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REPORTS OF ORIGINAL INVESTIGATIONS

Sevoflurane and desflurane protect cholinergic-induced bronchoconstriction of hyperreactive airways in rabbits

Le sévoflurane et le desflurane protègent les voies aériennes hyperréactives du lapin contre la bronchoconstriction induite par des agents cholinergiques

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Abstract

Purpose *The potential of desflurane to alter respiratory mechanics in the presence of bronchial hyperresponsiveness (BHR) is still a subject of debate. Accordingly, we evaluated the bronchoprotective potential of desflurane compared with sevoflurane following cholinergic lung constriction in rabbits with normal and hyperreactive airways.*

Methods *The input impedance of the respiratory system (Zrs) was measured during midazolam-based anesthesia before and during intravenous infusions of increasing doses of methacholine (MCh). The rabbits in the control group (Group C) were then randomized to receive either sevoflurane 1 MAC followed by desflurane 1 MAC or vice versa, whereas ovalbumin-sensitized rabbits received sevoflurane followed by desflurane (Group S-SD) or vice versa (Group S-DS). Baseline Zrs measurements and the MCh provocations were repeated under the maintenance of each volatile agent. Airway resistance (Raw), tissue damping (G), and elastance data were obtained from Zrs by model fitting.*

Results *Similar bronchoprotective effects of sevoflurane and desflurane against MCh-induced bronchoconstriction were observed independently of the severity of the bronchospasm and the presence of BHR. With sevoflurane, the decreases in Raw ranged from 22 (8.8)% to 44 (12)%, and with desflurane, they ranged from 22 (8.7)% to 50 (12)%. The increases in G reflecting the enhanced ventilation heterogeneities in the lung periphery were not affected by the volatile agents.*

Conclusions *If the contractile stimulus is cholinergic in origin, sevoflurane and desflurane exert similar bronchoprotective potentials to act against lung constriction independent of the presence of BHR. These volatile anesthetics otherwise lack a potential to improve the enhanced ventilation heterogeneities that develop particularly in the presence of BHR.*

Résumé

Objectif *Le potentiel de desflurane à altérer r la mécanique respiratoire en présence d'hyperréactivité bronchique (HRB) est encore sujet à controverse. C'est pourquoi nous avons évalué le potentiel de protection bronchique du desflurane par rapport au sévoflurane à la suite d'une constriction pulmonaire cholinergique chez des lapins présentant des voies aériennes normales et hyperréactives.*

Méthode *L'impédance dusystème respiratoire (Zrs) a été mesurée pendant une anesthésie réalisée à l'aide de*

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midazolam avant et pendant des perfusions intraveineuses de doses croissantes de méthacholine (MCh). Les lapins du groupe témoin (groupe C) ont ensuite été randomisés à recevoir soit 1 MAC de sévoflurane suivi de 1 MAC de desflurane ou vice versa, alors que les lapins sensibilisés à l'ovalbumine ont reçu du sévoflurane suivi de desflurane (groupe S-SD) ou vice versa (groupe S-DS). Les mesures de base de la Zrs et les provocations à la MCh ont été répétées pendant le maintien de chaque agent volatil. Les données concernant la résistance des voies aériennes (Raw), la composante résistive (G) et l'élastance du système respiratoire ont été obtenues de la Zrs par ajustement du modèle.

Résultats *Nous avons observé des effets bronchoprotecteurs semblables contre la bronchoconstriction induite par la MCh avec le sévoflurane et le desflurane, indépendamment de la gravité du bronchospasme et de la présence d'HRB. Avec le sévoflurane, les réductions de Raw se situaient entre 22 (8,8) % et 44 (12) %; avec le desflurane, elles se situaient entre 22 (8,7) % et 50 (12) %. Les augmentations de G, reflétant une augmentation de l'inhomogénéité ventilatoire en périphérie des poumons, n'ont pas été affectées par les agents volatils.*

Conclusion *Si le stimulus contractile est d'origine cholinergique, le sévoflurane et le desflurane exercent des potentiels de bronchoprotection semblables contre la constriction pulmonaire, indépendamment de la présence d'HRB. Néanmoins, ces agents anesthésiques volatils ne possèdent pas d'autre potentiel pour améliorer l'augmentation de l'hétérogénéité ventilatoire qui se manifeste particulièrement en présence d'HRB.*

Bronchospasm is one of the most challenging of the adverse respiratory events that occur during anesthesia, and it contributes greatly to perioperative morbidity.[1] This complication is manifested in a severe occasionally life-threatening form, particularly in the presence of respiratory diseases with associated bronchial hyperreactivity (BHR). As a consequence of the increasing impact of allergens worldwide, anesthesiologists are confronted ever more frequently to manage patients with chronic respiratory diseases associated with BHR.

