Anesthesiology 2005; 103:495–9

Desflurane Enhances Reactivity during the Use of the Laryngeal Mask Airway

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Background: **Desflurane and sevoflurane have markedly different pungencies. The tested hypothesis was that patients breathing equivalent concentrations of desflurane or sevoflurane through a laryngeal mask airway (LMA) would have similar responses.**

Methods: **After institutional review board approval and informed consent were obtained, 60 patients were enrolled and given intravenous midazolam (1⁄4 μg/kg) and fentanyl (1 μg/kg) 5 min before induction of anesthesia. The LMA was inserted at loss of consciousness after 2 mg/kg propofol. When spontaneous breathing returned, a randomly assigned volatile anesthetic was started at an inspired concentration of either 1.8% sevoflurane or 6% desflurane at a fresh gas flow of 6 l/min in air: oxygen (50:50). After 5 min, a controlled movement of the LMA took place. Three minutes later, the inspiratory anesthetic concentration was changed to either 3.6% sevoflurane or 12% desflurane for 3 min. A blinded observer recorded movements and airway events during the start of anesthetic, LMA movement, deepening of the anesthetic, and emergence before LMA removal.**

Results: **There were no differences at anesthetic start and LMA movement. Desflurane titration to 12% increased heart rate, increased mean arterial blood pressure, and initiated frequent coughing (53% *vs.* 0% sevoflurane) and body movements (47% *vs.* 0% sevoflurane). During emergence, there was a twofold greater incidence of coughing and a fivefold increase in breath holding in the desflurane group.**

Conclusions: **When airway responses to sevoflurane and desflurane were compared in elective surgical patients breathing through an LMA, there were significantly more adverse responses with desflurane at 12% concentrations and during emergence.**

DESFLURANE and sevoflurane represent our newest volatile anesthetics in clinical use and are unique in their low blood:gas solubilities. They seem to have different cardiovascular and respiratory effects.[1,2] Recent data have suggested that compared with sevoflurane, patients anesthetized with desflurane experienced greater responses to tracheal stimulation at 1 mean alveolar concentration (MAC) level of anesthesia.[3] In addition, desflurane has been associated with increases in airway resistance at inspired concentrations of 6% when compared to equipotent concentrations of sevoflurane, an effect that has been attributed to the greater pungency and irritant properties of desflurane.[2] These findings suggest that desflurane might be less well tolerated in patients who are not provided muscle relaxants and are breathing 1–2 MAC inspired concentrations *via* a laryngeal mask airway (LMA). However, a recent study suggested that desflurane *via* an LMA was associated with a similar low incidence of adverse airway responses compared with sevoflurane when these anesthetics were used with nitrous oxide and 2–4 μg/kg fentanyl.[4] The current study evaluated the airway responses and patient movement when administering desflurane and sevoflurane without nitrous oxide and minimal fentanyl at low and higher inspired concentrations. We tested the hypothesis that clinically relevant concentrations of sevoflurane and desflurane would result in similar airway and movement responses in spontaneously breathing patients.

Materials and Methods

After institutional review board approval was obtained (Zablocki VA Medical Center, Milwaukee, Wisconsin), patients who had an American Society of Anesthesiologists physical status classification of I–III and were scheduled to undergo elective surgery of less than 2 h in duration provided written, informed consent and were included in the study. Patients were excluded for a history of gastroesophageal reflux disease, hiatal hernia, morbid obesity, nonelective surgery, and any procedure requiring muscle relaxants; smokers were not excluded. Demographic data were collected. After measuring baseline vital signs, an intravenous line was established, and patients were provided with 1⁄4 μg/kg midazolam in the holding area and 1 μg/kg fentanyl 5 min before induction of anesthesia. At the time of arrival in the operating room, standard monitors were applied, and fluid deficits from fasting were replaced with 0.9% saline. After preoxygenation with 6 l/min oxygen through a facemask for 2–3 min, intravenous pretreatment with 30 mg lidocaine, 1%, was followed by induction of anesthesia with 2 mg/kg propofol. After loss of eyelash reflex, the appropriate size LMA, lubricated with plain water-soluble lubricant, was inserted. The cuff was inflated with the minimum amount of air required to maintain a seal at a pressure of 20 cm H_2O and a leak above this value. Fresh gas flow was set at 3 l each of air and oxygen. The patient was randomly assigned to receive either sevoflurane or desflurane. At the start of spontaneous breathing, the volatile anesthetic was started to keep the inspired concentration at 1 MAC equivalent (1.8% sevoflurane, 6% desflurane). During this time, heart rate (HR), mean arterial blood pressure (MAP), end-tidal carbon dioxide,

