Cardiothoracic Anesthesia, Respiration and Airway

The effect of isoflurane 0.6% on respiratory mechanics in anesthetized-paralyzed humans is not increased at concentrations of 0.9% and 1.2%

[L'effet de l'isoflurane à 0,6 % sur la mécanique respiratoire n'a pas augmenté chez l'humain anesthésie et paralysé à des concentrations de 0,9 % et 1,2 %]

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Purpose: To assess the dose-dependent effect of low concentrations of isoflurane on respiratory mechanics in normal subjects.

Methods: We studied 12 non-premedicated ASA I patients scheduled for lower abdominal or extremity surgery. After thiopental 5–7 $mg \cdot kg^{-1}$ *iv* and succinylcholine 1 $mg \cdot kg^{-1}$ *iv*, the trachea was intubated and an esophageal balloon was placed optimally by the occlusion test. After introduction of N_2O and muscle paralysis with vecuronium, we studied 0, 0.6, 0.9 and 1.2% isoflurane. We recorded flow (F), airway opening and esophageal pressures. Signals were amplified, filtered, sampled at 100 Hz, and then fed in a 12-bit analogue-digital converter in a personal computer. Data were collected and analyzed using LABDAT and ANADAT software. Signals were acquired for 60–90 sec during mechanical ventilation (10 $mL \cdot kg^{-1}$, 10 $breaths \cdot min^{-1}$, I:E ratio 1:2). We estimated respiratory system (RS), lung (L) and chest wall (W) dynamic elastance (E) and resistance (R) by $P(t) = EV_T(t) + RF(t) + K$, where t is time, V_T tidal volume from integration of F, and K an estimation of end-expiratory pressure. ANOVA was used for comparing the basal state with the three concentrations.

Results: E and R were statistically lower at 0.6, 0.9 and 1.2% compared to basal values for RS, L and W. Concentrations equal to or higher than 0.6% did not further change respiratory mechanics, except for $E_{L1,2}$ compared to $E_{L0.6,}$ 12.37 ± 5.72 and 13.52 ± 5.64 cm $H_2O.L^{-1}$, respectively.

Conclusion: Isoflurane concentrations between 0.6–1.2% are not associated to a dose-dependent effect on respiratory mechanics.

Objectif : *Évaluer l'effet relié à la dose de faibles concentrations d'isoflurane sur la mécanique respiratoire chez des sujets normaux.*

Méthode : *Nous avons étudié 12 patients, sans prémédication, d'état physique ASA I qui devaient subir une opération au bas ventre ou aux extrémités. Après l'administration de 5–7 $mg \cdot kg^{-1}$ iv de thiopental et de 1 $mg \cdot kg^{-1}$ iv de succinylcholine, la trachée a été intubée et un ballonnet œsophagien a été placé de façon optimale grâce au test d'occlusion. Suivant l'introduction de N_2O et la paralysie musculaire avec du vécuronium, nous avons étudié l'effet de l'isoflurane à 0, 0,6, 0,9 et 1,2 %. Nous avons noté le débit (D), l'ouverture des voies aériennes et les pressions œsophagiennes. Les signaux ont été amplifiés, filtrés, échantillonnés à 100 Hz et ensuite introduits dans un convertisseur analogique-numérique de 12-bits d'un ordinateur personnel. Les données ont été recueillies et analysées au moyen des logiciels LABDAT et ANADAT. Les signaux ont été acquis pendant 60–90 sec pendant la ventilation mécanique (10 $mL \cdot kg^{-1}$, 10 $respirations \cdot min^{-1}$, ratio I:E de 1:2). Nous avons évalué le système respiratoire (SR), l'élastance (E) dynamique et la résistance (R) des poumons (L) et de la paroi thoracique (W) par l'équation: $P(t) = EV_T(t) + RD(t) + K$, où t représente le temps time, V_T le volume courant provenant de l'intégration du débit (D) et K est une estimation de la pression télé-expiratoire. L'analyse de variance a été utilisée pour comparer la concentration initiale et les trois autres concentrations.*