The autonomic nervous system is of considerable importance in the development of bronchospasm that is associated with BHR. The parasympathetic nervous system is primarily involved in the vagally induced lung constriction via stimulation of the muscarinic receptors by acetylcholine.[2] Studies performed in various animal models of chronic pulmonary diseases provide increasing evidence that alterations in the non-adrenergic non-cholinergic autonomic nervous system (NANC) may also play an important role in the development of BHR via liberation of proinflammatory mediators that modulate airway reactivity.[3,4] Differences in the actions of these pathways were highlighted by demonstrating that cholinergic stimulation acting on the muscarinic receptors provokes primarily a central airway constriction, while allergen challenge induces adverse changes in the lung periphery.[5]

Among the anesthetic options for the management of patients with BHR, volatile anesthetics are usually regarded as first-line drugs for maintenance of anesthesia. Extensive investigations have led to consistent conclusions on the beneficial action of sevoflurane in the prevention and/or treatment of bronchospasm by counteracting the cholinergic stimulation of the airway smooth muscle.[6-9] However, there have been conflicting results on the potential of desflurane to alter the airway tone with various previous studies demonstrating a reduction of bronchoconstriction[6,10-15] or no effect on the basal[16] or elevated airway tone.[8,17,18] Since most of the adverse respiratory events are encountered in the presence of BHR, this discrepancy may be attributed to the different actions of desflurane on normal and allergically sensitized airways. Bronchoconstriction following exposure to an allergen is modulated primarily by an imbalance between the inhibitory and excitatory NANC pathways. Since these pathways play a major role in regulating the lung periphery via various neuropeptides, and since desflurane has been shown to stimulate the excitatory NANC activity,[19] it is possible that desflurane enhances the bronchoconstriction occurring in the lung periphery.

The present study was therefore designed to test the hypothesis that desflurane is able to prevent bronchoconstriction similarly to sevoflurane even in allergically sensitized airways if the triggering mechanism leading to the bronchospasm is cholinergic in origin. The validity of this hypothesis was evaluated by measuring the changes in the airway and tissue mechanics separately in an established model of BHR. The separate assessment of the changes in the flow resistance of the airways (Raw) and the viscoelastic properties of the respiratory tissues (G: tissue damping; H: tissue elastance) from the low frequency input impedance of the respiratory system (Zrs) may contribute to characterize the potential preventive effects of these volatile agents against an altered airway tone resulting from distinct cholinergic stimulation.

Methods

Animals, sensitization

Following approval of the study protocol by the Ethics Committee for Experimental Research of the University of Geneva (registration number 08-47) and the Animal Welfare

Committee (Office Véterinaire Cantonal de Genève, registration number 1051/3403/1), studies were performed on three groups of adult New Zealand white rabbits weighing 2-2.5 kg. Group C ($n = 7$) comprised naïve animals, while the rabbits in Groups S-SD ($n = 10$) and S-DS ($n = 8$) underwent active sensitization to ovalbumin (OVA). The sensitization procedure involved intraperitoneal injections of OVA 0.1 mg and aluminium hydroxide 10 mg on days 0 and 14. One week later, daily exposure to aerosolized OVA 10 $mg \cdot mL^{-1}$ was administered for a 20-min period for five consecutive days. Experiments were performed one day after administration of the final OVA aerosol.

Anesthesia and animal preparations

Anesthesia was induced in all animals by the injection of thiopental sodium 25 $mg \cdot kg^{-1}$ *iv* (Nesdonal, Rhone-Poulenc-Rohrer, Paris, France) via a 22G catheter introduced into the ear vein, and anesthesia was maintained by an intravenous infusion of benzodiazepine midazolam hydrochloride 0.2 $mg \cdot mL^{-1}$ at a rate of 0.1-0.2 $mg \cdot kg^{-1} \cdot hr^{-1}$. The rabbits were then tracheotomized, and a 3.5-mm-internal diameter polyethylene cannula was inserted into the distal trachea. They were mechanically ventilated with room air (Model 683, Harvard Apparatus, South Natick, MA, USA), while a tidal volume of 7-9 $mL \cdot kg^{-1}$, a frequency of 40 Hz, and a positive end-expiratory pressure of 2.5 cm H_2O were maintained. Fentanyl was infused at a rate of 2 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ *iv* to ensure an adequate level of analgesia. Muscle relaxation was achieved with atracurium besylate 2.5 $mg \cdot mL^{-1}$ at a rate of 0.5-1.0 $mg \cdot kg^{-1} \cdot hr^{-1}$. Anesthetic agents were administered by an infusion pump via the marginal ear vein. Arterial blood samples were analyzed radiometrically (Acid-Base Laboratory model 505, Copenhagen, Denmark), and the parameters of mechanical ventilation were adjusted to maintain normal gas exchange if necessary. The concentrations of end-tidal O_2 and CO_2 were monitored throughout the study (Ultima™, Datex/Instrumentarium, Helsinki, Finland). Airway pressures were measured continuously with a calibrated pressure transducer (Validyne DP45, Northridge, CA, USA).

