Hemodynamic and Catecholamine Responses to Tracheal Intubation during Inhalation of Isoflurane or Sevoflurane

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This study was designed to evaluate the hemodynamic and catecholamine responses to the inhalation of isoflurane and sevoflurane during anesthetic induction and to tracheal intubation in 46 adult patients who received elective surgery. Anesthesia was induced with thiamylal and vecuronium, followed by 3-min ventilation with 60% N_2O (final control group ; n = 13), 60% N_2O-3% isoflurane (final isoflurane group ; n = 15), or 60% N_2O-4.5% sevoflurane (sevoflurane group ; n = 16) in oxygen, and the trachea was then intubated. Isoflurane inhalation caused significant increases in heart rate and plasma norepinephrine, but attenuated the pressor response to tracheal intubation. Sevoflurane inhalation caused a decrease in systolic arterial pressure with an unchanged heart rate, and attenuated the pressor and tachycardia response to tracheal intubation to a greater extent than that observed in the control and isoflurane group. Plasma norepinephrine did not show any change in the sevoflurane group. Isoflurane induction increased the sympathoadrenal activity, resulting in marked tachycardia, but attenuated the pressor response to tracheal intubation. Sevoflurane caused milder hemodynamic change during inhalation and tracheal intubation, and was accompanied by stable plasma catecholamine levels, indicating a suppression of sympathoadrenal activity.

Keywords : isoflurane, sevoflurane, anesthetic induction, catecholamine responses

Introduction

Many anesthesiologists use an induction sequence of thiopental, neuromuscular blockade and a few minutes of manual ventilation of the patient's lungs with oxygen and nitrous oxide before laryngoscopy. This technique is frequently followed by hypertension and tachycardia in the patient in response to the tracheal intubation. An increase in the plasma concentrations of epinephrine and norepinephrine also occurs in response to this intubation stimulus.[1,2] These changes may produce arrythmias, myocardial ischemia, cardiac failure and intracranial hemorrhage. Various techiniques have thus been used to attenuate these undesirable responses ; the techniques depend on a reduction in input stimuli or the blockade of adrenergic responses, including alpha- or beta- blockade, direct-acting vasodilators, and opiates.

The inhalation of volatile anesthetics prior to tracheal intubation has also been shown to be useful for this purpose. Both halothane and enflurane alone or in combination with nitrous oxide attenuates the hemodynamic response to tracheal intubation.[3,4] Although isoflurane induction attenuates the pressor response to intubation, it causes increases in the heart rate and plasma norepinephrine concentration.[5]

Sevoflurane is a potent inhalational anesthetic for induction. Although sevoflurane has been reported to decrease sympathetic activity,[6] the sympathetic and hemodynamic responses to tracheal intubation during the inhalation of sevoflurane have not been fully investigated. The aim of the present study was to evaluate the hemodynamic and catecholamine responses to the inhalation of isoflurane or sevoflurane, and to tracheal intubation.

Methods

The protocol was approved by the Human Research Ethics Committee of Nagasaki University Hospital. Written informed consent was obtained from forty-six ASA PS 1 patients undergoing elective surgery. The patients were premedicated with atropine, 0.01 mg/kg, and hydroxyzine, 1 mg/kg intramuscularly 30 min before the start of anesthesia. Intravenous cannulation was performed, and 5 ml/kg of lactate Ringer's solution was infused prior to induction. The radial artery was also cannulated for blood pressure measurement and blood sampling. The heart rate was measured by ECG monitoring. After anesthesia was induced with thiamylal, 4mg/kg, and vecuronium, 0.15 mg/kg, the patients were randomly allocated into one of three groups to receive N_2O alone (control group, n = 14), N_2O+isoflurane (isoflurane group, n = 16), or N_2O+sevoflurane (sevoflurane group, n = 16). Controlled mask ventilation was initiated after diminution of the eye-lash reflex with a gas mixture of 60% N_2O in O_2 in control group and either 3% isoflurane in the isoflurane group or 4.5% sevoflurane in the sevo-

flurane group. The mean end-tidal carbon dioxide (EtCO2) and end-tidal isoflurane or sevoflurane was monitored by capnograph (Capnomac, Datex, Helsinki, Finland), and the EtCO2 was kept at 35~40 mmHg. After 3 min of ventilation, laryngoscopy lasting 15 sec was performed and the trachea was intubated. After intubation, ventilation was continued with a gas mixture of 60% N_2O in O_2 in the control group and either 1% isoflurane in the isoflurane group or 1.5% sevoflurane in the sevoflurane group.

