

Changes in heart rate variability during anaesthesia induction using sevoflurane or isoflurane with nitrous oxide

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Abstract

Background: The purpose of this study was to compare cardiac sympathetic and parasympathetic balance using heart rate variability (HRV) during induction of anaesthesia between sevoflurane and isoflurane in combination with nitrous oxide.

Methods: 40 individuals aged from 30 to 60 years, scheduled for general anaesthesia were equally divided into sevoflurane or isoflurane groups. After 100% oxygen inhalation for a few minutes, anaesthesia was induced with nitrous oxide 3 L min⁻¹, oxygen 3 L min⁻¹ and sevoflurane or isoflurane. Sevoflurane or isoflurane concentration was increased by 0.5% every 2 to 3 breaths until 5% was attained for sevoflurane, or 3% for isoflurane. Vecuronium was administered to facilitate tracheal intubation. After intubation, sevoflurane was set to 2% while isoflurane was set to 1% with nitrous oxide with oxygen (1:1) for 5 min.

Results: Both sevoflurane and isoflurane provoked a decrease in blood pressure, total power, the low frequency component (LF), and high frequency component (HF) of HRV. Although the heart rate increased during isoflurane anaesthesia, it decreased under sevoflurane. The power of LF and HF also decreased in both groups. LF was higher in the isoflurane group while HF was higher in the sevoflurane group. The LF/HF ratio increased transiently in the isoflurane group, but decreased in the sevoflurane group.

Conclusion: Anaesthesia induction with isoflurane-nitrous oxide transiently increased cardiac sympathetic activity, while sevoflurane-nitrous oxide decreased both cardiac sympathetic and parasympathetic activities. The balance of cardiac parasympathetic/sympathetic activity was higher in sevoflurane anaesthesia.

Key words: general anaesthesia, induction, volatile; volatile anaesthetics, sevoflurane, isoflurane; autonomic nervous system; heart rate variability

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Heart rate variability (HRV) is a widely used, non-invasive method to investigate the balance of cardiac sympathetic and parasympathetic activities. A low frequency component (LF, 0.04–0.15 Hz) indicates cardiac sympathetic and parasympathetic activities, while a high frequency component (HF, 0.15–0.4 Hz) shows cardiac parasympathetic activity. Therefore, LF/HF reveals cardiac sympathetic activity [1].

There have been some studies aimed at investigating HRV changes during isoflurane [2–4] or sevoflurane [5–10] anaesthesia. Although we previously compared HRV between two kinds of induction: sevoflurane and thiopental-isoflurane [11], no studies have been conducted in order to compare HRV between isoflurane and sevoflurane anaes-

thesia without intravenous anaesthetics, especially at the induction of anaesthesia. The present study was conducted in order to compare HRV changes during anaesthesia induction with sevoflurane or isoflurane in combination with nitrous oxide.

METHODS

After the approval of the appropriate research committee and obtaining of informed consent, 40 individuals, aged from 30 to 60 years, scheduled for general anaesthesia were equally divided into sevoflurane and isoflurane groups. Those who had cardiac, respiratory, liver, renal or cerebral disease, along with those who were obese (body mass index

Table 1. Demographic data (mean \pm SD)

	Sevoflurane	Isoflurane
Age (years)	50 \pm 8	48 \pm 10
Body mass (kg)	59 \pm 8	60 \pm 5
Height (cm)	159 \pm 7	162 \pm 7
Duration of surgery (min)	194 \pm 78	214 \pm 88

> 30 kg m⁻²), as well as those who had use sedatives daily or habitually before surgery, were excluded from this study.

Midazolam 3 to 5 mg was administered intramuscularly 15 to 30 minutes before entering the operating room for premedication. After 100% oxygen inhalation for a few minutes, anaesthesia was induced using nitrous oxide 3 L min⁻¹, oxygen 3 L min⁻¹ and sevoflurane or isoflurane. Sevoflurane or isoflurane concentration was increased by 0.5% every 2 to 3 breaths until 5% was attained for sevoflurane, or 3% for isoflurane.

Once consciousness was lost, vecuronium at 0.15 mg kg⁻¹ was administered intravenously. When the train of four ratio reached 0, endotracheal intubation was performed. After intubation, sevoflurane end-tidal concentration was set to 2% while isoflurane was set to 1% with nitrous oxide and oxygen (1: 1) for 5 min.

HRV was measured with LRR-03TM (GMS, Tokyo, Japan) and analyzed with Mem CalcTM (Suwa Trust, Tokyo, Japan).