Résultats : *E et R ont été statistiquement plus faibles aux concentrations de 0,6, 0,9 et 1,2 % comparées aux valeurs initiales du SR, de L et de W. Les concentrations égales à 0,6 % ou plus élevées n'ont pas modifié ultérieurement la mécanique respiratoire, sauf pour $E_{L1,2}$ comparée à $E_{L0,6}$, 12,37 ± 5,72 et 13,52 ± 5,64 cm $H_2O.L^{-1}$, respectivement.*

Conclusion : *Les concentrations d'isoflurane de 0,6–1,2 % n'ont pas d'effet relié à la dose sur la mécanique respiratoire.*

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VOLATILE agents are potent bronchodilators and can be used in severe status asthmaticus. Considering the potentially therapeutic properties of those agents, we assessed the dose-dependent effect of three different concentrations of isoflurane on respiratory mechanics to define the lowest useful concentration for bronchodilation while limiting side effects.

Methods

After hospital Ethics Committee approval and patient informed consent, we studied 12 ASA I patients undergoing general anesthesia for lower abdominal or extremity surgery. None had previous evidence of respiratory disease and presented normal forced vital capacity and forced expiratory volume in one second preoperative values. No premedication was given and standard monitoring was used. Induction consisted of thiopental 5–7 $mg{\cdot}kg^{-1}$ *iv* and succinylcholine 1.0 $mg{\cdot}kg^{-1}$ *iv*. Anesthesia was maintained with isoflurane and a 1:1 N_2O: O_2 mixture. An esophageal balloon was inserted during spontaneous breathing and the esophageal pressure used for estimating pleural pressure. The patient was then paralyzed with vecuronium (0.08 $mg{\cdot}kg^{-1}$ *iv*) followed by intermittent doses according to neuromuscular monitoring. We studied the effects of 0.6, 0.9 and 1.2% isoflurane after the basal condition (no isoflurane). Data were recorded after obtaining the steady end-tidal concentration for each condition. Flow (F), and tracheal and esophageal pressures (Ptr and Pes) signals were sampled at 100 Hz and then fed into a 12-bit analogue digital converter (DT2801A, Data Translation) installed in a personal computer. Data were collected and analyzed using LABDAT and ANADAT software (RHT - InfoData USA Inc.). A 60–90 sec sample was obtained during mechanical ventilation using a tidal volume of 10 $mL{\cdot}kg^{-1}$, an I:E ratio of 1:2, and a respiratory rate of 10 $cycles{\cdot}min^{-1}$. Analysis of F, Ptr and Pes signals enabled us to estimate dynamic elastance (E) and resistance (R) of the total respiratory system (E_{RS}, R_{RS}), lungs (E_L, R_L) and chest wall (E_W, R_W). We estimated variables for chest wall and lung using Pes and transpulmonary pressure, obtained by subtracting Pes from Ptr. Ptr was corrected for tracheal tube resistance. We estimated respiratory system (RS), lung (L) and chest wall (W) dynamic elastance (E) and resistance (R) by $P(t) = EV_T(t) + RF(t) + K$, where t is time, V_T tidal volume from integration of F, and K an estimation of end-expiratory pressure. ANOVA test, Levene's test for the H0 hypothesis, Bartlett's test for homogeneity of variances and Bonferroni's correction were used for statistical analysis. $P < 0.05$ was considered statistically significant.

Results

The Table and Figures 1 and 2 describe the values of E and R (mean ± SD). Baseline E_{RS} (E_{RS0}) is statistically higher than E_{RS} under 0.6, 0.9 and 1.2% isoflurane ($E_{RS0.6}$, $E_{RS0.9}$ and $E_{RS1.2}$ respectively). Increasing isoflurane concentration showed no significant effect for E_{RS}. Baseline E_L was significantly higher than $E_{L0.6}$, $E_{L0.9}$ and $E_{L1.2}$. Values for $E_{L0.6}$ were higher than $E_{L1.2}$, and $E_{W0.9}$ was similar to $E_{W1.2}$. Baseline E_W was statistically higher than $E_{W0.6}$, $E_{W0.9}$ and $E_{W1.2}$. Values of $E_{W0.6}$, $E_{W0.9}$ and $E_{W1.2}$ were comparable.

