ABSTRACT

Background: Inhalational anesthetic effects on upper airway muscle activity in children are largely unknown. The authors tested the hypothesis that phasic inspiratory genioglossus and palatoglossus activity increases during recovery from sevoflurane anesthesia in a dose-dependent manner in children.

Methods: Sixteen children, aged 2.0 to 6.9 yr, scheduled for elective urological surgery were studied. Electromyogram recordings were acquired using intramuscular needle electrodes during spontaneous ventilation. After a 15-min period of equilibration, electromyogram activity was recorded over 30 s at each of three end-tidal concentrations, 1.5, 1.0, and 0.5 minimum alveolar concentration (MAC), administered in sequence.

Results: Phasic genioglossus activity was noted in four children at 1.5 MAC, five at 1.0 MAC, and six children at 0.5 MAC sevoflurane. Phasic palatoglossus activity was noted in 4 children at 1.5 MAC, 6 at 1.0 MAC, and 10 children at 0.5 MAC sevoflurane. Both the proportion of children exhibiting phasic activity, and the magnitude of phasic activity increased during recovery from anesthesia. For the genioglossus, decreasing the depth of sevoflurane anesthesia from 1.5 to 1.0 MAC increased phasic activity by approximately 35% and a further decrease to 0.5 MAC more than doubled activity (median [range] at 1.5 and 0.5 MAC: 2.7 μV [0 to 4.0 μV] and 8.6 μV [3.2 to 17.6], respectively; \( P = 0.029 \)). A similar dose-related increase was recorded at the palatoglossus (\( P = 0.0002 \)).

Conclusions: Genioglossus and palatoglossus activity increases during recovery from sevoflurane anesthesia in a dose-dependent manner over the clinical range of sevoflurane concentrations in children.

What We Already Know about This Topic

- General anesthesia suppresses the neural control of the upper airway dilating muscles
- Little is known about responses of these muscles to recovery from general anesthesia, particularly in children

What This Article Tells Us That Is New

- Phasic, but not tonic, inspiratory activity of the genioglossus and palatoglossus muscles increases progressively with decreasing depth of sevoflurane anesthesia in spontaneously breathing children

GENERAL anesthesia induces changes in upper airway caliber and configuration that predispose to partial or complete airway obstruction in spontaneously breathing patients. The mechanisms underlying anesthesia-induced changes in upper airway caliber are not fully understood. Phasic and tonic electromyogram activity in upper airway dilator muscles, such as the genioglossus and palatoglossus, stabilizes the airway during the ventilatory cycle. Phasic augmentation of upper airway muscle activity with inspiration maintains airway patency in the face of the negative intraluminal pressure generated by inspiratory muscles. General anesthesia decreases the activity of upper airway muscles, with suppression of phasic activity being greater in younger compared with adult animals.

Previous studies evaluating dose-related anesthetic actions on upper airway muscle activity and/or airway caliber have yielded conflicting results. Inhibition of upper airway muscle activity by isoflurane was independent of dose in adults, with profound inhibition occurring even at subanesthetic concentrations of isoflurane. In contrast, increasing depth of propofol anesthesia was associated with a
dose-related inhibition of genioglossus activity, and a graded reduction in upper airway caliber in children, which were similar to findings reported for sevoflurane. Several explanations may be offered for these disparate observations, including age and anesthetic-related factors; however, the effect of age in humans is unclear, given that no study has evaluated anesthetic influences on upper airway muscle activity in children.

Although the genioglossus remains the most commonly studied upper airway dilator muscle, other muscles such as palatal muscles are important dilators of the upper airway. Indeed, the soft palate is a common site of airway obstruction in children and adults. The palatoglossus muscle exhibits phasic activity with inspiration and alters palatal position to facilitate the nasal route of ventilation. The effect of general anesthesia on palatoglossus muscle activity in humans is largely unknown.

