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Airway occlusion pressure is an indicator of respiratory depression with isoflurane

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Abstract: The purpose of this study was to elucidate the respiratory depressant effects of isoflurane (0%–1.0%) using airway occlusion pressure ($P_{0.1}$), a known index of the output of the respiratory centers, in ten anesthetized patients. $P_{0.1}$ was measured as the pressure change obtained after the first 0.1 sec of spontaneous inspiration against the occluded airway. A significant decrease in minute volume ($\dot{V}_E$) and a significant increase in $Paco_2$ were not observed during the periods of isoflurane 1.0% at the end-tidal concentration compared with those of control period (0% isoflurane) ($P < 0.05$), whereas a significant decrease in $P_{0.1}$ was observed during the period of isoflurane 0.5%. Our results suggested that $P_{0.1}$ was a more sensitive indicator of respiratory depression than $Paco_2$ or $\dot{V}_E$, and the respiratory center was depressed with a considerably lower concentration (0.5%) of isoflurane.

Key words: Airway occlusion pressure ($P_{0.1}$), Isoflurane

Introduction

Airway occlusion pressure ($P_{0.1}$) is defined as the pressure generated after the first 0.1 sec of inspiration when the airway is occluded at functional residual capacity (FRC) and is considered to be an index of the output of the respiratory centers [1]. Recently, $P_{0.1}$ has been reported to be a useful predictor for successful weaning in mechanically ventilated patients with chronic obstructive plumonary disease (COPD) [2]. The respiratory depressant effects of volatile anesthetics have been evaluated using minute volume ($\dot{V}_E$) and blood gas analysis. However, the effects of volatile anesthetics on $P_{0.1}$ have never been reported. This study was performed in an attempt to clarify the respiratory depressant effect of isoflurane using $P_{0.1}$ as an alternative index.

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Patients and methods

Ten female patients undergoing gynecological surgery were included in the study after approval by the ethical committee of the Toride Kyodo General Hospital, and informed consent was obtained from the patients. The patients ranged in age from 31 to 52 years and were of ASA physical status I or II. All patients were free of cardiovascular, respiratory, and neuromuscular diseases.

No patient received preanesthetic medication. The study was performed in a supine position. Anesthesia was induced with thiopental 4–5 $mg \cdot kg^{-1}$ I.V., and succinylcholine 1 $mg \cdot kg^{-1}$ I.V. was administered to facilitate tracheal intubation. After intubation with an endotracheal tube, spontaneous breathing was allowed to resume while the patients breathed 66% nitrous oxide in oxygen. A 22-gauge catheter was placed in the radial artery for blood sampling. No muscle relaxant was used other than the induction of anesthesia. Rectal temperature was monitored and maintained at 37° ± 1°C.

The patient's endotracheal tube was connected to an experimental apparatus incorporated into a semiclosed anesthetic circuit. This consisted of a pressure transducer (Nihon Kohden, Tokyo, Japan), a one-way Hans-Rudolph valve and a side stream spirometer [3]. $\dot{V}_E$ was measured from this spirometer and a Datex anesthetic/respiratory gas analyzer (Capnomac, Ultima, Helsinki, Finland). Esophageal pressure (P_{es}) was measured by means of a thin-walled latex balloon positioned in the middle third of the esophagus and a pressure transducer. Transpulmonary pressure (P_{tp}), the difference between tracheal airway pressure (P_{aw}) and P_{es}, was monitored to maintain the FRC. $P_{0.1}$ was measured as

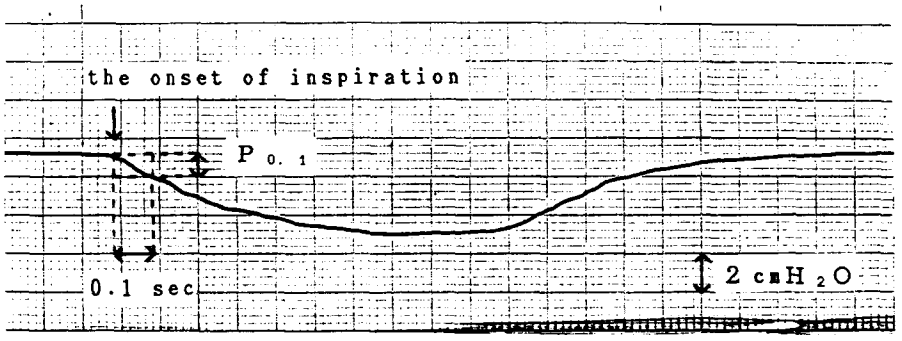

Fig. 1. Measurement of airway occlusion pressure ($P_{0.1}$)

the change of P_{aw} during the first 0.1 s of spontaneous inspiratory effort against the airway closed by a one-way valve (Fig. 1). Heart rate and arterial blood pressure were measured noninvasively. Arterial blood gas was measured with a 178 pH/blood gas analyzer (Corning, Medfield, England).

When all of the respiratory and hemodynamic variables were stable, isoflurane was administered through a vaporizer. The concentration of isoflurane was monitored with a Datex anesthetic/respiratory gas analyzer (Capnomac, Ultima). After control measurements (0% isoflurane), isoflurane was added stepwise to the inspired gas to end-tidal concentrations of 0.5% and 1.0%, in this order. All variables were measured after achieving 10 min of each stable end-tidal isoflurane. All the measurements were done without surgical intervention.

All values were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) and paired *t*-tests corrected for multiple comparisons were used to compare the data acquired at each concentration of isoflurane with control data. A probability value of less than 0.05 was regarded as statistically significant.