The carotid artery was cannulated for continuous arterial blood pressure monitoring (Honeywell, model 156 PC 06-GW2, Zurich, Switzerland), and the jugular vein was also cannulated for methacholine (MCh) delivery. Rectal temperature was monitored with a temperature sensor (Thermalert model TH-8, Physitemp, Clifton, NJ, USA) and was maintained at 39.3 (0.5)°C with a heating pad (Miostar, Zurich, Switzerland). Airway and arterial pressures, heart rate, and rectal temperature were displayed and stored on a computer at a sampling rate of 50 Hz via an analogue/digital interface converter (Biopac Systems, Inc., Santa Barbara, CA, USA).

Forced oscillatory measurements

The measurement set up used to collect input impedance data for the total respiratory system (Zrs) was described in detail previously.[20] Briefly, the endotracheal tube was switched to a loudspeaker-in-box system at end-expiration. The loudspeaker generated a small-amplitude pseudorandom signal containing 15 noninteger multiple components in the frequency range 0.5-21 Hz through a 100-cm-long 5-mm-internal diameter polyethylene wave tube. Lateral pressures were measured at the loudspeaker (Pbox) and the tracheal end (Ptr) of the tubing with two identical miniature pressure transducers (ICS model 33NA002D). The Pbox and Ptr signals were low-pass filtered and digitized by an analogue-to-digital board of a computer at a sampling rate of 128 Hz. The pressure-transfer functions Pbox/Ptr were computed by fast Fourier transformation from the 8-s recordings by using a four-second time window and 95% overlapping. The Zrs was calculated as the load impedance of the wave tube.[20]

Separation of airway and tissue mechanical properties

A well-established and verified[20,21] linear model containing a frequency-independent airway resistance (Raw) and inertance in series with the tissue damping (G) and elastance (H) of a constant-phase tissue compartment[22] was fitted to the Zrs spectra by minimizing the weighted difference between the measured and the modelled impedance data:

$$\mathrm{Zrs} = \mathrm{Raw} + \mathrm{j}\omega\mathrm{Iaw} + (\mathrm{G} - \mathrm{jH})/\omega^{\alpha}$$

where j is the imaginary unit, ω is the angular frequency, and $\alpha = 2/\pi \arctan(\mathrm{H/G})$.

Study protocol

The experimental timeline and the protocol groups are shown in Fig. 1. When stable respiratory mechanical and systemic hemodynamic conditions had been established, 4-6 Zrs recordings were collected in all animals to establish the baseline. Increasing doses of MCh were then infused through the jugular venous line at rates of 2.5, 5, and 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$. A period of six minutes was allowed after the onset of each MCh perfusion, and the collection of Zrs was started at one-minute intervals thereafter until a steady-state constriction had developed. Next, four Zrs data epochs were collected at each infusion level under the steady-state conditions (i.e., Raw values were within 5%) in order to assess the lung responsiveness during intravenous anesthesia. Depth of anesthesia was then altered in accordance with the group allocation of the animals: the rabbits in Group C were assigned randomly to receive

