Absence of Bronchodilation during Desflurane Anesthesia

A Comparison to Sevoflurane and Thiopental

Mitchell J. Goff, B.S.,* Shahbaz R. Arain, M.D.,† David J. Ficke,‡ Toni D. Uhrich, M.S.,§ Thomas J. Ebert, M.D., Ph.D.||

Background: Bronchospasm is a potential complication in anyone undergoing general anesthesia. Because volatile anesthetics relax bronchial smooth muscle, the effects of two newer volatile anesthetics, desflurane and sevoflurane, on respiratory resistance were evaluated. The authors hypothesized that desflurane would have greater bronchodilating effects because of its ability to increase sympathetic nervous system activity.

Methods: Informed consent was obtained from patients undergoing elective surgery with general anesthesia. We recorded airway flow and pressure after thiopental induction and tracheal intubation (baseline) and for 10 min after beginning volatile anesthesia (−1 minimum alveolar concentration inspired). Respiratory system resistance was determined using the isovolume technique.

Results: Fifty subjects were randomized to receive sevoflurane (n = 20), desflurane (n = 20), or thiopental infusion (n = 10, 0.25 mg · kg⁻¹ · h⁻¹). There were no differences between groups for age, height, weight, smoking history, and American Society of Anesthesiologists physical class. On average, sevoflurane reduced respiratory resistance 15% below baseline, whereas both desflurane (+5%) and thiopental (+10%) did not decrease respiratory resistance. The respiratory resistance changes did not differ in patients with and without a history of smoking during sevoflurane or thiopental. In contrast, administration of desflurane to smokers resulted in the greatest increase in respiratory resistance.

Conclusions: Sevoflurane causes moderate bronchodilation that is not observed with desflurane or sodium thiopental. The bronchoconstriction produced by desflurane was primarily noted in patients who currently smoked. (Key words: Bronchospasm; respiratory resistance; volatile anesthetics.)

PATIENTS undergoing general anesthesia are at risk for a number of rare but serious complications, including bronchospasm.¹,² Of the volatile anesthetics used to treat bronchospasm, halothane has been the preferred agent, but recent evidence suggests that other agents may be better choices. For example, a study comparing the effects of isoflurane, halothane, sevoflurane, and thiopental/nitrous oxide on respiratory system resistance after tracheal intubation showed that sevoflurane decreased respiratory resistance more than halothane or isoflurane.³ Sevoflurane as an alternative to halothane for the management and/or prevention of bronchospasm has the added advantage of low blood solubility and, therefore, anesthetic depth can be rapidly adjusted. The effects of desflurane on bronchodilation have not been characterized. One potential disadvantage of desflurane might be its extreme pungency.⁴,⁵ In fact, the airway irritation caused by administering desflurane after intravenous induction of anesthesia has been associated with a marked increase in the activity of the neuroendocrine axis.⁶–⁹ Despite its pungency, we hypothesized that after intravenous induction of anesthesia, desflurane might be a better bronchodilating agent than sevoflurane because of the potential beneficial effect of increased sympathetic nervous system activity on bronchial smooth muscle.
Materials and Methods

After receiving approval from the Human Studies Review Board, we obtained written consent from patients scheduled to undergo elective surgery with general anesthesia. Patients were excluded for use of β₂-agonists, steroids, an ipratropium inhaler, or theophylline. Demographic information included gender, age, height, weight, smoking status, American Society of Anesthesiologists physical status, and pulmonary history. As a baseline measurement of pulmonary function, peak expiratory flow was measured in triplicate with the patient in the awake, sitting position using a peak flow meter (TruZone; Monaghan Medical Corp., Plattsburgh, NY) before the administration of premedication. The highest achieved value was expressed as a percentage of expected value for peak flow based on the patient’s gender, height, and age. Patients then were administered 1 mg midazolam and 50 μg fentanyl in the holding area. They were transported to the operating room, and standard monitors were applied. Another 1 mg midazolam and additional fentanyl to total 2.0 μg/kg were administered 5 min before induction. Anesthetic induction was achieved with 5 mg/kg sodium thiopental and 1.25 mg/kg succinylcholine. Tracheal intubation was achieved using a Macintosh 3-4 blade and an 8-mm diameter cuffed endotracheal tube. Immediately after intubation, 0.3 mg/kg rocuronium was given. All procedures for all patients were performed by a single anesthesiologist.