The heart rate (HR) and direct systolic arterial pressure (SAP) were continuously recorded starting just before the induction of anesthesia and lasting until 5 min after intubation. Blood samples from the radial artery were drawn before the induction of anesthesia, after the administration of vecuronium, 3 min after ventilation by mask, and 1 min after laryngoscopy. The blood samples were collected in ice-cold plastic tubes containing EDTA, and centrifuged at 4℃. Plasma was stored at −40℃ until analyzed for the plasma concentration of epinephrine (E) and norepinephrine (NE). E and NE in plasma were determined by high-performance liquid chromatography.[7] This assay method has a limit of sensitivity of 20 pg for each catecholamine. The interassay and intraassay variations are less than 5%. Data were analyzed by ANOVA followed by Student's t-test. A p value less than 0.05 was considered significant.

Results

The three groups were comparable with regard to age, height and weight (Table. 1). Two patients (1 patient in the control group and 1 patient in the isoflurane group) who moved during ventilation and tracheal intubation were excluded from this study. After the 3-min ventilation, the EtCO2 values were 36.0±1.4 mmHg in the control group, 37.2±2.5 mmHg in the isoflurane group, and 35.2 ±1.8 mmHg in the sevoflurane group, respectively, with no significant differences among the groups. The end-tidal concentrations of the inhalational anesthetics after the 3-min ventilation were 2.1±0.3% of isoflurane and 3.3± 0.4% of sevoflurane, and the concentration of each anesthetic was comparable with respect to minimum alveolar concentration (MAC), i. e., 1.82±0.03 MAC in isoflurane and 1.91±0.04 MAC in sevoflurane.

Fig. 1 shows the SAP and HR changes during anesthetic induction, laryngoscopy, and tracheal intubation. The baseline values of SAP and HR were comparable among the groups. In the control group, the SAP decreased significantly (p<0.05) during the manual ventilation with HR unchanged, and both the SAP and HR increased significantly (p<0.01) 1 min after tracheal intubation. In the isoflurane group, the SAP did not change and was significantly higher than that of the control group

Table 1. Demongraphic Characteristics for Three Anesthetic Induction Groups

	control	isoflurane	sevoflurane
Number of patients	13	15	16
Age (yrs)	46.2±2.2	49.6±3.0	44.9±3.2
Weight(kg)	51.8±3.8	59.0±2.4	56.0±3.3
Height(cm)	161.8±3.1	162.0±3.0	159.3±2.9

Values = mean±SEM. control = control group.
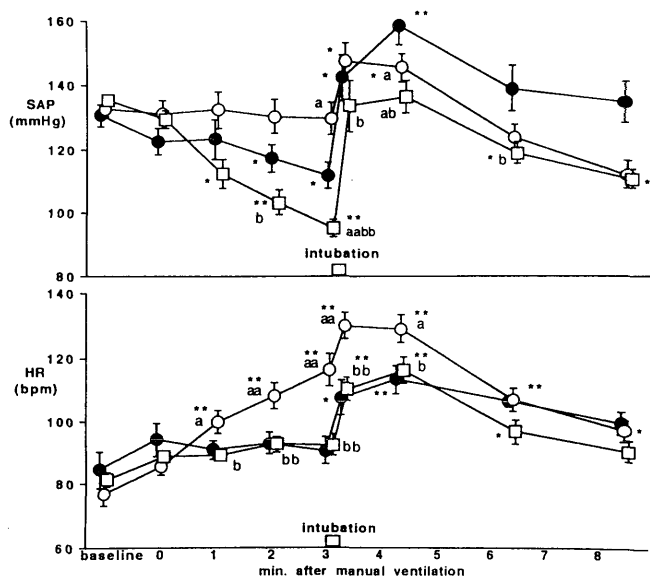isoflurane = isoflurane group. sevoflurane = sevoflurane group.