The main purpose of this study was to evaluate the phasic electromyogram activity of the genioglossus and palatoglossus muscles during recovery from sevoflurane anesthesia in spontaneously breathing children. We defined phasic activity as the peak electromyogram activity that occurs in phase with each inspiration, whereas tonic activity was defined as the nadir activity during expiration. Our hypothesis was that phasic genioglossus and palatoglossus muscle activity increases during recovery from sevoflurane anesthesia in a dose-dependent manner over the clinical range of sevoflurane concentrations.

Materials and Methods

The Research Ethics Board at the Hospital for Sick Children, Toronto, approved the protocol for this single-center observational study. Written informed parental consent and patient assent, where appropriate, were obtained to study 16 healthy (American Society of Anesthesiologists’ physical status 1 or 2) unpremedicated children aged 2 to 10 yr, who were scheduled for elective hypospadias repair. This prospective observational study was conducted between March 2007 and February 2009. Children with a history of adenotonsillar hypertrophy or other pathology of the upper or lower airway, obstructive sleep apnea, gastroesophageal reflux, developmental delay, craniofacial anomalies, and neurological disorders were excluded. In addition, failure to maintain a patent airway (defined as the presence of stridor, paradoxical chest wall motion, oxygen desaturation, or other clinical evidence of airway obstruction), failure of the caudal block, and need for intraoperative opioid supplementation were considered withdrawal criteria during the study. Children needing any type of upper airway intervention to maintain the patent of the upper airway were withdrawn from the study.

Anesthesia was induced with sevoflurane, and maintained with air, oxygen (fraction of inspired oxygen, 0.3), and sevoflurane, using an air-cushioned facemask and a 1.5-cm diameter pediatric circle breathing circuit (183 cm in length, Portex; Smiths Medical International Ltd., Kent, United Kingdom). Anesthesia was maintained with a Primus anesthesia workstation equipped with a standard carbon dioxide absorber (Amsorb®; Armstrong Medical Ltd., Coleraine, Northern Ireland) and set to deliver a fresh gas flow of 6.0 l/min. Standard intraoperative monitors were applied, including axillary temperature (SC9000XL, Dräger, Lübeck, Germany). Respiratory variables, expired carbon dioxide concentration, and sevoflurane concentration were monitored during the study. A caudal block was performed after induction of anesthesia to provide intraoperative and postoperative analgesia. The dosage of bupivacaine used for caudal analgesia was standardized (1 ml/kg of 0.25% bupivacaine with epinephrine 1:200,000). No opioids, nonsteroidal antiinflammatory agents, or acetaminophen were administered intraoperatively.

The caudal block was evaluated on surgical incision (in the presence of 1.5 minimum alveolar concentration [MAC] sevoflurane) and throughout surgery as the depth of anesthesia was decreased. The caudal block was considered inadequate if the heart rate and/or mean arterial blood pressure increased by 20% or more of the baseline value.

All electromyogram data were collected while the children breathed spontaneously. Head position was standardized to obtain an angle of 110° between the horizontal plane and a line connecting the tragus and the lateral corner of the ipsilateral eye. In previous studies, the majority of children anesthetized with sevoflurane (0.5 to 1.5 MAC) maintained a clear unobstructed airway when breathing spontaneously with the head in this position.

Two experienced pediatric anesthesiologists were present at all times during the study. Each anesthesiologist assessed the patency of the upper airway independently. Each anesthesiologist was aware that partial or complete upper airway obstruction was a criterion for patient withdrawal from the study. For every patient included in the study, both anesthesiologists independently agreed that there was no clinical evidence of airway obstruction at any point during the period of data acquisition.

Genioglossus and palatoglossus electromyogram recordings were acquired using intramuscular, disposable needle electrodes inserted after induction of anesthesia. For genioglossus recordings, two needle electrodes were inserted orally under the tongue, each 5 mm to the left or right of the frenulum, and midway between the mandibular incisor and the sublingual fold. For palatoglossus recordings, two needle electrodes were inserted orally into the palatoglossal arch of the pharyngeal fauces, each 5 mm to the left or right of the uvula at the level of the uvular–isthmus junction. For each muscle, left and right electrodes were referenced to each other, recording the combined electromyogram activity to produce a bipolar recording. A sterile, pregelled, silver-silver chloride surface electrode was placed on the forehead and used as a ground for all recording electrodes. All needle
electrodes were sterile, single-use, 6 mm, 29-gauge stainless steel. The resistance at each electrode was monitored using an impedance meter (Prep-Check; General Devices, Ridgefield, NJ), and maintained below 5 kilohm, to ensure low impedance and a high signal to noise ratio. Electromyograms were recorded using a differential amplifier, and band-passed filtered between 10 and 5,000 Hz (EMG100C; Biopac Systems Inc., Goleta, CA), using a sampling rate of 1,000 samples per second. Electromyogram activity was measured as a simple moving time average of the root mean square with a time constant of 20 ms and peak inspiratory and expiratory amplitudes were calculated.