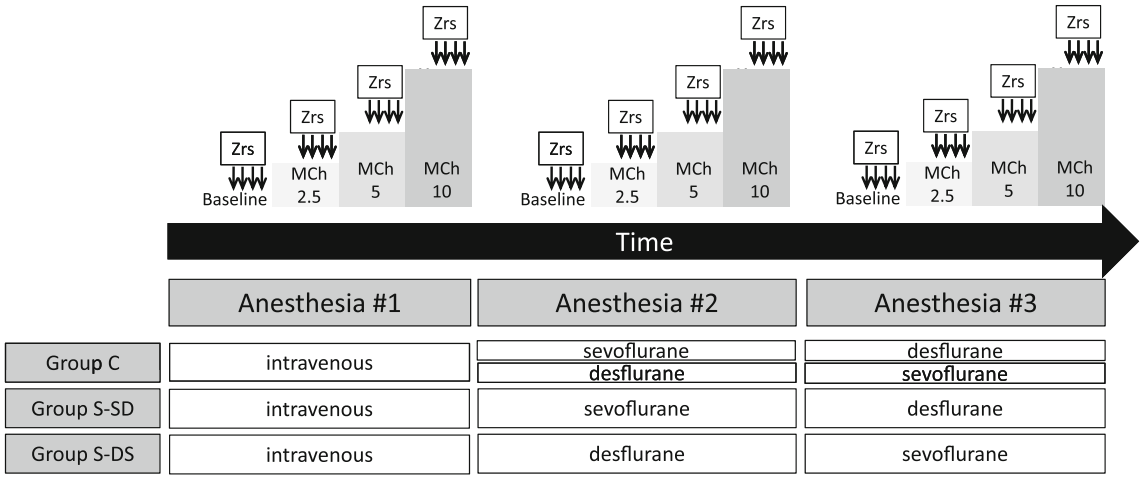

Fig. 1 Experimental timeline and protocol groups

either 3.7% sevoflurane ($n = 3$) or 8.9% desflurane ($n = 4$) first (the concentration of anesthetic volatile agent corresponding to 1 MAC)[23]; the animals in Group S-SD received sevoflurane first followed by desflurane, whereas the reverse sequence of administering the volatile agents was used for the rabbits in Group S-DS. The random sequencing of the volatile agents was done to minimize the possible biasing effect of measurement times and the interactions between them.

After establishment of a steady-state concentration of the first volatile anesthetic agent, a five-minute period was allowed for the agent to exert its effect and a series of Zrs measurements was then performed. The dose-response curve for increasing doses of intravenous MCh was next recorded in the presence of the first volatile agent. After completion of these recordings, the first volatile agent was discontinued and maintenance of anesthesia was switched to the second volatile agent. When the clearance of the first volatile anesthetic had been attained (as confirmed by exhaled gas analysis) and a steady-state concentration with the second volatile anesthetic had been established (approximately 15 min), another set of Zrs measurements, including recordings of the baseline and during MCh infusion, was obtained in the same manner as earlier.

After completion of the protocol during intravenous anesthesia and with both volatile agents, the animals in the sensitized groups (Groups S-SD and S-DS) received an intravenous bolus of OVA 1 mg to validate the efficiency of the allergen of sensitization.

Statistical analysis

Individual data points and group mean averages with standard deviation values are reported.[24] A logarithmic transformation was applied to normalize the variables before statistical testing. Three-way repeated measures of analysis of variance (ANOVA) was used with within-subject factors of anesthetic agents (intravenous sevoflurane and desflurane) and MCh dose, and between-subject factor of sensitization (control *vs* sensitized) to establish the effects of the volatile anesthetics and OVA-sensitization on the lung responsiveness (Fig. 2). This statistical method was used to test the hypotheses that 1) the presence of volatile agents affect the respiratory mechanical parameters; 2) the affinities of the two volatile agents (sevoflurane and desflurane) are identical in protecting cholinergic-induced bronchoconstriction; and 3) these affinities are independent of the OVA-sensitization. Another three-way repeated measures ANOVA was applied with the volatile agent (sevoflurane and desflurane) and the MCh dose as within-subject variables and the experimental group (Group C, S-SD, and S-DS) as the between-subject variable to test the hypothesis that the magnitude of bronchodilation potential of the volatile agents were not affected by the degree of the airway tone (Fig. 3). In case of significant effects, pairwise comparisons of interest were performed based on estimated marginal means to compare the lung mechanical parameters under different conditions. Holm's step-down method was used to correct *P* values of pairwise comparisons. The statistical tests were performed with a SPSS® statistical software package version 17 (IBM Corporation, Somers, NY, USA). In each test, all reported *P* values are two-sided.