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Received from the Department of Anesthesiology, Zablocki VA Medical Center, Milwaukee, Wisconsin. Submitted for publication February 24, 2005. Accepted for publication June 6, 2005. Supported by a contract with Abbott Laboratories, Abbott Park, Illinois.

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oxygen saturation, and end-tidal gas concentration were recorded. A blinded observer noted any coughing, breath holding, movement, or laryngospasm. After 5 min, the cuff of the LMA was deflated, moved up and down three consecutive times (approximately a 5-cm span of movement over approximately 10 s), and then reinflated while the blinded observer noted hemodynamic and patient responses. Three minutes after this stimulus, the inspired concentration of the volatile anesthetic was increased to 2 MAC equivalent, 3.6% sevoflurane or 12% desflurane, while the blinded observer recorded hemodynamic and patient responses for an additional 3 min. Hemodynamic data were collected at minutes 1, 4, 5, 6, 7, 8, 9, and 11 of this 11-min experimental period and at 1-min intervals during emergence. When the scrub technician began to prepare the patient, the fresh gas flow was reduced to 2 l/min, and the volatile anesthetic was titrated to maintain an adequate anesthetic depth for surgery. Additional doses of fentanyl were permitted intraoperatively at the discretion of the anesthesia provider if adjustments of the volatile anesthetic (from one third MAC up to 2 MAC) were insufficient to control HR, blood pressure, or movement. At the conclusion of surgery, the volatile anesthetic and air were discontinued, the oxygen was increased to 6 l/min, and LMA removal was completed when the patient responded to verbal commands (*e.g.*, patient's first name, "open your eyes"). This command was given at 15-s intervals. The blinded observer recorded hemodynamics and patient responses until LMA removal.

Movements were graded as 0 for no movement, 1 for isolated flexion movement, 2 for flexion and extension movement occurring less than three times, and 3 for flexion and extension movement occurring more than three times. Cough was graded as 0 for no cough, 1 for a single cough, 2 for two or three coughs, and 3 for more than 3 coughs. Breath holding was graded as 0 for none, 1 for less than 20 s, 2 for 20–30 s, and 3 for greater than 30 s. Secretions at the end of surgery were graded as 0 if there were no secretions, 1 if there was a small amount of secretions not requiring suctioning, 2 if secretions required suctioning once, and 3 if secretions required multiple suctioning. Laryngospasm was graded as 0 if none occurred, 1 if the duration was less than 20 s with no decrease in oxygen saturation measured by pulse oximetry (Spo_2), 2 if the duration was greater than 20 s with a decrease of 4% or greater in Spo_2 and briefly assisted ventilation but no requirement for muscle relaxant, and 3 if the duration was greater than 20 s with a decrease of 10% or greater in Spo_2 requiring muscle paralysis and mechanical ventilation.