The genioglossus and palatoglossus electromyograms were recorded over 30 s during the recovery from sevoflurane anesthesia at each of three end-tidal sevoflurane concentrations, 1.5, 1.0 (2.5 volume%), and 0.5 MAC administered in sequence. Recordings at 0.5 MAC were acquired after completion of surgery. For each end-tidal concentration of sevoflurane, 15 min were allowed for equilibration of inspired and end-tidal concentrations of sevoflurane before acquisition of electromyogram recordings. During acquisition of electromyogram recordings, the air-cushioned facemask rested gently on the face, taking care to ensure an airtight seal and avoid mandibular displacement.

**Statistical Analysis**

The primary outcome was the peak phasic inspiratory electromyogram activity of the genioglossus muscle, presented as median (interquartile range). An *a priori* sample size calculation was based on an estimated 35% reduction in phasic genioglossus activity during anesthesia and a baseline mean and SD (379 ± 110 μV) similar to that found for the single-fiber electromyogram in awake adults. Assuming a two-tailed α level of 0.05 and a study power of 0.80, a total of 12 patients were required. We enrolled 16 patients to account for dropouts. Graph Pad Prism statistical software (version 5) (GraphPad Software Inc., San Diego, CA) was used for analysis. Electromyogram data were compared using the Friedman statistic and Dunn multiple comparison tests. Nominal data were compared using chi-square analysis. Cardiorespiratory variables were compared using repeated measures ANOVA and the Student–Newman–Keuls post hoc multiple comparison test. Statistical tests were two-tailed and a P value less than 0.05 was considered statistically significant.

**Results**

Sixteen children were recruited to the study. Of three children excluded, two had poor electromyogram signal quality, and one needed a jaw thrust to maintain airway patency. The median age (range) of children in the study was 3.9 yr (2.0 to 6.9 yr). The median weight (range) was 15.2 kg (12.0 to 26.3 kg). All children underwent hypopneas during recovery. The respiratory rate was significantly greater at 1.5 MAC sevoflurane compared with lighter levels of anesthesia (P = 0.004; table 1), consistent with the general pattern of ventilation observed during inhalational anesthesia. The capnographic waveform remained constant throughout the study, and no child included in the study demonstrated clinical or capnographic evidence of upper airway obstruction. There were no statistically significant differences in peak-expired carbon dioxide concentration or axillary temperature at the three concentrations of sevoflurane studied (table 1). There were no significant increases in heart rate or mean arterial pressure as the depth of sevoflurane anesthesia decreased, indicating that the caudal block was effective in all children (table 2); in no child did the heart rate or mean arterial pressure increase by more than 20% of the baseline value. Surgical and anesthetic durations were 80 ± 28 and 126 ± 28 min, respectively. Data for electromyogram activity at 1.5, 1.0, and 0.5 MAC sevoflurane were acquired at 37 ± 6, 73 ± 9, and 104 ± 15 min after induction of anesthesia, respectively.

