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The effects of pressure-controlled and volume-controlled ventilation modes on the nasal mucociliary activity during general anaesthesia.

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Abstract

The aim of this prospective randomized, double-blind study was to investigate the effects of pressure controlled and volume controlled ventilation on mucociliary clearance under general anaesthesia maintained with total intravenous anaesthesia. After approval by the Ethics Committee, 60 patients scheduled for tympanoplasty or tympanomasteidectomy under general anaesthesia were enrolled in the study. In Group I (n=30), the lungs of the patients were ventilated using volume-controlled mode with 8 ml/kg tidal volume. In Group II (n=30) pressure controlled ventilation mode was used with 10 cm H_2O pressure support. Mucociliary clearance was assessed by *in vivo* saccharine transit time in preoperative and postoperative periods. The groups showed no significant differences regarding age, height, body mass index, peak and plateau airway pressures. Saccharine transit time values did not differ significantly between the groups. In conclusion, volume-controlled and pressure-controlled ventilation modes have no significant impact on nasal saccharine transit time.

Keywords: Mucociliary clearance, Mechanical ventilation, General anaesthesia.

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Introduction

Mucociliary clearance is an important part of the respiratory defence mechanism, which protects the upper and lower respiratory tract and alveoli [1]. Impairment of the mucociliary clearance may cause pulmonary complications such as atelectasis, retention of secretions and lower respiratory tract infections in the postoperative period [2]. Abnormality of nasal mucociliary clearance indicates inflammatory and pathological events in the lower respiratory tract because of the similarity of its epithelium with trachea and bronchi [3]. There is known to be a close inter-relationship between nasal and tracheobronchial clearance and abnormalities of nasal clearance project to the injured lung [4,5].

During general anaesthesia, the mucociliary mechanism can be impaired by tracheal intubation, volatile anaesthetics, high tidal volume or pressure [6]. General anaesthesia promotes pulmonary atelectasis and anaesthetics impair mucociliary clearance [7,8]. Mechanical ventilation is usually mandatory under general anaesthesia for surgery and the effects of short-term intraoperative ventilation may be harmful. Inappropriate application of invasive mechanical ventilation can damage healthy lungs within 30 minutes by provocative or resumable alveolar inflammatory response systems [9,10].

Volume-Controlled Ventilation (VCV) is the traditional mode of ventilation used in patients undergoing general anaesthesia. Pressure-Controlled Ventilation (PCV) is an alternative mode of ventilation which is used in severe respiratory failure [11]. Pressure-Controlled Ventilation (PCV) has been shown to improve arterial oxygenation and decrease peak inspiratory airway pressure by decelerating inspiratory flow [12]. The aim of this study was to investigate the effects of pressure controlled and volume controlled ventilation on mucociliary clearance under general anaesthesia maintained with total intravenous anaesthesia. It was hypothesized that pressure-controlled ventilation during general anaesthesia is more reliable than volume-controlled ventilation which has the effect of decelerating inspiratory flow.

Methods

Approval for the study was granted by the Ethics Committee of the University of Kirikkale School Of Medicine (01/03; 06/01/2013). Informed consent was obtained from all patients. A total of 60 patients aged between 18 and 45 years, classified as American Society of Anaesthesiologists (ASA) Grade I-II risk group, scheduled for tympanoplasty or tympanomasteidectomy under general anaesthesia, were enrolled in the study. Smokers, pregnant women and patients