Statistical Analysis

Based on preliminary studies, sample sizes were sufficient to detect a 20% reduction in the incidence of coughing, with an α of 0.5 and a β of 0.8. Continuous variables are presented as mean ± SEM. Categorical data are presented as number or percentage. Two-way repeated-measures analysis of variance was performed to determine differences between groups and changes from baseline for continuous variables (*e.g.*, HR, MAP, respiration) during each of three experimental settings. Baseline values represent the average of preoperative and preinduction data. After LMA placement, the experimental timer was reset to zero, and the volatile agent was started. The three experimental sections, all timed from the start of the volatile agent, were from baseline through 5 min at 1 MAC anesthesia (section 1), from the last minute of section 1 through 3 min after LMA movement (section 2), and from the last minute of section 2 through the transition to approximately 2 MAC inspired concentrations (section 3). *Post hoc* testing was with the Scheffé test. Chi-square analyses were performed to determine differences in the incidence of movements, coughing, breath holding, and secretions between the anesthetics. Chi-square analyses also were performed within the desflurane group to determine whether the incidence of coughing was higher in patients who smoked. Although the responses of body movement, coughing, breath holding, and secretions were graded, the percent of patients who experienced each complication, regardless of degree, was calculated for each anesthetic. Unpaired *t* tests were used to compare demographic information and fentanyl use between anesthetic groups. Statistical significance was set at $P < 0.05$.

Table 1. Baseline Hemodynamic Data

	Sevoflurane	Desflurane
Heart rate, beats/min	71.3 ± 10.7	73.3 ± 14.8
Mean arterial pressure, mmHg	72.9 ± 10.3	69.9 ± 9.4
Oxygen saturation, %	97.7 ± 1.5	97.8 ± 1.4
Respiratory rate, breaths/min	16.0 ± 2.5	15.6 ± 1.7

n = 30/group. Data are presented as mean ± SEM.

Results

Sixty patients participated in this research study, 30 in each anesthetic group. Groups were similar with regard to average age (58 yr; range, 22–89 yr), height (178 cm; 163–193 cm), weight (91 kg; 59–125 kg), incidence of preexisting pulmonary disease (approximately 50%), smokers (approximately 50%), pack-year history (34/group), patients with chronic obstructive pulmonary disease (2 or 3/group), and patients with mild asthma (2/group). The majority of cases were genitourinary, orthopedic, and minor general surgical procedures such as inguinal hernias.

There were no differences between groups for hemodynamic variables (HR, MAP, oxygen saturation, respiratory rate) during baseline measurements (table 1), dur-