Mechanical ventilation commenced, and airway pressure and flow measurements (Datex Capnomac Ultima, Helsinki, Finland) were taken 30 s after tracheal intubation but before administering further anesthesia (30-s sample). Specific ventilation guidelines were established as quickly as possible (8 breaths/min, tidal volume of 10 ml/kg, fresh gas flow of 4 l/min, inspiratory to expiratory ratio of 1:3). Patients were randomly assigned to receive desflurane or sevoflurane. The vaporizer was set at an inspired anesthetic concentration of 7% desflurane in oxygen-air (fraction of inspired oxygen ~ 70%) or 2.3% sevoflurane in oxygen-air (~ 1 minimum alveolar concentration [MAC]). A control group was included in the randomization after enrolling 20 patients. This group was randomized to received 0.25 mg · kg⁻¹ · min⁻¹ sodium thiopental for 10 min. At 2.5, 5, 7.5, and 10 min after initiating the volatile anesthetic or thiopental, pressure and flow measurements were repeated. Mean arterial pressure (MAP), heart rate, end-tidal carbon dioxide, and end-tidal gas concentration were measured and recorded simultaneously to the respiratory system resistance (Rrs) measurements. Hypotension (MAP decrease > 25% from preinduction baseline) was treated with 100 μg phenylephrine.

The procedure for deriving Rrs is termed the isovolume technique. Briefly, Rrs is a measurement that comprises the sum of the resistance from the chest wall and elastic forces of the lung as well as the resistance from the small and large airways. The technique is based on measuring airway pressure and flow at identical volumes during inspiration and exhalation. The inspiratory (and expiratory) pressure is a function of the respiratory system compliance, the inspiratory (or expiratory) flow, and resistance. Rrs was calculated offline. The flow waveform was integrated to obtain a volume waveform. The resistance is calculated as the change in pressure divided by the change in flow between inspiration and expiration while the lungs are at the same volume to minimize elastic force differences. Finally, the resistance because of the 8-mm endotracheal tube was determined and subtracted from the calculated value of Rrs.

Continuous variables were expressed as mean ± SD. Comparisons for continuous variables within and between groups were performed using repeated-measures analysis of variance. Measurements of Rrs at 2.5, 5, 7.5, and 10 min were analyzed as percent change from the thiopental baseline before initiating the gas or infusion. Correlation analysis was used to seek relations between pack-year smoking history and respiratory resistance changes with each anesthetic treatment. Patients who had smoked in the past were considered nonsmokers for this evaluation if they had quit for at least 10 yr. Statistical significance was set at the 0.05 level.

Results

Fifty patients participated in this study: 20 received sevoflurane, 20 desflurane, and 10 thiopental. There was one female in each of the inhalational anesthetic groups. Average age, height, weight, American Society of Anesthesiologists physical status, and smoking history did not differ between treatment groups (table 1). The percentage of patients who smoked was 42%, 55%, and 50% in the desflurane, sevoflurane, and thiopental groups, respectively. Peak expiratory flow measurements were not different between the groups (398, 405, 444 l/min for desflurane, sevoflurane, and thiopental, respectively, with a range of 200–750 l/min; table 1). Four patients had mild chronic obstructive pulmonary disease (two...
desflurane, one sevoflurane, one thiopental), two patients had shortness of breath with moderate exertion (one desflurane, one sevoflurane), and none had emphysema. Hemodynamics were recorded and compared on the last 10 patients in each group. The baseline MAP recorded before anesthetic induction did not differ between the three groups. Resting MAP averaged 98 ± 20, 93 ± 18, and 101 ± 20 mmHg in the desflurane, sevoflurane, and thiopental groups, respectively. The average maximum decrease in MAP from baseline during the 10-min induction sequence ranged from −219 to −228 mmHg and did not differ between groups. The baseline heart rate in the three groups did not differ, nor did the heart rate change during the induction sequence.