Baseline R_{RS}, R_L and R_W were significantly higher than those obtained under 0.6, 0.9 and 1.2% isoflurane, although no effect was showed for a higher concentration of isoflurane.

Discussion

As expected, isoflurane at 0.6% reduced R_{RS}, R_L and R_W. Nonetheless, increasing isoflurane concentration to 0.9 and 1.2% had no further effect on these variables. Wu *et al.* observed no bronchodilation potentialization when a $ß_2$-adrenergic agonist was administered simultaneously to 1.3% isoflurane.[1] The mechanisms controlling bronchomotor tonus could present a "ceiling effect", or once a maximum effect on smooth muscle has been reached, it does not change regardless of the

TABLE Mean ± SD values of total respiratory system elastance (E_{RS}), lung elastance (E_L), chest wall elastance (E_W), total respiratory system resistance (R_{RS}), lung resistance (R_L) and chest wall resistance (R_W) at baseline, 0.6%, 0.9% and 1.2% conditions in cm $H_2O.L^{-1}$ cm $H_2O.L^{-1}{\cdot}sec^{-1}$, respectively

	Baseline	*0.6%*	*0.9%*	*1.2%*
E_{RS}	31.73 ± 4.98*	25.34 ± 6.45	24.91 ± 6.29	24.39 ± 6.42
E_L	15.85 ± 5.78*	13.52 ± 5.64**	12.49 ± 5.94	12.37 ± 5.72
E_W	15.88 ± 4.45*	11.82 ± 4.62	12.01 ± 4.9	12.0 ± 5.63
R_{RS}	4.76 ± 1.4*	3.82 ± 1.55	3.74 ± 1.58	3.68 ± 1.66
R_L	3.06 ± 1.58*	2.63 ± 1.48	2.48 ± 1.53	2.49 ± 1.58
R_W	1.71 ± 0.66*	1.16 ± 0.59	1.18 ± 0.69	1.18 ± 0.56

*$P < 0.05$ compared to 0.6, 0.9 and 1.2% isoflurane; **$P < 0.05$ compared to 1.2% isoflurane.

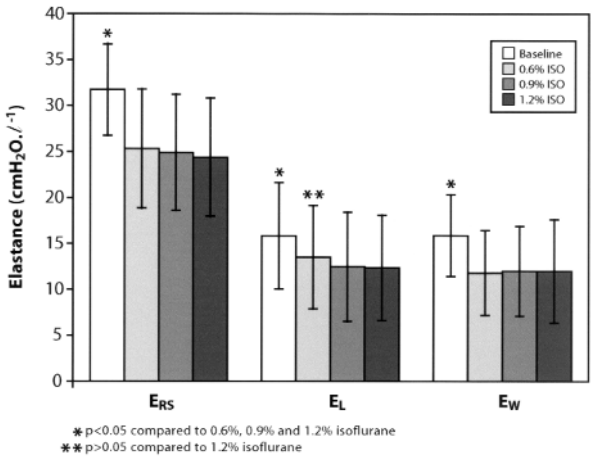

FIGURE 1 Mean ± SD values of total respiratory system elastance (E_{RS}), lung elastance (E_L), chest wall elastance (E_W) at baseline, 0.6%, 0.9% and 1.2% conditions in cm $H_2O.L^{-1}$.