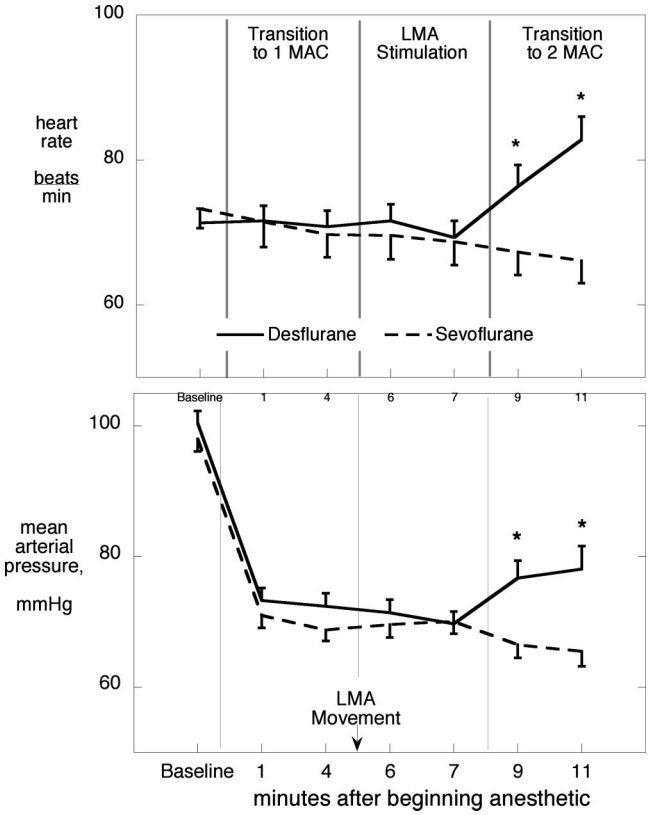

Fig. 1. Heart rate (*top*) and mean arterial pressure (*bottom*) responses to various stimuli during sevoflurane and desflurane. There were no differences between groups except at the 2 minimum alveolar concentration (MAC) transition. * Desflurane caused increases in both heart rate and mean arterial pressure when increased from 1 to 2 MAC compared with sevoflurane ($P < 0.05$). Data are presented as mean ± SEM. LMA = laryngeal mask airway.

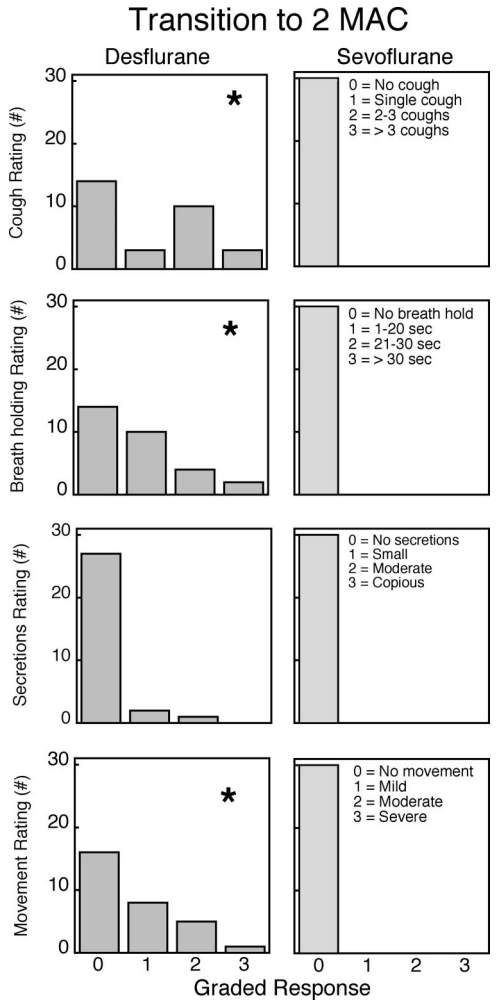

Fig. 2. Graded responses to coughing, breath holding, secretions, and movement during transition to 2 minimum alveolar concentration (MAC) desflurane and sevoflurane anesthesia. Small secretions are defined as no suction needed; moderate secretions required a single suction; copious secretions required multiple suctions. * Desflurane caused more events compared with sevoflurane ($P < 0.05$). n = 30 patients/anesthetic group.

ing 5 min of low anesthetic concentration, or as the result of LMA movement. Respiratory rate significantly slowed by approximately 3 breaths/min in both groups at the low anesthetic concentration (approximately 1 MAC) compared with baseline. Significant differences between groups were not noted until the transition toward 2 MAC. In desflurane-treated patients, HR increased by an average of 12 ± 2%, and MAP increased by an average of 7 ± 3%. This was a significantly different response from the unchanged HR and MAP in the sevoflurane-treated patients. Changes in HR and MAP are depicted in figure 1.

Average intraoperative fentanyl use was not significantly different between the desflurane and sevoflurane groups (138 v 91 μg, respectively). No fentanyl was needed in five patients in the desflurane group and seven patients in the sevoflurane group.