**Genioglossus Electromyogram**

Phasic electromyogram activity of genioglossus was noted in four children at 1.5 MAC, five at 1.0 MAC, and six children at 0.5 MAC sevoflurane. All four children demonstrating phasic activity at 1.5 MAC subsequently demonstrated phasic activity at 1.0 MAC and 0.5 MAC. Similarly, all five children demonstrating phasic activity at 1.0 MAC subsequently demonstrated phasic activity at 0.5 MAC. The magnitude of phasic activity increased progressively with decreasing depth of sevoflurane anesthesia. Decreasing the depth of sevoflurane anesthesia from 1.5 to 1.0 MAC increased phasic genioglossal activity by approximately 35% from 2.7 (0 to 4.0 μV) to 3.7 μV (1.8 to 9.4 μV; fig. 1). A further decrease from 1.0 to 0.5 MAC more than doubled phasic activity (median at 0.5 MAC = 8.6 μV [3.2 to 17.6]; P = 0.029 vs. 1.5 MAC). In contrast, the magnitude of tonic activity was unchanged by depth of anesthesia (table 1).

**Palatoglossus Electromyogram**

Phasic electromyogram activity of palatoglossus was noted in 4 children at 1.5 MAC, 6 at 1.0 MAC, and 10 children at 0.5 MAC sevoflurane. All four children demonstrating phasic activity at 1.5 MAC subsequently demonstrated phasic activity at 1.0 MAC and 0.5 MAC. Similarly, all six children demonstrating phasic activity at 1.0 MAC, subsequently demonstrated phasic activity at 0.5 MAC. Overall, the number of children exhibiting phasic activity was significantly greater at 0.5 MAC compared with 1.5 MAC (chi-square [1 df] = 4.9; odds ratio = 3.6; 95% CI, 1.1 to 11.3; P = 0.03). The magnitude of phasic palatoglossus activity progressively increased with decreasing depth of anesthesia in children exhibiting phasic activity, it being 0 μV (0, 5.9) at 1.5 MAC, 2.5 μV (0, 7.0) at 1 MAC, and 6.6 μV (3.2, 15.2) at 0.5 MAC (P = 0.0002 vs. 1.0 and 1.5 MAC; fig. 1). The magnitude of the tonic activity was unchanged by depth of anesthesia (table 1).

Changes in the phasic electromyogram of the palatoglossus with decreasing depth of anesthesia are shown in...
representative images from one patient (fig. 2). No child experienced oxygen desaturation or other complication. There were no complications related to placement of the needle electrodes.

Discussion

The current study evaluated phasic and tonic electromyogram activity of the genioglossus and palatoglossus during recovery from sevoflurane anesthesia in spontaneously breathing children. The results show a progressive increase in genioglossus and palatoglossus phasic inspiratory activity with decreasing depth of sevoflurane anesthesia. Both the proportion of children exhibiting phasic activity, and the magnitude of the phasic activity increased with decreasing end-tidal sevoflurane concentration. These findings support the hypothesis that phasic genioglossus and palatoglossus muscle activity increases during recovery from sevoflurane anesthesia in a dose-dependent manner over the clinical range of sevoflurane concentrations. This increase in upper airway muscle activity may contribute to the decreased propensity of the upper airway to collapse as the depth of sevoflurane anesthesia decreases. In contrast, we found no difference in tonic genioglossus and palatoglossus activity at the different levels of sevoflurane anesthesia, suggesting that tonic activity might be either unaffected or profoundly suppressed even at lighter planes of anesthesia.

Phasic and tonic neurogenic activity in upper airway dilator muscles, such as the genioglossus and palatoglossus, is controlled by hypoglossal motor neurons, and modulated by cortical influences, chemoreceptor drive, mechanoreceptor-mediated reflexes from the upper airway, and lung inflation. Anesthetic agents could in theory influence upper airway muscle activity by various actions at these multiple sites, as summarized by Eikermann.9 For example, anesthetic agents decrease respiratory-related hypoglossal nerve activity,4,5,20 they induce a dose-dependent reduction in peripheral chemoreceptor responses to hypercapnia and hypoxia,21,22 and they abolish pharyngeal mechanoreceptor-mediated reflexes, even at subanesthetic concentrations.8 In an isolated upper airway model, this reflex suppression was found to be age-dependent, with young but not adult dogs being susceptible.23 General anesthesia also decreases lung volume and could potentially alter upper airway wall tension and caliber indirectly through lung–airway interdependence.24,25 In addition, anesthetics may influence electromyographic activity through a vagolytic action,9 by decreasing synaptic neuromuscular transmission,26 or by a direct action on skeletal muscle to decrease contractility.27