Figure 1. Changes of systolic arterial pressure (SAP) and heart rate (HR) in three anesthetic induction groups. (mean ± SEM). Closed circle reveals control group. Open circle reveals isoflurane group. Open square reveals sevoflurane group.
*: p<0.05, **p<0.01, vs baseline value. a : p<0.05, aa : p<0.01, vs control group. b : p<0.05, bb : p<0.01, vs isoflurane group.

(p<0.05) during manual ventilation. The HR increased significantly and to a higher level than that of the control patients after the initiation of isoflurane inhalation. The SAP (p<0.05) and HR (p<0.01) increased significantly after laryngoscopy and tracheal intubation, but the SAP after tracheal intubation was significantly lower than that in the control group (p<0.05). In the sevoflurane group, the SAP decreased significantly (p<0.01) during sevoflurane inhalation, with HR unchanged. The increase in SAP after laryngoscopy and tracheal intubation was significantly less than those of the control and isoflurane groups. Although the HR increased significantly after laryngoscopy, the increase was significantly less than that of the isoflurane group both after laryngoscopy (p<0.01) and after tracheal intubation (p<0.05).

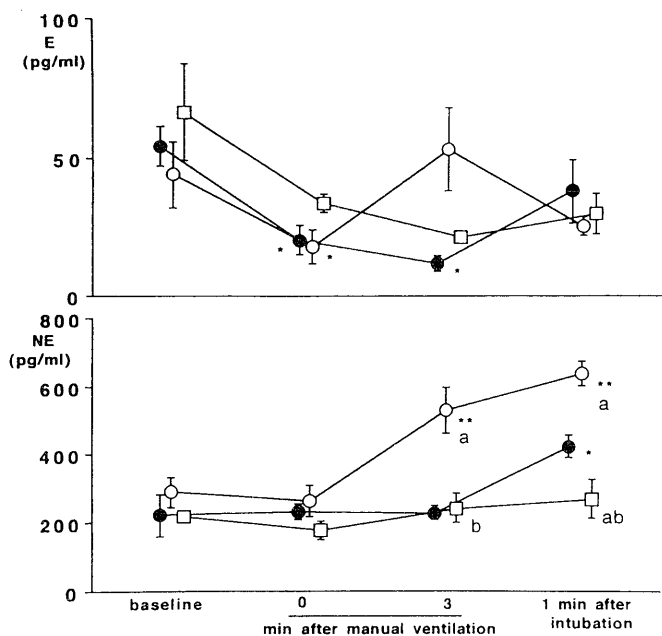**Figure 2.** Changes of plasma concentrations of epinephrine (E) and norepinephrine (NE) in three anesthetic induction grpups (mean±SEM). Closed circle reveals control group. Open circle reveals isoflurane group. Open square reveals sevoflurane grpup.
*: $p<0.05$, **: $p<0.01$, vs baseline value. a : $p<0.05$, vs control grop. b : $p<0.05$, vs isoflurane grop.

Fig. 2 shows the changes in plasma NE and E concentrations. The baseline values were comparable among the groups. In the control group, NE increased significantly after the tracheal intubation ($p<0.05$). In the isoflurane group, NE increased significantly ($p<0.01$) after the 3-min inhalation of isoflurane and after tracheal intubation , and was significantly higher than that in the control group. In the sevoflurane group, the concentration of NE showed no change during the time course, and was significantly lower than that in the control group after tracheal intubation ($p<0.05$) and that in the isoflurane group after the 3-min ventilation and tracheal intubation ($p<0.05$). The plasma E concentration showed levels lower than the baseline values in all groups throughout the study period, except at 3 min after the inhalation of isoflurane.