The body movement and airway responses at low anesthetic concentrations and during LMA movement were negligible and not significant. In contrast, there were substantially greater movement responses (desflurane:sevoflurane, 47%:0%), coughing (53%:0%), and breath holding (53%:0%) in the desflurane group during transition toward 2 MAC compared with sevoflurane. The effect of smoking on the incidence of coughing and breath holding in the desflurane group was not significant. Figure 2 summarizes the gradation of airway and movement responses to desflurane and sevoflurane during the transition to higher concentrations of desflurane and sevoflurane. Significantly greater responses occurred with desflurane. There were statistically similar end-tidal gas concentrations expressed as a percentage of 1 MAC during the three observation periods and at emergence: At approximately 1 MAC, the average end-tidal sevoflurane concentration was 1.1 ± 0.3, and the average end-tidal desflurane concentration was 3.9 ± 0.08; during LMA movement, the average end-tidal sevoflurane concentration was 1.2 ± 0.02, and the average end-tidal desflurane concentration was 4.4 ± 0.14; at approximately 2 MAC, the average end-tidal sevoflurane

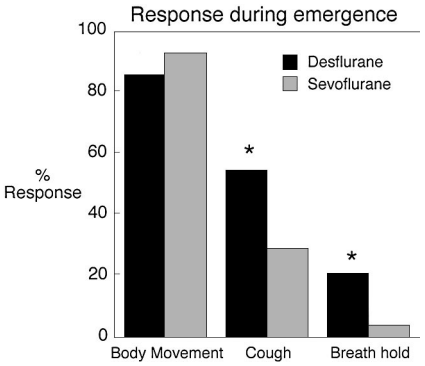

Fig. 3. Percentage of patients experiencing body movement, coughing, and breath holding during emergence associated with sevoflurane and desflurane. * Desflurane resulted in more coughing and breath holding than sevoflurane during emergence ($P < 0.05$).

concentration was 2.4 ± 0.06, and the average end-tidal desflurane concentration was 8.6 ± 0.19.

The movement and airway responses to emergence are depicted in figure 3. The majority of patients moved during emergence regardless of anesthetic. However, the incidences of coughing (55%) and breath holding (21%) were significantly greater in the desflurane-treated group compared with the sevoflurane-treated group (29% cough; 4% breath holding). No patient developed laryngospasm, and secretions were not different between groups.

Discussion

The major finding of this clinical study was the high incidence of adverse events (coughing, breath holding, and movement) with desflurane above 6% compared with the absence of these effects with sevoflurane above 1.8%. This occurred despite all patients receiving a small dose of fentanyl before induction of anesthesia. There also were higher incidences of airway events during the emergence period in patients receiving desflurane.

Compared with tracheal intubation, advantages to LMA use include simplicity of placement and fewer adverse hemodynamic and respiratory events associated with both placement and removal. Previous research from our laboratory has identified that LMA placement results in a 50% reduction in the typical sympathetic activation associated with tracheal intubation.[5] In addition, the incidence of laryngospasm and bronchospasm is less with the LMA compared with conventional laryngoscopy and intubation.[6] However, there are caveats associated with its safe use. Aside from those related to gastrointestinal concerns of full stomach, hiatal hernia, or gastroesophageal reflux disease, the current study suggests that the use of higher concentrations of desflurane with an LMA after induction of anesthesia may be problematic. Furthermore, at lower concentrations of desflurane, adverse reactions were noted at emergence.

After propofol induction, LMA placement, and the resumption of spontaneous ventilation, the initiation of 6% desflurane or 1.8% sevoflurane inspired concentrations did not result in any adverse airway events or movement responses. However, higher concentrations of the volatile anesthetics are often needed in spontaneously breathing patients to assure patient immobility and to suppress autonomic responses to surgical discomfort. In this study, we determined whether adequate ventilation, immobility, and hemodynamic stability could be maintained when initiating inspired concentrations of desflurane and sevoflurane above 1 MAC. We found substantial adverse responses of movement, coughing, breath holding, tachycardia and hypertension from high concentrations of desflurane that did not exist with sevoflurane. As a percent of MAC, we achieved 143% with desflurane and 135% with sevoflurane; these were not statistically different. We believe that at high concentrations, desflurane activated airway irritant receptors,[1,7] thereby triggering reflexes in the anesthetized patient. Approximately half of the patients in this study had a positive smoking history. We have previously shown that higher concentrations of desflurane in smokers result in increases in respiratory resistance compared with sevoflurane.[2] The effects of smoking did not influence the findings in the current study because approximately 44% of the patients with a cough response to high concentrations of desflurane were nonsmokers.