The Rrs at thiopental baseline did not differ between the sevoflurane, desflurane, and thiopental groups (table 1). The changes in Rrs over the 10-min recording period were significantly different between sevoflurane and desflurane and between sevoflurane and thiopental, but not between desflurane and thiopental (fig. 1). The percentage change from baseline Rrs in the sevoflurane group (average = −15 ± 5%) was significantly different from the Rrs response in the desflurane group (5 ± 4%) and the thiopental group (10 ± 4%) by repeated-measures analysis of variance. Further analysis based on presence or absence of smoking revealed that the magnitude of the Rrs increase during desflurane could be accounted for by a positive history of smoking. In non-smokers receiving desflurane, no significant change in Rrs was observed. In contrast, smoking did not influence the bronchodilation (Rrs) from sevoflurane or the airway effects of thiopental (fig. 2).

We also recorded the level of anesthesia during the 10-min recording period in 2.5-min increments as a percentage of age-adjusted MAC. There were no differences between sevoflurane and desflurane in the achieved percent of MAC at each of the 2.5-min recording epochs. At the 10-min time point, the average percent MAC in the sevoflurane group was 0.97 ± 0.2 and in the desflurane group was 1.03 ± 0.2. The end-tidal carbon dioxide concentrations were similar at baseline (40 ± 4 mmHg) and did not differ between any treatment group during any recording period during the 10-min study period (average end-tidal carbon dioxide = 35 ± 4, 34 ± 4, and 35 ± 4 mmHg for desflurane, sevoflurane, and thiopental, respectively).

**Discussion**

The purpose of this study was to compare, after tracheal intubation, the effect of desflurane and sevoflurane on respiratory resistance. Our hypothesis was that desflurane, through its activation of the sympathetic nervous system, might decrease Rrs more effectively than sevoflurane. Our major finding was that Rrs was not decreased at all by the initial administration of desflurane. Rather, it was increased by 5% in contrast to the 15% decrease in respiratory resistance noted with sevoflurane. The effect of thiopental on respiratory resistance was similar to that of desflurane. Furthermore,

![Fig. 1. Changes in respiratory system resistance (Rrs) expressed as a percentage of the thiopental baseline recorded after tracheal intubation but before administration of sevoflurane or desflurane to the inspired gas mixture (or beginning infusions of thiopental). Airway resistance responses to sevoflurane were significantly different from desflurane and thiopental (P < 0.05).](https://example.com/fig1.png)

Table 1. Demographic Characteristics of Study Patients

<table>
<thead>
<tr>
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<th>Desflurane</th>
<th>Sevoflurane</th>
<th>Thiopental</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>61 ± 12</td>
<td>60 ± 12</td>
<td>59 ± 12</td>
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<tr>
<td>Height (cm)</td>
<td>178 ± 10</td>
<td>177 ± 7</td>
<td>177 ± 11</td>
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<tr>
<td>Weight (kg)</td>
<td>87 ± 20</td>
<td>88 ± 18</td>
<td>90 ± 19</td>
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<tr>
<td>ASA physical status I/II/III (n)</td>
<td>1/9/10</td>
<td>1/9/10</td>
<td>1/5/4</td>
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<tr>
<td>Smokers/nonsmokers (n)</td>
<td>8/12</td>
<td>11/9</td>
<td>5/5</td>
</tr>
<tr>
<td>Smoking (pack/yr)</td>
<td>48 ± 22</td>
<td>46 ± 35</td>
<td>42 ± 21</td>
</tr>
<tr>
<td>Respiratory system resistance (cm H₂O · l⁻¹ · s⁻¹)</td>
<td>9.7 ± 4.2</td>
<td>11.7 ± 7.8</td>
<td>7.4 ± 3.1</td>
</tr>
<tr>
<td>Peak expiratory flow (% predicted)</td>
<td>79 ± 23</td>
<td>78 ± 23</td>
<td>87 ± 26</td>
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Data are mean ± SD.
ASA = American Society of Anesthesiologists.
the majority of the increase in Rrs from desflurane occurred in patients who smoked. Smoking history did not influence the bronchodilation from sevoflurane.