with a history of respiratory tract pathology e.g. chronic obstructive pulmonary disease or history of nasal surgery, atopy, septal deviation, nasal polyposis, and allergic reaction to any of the study drugs, cardiac, hepatic and renal failure were excluded from the study. Patients were also excluded if taking any medication known to influence the bronchial mucus such as β-adrenoceptor antagonists, cortisone, atropine, theophylline, and antihystaminics. Saccharin Transit Time (STT) was measured to assess mucociliary activity on the day before the operation. All saccharin tests were performed by the same otorhinolaryngologist blinded to the study under the same climatic conditions (room temperature 23˚C, relative humidity 60%) and the patients were rested for 30 minutes before the saccharin test [13]. The patient was placed in a head-upright sitting position while breathing normally, and asked not to sneeze, sniff, eat or drink. A saccharin tablet (12.5 mg Dulcaryl) was divided into 4 pieces and one of these pieces was placed approximately 0.5 cm behind the anterior end of the inferior turbinate to the contralateral of the operation side. Every 30 seconds, the patient was asked for swallow to be able to record when they tasted the saccharin. The time of the first perception of the sweet taste was recorded as the saccharin transit time.

Premedication was not administered to any of the patients. On admission to the operating room, a 22 G peripheral intravenous (i.v.) cannula was inserted in the dorsum of the patient's hand and 4-6 $ml.kg^{-1}$ min 0.9% NaCl infusion was started. Electrocardiogram (ECG), non-invasive Mean Arterial Blood Pressure (MAP), Peripheral Oxygen Saturation ($Sp0_2$) heart rate, end-tidal concentration of oxygen and carbon dioxide measures were monitored and recorded at baseline and at the 5^{th} minute then every 10 minutes thereafter. The temperature of the operating room was kept at 21-22˚C. Induction of anaesthesia was achieved by intravenous administration of 1.5 $mg.kg^{-1}$ propofol, 1 mcg kg^{-1} remifentanyl and 0.6 $mg.kg^{-1}$ rocuronium bromide. Anaesthesia was maintained by an intravenous infusion of propofol 100 mcg/kg/min and remifentanyl 0.25 $mcg.kg^{-1}$ min. Neuromuscular blocking was maintained with intermittent boluses of rocuronium 0.1 $mg.kg^{-1}$ as needed. The dose of remifentanyl was titrated to maintain the Mean Arterial Blood Pressure (MAP) and Heart Rate (HR) at 20% decrease of the baseline measures. Volatile anaesthetic agents were not used for induction or for maintenance of anaesthesia. A size of 7.5 mm Inner Diameter (ID) Endotracheal Tube (ETT) for female and 8.0 Inner Diameter (ID) Endotracheal Tube (ETT) for male patients was used for intubation of the trachea. The cuff was inflated with air until no air leakage was heard while manually ventilating at 25 cm H_2O pressure of Adjustable Pressure-Limiting (APL) valve. In Group I (n=30), the lungs of the patients were ventilated using volume-controlled mode with 8 ml/kg tidal volume. The tidal volumes were adjusted to the predicted body weight. In Group II (n=30), pressure-controlled ventilation mode was used with 10 cm H_2O pressure support. The respiratory rate was adjusted to maintain normal end tidal carbon dioxide (ET CO_2) (32-36 mmHg). Fresh gas flow was 4 l min^{-1} with an oxygen fraction of 0.5 in oxygen-air mixture and a Positive End-Expiratory Pressure (PEEP) of 5 cm H_2O, with an inspiration: expiration ratio of 1:2 was used in both of the groups. Peak inspiratory pressure, plateau pressure, $ETCO_2$, consumption of fluid, Heart Rate (HR), and Mean Arterial Blood Pressure (MAP) were recorded before the induction of anaesthesia (baseline measurement), at the first 5^{th} minute of the operation and then every ten minutes during the operation after the baseline measurement. (GE Datex-Ohmeda S/5 Avance, Munich, Germany) At the end of the operation, neuromuscular blockade was reversed with neostigmine 0.04 $mg.kg^{-1}$ and atropine 0.02 $mg.kg^{-1}$.

