesia on nasal mucociliary clearance rate using the saccharin test.

In the current study, low and high flow desflurane anesthesia was found to significantly elongate the SN TT levels, thus negatively affecting the nasal mucociliary clearance. However, low flow desflurane anesthesia had a statistically more significant effect extending SNTT compared to high flow anesthesia. Nasal mucociliary clearance includes two major components. One is the physicochemical quality and quantity of the mucus. Increase in air humidity and temperature can affect the physicochemical properties of the mucus. The second is the beat frequency of the cilia and coordination. It has been reported that in asthma patients, the mucociliary impairment is due to quality and quantity changes of the airway secretions rather than the changes of the ciliary beat.\[25,30\]

The mucociliary functions of the upper airways are regulated by complex and partially neurological mechanisms. It has been reported that tobacco smoke and ammonium vapour increase mucociliary activity and this increase can be partially prevented with atropine and substance P.\[31,32\] Knill et al. showed that halothane and enflurane reduced the peripheral chemoreceptor response to hypoxia and doxapram.\[33,34\] Coleridge stated that anesthetic agents change the high pulmonary tension and the activity of high-threshold receptors.\[35\] It has been stated that vagal or sympathetic nerve impulses increase the ciliary beat frequency.\[36,37\] Considering that volatile anesthetics may affect the autonomic nervous system, they may also affect the frequency of ciliary beats.

It was expected that low-flow anesthesia, and proper humidification and heating of anesthetic gases would have a positive effect on mucociliary clearance. The physico-chemical features of nasal mucus were not evaluated; therefore we were unable to state which one prolonged the SNTT. However, high agent concentrations to recreate the necessary alveolar concentration may lead to elongation of SNTT in low-flow desflurane anesthesia. Wilkes et al. stated that desflurane was the most irritant agent of the upper respiratory tract.\[38\] Cervin and Lindberg found that NK1 receptors are influenced in airway irritants and atropine does not decrease the early ciliary beat frequency due to desflurane. Use of NK1 antagonists may prevent the elongation of SNTT.

Ho et al. compared nasal mucociliary clearance between genders and found no statistically significant difference.\[39\] Another study comparing differences between the genders had similar results. In the current study, both low-flow and high-flow desflurane anesthesia elongated SNTT in both genders.

**Conclusion**

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The saccharin nasal transit time was extended in both flow types while being more prolonged with the use of low-flow desflurane anesthesia. Although clinically non-relevant elongation was detected in the current study, further extended studies are required to reveal the cause of extension.

References

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