Discussion

The hemodynamic and catecholamine response data of the present control group were comparable to those of other studies.[1,2] As Joyce et al.[8] suggested, the administration of thiopental before nitrous oxide stabilized the plasma concentration of catecholamines. However, the hemodynamic and catecholamine responses to laryngoscopy and tracheal intubation were not attenuated by this induction method.

The induction method of the isoflurane group was adopted according to the studies of Randell et al.[5] and Frink et al.[9] The inhalational concentration of sevoflurane was chosen to provide the alveolar concentration of the same potency as that of isoflurane after the 3-min inhalation. With respect to the MAC of sevoflurane in humans, Katoh et al.[10] reported that it as 1.71, and Scheller et al.[11] reported it as 2.05. Because the mean age of the patients who participated in the present study was 46.9± 2.6, closer to that of the patients of Katoh et al., 1.71 was adopted as the MAC of sevoflurane in this study. Ventilation with 3% isoflurane or 4.5% sevoflurane produced comparable end - tidal MAC after 3 min.

In the isoflurane group, the supplementary administration of 3% isoflurane in the gas mixture of N_2O and O_2 attenuated the pressor response to tracheal intubation. However, the inhalation of isoflurane caused an increase in the plasma concentration of NE and was associated with an increase in HR. Although the mechanisms involved in the isoflurane-induced increase in HR are unclear, some explanations are offered as follows. 1) Isoflurane anesthesia is associated with marked vasodilation,[5,12] and depresses baroreflex function less than other inhalational anesthetics such as enflurane and halothane.[2,4] 2) Isoflurane depresses parasympathetic activity to a greater extent than sympathetic activity, and has beta sympathomimetic action.[13,14] 3) The stimulation of sensory afferent nerve endings in the lungs by a high inspired concentration of isoflurane might be the source of the sympathoadrenal response, because isoflurane is an irritating vapor.[15-17]

In the present study, not only the HR, but also the SAP was higher in the isoflurane group than in the control group during manual ventilation, indicating that the vasodilatory effect of isoflurane might be counteracted by the cardiac sympathetic stimulation. Despite the sympathetic stimulation, the pressor response to tracheal intubation was significantly attenuated by isoflurane. This attenuation may be due to a vasodilatory effect of isoflurane, as suggested by several previous studies.[12,13,18]

The inhalation of sevoflurane caused a gradual decline of the SAP with a stable HR. The finding of a stable HR in spite of the decreased SAP during sevoflurane inhalation is consistent with previous studies.[19,20] It seems possible that sevoflurane would depress the baroreflex function to a greater extent than does isoflurane. Additionally, the lower pungency of sevoflurane even at a high inspired concentration may explain the milder hemodynamic change. The increase in plasma NE concentration and the pressor response to laryngoscopy and tracheal intubation were significantly attenuated during sevoflurane inhalation. There was an increase in the HR in response to the tracheal intubation, but no change in the plasma catecholamine concentration. Because plasma NE represents only a small fraction of the NE released at the nerve

endings,[8] it seems possible that there was an increase in the sympathetic nerve activity in the heart without an increase in the plasma NE. Kurosawa et al.[6] evaluated the cardiac sympathetic and parasympathetic activities during sevoflurane inhalation in rats at rest and with noxious mechanical stimulation, and suggested that sevoflurane depressed the sympathetic activity without altering the parasympathetic activity, and attenuated the sympatheic response to painful stimuli. The present results also indicate that sevoflurane attenuates the sympathetic response to tracheal intubation in humans.

In conclusion, isoflurane induction increased the sympathoadrenal activity, resulting in marked tachycardia, but attenuated the pressor response to tracheal intubation. Sevoflurane caused milder hemodynamic changes during inhalation and tracheal intubation, and was accompanied by more stable plasma catecholamine levels than those observed in the control and isoflurane groups, indicating a suppression of sympathethoadrenal activity .

Acknowledgement

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