Laboratory Investigation

Tracheobronchial consequences of the use of heat and moisture exchangers in dogs

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Purpose: To determine the effect of heat and moisture exchange (HME) on the tracheobronchial tree (TBT) using a unidirectional anesthesic circuit with or without CO_2 absorber and high or low fresh gas flow (FGF), in dogs.

Methods: Thirty-two dogs were randomly allocated to four groups: G1 (n=8) valvular circuit without CO_2 absorber and high FGF (5 $L \cdot min^{-1}$); G2 (n=8) as G1 with HME; G3 (n=8) circuit with CO_2 absorber with a low FGF (1 $L \cdot min^{-1}$); G4 (n=8) as G3 with HME. Anesthesia was induced and maintained with pentobarbital. Tympanic temperature (TT), inhaled gas temperature (IGT), relative (RH) and absolute humidity (AH) of inhaled gas were measured at 15 (control), 60, 120 and 180 min of controlled ventilation. Dogs were euthanized and biopsies in the areas of TBT were performed by scanning electron microscopy.

Results: The G2 and G4 groups showed the highest AH (>20 $mgH_2O \cdot L^{-1}$) and G1 the lowest (< 10 $mgH_2O \cdot L^{-1}$) and G3 was intermediate (< 20 $mgH_2O \cdot L^{-1}$) ($P < 0.01$). There was no difference of TT and IGT among groups. Alterations of the mucociliary system were greatest in G1, least in G2 and G4, and intermediate in G3.

Conclusion: In dogs, introduction of HME to a unidirectional anesthetic circuit with/without CO_2 absorber and high or low FGF preserved humidity of inspired gases. HME attenuated but did not prevent alterations of the mucociliary system of the TBT.

Objectif : Déterminer, chez des chiens, l'effet de l'échange de chaleur et d'humidité (ECH) sur l'arbre trachéobronchique (ATB) en utilisant un circuit anesthésique unidirectionnel avec ou sans absorption de CO_2 et un haut ou bas débit de gaz frais (DGF).

Méthode : Trente-deux chiens ont été répartis au hasard en quatre groupes : G1 (n=8), un circuit à valve sans absorption de CO_2 et avec un haut DGF (5 $L \cdot min^{-1}$); G2 (n=8), comme G1 avec ECH; G3 (n=8), un circuit avec absorption de CO_2 et un bas DGF (1 $L \cdot min^{-1}$); G4 (n=8), comme G3 avec ECH. L'anesthésie a été induite et maintenue avec du pentobarbital. La température tympanique (TT), la température des gaz inhalés (TGI), l'humidité relative (HR) et absolue (HA) des gaz inhalés ont été mesurées après 15 (témoin), 60, 120 et 180 min de ventilation contrôlée. Les chiens ont été sacrifiés et des biopsies de l'ATB ont été réalisées par microscopie électronique à balayage.

Résultats : Les groupes G2 et G4 ont affiché les plus hauts taux d'HA (>20 $mgH_2O \cdot L^{-1}$), G1 avait le plus bas taux (< 10 $mgH_2O \cdot L^{-1}$) et G3 était intermédiaire (< 20 $mgH_2O \cdot L^{-1}$) ($P < 0,01$). Il n'y a pas eu de différence intergroupe concernant la TT et la TGI. Les modifications du système mucociliaire ont été plus importantes dans le G1, moindres dans les G2 et G4 et intermédiaires dans le G3.

Conclusion : L'introduction, chez des chiens, d'un ECH à un circuit anesthésique avec ou sans absorption de CO_2 et avec un haut ou bas DGF a préservé l'humidité des gaz inhalés. L'ECH a diminué, mais n'a pas empêché, les modifications du système mucociliaire de l'ATB.

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URING respiration, inhaled air is heated and humidified when passing through the nose and upper airway, reaching the alveoli at body temperature (37°C) with 100% relative humidity and approximately 44 $mgH_2O \cdot L^{-1}$ absolute humidity. During expiration, heat and moisture are conserved by the upper airway and nose to minimize these losses from the lower airways.[1,2]

When tracheal intubation or tracheostomy is performed, this counter-current mechanism is partly bypassed and ventilation with dry (i.e. < 5% relative humidity) and cold medical gases produces loss of water from the respiratory tract, unless appropriate means of humidification and heating are used.[2,3] Failure to achieve and maintain adequate humidification may predispose patients to airway damage, such as destruction of cilia and mucus glands, decrease in surfactant and ciliary transport.[3-8]