Results

The mean values of age, height, and weight of the patients were 44.3 ± 6.3 years, 156.2 ± 5.3 cm, and 51.0 ± 6.3 kg, respectively.

Mean arterial pressure during the period of isoflurane 0.5% was decreased in comparison with the control value ($P < 0.01$) and decreased with increasing concentration of isoflurane. No difference in heart rate was observed (Table 1).

Arterial blood gas tensions are summarized in Table 2. No difference in pH, $Paco_2$, Pao_2, HCO_3^- and base excess was observed.

There was no difference in $\dot{V}_E \cdot P_{0.1}$ during the period of isoflurane 0.5% was decreased compared with the control value ($P < 0.01$) and the decrease in $P_{0.1}$ was related to the increase in the end-tidal concentration of isoflurane (Table 1).

Discussion

The main finding of this study was that isoflurane at an end-tidal concentration of less than 1.0% had no significant effect on $\dot{V}_E$ and $Paco_2$ in spontaneously breathing patints while $P_{0.1}$ was reduced even at the lower concentration of 0.5% in comparison with the control value ($P < 0.01$).

Isoflurane has ventilatory depressant effects which are variously expressed as an increase in $Paco_2$, a decrease in CO_2 response, and a decrease in tidal volume and $\dot{V}_E$ [4]. However, our results showed neither an increase in $Paco_2$ nor a decrease in $\dot{V}_E$ during the period of isoflurane 1.0% ($P < 0.05$).

The output of the respiratory centers is influenced by the chemical or mechanical stimulation. The chemical stimuli are hypercapnia and hypoxia [1], while the mechanical stimuli include the changes in the elastic and resistive component of the respiratory system [5,6]. In

Table 1. Hemodynamic and respiratory variables

Variable	Isoflurane (%)		
	0 (Control)	0.5	1
HR (bpm)	84 ± 11	81 ± 7	84 ± 7
MAP (mmHg)	102 ± 17	91 ± 17*	84 ± 17*
$\dot{V}_E$ (l)	5.7 ± 1.2	5.4 ± 0.9	5.3 ± 1.1
$P_{0.1}$ (cmH_2O)	2.7 ± 0.5	2.0 ± 0.5*	1.8 ± 0.6*

All values are expressed as mean ± SD ($n = 10$).
HR, heart rate; MAP, mean arterial pressure; $\dot{V}_E$, minute volume; $P_{0.1}$, airway occlusion pressure. * $P < 0.01$ (vs control).

Table 2. Arterial blood gas tensions

Arterial blood gas	Isoflurane (%)		
	0 (Control)	0.5	1
pH	7.40 ± 0.02	7.40 ± 0.02	7.39 ± 0.02
$Paco_2$ (mmHg)	35.7 ± 1.5	35.5 ± 2.8	36.2 ± 3.8
Pao_2 (mmHg)	183 ± 35	183 ± 26	183 ± 24
HCO_3^- ($mEq \cdot l^{-1}$)	22.4 ± 1.5	21.7 ± 1.8	22.2 ± 2.1
B.E. ($mEq \cdot l^{-1}$)	−0.9 ± 1.9	−1.6 ± 1.9	−1.2 ± 2.4

All values are expressed as mean ± SD ($n = 10$).
BE, base excess.

this study, there was no increase in $Paco_2$ during the period of isoflurane 1.0%. Therefore, it is predicted that the output of respiratory centers would not be increased. However, $P_{0.1}$, an index of the output of the respiratory centers, was reduced markedly at that concentration.

Alternatively, it is reported that isoflurane at a concentration of 1.1% causes no change in $\dot{V}_E$ and $Paco_2$, and does not inhibit the output of the respiratory centers [7]. In our study, however, a significant decrease in $P_{0.1}$ was observed at a concentration of 0.5% which produced no change in $\dot{V}_E$ and $Paco_2$. Therefore, it can be assumed that $P_{0.1}$ is a more sensitive index of the respiratory drive than $\dot{V}_E$ or $Paco_2$.

It is well known that isoflurane induces muscle relaxation and decreases the ability of the muscles to sustain contraction. It is demonstrated that $P_{0.1}$ is measured during an isometric contraction of respiratory muscles [1], which may be affected by isoflurane. However, a potent muscle relaxing effect appears after approximately 90 min administration of isoflurane 0.5% [8]. In our study, the duration of isoflurane 0.5% inhalation was no more than 10 min. Therefore, it is supposed that isoflurane 0.5% has a little effect on the measurement of $P_{0.1}$. However, it is possible that this volatile agent, at concentrations over 0.5%, may cause $P_{0.1}$ to be underestimated.

It is known that the activity of the respiratory centers partially depends on the level of functional residual capacity (FRC). The elevated FRC inhibits the pressure development by decreasing the electrical activity of the diaphragm [9] and also by reducing the diaphragmatic contractility depending on the relationship between length and tension [10]. There is a possibility that FRC was reduced by thiopental-induced anesthesia in the present study. However, FRC after the induction of anesthesia seems to be well controlled as the end-tidal P_{tp} was kept constant before each measurement. Additionally, it has been reported that FRC falls initially with the induction of anesthesia but does not continue to fall with time [11].

In conclusion, $P_{0.1}$ seems to be a more sensitive indicator of respiratory suppression than $Paco_2$ and $\dot{V}_E$. With this index, the respiratory depression with isoflurane seemed to be detected in patients at end-tidal concentrations as low as 0.5%.

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