Given multiple potential sites of interaction and various age- and agent-dependent anesthetic actions, it is not unexpected that the results of clinical studies have been highly variable.7,9-11 To our knowledge, this is the first study to report a graded increase in genioglossus and palatoglossus muscle activity during recovery from sevoflurane anesthesia in humans, which is consistent with previous studies in animals showing a dose-dependent effect of halothane on phasic genioglossus3 and hypoglossal nerve28 activity. We recently demonstrated in children undergoing magnetic resonance imaging that increasing depth of sevoflurane anesthesia caused a progressive dose-dependent reduction in the caliber of the pharyngeal airway.13 It is our speculation that dose-dependent electromyogram changes, similar to those noted in our current study, could explain the graded reduction in airway dimension seen in our previous study. However,
although there is tacit agreement that suppression of upper airway muscle activity is responsible for anesthesia-induced airway narrowing, although there is tacit agreement that suppression of upper airway muscle activity is responsible for anesthesia-induced airway narrowing,

Other physiologic factors that may influence upper airway caliber and muscle activity include body position, head and neck position, and mandibular position. To control for these factors in the current study, subjects were supine, a standard head position was used, and airway maneuvers, airway instrumentation, mandibular displacement, and continuous positive airway pressure were avoided.

Studies evaluating the effects of general anesthesia on the activity of upper airway muscles have focused almost exclusively on the genioglossus. The reasons are that the genioglossus is considered a major dilator of the upper airway and is easily accessible via intraoral or percutaneous approaches during general anesthesia. Inhibition of genioglossus activity is believed to cause posterior displacement of the tongue, resulting in partial or complete oropharyngeal obstruction. However, it has been shown that the velopharynx may also be an important site of airway obstruction during general anesthesia and sleep. Using a variety of imaging techniques, recent studies show that anesthesia-induced airway obstruction can occur at multiple sites, and in particular, in the velopharynx. The palatoglossus exhibits phasic inspiratory electromyogram activity in awake normal subjects and is prominently involved in moving the soft palate forward, thereby increasing retropalatal patency, and facilitating the nasal route of respiration. The two palatoglossus muscles form the anterior pillars of the palatal arch. They connect the palatal aponeurosis to the sides of the tongue and function to lower the soft palate onto the back of the tongue, thereby enlarging the velopharynx. Our data provide insights into the mechanisms by which velopharyngeal patency may be enhanced during recovery from sevoflurane anesthesia in children.

![Box and whisker plot showing phasic inspiratory genioglossus and palatoglossus activity during recovery from sevoflurane anesthesia.](image1)

Fig. 1. Box and whisker plot showing phasic inspiratory genioglossus (n = 6) and palatoglossus (n = 10) activity during recovery from sevoflurane anesthesia. The horizontal line within the box represents the median activity, the outer horizontal lines of the box are the 25th and 75th quartiles, the horizontal lines of the whiskers are the Tukey inner fences, and the closed circles represent outliers. * P = 0.029 versus 1.5 minimum alveolar concentration (MAC; genioglossus). † P = 0.0002 versus 1.0 and 1.5 MAC (palatoglossus). EMG = electromyogram.

![Representative raw recordings of electromyographic activity of the palatoglossus muscle showing increasing phasic activity during recovery from sevoflurane anesthesia in one child.](image2)