The Saccharin Transit Time (STT) was repeated again at 6 hours postoperatively. No complication was encountered such as bradycardia, hypotension or arrhythmia. Hypotension and bradycardia were accepted as a 20% decrease of the baseline measurements. One anaesthesiologist performed the study, evaluated and recorded data and the Saccharin Transit Time (STT) was evaluated by the only otorhinolaryngologist who participated in the study. The otorhinolaryngologist and patients were blinded to the group allocation. The saccharin transit time was the primary outcome variable on which sample size estimation was based. Power analysis identified at least 48 patients (16 per group) as the total sample size required to detect a three minute difference between preoperative and postoperative Saccharin Transit Time (STT) measurements with a power of 80% at 5% significance level on the basis of the study of Kesimci et al. [8]. Statistical analysis of data was performed using Statistical Package for Social Sciences (SPSS) for Windows v.17. The results were expressed as mean and Standard Deviations (SD). A value of $p<0.05$ was considered statistically significant.

Results

No statistically significant differences were determined between the groups in respect of age, height, body mass index, peak and plateau airway pressures as shown in Table 1. The Saccharin Transit Time (STT) values were statistically similar between the two groups as shown in Table 2.

Table 1. *Demographic variables, operation and anaesthesia time of groups ($p<0.05$).*

	Group I (mean ± SD) (n=30)	Group II (mean ± SD) (n=30)	P value
Age (year)	35.09 ± 13.54	35.38 ± 10.98	0.157
Weight (kg)	72.59 ± 15.71	69.76 ± 10.89	0.05
Height (cm)	169.45 ± 7.91	168.10 ± 7.82	0.7
Body Mass Index (BMI) (kg/m^2)	25.22 ± 4.91	24.79 ± 4.46	0.45
Operation time (min)	115.90 ± 45.60	95.47 ± 25.68	0.05
Anaesthesia time (min)	100.00 ± 43.20	80.00 ± 25.14	0.06
Total fluid (ml)	1162.27 ± 350.27	1071.42 ± 307.23	0.32

Table 2. *Preoperative and postoperative saccharin transit time of groups (p<0.05).*

	Pre-operative STT	Post-operative STT	P value
Group I (mean ± SD) (n=30)	8.72 ± 3.32	8.62 ± 3.05	0.84
Group II (mean ± SD) (n=30)	7.96 ± 2.67	7.93 ± 3.00	0.96

STT: Saccharin Transit Time.

Discussion

Mucociliary clearance is an important part of the pulmonary defence mechanism that transports the mucus layer by ciliary beating at a frequency of 7-16 Hz at body temperature and is controlled by certain physiological, anatomic, and biochemical variables [14]. The impairment of cilia beat frequency deteriorates the defence mechanism of the mucociliary clearance and thus the bronchial mucus transport velocity which is associated with pulmonary complications in ventilated patients [15]. Several methods have been used to evaluate mucociliary clearance, by photo transducer recorded photo electrically, or by a video camera using light microscope (x 10) *in vivo* [3,6]. Keller et al. determined bronchial mucus transport velocity with a calculation of the transmission of methylene blue dye by fiberoptic bronchoscope [16]. Millar et al. used teflon particles with radiolabelled 99 mTc to determine nasal clearance and a radio aerosol technique for tracheobronchial clearance and a close correlation was shown between tracheobronchial clearance and nasal clearance [4]. In the current study, the saccharin test was used to evaluate mucociliary clearance. The measurements represent the changes in responses and pathophysiological mechanisms in the distal airway. The saccharin test is easy to perform, non-invasive, inexpensive and comfortable for the patient. The Saccharin Transit Time (STT) was evaluated first before anaesthesia and secondly after anaesthesia at 6 hours postoperatively to determine the effects of the two different mechanical ventilation modes of pressure- controlled and volume controlled.