The early adverse effects of desflurane might have been avoided had our protocol design incorporated higher doses of fentanyl, nitrous oxide, or both. For example, 5 μg/kg fentanyl can significantly obtund the sympathetic activation from high concentrations of desflurane.[8] Nitrous oxide has analgesic effects that also might lessen the response to desflurane. Previous work by Eshima *et al.*[4] used both supplemental analgesic strategies in a study evaluating the effects of desflurane and sevoflurane with an LMA. They compared responses in patients who simultaneously received 40–50% nitrous oxide and 2–4 μg/kg fentanyl. They noted 27–48% of patients briefly received over 1 MAC exposures, although the average MAC fraction of each volatile agent was less than 1 MAC. They found no differences in the effects of desflurane and sevoflurane when used with analgesic adjuvants in conjunction with an LMA.[4] Our study design used only 1 μg/kg fentanyl and no nitrous oxide. These adjuvants are commonly avoided when volatile anesthetics are used in an ambulatory setting to circumvent their undesirable side effects of postoperative nausea and vomiting.[9] Higher doses of fentanyl also may lead to unwanted side effects of apnea, inadequate ventilation, or both.[10,11]

A secondary objective of this research was to seek evidence for heightened airway reactivity from the use of desflurane with an LMA. Recently, Klock *et al.*[3] studied airway reactivity in patients after tracheal intubation

who were randomly assigned to receive either 1 or 2 MAC concentrations of sevoflurane or desflurane. At each MAC, the authors stimulated the airway by inflating and deflating the cuff on the endotracheal tube. At 1 MAC concentrations, patients receiving desflurane had more adverse airway responses than patients receiving sevoflurane. MAC by definition represents the concentration of anesthetic gas that prevents purposeful movement response to a noxious peripheral stimulus in 50% of patients. Their work suggests that the MAC was sufficient to prevent a response to tracheal stimulation when sevoflurane was used but not sufficient when desflurane was being administered. We sought a similar effect of "sensitizing" or "inadequate desensitization" of the airway from desflurane by deflating the LMA and making three controlled movements of the device before reinflating the cuff. The LMA device was not lubricated with lidocaine jelly. This maneuver, to stimulate the posterior pharyngeal area, did not cause any undesired response during either anesthetic. This test occurred approximately 7–8 min after anesthetic induction, and it is likely that both propofol and fentanyl might have contributed to the absence of response. More likely, the lesser stimulus of LMA movement *versus* tracheal stimulation as performed by Klock *et al.*[3] could account for the lack of response.

Finally, we noted significantly increased airway events in the desflurane group during emergence. Patients in both groups had substantial movement as expected. However, during declining concentrations of desflurane, patients had a greater than 20% incidence of breath holding and a greater than 50% incidence of coughing compared with only a 4% incidence of breath holding and a 29% incidence of coughing in the sevoflurane group. Some of these differences might be explained by the slightly greater incidence of secretions in patients receiving desflurane, which might promote coughing and breath holding.

In summary, when airway responses to desflurane and sevoflurane are compared in elective surgical patients breathing through an LMA, there were significant adverse responses with desflurane when higher concentrations of volatiles were used. Compared with equipotent concentrations of desflurane, sevoflurane was associated with substantially fewer adverse movement and airway effects. It is proposed that the airway irritant properties of desflurane serve as a trigger for these events. It is also proposed that additional analgesic adjuvants be considered if desflurane is chosen as the primary anesthetic for use with an LMA. Finally, during emergence when anesthetic concentrations are declining, a higher incidence of coughing and breath holding might occur in patients receiving desflurane.

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