Fig. 2. Representative raw recordings of electromyographic activity of the palatoglossus muscle showing increasing phasic activity during recovery from sevoflurane anesthesia in one child. MAC = minimum alveolar concentration.
Our study has several limitations. First, given the age range of our study population, awake recordings of muscle activity could not be obtained, and therefore, recordings at deeper levels of anesthesia were compared with those at 0.5 MAC. Accordingly, differences in electromyogram activity during recovery from anesthesia might have been underestimated. Second, we did not measure surrogates of airway patency such as tidal volume, inspiratory flow, and airway collapsibility because these techniques depend on the presence of a tight-fitting facemask or instrumentation of the airway, and could introduce varying degrees of mandibular displacement, alterations in upper airway dimension, and/or application of continuous positive airway pressure, all of which have the potential to introduce confounding effects in a highly variable and unpredictable manner. To avoid these confounding factors, we relied on the independent clinical assessment of airway patency by two experienced pediatric anesthesiologists. Each child included in the study demonstrated quiet unobstructed breathing throughout each respiratory cycle. Throughout the study period, the shape of the capnographic waveform remained constant and was consistent with the absence of upper airway obstruction. Despite the apparent lack of clinical signs, subclinical airway obstruction might still have been present, as demonstrated by Keidan et al., who found that the use of continuous positive airway pressure or an oral airway decreased the work of breathing (a measure of upper airway patency), even when partial upper airway obstruction was not clinically apparent. In applying the air-cushioned facemask, we ensured an airtight seal while avoiding mandibular displacement. Although it is possible that we did not capture a true end-tidal carbon dioxide or sevoflurane concentration, we believe this is unlikely. Given that the accuracy of expired sevoflurane concentrations is central to our study, we took several precautions to ensure the accuracy of these data. First, we allowed 15 min for equilibration of inspired alveolar and expired sevoflurane concentrations, before acquisition of electromyogram data. Second, as noted above, we were careful to ensure a secure seal around the air-cushioned mask to avoid leaks and entrainment of room air, while avoiding displacement of the mandible. Third, we also observed that the expired sevoflurane concentration were stable throughout the period of data acquisition. For these reasons, we believe that the data for expired sevoflurane concentration are accurate.

Another limitation is that we did not randomize the sequence of anesthetic concentration, given that we sought to determine the changes in upper airway muscle activity, which occur during recovery from anesthesia. We were primarily concerned with the recovery phase because this is when children are most susceptible to unrecognized upper airway obstruction. The study protocol mimicked the usual course of anesthesia, with higher sevoflurane concentrations during maintenance of anesthesia and lower concentrations toward the end of surgery. In order to randomize the order of anesthetic depth (including 0.5 MAC), the entire study would have to be conducted either before, or after surgery, which would prolong the duration of anesthesia well beyond the surgical time, and could be considered ethically unacceptable. Our methodology minimized the time that children were anesthetized for the study protocol only. Given that the data were acquired in part during surgery, caudal analgesia was used to minimize any effect of varying degrees of surgical stimulation on outcome variables. The efficacy of the caudal block was evaluated on surgical incision and throughout surgery as the depth of anesthesia decreased by monitoring hemodynamic changes. In no child did the heart rate or mean arterial pressure increase by 20% or more of the baseline value, suggesting that the caudal block provided effective analgesia in all children.

Our study has clinical implications. Children, and in particular infants, are especially vulnerable to anesthesia-induced upper airway obstruction because of their small airway dimensions and their relative dependence on neural mechanisms for airway maintenance. Residual anesthesia is believed to be an important cause of postoperative airway obstruction. Our results suggest that the likelihood of airway obstruction decreases as the end-tidal concentration of the volatile anesthetic decreases; however, it is not known at what specific anesthetic depth during recovery is the airway no longer susceptible to obstruction. Increasingly, a role for the soft plate is being recognized as important in maintaining airway patency. Although studies in anesthetized patients are lacking, evidence from patients with sleep apnea indicates that the palatoglossus is important in maintaining the nasal route of respiration, and studies on children suggest that palatoglossus activity is crucial in maintaining upper airway patency. Our results indicate that sevoflurane alters the activity of both palatoglossus and genioglossus, suggesting that anesthesia-induced obstruction may occur at multiple sites in the upper airway.

In summary, the current study suggests that the phasic electromyogram activity of the genioglossus and palatoglossus increases in a dose-related fashion during recovery from anesthesia with sevoflurane. These results suggest that recovery of upper airway muscle activity may contribute to the decreased propensity of the upper airway to collapse as the depth of sevoflurane anesthesia decreases. Suppression of genioglossus and palatoglossus muscle activity may be contributory to airway obstruction at deeper planes of anesthesia.

References

Anesthesiology 2013; 119:562-8