Results

The effectiveness of the sensitization procedure was confirmed at the end of the experiment. The injection of the allergen into the sensitized animals led to a heterogenous

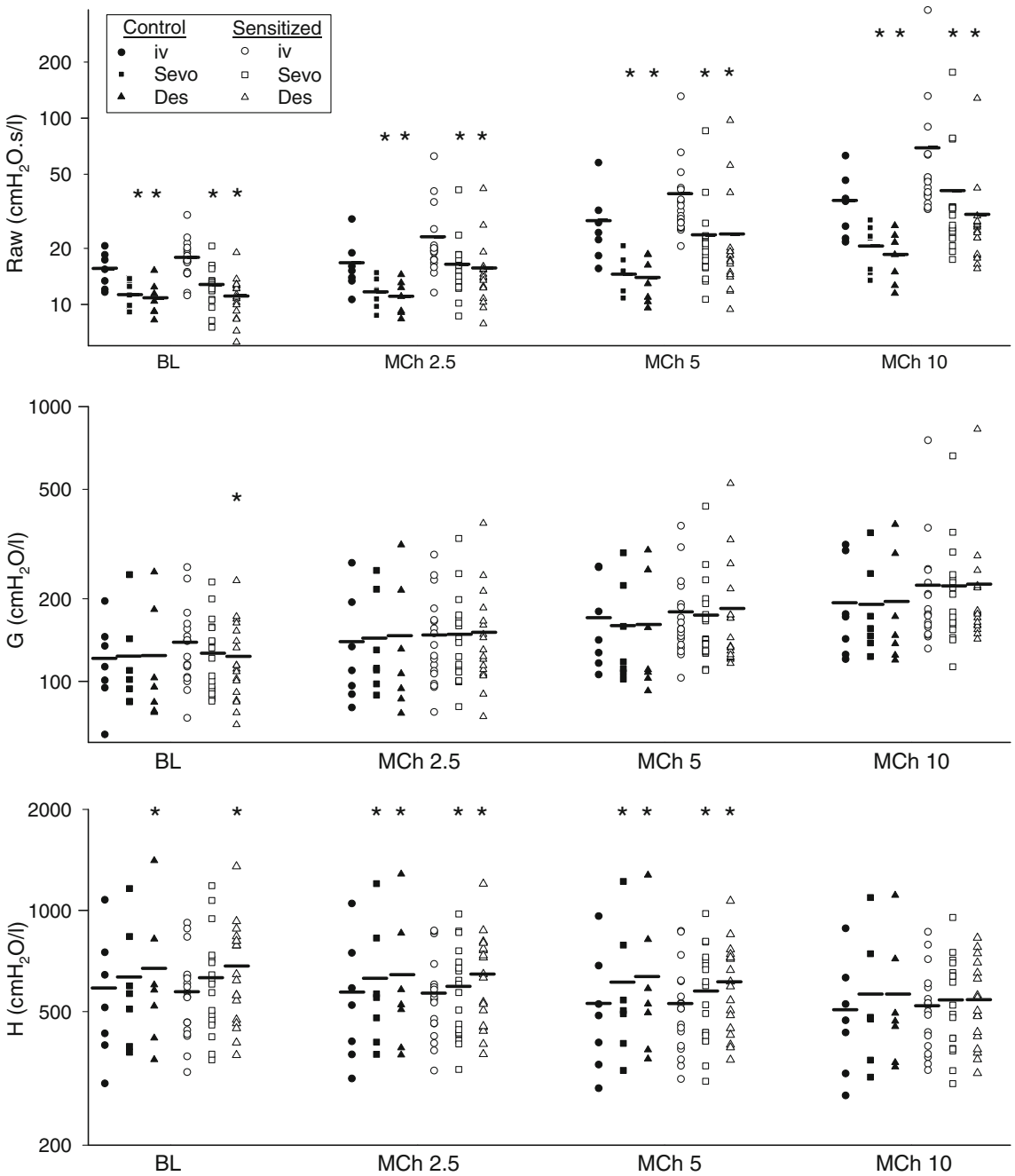

Fig. 2 Individual (small symbols) and group mean (SD) values (large symbols) of airway resistance (Raw), tissue damping (G), and elastance (H) under baseline conditions (BL) and during infusions of increasing doses of methacholine (MCh) 2.5-10 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Closed symbols: data obtained in the naïve animals (Group C); open symbols: pooled data obtained in the ovalbumin-sensitized animals (Groups S-SD and S-DS). Data were obtained during midazolam-based intravenous anesthesia (circles) and during inhalation of sevoflurane (squares) or desflurane (triangles). *Statistical significance *vs* the corresponding value obtained during intravenous anesthesia. Horizontal lines: mean values

bronchoconstriction (increases in Raw, 56-513%; $P = 0.0001$) and significant increases in G (15-202%; $P = 0.005$), while H remained unaffected (−26-33%; $P = 0.94$). Ovalbumin induced similar lung responses in Groups S-SD and S-DS ($P = 0.14$ and $P = 0.66$ for Raw and G, respectively, data not shown). Complete recovery of all mechanical parameters was observed following each MCh challenge with no statistically significant changes ($P = 0.12$, $P = 0.1$, and $P = 0.28$ for Raw, G, and H, respectively).