During anesthesia, ventilator systems are frequently equipped with circle systems with carbon dioxide absorbers, that have inherent humidifying properties as a result of rebreathing of expired humidity and of the production of water in the CO_2 absorber, but data concerning the level of absolute humidity from studies with rebreathing system are contradictory.[9,10]

Heat and moisture exchangers (HME) placed between the endotracheal tube and the ventilation circuit conserve heat and moisture during expiration, mixing expired air with the cool, dry gases inspired by the patient.[10,11]

The aim of the present investigation, in dogs, was to determine the effect of HME on the tracheobronchial tree assessed by scanning electron microscopy, using a unidirectional anesthetic circuit with or without CO_2 absorber and high or low fresh gas flow.

Methods

The study was approved by the University Ethics Commission for Research in Animals. Thirty-two mongrel dogs, of both sexes, weighing 15 - 20 kg were used. They were considered healthy after clinical examination and normal red blood cell count. Before induction of anesthesia, the dogs were randomly allocated, by opening a sealed envelope, to one of four groups, as follows: G1 (n=8) a unidirectional anesthesia system without CO_2 absorber with a high fresh gas flow of 5 $L \cdot min^{-1}$ (2 $L \cdot min^{-1}$ O_2 and 3 $L \cdot min^{-1}$ air); G2 (n=8) as G1 with an HME; G3 (n=8) a circuit with CO_2 absorber was used with a low fresh gas flow of 1 $L \cdot min^{-1}$ (0.4 $L \cdot min^{-1}$ O_2 and 0.6 $L \cdot min^{-1}$ air); G4 (n=8) as G3 with an HME. In G2, the hydrophobic HME (Hygrobac S, from DAR, Italy) was placed between the tracheal tube and the unidirectional valve, and in G4, between the tracheal tube and the Y piece of the breathing system.

After starvation of 12 hr, a 20 G catheter was placed in the cephalic vein. The dogs received an initial dose of 25 $mg \cdot kg^{-1}$ pentobarbital, followed by an intravenous infusion maintenance at 5 $mg \cdot kg^{-1} \cdot hr^{-1}$, using an infusion pump (Anne, Abbott, Chicago, USA). The dogs were placed in dorsal recumbency and the tracheas intubated with a tracheal tube 8.5 - 9.0 mm internal diameter. A 20 G catheter was placed in the right femoral artery for blood pressure measurement (AS 3, Datex - Engstrom, Helsinki, Finland). An 18 G catheter was placed in the right jugular vein for infusion of 5 $ml \cdot kg^{-1} \cdot hr^{-1}$ lactated Ringer's solution.

The dogs were maintained under controlled ventilation according to the group, using a pneumatic ventilator, generating a continuous input in the inspiratory phase with pressure cycling from inspiratory to expiratory, and volume limited (K.Takaoka, model Nikkei, São Paulo, Brazil), converted to low-flow anesthesia. In groups G3 and G4, the capacity of the circuit, including the CO_2 absorber, was about 5.12 L, the volume of the soda lime in the absorber was about 1 L. Before each anesthesia, the circuit was replaced with clean, dry corrugated tubes of the same length, and the soda lime was changed (Wilson, USA). Neuromuscular block was performed with an initial dose of 0.1 $mg \cdot kg^{-1}$ pancuronium and maintenance doses of 0.03 $mg \cdot kg^{-1}$ every 45 min.

The tidal volume was set at 20 $ml \cdot kg^{-1}$ and the ventilator frequency was adjusted to provide a $P_{ET}CO_2$ between 30-35 mmHg. Pulse rate and pulse oximeter arterial O_2 saturation were measured using a sensor placed on the tongue (4700 Oxicap, Ohmeda, USA). The $P_{ET}CO_2$, respiratory rate and O_2 inspired fraction were measured with a sidestream capnometer (4700 Oxicap, Ohmeda, USA). Tidal volume was measured using a Mark 8 Wright respirometer (Ferraris, England). The tympanic temperature was measured at the external auditory conduct using an electrical thermometer (Yellow Springs Instruments Co, model 4000 A, China). The temperature and relative humidity of the inspired gas was measured using a thermohygrometer (Gulton, São Paulo, Brazil) attached between the tracheal tube and the unidirectional valve (G1), or HME (G2 and G4) or the Y piece of the breathing system (G3). The relative humidity sensor operated on a capacitative principle. The stated system accuracy is ± 2% for relative humidity and ± 0.5°C for temperature. The rise times are 1.5 sec for 90% relative humidity response and < 150 msec for a 90% temperature response. The highest values of temperature and relative humidity were collected over four respira-

tory cycles for statistical analysis. Absolute humidity was calculated using the formulae:

AH = RH.MH, in which **AH** = absolute humidity ($mgH_2O \cdot L^{-1}$);
RH = relative humidity (percent);
MH = maximum humidity ($mgH_2O \cdot L^{-1}$).