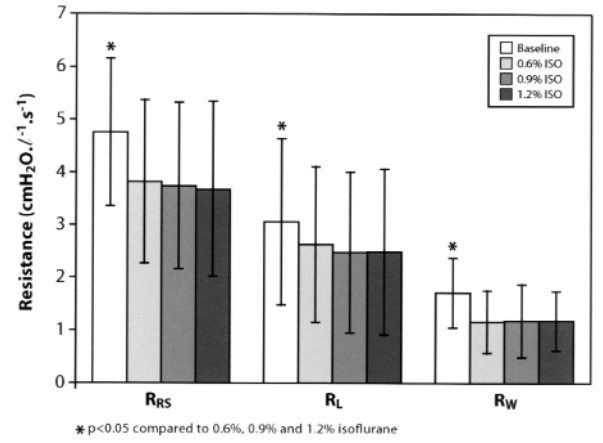

FIGURE 2 Mean ± SD values of total respiratory system resistance (R_{RS}), lung resistance (R_L) and chest wall resistance (R_W) at baseline, 0.6%, 0.9% and 1.2% conditions in cm $H_2O.L^{-1}.sec^{-1}$.

association of pathway-acting drugs. Rooke *et al.* compared the effects of 1.1 MAC of halothane, sevoflurane and isoflurane on R_{RS} to thiopental 0.25 $mg{\cdot}kg^{-1}{\cdot}min^{-1}$ *iv* infusion.[2] While R_{RS} increased under thiopental, equipotent doses of halothane and sevoflurane reduced R_{RS} by 31% and 42%, respectively. Isoflurane (1.1 MAC) reduced R_{RS} by 25%, similar to our results. We observed a decrease of E_{RS} after isoflurane, although concentrations above 0.6% did not cause further decrease of E_{RS}. Others, using 0.5 and 0.6% isoflurane also observed a significant decrease of E_{RS} compared to baseline.[3] Similarly, Canet *et al.* observed that increasing the dose of isoflurane from 1.2 to 2.0 MAC does not produce a significant effect on respiratory mechanics.[4] We observed that 0.6% isoflurane also reduced E_L but there was no difference between 0.6 and 0.9% isoflurane. Compared to 0.6% however, E_L at 1.2% is statistically lower. Although the lower airway resistance during 1.2% isoflurane was not enough to change E_{RS} statistically it might be sufficient to change E_L. Barnas *et al.* studied E_L during mechanical ventilation at 0.5% and 0.6% isoflurane, reporting a similar effect on pulmonary elastance.[3] Few studies draw attention to the effects of inhalation anesthesia on the elastic properties of the chest wall, probably due to technical difficulties associated to accurate recording of pleural pressure. Our E_W values are similar to those reported by others using 1–2% isoflurane.[3,5,6] The chest wall anatomical configuration is important for its elastic properties, and concentrations above 0.6% do not seem to affect its structure enough to change it.

Inhalation agents can have at least two potentially antagonistic effects over airway resistance. First, they can relax airway smooth muscles either by inhibiting the parasympathetic neural pathway or by a direct effect on muscle fibres and receptors.[7,8] But volatile agents can also change thoracic configuration reducing functional residual capacity (FRC). As airway resistance increases with the decrease in lung volume, decreasing FRC is followed by an increase in airway resistance. Thus, the final effect of volatile agents will depend on the interaction between both factors. However, the relationship between pulmonary volume and respiratory resistance has been stated to depend on airway muscle tonus: the tonus relaxation decreases the dependence of the resistance regarding lung volume.[9] We may say that by relaxing smooth muscle tonus, volatile agents make the changes of FRC play a smaller role on pulmonary resistance. Anticipated changes of airway resistance associated with anesthesia are still complicated by another factor. Although the majority of *in vivo* studies assessing the airway muscle tonus use lung resistance as an index of the airway diameter, the parameter is a sum of two resistances. The first depends on airflow resistive properties and the other is associated to the elastic properties of the pulmonary tissue. Like the first resistance, tissue resistance also depends on lung volume and on bronchial tonus.[10] However, differently from the first, tissue resistance decreases as lung volume decreases, putting another variable in the equation describing the respiratory resistance behaviour. In conclusion, we

observed that the effect of isoflurane 0.6% on the resistance and elastance of the respiratory system and its subcomponents was not increased with concentrations of 0.9% and 1.2%.

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