Changes in the airway and tissue parameters during anesthesia with intravenous or inhalation agents in the

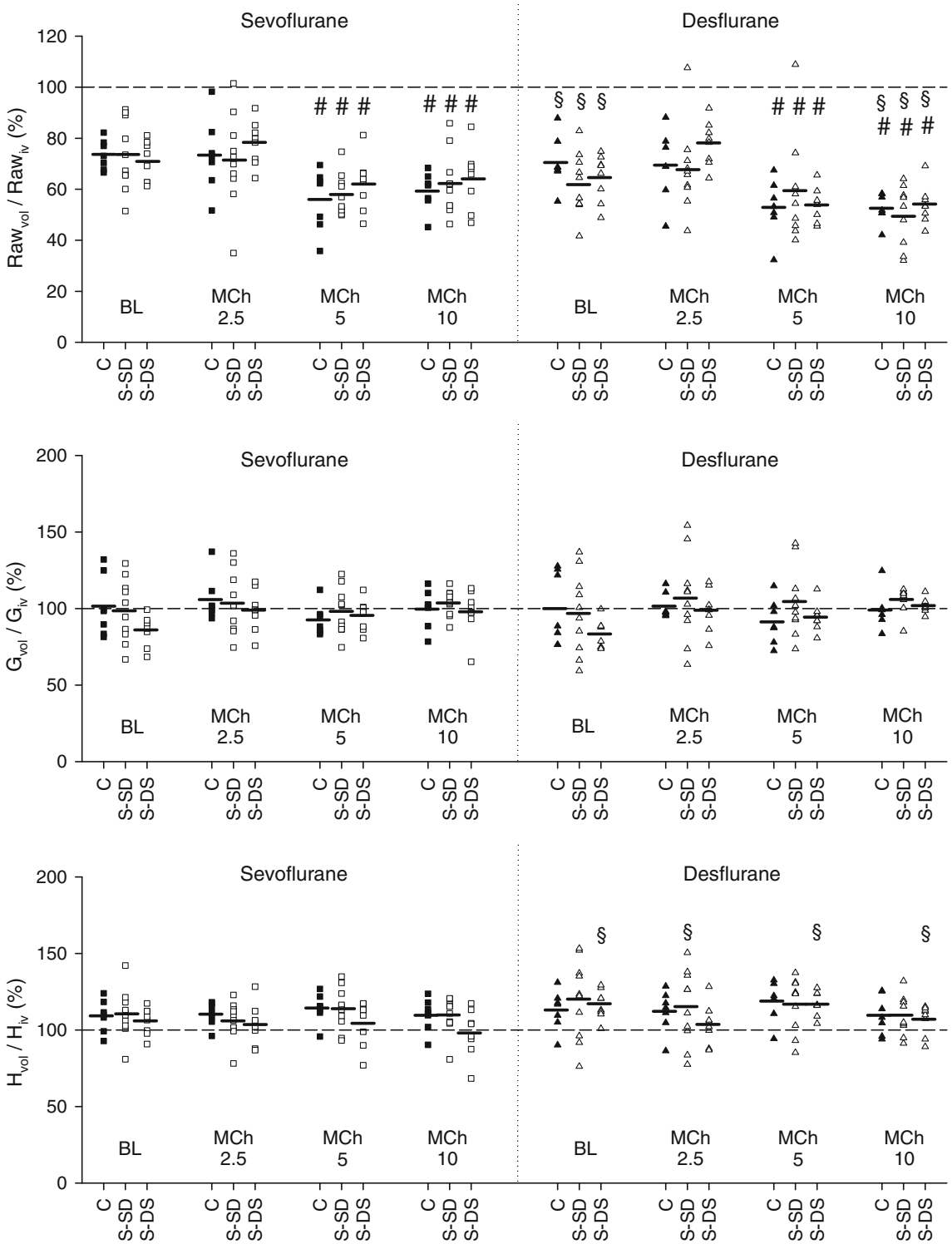

Fig. 3 The percentage ratio in the airway resistance (Raw), tissue damping (G), and elastance (H) obtained during the inhalation agents relative to those observed during the midazolam-based intravenous anesthesia. Closed symbols: data obtained in the naïve animals (Group C); open symbols: data obtained in the ovalbumin-sensitized animals (Groups S-SD and S-DS). Squares: data obtained during inhalation of sevoflurane relative to intravenous anesthesia; triangles: data obtained during inhalation of desflurane to intravenous anesthesia. #Statistical significance *vs* the corresponding baseline; §Statistical significance between the volatile agents within Group S-DS or Group S-SD. Horizontal lines: mean values