Absolute humidity was calculated from relative humidity and temperature according to a specific table.[12] Room temperature was maintained between 22-25°C.

The following parameters were evaluated: tympanic temperature (TT) (°C), inspired gas temperature (IGT), relative humidity (RH) (%), and absolute humidity (AH) ($mgH_2O \cdot L^{-1}$). Anesthesia was maintained for three hours and the measurements were performed 15 min after the beginning of controlled ventilation (control - M1) and 60 (M2), 120 (M3) and 180 (M4) min afterwards. In G2 and G4, an HME was installed 10 min after the beginning of controlled ventilation and 5 min before M1.

At the end of the study, the animals were euthanized. Thoracotomy and removal of the tracheobronchial tree were performed and biopsies (1 x 1 cm) in pre-determined areas of the trachea (below the endotracheal tube cuff and carina), primary and secondary bronchi were performed. The specimens were fixed in glutaraldehyde 2.5% in an 0.1 M sodium phosphate buffer solution (pH 7.3) for at least 24 hr for scanning electron microscopy (SEM). They were then fixed in osmium tetroxide 2% solution with the same buffer for one hour and dehydrated in a graded concentration of ethanol. The samples were dried to a critical point, placed on a metal stub, spatter coated with gold and examined in a scanning electron microscope (515 Philips, Holland). The SEM was accom-

TABLE I Tympanic temperature (TT) and inspired gas temperature (IGT) in the groups. Values are given in mean ± SD.

FGF: 5L·min⁻¹		*15 min (control)*	*60 min*	*120 min*	*180 min*
Without HME (G1)	TT (°C)	37.7 ± 0.6	37.0 ± 0.8*	36.5 ± 1.1*	36.0 ± 1.5*
With HME (G2)	TT (°C)	38.1 ± 1.2	37.7 ± 1.4†	37.5 ± 1.5†	37.3 ± 1.7†
Without HME (G1)	IGT (°C)	25.5 ± 2.0	25.4 ± 1.6	25.3 ± 1.7	25.7 ± 1.4
With HME (G2)	IGT (°C)	26.1 ± 1.3	26.5 ± 1.1	26.5 ± 1.3	26.6 ± 1.7
FGF: 1L·min⁻¹		*15 min (control)*	*60 min*	*120 min*	*180 min*
Without HME (G3)	TT (°C)	36.7 ± 1.4	36.5 ± 1.2	36.0 ± 1.2*	35.4 ± 1.2*
With HME (G4)	TT (°C)	37.8 ± 0.9	37.4 ± 1.2†	37.2 ± 1.4†	37.1 ± 1.5†
Without HME (G3)	IGT (°C)	24.6 ± 1.7	25.5 ± 1.9	24.7 ± 1.5	25.4 ± 1.6
With HME (G4)	IGT (°C)	25.8 ± 1.7	27.0 ± 1.8	26.7 ± 1.6	26.8 ± 1.4

* $P < 0.01$ in the groups, compared with control (M1)
† $P < 0.05$ in the groups compared with control (M1)

TABLE II Relative (RH) and absolute (AH) humidity of the inspired gas in the studied groups. Means ± SD.