Several studies have confirmed that volatile anaesthetics affect mucociliary function. Raphael et al. demonstrated a depression of cilia beat frequency *in vitro* with three volatile anaesthetics; halothane, enflurane, isoflurane at 3 Minimum Alveolar Concentration (MAC) [17]. Cervin et al. investigated the mechanism of the mucociliary system in response to halothane, isoflurane and desflurane in rabbit maxillary sinus and it was concluded that the inflammatory, NK1 mediated pathway, may reflect the airway-irritating effects of the volatile anaesthetics [3]. Kesimci et al. determined no significant difference between desflurane and isoflurane but the saccharin transit time was prolonged with both of the volatile anaesthetics [8]. Raphael et al. demonstrated that the nasal ciliary beat frequency was significantly decreased in patients anaesthetized with isoflurane compared to total intravenous anaesthesia maintained by propofol and alfentanyl [18]. In the current study, the undesired effects of volatile anaesthetics were eliminated as only total intravenous anaesthesia with propofol and remifentanyl was used in both groups. In addition, the air flow was standardized at 4 l min^{-1} in accordance with the study of Bilgi et al. that demonstrated that mucociliary clearance is better protected by low flow anaesthesia than high flow anaesthesia technique [19]. In both groups, the patients were ventilated within air flow at 4 l min^{-1}, therefore, the air flow could not influence the study results.

During general anaesthesia, mechanical ventilation is mostly mandatory for surgery. The effects of short-term mechanical ventilation on pulmonary integrity have yet to be defined [20]. Lung protective ventilation, which originated in the critical care unit, has low Tidal Volume (TV) and lung recruitment, and is a simple inexpensive intervention that reduces postoperative morbidity without adverse effects [21]. Lung protective ventilation may be obtained by the monitoring of peak and plateau pressure with a volume-controlled mode or through the use of pressure-controlled ventilation [22]. While volume-controlled mode does not provide control over peak airway pressures, pressure-controlled mode allows control over peak inspiratory pressures [23]. Volume controlled mode is the most commonly used (85%) technique by anaesthesiologists in the operating room [24]. Pressure-controlled mode is an alternative mode of ventilation which is widely used especially in severe respiratory failure [25]. Pressure-Controlled Ventilation (PCV) has been shown to improve arterial oxygenation and decrease peak airway pressure because of its decelerating effect on inspiratory flow [25]. Thus, Pressure-Controlled Ventilation (PCV) provides uniform distribution of inspired gas hence it is used for better arterial oxygenation in patients with respiratory failure [25,26]. Positive End Expiratory Pressure (PEEP) is applied during the end of expiration to maintain the alveolar pressure above atmospheric pressure [27]. Although the role of Positive End Expiratory Pressure (PEEP) in mechanical ventilation has been investigated in different types of surgery, the results have not shown sufficient evidence to assess the role of intraoperative Positive End Expiratory Pressure (PEEP) [28]. Applying Positive End Expiratory Pressure (PEEP) may affect cardiac function and vital organ perfusion [27]. In the current study, Positive End Expiratory Pressure (PEEP) was set at 5 cm H_2O to prevent adverse effects with hypotension maintained by total intravenous anaesthesia. Knowledge of the intraoperative mechanical ventilation setting is largely lacking. One observational study of 49 centres in France showed that 18% of patients received tidal volumes of more than 10 ml/kg predicted body weight during mechanical ventilation in the operating room and 81% received mechanical ventilation without Positive End Expiratory Pressure (PEEP) [24]. In the current study, no significant difference was determined between the two groups, and these results can be interpreted as being related to no difference between the tidal volume and peak pressure in healthy lungs.

There have been a limited number of investigations of the relationship of mucociliary clearance and mechanical ventilation strategies in the operating room. The present study is the first in which Volume-Controlled Ventilation (VCV) is compared with Pressure-Controlled Ventilation (PCV) to investigate the effects on mucociliary clearance, rather than oxygenation or ventilation parameters.

Conclusion

The present study demonstrated that volume-controlled and pressure controlled ventilation modes have no significant impact on nasal Saccharin Transit Time (STT). Further studies using different Positive End Expiratory Pressure (PEEP) values are required to investigate the effects of ventilation modes on mucociliary clearance under general anaesthesia to clarify the risks of postoperative pulmonary complications.

Competing Interest

No external funding and competing interests declared.

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