naïve and OVA-sensitized animals are illustrated in Fig. 2. The statistical analyses revealed that the MCh dose and the mode of anesthesia management affected the Raw values significantly ($P < 0.001$). The between-subject effect was not significant ($P = 0.22$, $P = 0.56$, and $P = 0.57$ for Raw, G, and H, respectively), suggesting that sensitization did not affect the parameter values. Under baseline conditions, both inhalation anesthetics decreased the airway tone significantly ($P < 0.001$), whereas desflurane increased the respiratory elastance (H) in both the naïve ($P = 0.005$) and the sensitized animals ($P = 0.001$). Methacholine induced dose-dependent increases in Raw; these changes were markedly greater in the sensitized animals, demonstrating the presence of BHR ($P = 0.001$). The analysis revealed strong interactions between the administration of the inhalation agents and the magnitude of the MCh-induced increases in Raw ($P = 0.001$), revealing that the elevations in Raw were inhibited both by sevoflurane and by desflurane, independently of the presence of BHR. In contrast, the ANOVA did not show evidence of a significant interaction between the effects of MCh on G and the anesthesia technique ($P = 0.72$), indicating that the anesthetic agents had no appreciable effects on the MCh-induced increases in G.

The ratio of the airway and tissue mechanical parameters obtained in response to the inhalation agents relative to those observed during the intravenous anesthesia are shown in Fig. 3. The Raw ratios were affected significantly by the presence of the different volatile anesthetic agent (sevoflurane or desflurane; $P < 0.001$). Furthermore, significant interaction was observed between the presence of the different volatile agents and the MCh ($P = 0.047$). Both volatile agents exhibited fairly similar bronchodilation potentials, independently of the level of the airway tone, i.e., the decreases in Raw in the presence of sevoflurane and desflurane were around 30-40% during maintenance of a basal airway tone (corresponding to an airway resistance of around 15 cm H_2O.s/l), and this inhibition was fairly similar when the airway tone was markedly elevated (corresponding to an airway resistance of about 70 cm H_2O.s/l). Furthermore, the protective potential of the inhalation agents was not influenced by the presence of BHR following allergic sensitization ($P = 0.76$). Regarding the role of the sequence of administration of the volatile anesthetics (i.e., whether sevoflurane or desflurane was given first or second), we did not observe any difference in the bronchoprotection potentials of sevoflurane and desflurane ($P = 0.8$). However, partitioning of the airway and tissue changes revealed that the inhalation agents displayed variability in their abilities to influence the different lung compartments, with a more pronounced bronchoprotective effect of desflurane, whereas sevoflurane was able to reverse the deleterious effects of desflurane on the respiratory elastance.

Discussion

The results of the present study show that sevoflurane and desflurane are similar in their abilities to prevent bronchoconstriction of cholinergic origin occurring in allergically sensitized airways. The bronchoprotective potential of both volatile anesthetics was largely independent of the degree of airway smooth muscle contraction but limited in its extent. Separate assessment of the airway and respiratory tissue mechanical changes revealed that both inhalation agents act mainly on the central conducting airways, whereas they exhibit only minor affinities to alter the mechanical parameters related to the lung periphery.

To explore whether the effects of inhalation agents depend on the presence of BHR, we adopted a well-validated sensitization procedure with OVA to produce allergic inflammation and subsequent BHR in rabbits.[25,26] Independently of the anesthetic management, the presence of airway hyperresponsiveness to MCh that mimics cholinergic stimuli was confirmed in the present study. Additionally, consistent with previous results, all animals in the present study exhibited a response to OVA, with marked increases in all resistive mechanical parameters, confirming that the allergic sensitization was the major cause of BHR.

The present study focused on one specific pathway triggering lung constriction, as is commonly observed during anesthesia following airway instrumentation and endotracheal intubation. Since this adverse respiratory event is controlled by activation of the cholinergic autonomous nervous system, we applied a common stimulus, MCh, to activate the muscarinic receptors located primarily in the central airways. The magnitude and the pattern of the lung response to MCh were similar to those previously measured in naïve and sensitized animals with a similar technique, with the dominance of Raw elevations associated with parallel increases in G and minor changes in H.[5,18,25,27] The increases in Raw proved to be related to the decrease in the cross-sectional area of the central conductive airways. These changes were similarly prevented by the administration of either of these volatile anesthetics, demonstrating that these agents have a marked potential to block a central airway constriction that develops following cholinergic stimulation. Moreover, the increases in G observed during MCh infusions with fairly constant H can be attributed to the enhanced ventilation heterogeneities that develop in the lung periphery, which was consistently confirmed in previous studies by using foreign gases and imaging techniques.[5,21] In this scenario, neither of the volatile anesthetics had a detectable effect on the elevated G. Despite the strong bronchoprotective action of these agents on the central airway tone, this finding suggests that they have no affinity to prevent a heterogeneous deterioration of the peripheral airway function. Since we observed

a complete recovery in all mechanical parameters following each MCh challenge, no residual effect of MCh may have biased our results.