FGF: 5L·min⁻¹		*15 min (control)*	*60 min*	*120 min*	*180 min*
Without HME (G1)	RH (%)	39.3 ± 11.6	37.0 ± 13.6	37.3 ± 16.2	37.7 ± 13.7
With HME (G2)	RH (%)	89.2 ± 13.9*	89.9 ± 10.6*	94.1 ± 5.6*	93.2 ± 5.9*
Without HME (G1)	AH ($mgH_2O \cdot 1^{-1}$)	9.2 ± 2.4	8.5 ± 2.6	8.5 ± 3.3	9.0 ± 3.3
With HME (G2)	AH ($mgH_2O \cdot 1^{-1}$)	22.3 ± 4.0 (	22.6 ± 3.4 (	23.5 ± 2.0 (	23.3 ± 2.5 (
FGF: 5L·min⁻¹		*15 min (Control)*	*60 min*	*120 min*	*180 min*
Without HME (G3)	RH (%)	70.2 ± 8.0*	62.5 ± 10.5*	71.8 ± 5.9*	75.2 ± 4.2*
With HME (G4)	RH (%)	91.3 ± 4.7*	88.4 ± 12.2*	94.1 ± 9.2*	93.5 ± 11.3*
Without HME (G3)	AH ($mgH_2O \cdot 1^{-1}$)	15.7 ± 1.9*	15.7 ± 1.7*	16.3 ± 1.8*†	17.8 ± 2.3*†
With HME (G4)	AH ($mgH_2O \cdot 1^{-1}$)	22.1 ± 2.5*	22.7 ± 3.5*	23.8 ± 2.9*	23.8 ± 3.2*

* $P < 0.01$ in the comparison of the groups: G1<G3<(G2=G4)
† $P < 0.01$ in the groups, compared with the control moment (M1)

plished without knowledge of the groups and by the same physician.

Three other dogs (G0-control) were euthanized with excessive doses of pentobarbital and thoracotomy and removal of the tracheobronchial tree was performed immediately. Preparation of the specimens was performed as in other groups and they were considered as a normal standard for the SEM.

The Kruskal-Wallis test was used for analysis of differences of weight. Continuous data were compared using analysis of variance for repeated measures followed by Tukey's test, to investigate differences over time. A descriptive analysis was used for the scanning electron microscopy. Data are reported as means ± SD. Probability levels < 0.05 were considered significant.

Results

There was no difference in the weight of the dogs among groups: G1 (17.6 ± 2.0 kg), G2 (17.3 ± 2.0 kg), G3 (18.2 ± 2.0 kg) and G4 (18.3 ± 1.0 kg). The tympanic temperature decreased to a similar extent in all groups compared with control ($P < 0.05$) but there was no difference among groups in relation to the inspired gas temperature ($P > 0.05$) (Table I).

The non-rebreathing circuit with a high fresh gas flow group (G1) showed lower relative and absolute humidity than the other groups ($P < 0.01$). The groups with HME (G2 and G4) had the highest values ($P < 0.01$) but with no difference between them. The CO_2 absorber group (G3) showed intermediate values, which increased during the study ($P < 0.01$) (Table II).

Specimens from control animals (G0) were lined with a ciliary epithelium in a "wheat field" pattern projecting into the lumen of the trachea, primary and secondary bronchi. The cilia were "loose" with no adherence among them (Figure 0a). No areas of absence of cilia were observed. Spherical mucus droplets were present at the tips of the cilia in a diffuse pattern, giving an impression of being floating above them (Figure 0b).

In all specimens from animals from G1, trachea, primary and secondary bronchi showed mucus droplets with considerable changes in size and shape, surface rough and wrinkly. Occasionally, they were completely desiccated and strawberry-shaped (Figure 1a). The mucus droplets were mostly grouped, losing the characteristic of floating over the cilia. The cilia showed a tendency to be grouped, adhering to each other, and losing their characteristic of regular array (Figure 1b). Focal areas with absence of cilia or cilial rarefication covered with defective cilia were observed.

In all specimens from G3, and in 75% and 62.5%, respectively, from G2 and G4 showed less alteration of the mucociliary system of the tracheobronchial tree than did specimens from G1. They showed formation of groups of cilia and focal areas with absence of cilia or cilial rarefication covered with defective cilia, but less than in G1. The mucus droplets were of irregular size, showing rough ridges in their surface, but they were more superficial and not as rough as in G1 (Figures 3). Some specimens from G2 (25%) and G4 (37,5%) showed no pathological changes in the ciliary epithelium or mucus.

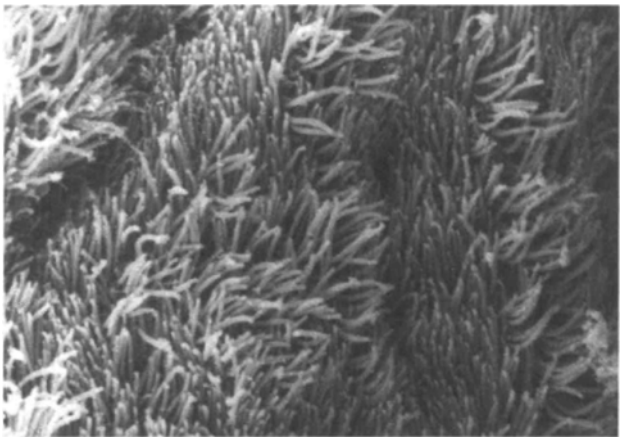

FIGURE 0A Electron microscopic scanning of normal epithelial surface of the tracheobronchial tree of animals of a control dog. The cilia show a regular array. (× 5280)