Demographic characteristics, American Society of Anesthesiologists physical status, and pulmonary history did not differ among treatment groups. The type of surgery performed on each patient was not relevant to the protocol or outcome because all data were collected before surgery (or Foley placement) had begun. This eliminated confounding variables such as sympathetic nervous system activation by pain. All treatment groups experienced statistically similar hemodynamic effects, including decreases in MAP and insignificant heart rate changes. The isovolume technique for measuring respiratory resistance relies on the sound physiologic principle that resistance is simply pressure divided by flow. The technique does not measure solely airway resistance, but includes resistance from the chest wall and elastic forces from the lung. It relies on the assumption that at a given volume, the elastic forces are the same in expiration as they are in inspiration. This, in fact, is not the case. The difference in elastic forces at the same volume is termed hysteresis and is a potential source of error in our measurements. But, because the potential error would affect measurements equally in all patients, it would not likely change the results.

Approximately half of the patients were smokers with a history ranging from 8 to 125 pack-years. It is possible that increased lung compliance or bronchial reactivity associated with a smoking history might affect the results, but this effect should have been equal between groups because smoking histories were similar between groups. Because of the positive association of smoking status and respiratory resistance with desflurane, we also sought significant correlations between pack-year smoking history and the average Rrs response to anesthesia. There were no significant relationships for any of the anesthetics. Therefore, it seems that regardless of small versus large pack-year smoking history, the initial administration of desflurane after induction of anesthesia with thiopental caused significant increases in Rrs (bronchoconstriction). It is well-known that smoking increases the reactivity of bronchial smooth muscle to exogenous stimuli. Because smoking history did not counteract the bronchodilation from the nonpungent sevoflurane but did affect the response to desflurane, a logical conclusion would be that the pungency and presumed irritation of the airway from desflurane was sufficient to trigger bronchoconstriction. Even in nonsmokers receiving desflurane, the absence of changes in Rrs from baseline contrasts to the bronchial dilation noted with sevoflurane.

The decision to include thiopental in our study at approximately the midway point was to confirm the sensitivity of our measurement technique for Rrs, because the findings with desflurane were opposite of those we had expected. Thiopental has been associated with histamine release and increases in Rrs. Our technique of measuring Rrs was sufficiently sensitive to detect an increase with thiopental.

Traditionally, halothane has been considered the drug of choice among volatile anesthetics for the treatment and prevention of bronchospasm. Rooke et al. demonstrated that the nonpungent, low-solubility anesthetic, sevoflurane, had a more pronounced ability to decrease Rrs than isoflurane, halothane, or thiopental–nitrous oxide. Our results confirm these findings, demonstrating that sevoflurane is an effective bronchodilating inhala-

Fig. 2. Respiratory system resistance (Rrs) during the 10 min after thiopental (baseline), separated by current smoking status. Administration of desflurane to patients who are smokers caused significant bronchoconstriction compared with nonsmokers receiving desflurane (*P < 0.05).
tion anesthetic. We have extended these findings to show that desflurane may not be an effective bronchodilating anesthetic in the first 10 min after tracheal intubation and may, in fact, cause bronchoconstriction in patients with a positive history of smoking.

There are several observations that can be made regarding the absence of bronchodilatation with desflurane anesthesia. First, we measured Rrs in patients exposed to an inspired concentration of inhaled anesthetic that achieved 1 MAC over a 10-min period. We avoided higher levels of desflurane in an effort to reduce hemodynamic alterations such as tachycardia and hypertension that are known to occur with high levels of desflurane.\(^8,9,14\) Nonetheless, because desflurane is the least potent of modern inhaled anesthetics, it mandates delivery at a higher percentage of the total inspired gas mixture. The combination of an extremely pungent gas delivered in a high concentration exposes “at risk” patients to a bigger airway stimulus then might occur with a pungent but potent anesthetic such as isoflurane. It is currently unknown whether the effects of desflurane on Rrs are different at lower (or higher) inspired concentrations than that used in this study.

It is possible that desflurane may simply require more time to achieve a state of bronchodilatation, and that desflurane and sevoflurane might converge at a common Rrs at some time point that is beyond the scope of this protocol (10 min). Finally, our hypothesis that desflurane might be a better bronchodilator than sevoflurane because of its positive effect on the sympathetic nervous system was likely flawed because neuronal sympathetic nervous system activation provides little, if any, bronchodilatation.\(^15-18\)

This study indicates that desflurane lacks the ability to cause an early decrease in Rrs after tracheal intubation and, in fact, causes significant increases in Rrs in patients with positive smoking status. Sevoflurane causes significant decreases in Rrs, regardless of smoking status or history, which is not observed with desflurane or sodium thiopental.

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