Desflurane is often recommended for the maintenance of anesthesia because of its low blood solubility which allows rapid recovery.[28] However, despite its beneficial pharmacodynamic profile, the interaction of desflurane with the respiratory system is still a subject of debate. Evidence has accumulated recently which suggests that this debate is related to the distinct effect of desflurane on the neural pathways regulating the airways.[19,29] The bronchial smooth muscle tone is regulated by two different neural pathways, i.e., the cholinergic parasympathetic efferent system and the NANC pathway activated by stimulation of the afferent bronchopulmonary sensory C fibres.[30,31] The allergic inflammation that developed in the sensitized animals in the present study was likely to affect both regulatory mechanisms.[31] Although the disturbance in the NANC pathway was shown to be responsible for the deleterious effects of desflurane by further elevating the airway tone,[19,29] our data demonstrate the beneficial properties of this agent if the triggering mechanism leading to the bronchospasm is cholinergic in origin. This finding may explain the controversy in the literature related to the fact that desflurane exhibits beneficial bronchoprotective properties when the airway constriction results from cholinergic activation,[6,10,11,15] whereas it may worsen the airway constriction if this develops via the NANC pathway.[19,29]

A noteworthy aspect of our findings is the similarity in magnitude of the bronchoprotective properties of sevoflurane and desflurane independently of the level of airway constriction and the presence or not of allergic airway inflammation (Fig. 3, top). Consistent with previous results obtained in isolated perfused rat lungs,[15] both inhalation agents inhibited basal bronchial tone by around 30-40%. This clinically relevant magnitude of inhibition persisted if the Raw was further increased by more than threefold following infusion of the highest dose of MCh. This suggests the presence of a threshold in the degree of bronchoprotection by the volatile anesthetics against the central airway constriction induced via cholinergic activation. These properties of sevoflurane and desflurane are manifested in similar proportional decreases in Raw in animals with normal and sensitized airways. While the airway tone enhancement following cholinergic stimulation can be prevented effectively, even in the presence of BHR, the existence of this phenomenon suggests that administration of the volatile agents would have the potential to restore airway tone to a certain extent.

Whereas sevoflurane is indicated for both induction and maintenance of general anesthesia, we recognize that, due to moderate pungency, desflurane is indicated for maintenance of anesthesia only. Some clinicians use sevoflurane for the induction period then switch to desflurane for maintenance of anesthesia. The present study demonstrates that the sequence of administration of these volatile agents is immaterial as regards the airway tone and that the extent of bronchoprotection is determined primarily by the presence of a volatile agent rather than the specific agent applied, no matter what the sequence of administration.

The apparent controversy between the present findings with desflurane and those where airway irritation was reported previously in the presence of enhanced airway tone[8,32] ensues primarily from the differences in the initial conditions before administering this volatile agent. Airway constriction was present prior to desflurane inhalation both in children with susceptible airways[8] and in OVA-sensitized guinea pigs,[18] indicating that desflurane may exert its deleterious effects on the airway tone only if it was already compromised before the onset of the volatile agent. In addition, initially impaired airway and respiratory tissue mechanics were a consequence of a complex mechanism involving both the cholinergic and NANC pathways in children with susceptible airways.[8] The deleterious effect of desflurane under this scenario further confirms that this volatile agent exerts its irritation potential via stimulation of the NANC pathway.

In summary, the present study has demonstrated the similar bronchoprotective potentials of sevoflurane and desflurane against lung constriction induced by activation of the cholinergic pathway. This ability was independent of the presence or not of allergic inflammation in the airways and the subsequent development of BHR. The severity of the lung constriction induced by different levels of MCh provocation did not influence the degree of bronchoprotection exerted by the volatile agents studied. When using these agents in clinical practice, our findings suggest that clinicians should be aware that these agents are unable to counteract an enhanced airway tone completely, and they have no beneficial profile against the resulting ventilation inhomogeneities in the lung periphery that develop, particularly in the presence of airway hyperresponsiveness.

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Competing interests None declared.

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