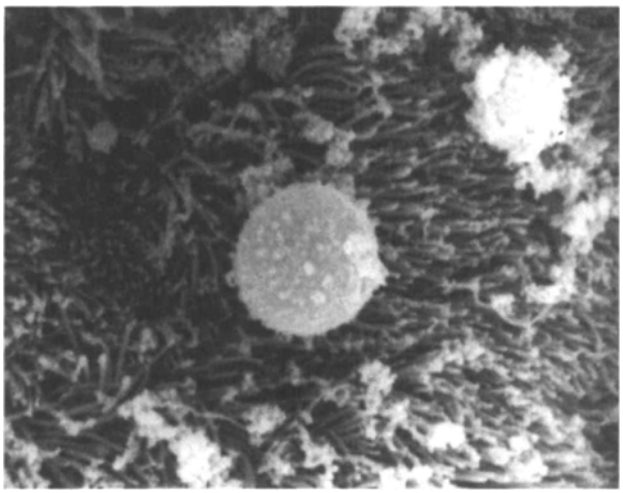

FIGURE 0B Electron microscopic scanning of normal epithelial surface of the tracheobronchial tree of a control dog. Spherical mucus droplets are present at the tips of the cilia (× 4500).

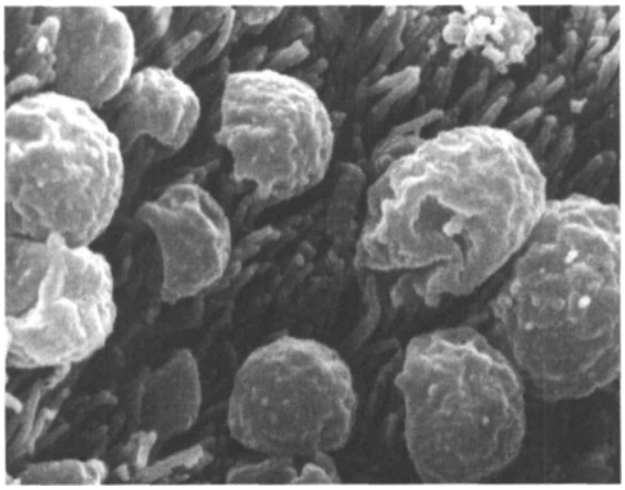

FIGURE 1A Electron microscopic scanning of epithelial surface of the tracheobronchial tree of animals in G1. Mucus droplets show marked variation in size and shape, and some are broken into pieces with irregular surface. (× 7800)

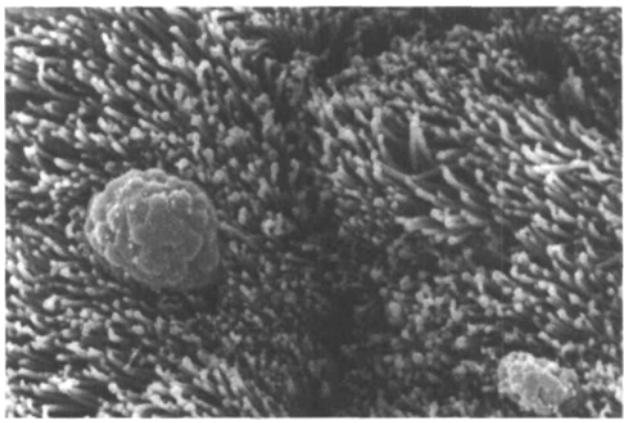

FIGURE 1B Electron microscopic scanning of epithelial surface of the tracheobronchial tree of animals in G1. Cilia forming groups. (× 5500)

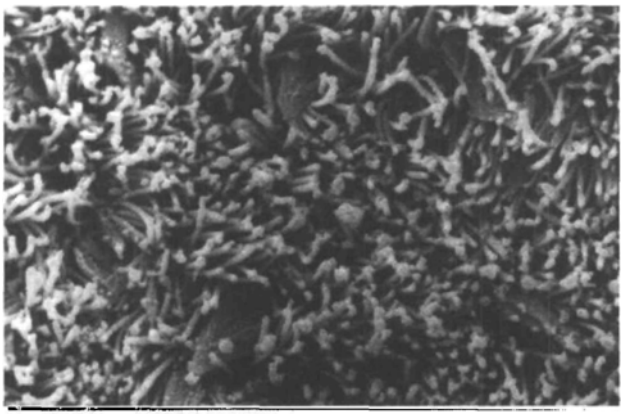

FIGURE 3 Electron microscopic scanning of epithelial surface of the tracheobronchial tree of animals in G3. The mucus droplets with wrinkling on the surface, but always more superficial and not so rough as in G1 (× 5700)

Discussion

The addition of HME in the respiratory circuit of G2 and G4 increased the humidity of inhaled gas, with relative humidity reaching 90%-94% and absolute humidity 22 to 24 $mgH_2O \cdot L^{-1}$ (Table II), without an increase in the temperature of the inhaled gas (Table I). Thus, absolute humidity increased by 150% compared with the system without CO_2 absorber (G2), and by about 33% compared with the system with CO_2 absorber (G3) (Table II). These findings are within the recommended lower limit for absolute humidity during anesthesia, (>20 $mgH_2O \cdot L^{-1}$) to reduce dehydration of the respiratory tract.[6–10] However, these levels of humidity were insufficient to avoid morphological alterations of the cilia and mucus of the tracheobronchial surface.

The use of HME in human beings during anesthesia has increased recently, because it may reduce the loss of water[13–17] and offers other advantages, such as low cost, facility of use, microbiological filter[18] and does not need an energy source. The limited data available regarding the efficiency of HME in humidifying inspired gas of anesthetized patients has shown favourable results, achieving humidification between 25-32 $mgH_2O \cdot L^{-1}$.[10,13,19–21]

The circuit with CO_2 absorption and low fresh gas flow of 1 $L \cdot min^{-1}$ produced maximum absolute humidity of inspired gas of 17.8 ± 2.3 $mgH_2O \cdot L^{-1}$ after three hours (Table II). These results are similar to those obtained by other authors.[9,22] However, the levels are lower than the lowest absolute humidity of the recommended inspired gas.[6–10] This may explain the alterations in the tracheobronchial mucosa observed during SEM in group G3, with relative desiccating effect in the areas of the cilia and mucus droplets (Figure 3). The levels of absolute humidity and the time needed to reach the high levels of humidity with a rebreathing system, depend on the anesthesia machine, the volume of fresh gas flow and the inspired gas temperature.[9,10,22]

Previous studies have recommended absolute humidity of inspired gas between 20-33 $mgH_2O \cdot L^{-1}$ to reduce the risk of dehydration of the respiratory

tract.[9,10,23–25] The accepted lower limit of absolute humidity during prolonged ventilation is 30 $mgH_2O \cdot L^{-1}$,[4] but, in our opinion, the lower limit of humidification during anesthesia is difficult to determine,[5] because it depends on the duration of anesthesia, previous pulmonary conditions of the patient, and on the anesthetic circuit. Humidification requirements are based mainly on animal studies.[2,6,7,15,25] Investigations in man are limited by the small number of patients and lack of data on the patients involved.[9,10] There is little new data on upper airway function,[5] and even less data on changes in disease states and none on advances in measurement techniques.

Inhaled gases and tympanic temperatures showed no alterations although, in G2 and G4, there was a tendency to higher values of temperature (Table I). The lack of a difference in these temperatures may have been due to the small number of animals in each group.

The use of a neuromuscular blocking drug such as pancuronium, with vagolytic properties in the experimental groups but not in the control animals, may have contributed to the relative dryness of the mucociliary system of the experimental groups when compared with control. However, the dose-response curve for the vagolytic property of pancuronium lies to the right of the neuromuscular blocking effect, so it is probably only partially vagolytic in clinical practice[26] and the vagolytic effect is limited to receptors in the sinus node. Other muscarinic sites in the parasympathetic nervous system such as bowel, bladder, bronchi and pupils, are not affected.[26]

In conclusion, under these experimental conditions, the introduction of HME in a unidirectional anesthetic circuit with or without CO_2 absorber, with high or low fresh gas flow in dogs, increased absolute humidity of inhaled gas, without altering the inhaled gas temperature. The HME attenuated, but did not prevent alterations of the mucociliary system of the tracheobronchial tree, as observed by the scanning electron microscopy, particularly in the group without the CO_2 absorber.

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