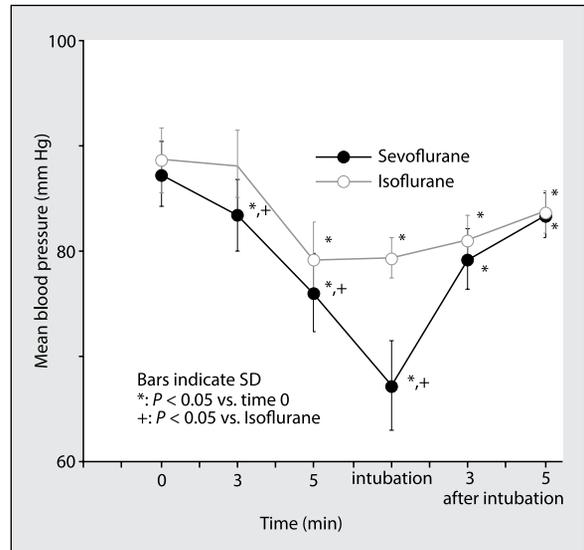
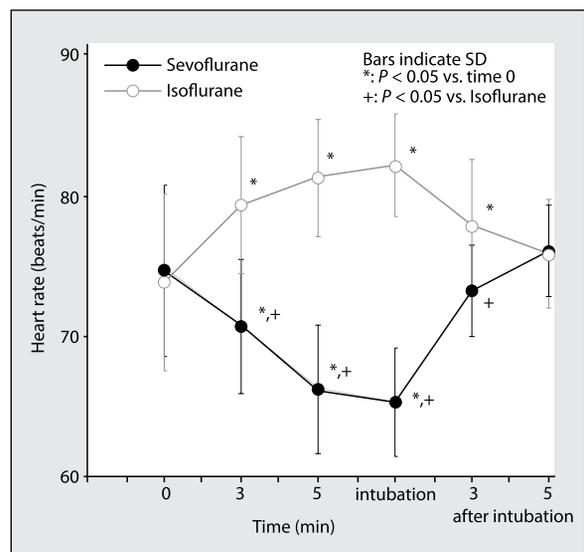
STATISTICAL ANALYSIS

Power analysis was performed in order to detect the inter-group differences of LF and LF/HF with a power of 0.95 and an effect size of 0.2, using G PowerTM software (University of Mannheim, Germany). This revealed that 28 individuals was minimal sample size. Therefore, 40 patients were considered enough to evaluate the difference between sevoflurane and isoflurane.

Statistical analysis was performed with factorial analysis of variance (ANOVA) and the chi-square test and repeated measures ANOVA followed by the Student-Newman-Keuls test. A *P*-value less than 0.05 was considered to be statistically significant.

RESULTS

The demographic data did not differ between the two groups (Table 1). The decrease in blood pressure before intubation was more profound in the sevoflurane group (Fig. 1). Although the heart rate decreased in the sevoflurane group, it increased in the isoflurane group (Fig. 2). The end-tidal CO₂ concentration was lower in the sevoflurane group before intubation, as well as the minimum alveolar concentration (MAC) value (Data not shown). While the

**Figure 1.** Mean blood pressure changes during study**Figure 2.** Heart rate changes during study

total power of HRV decreased in both groups, the isoflurane group showed greater power (Fig. 3).

The power of LF and HF also decreased in both groups. Although LF was higher in the isoflurane group, HF was higher in the sevoflurane group (Fig. 4, 5). LF/HF ratio increased transiently in the isoflurane group, but decreased in the sevoflurane group (Fig. 6).

DISCUSSION

The present study showed that both sevoflurane and isoflurane decreased blood pressure, total power, LF, and HF

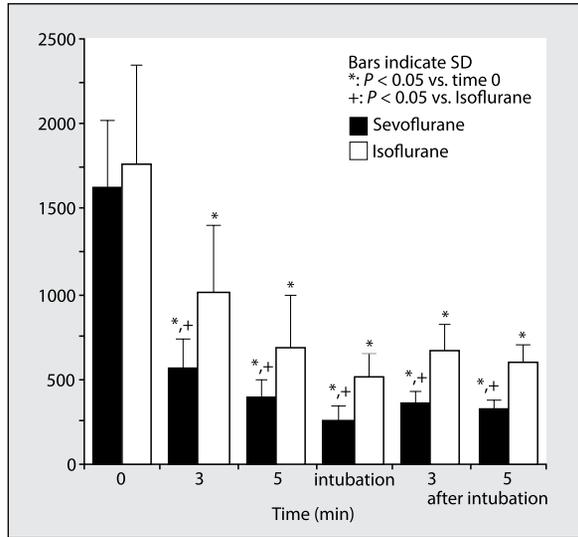


Figure 3. Total power of heart rate variability

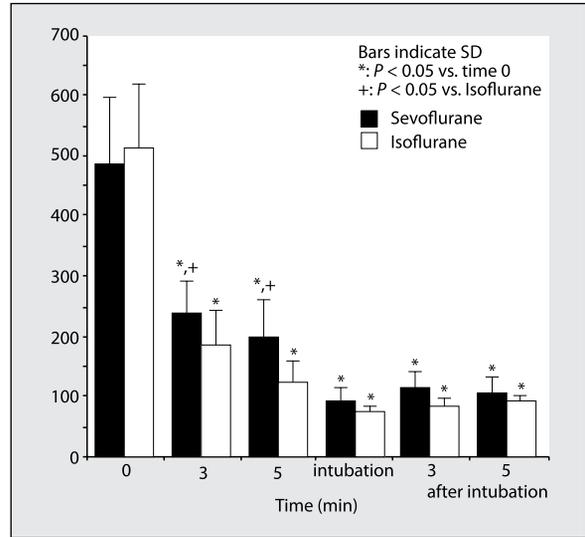


Figure 5. High frequency component of heart rate variability

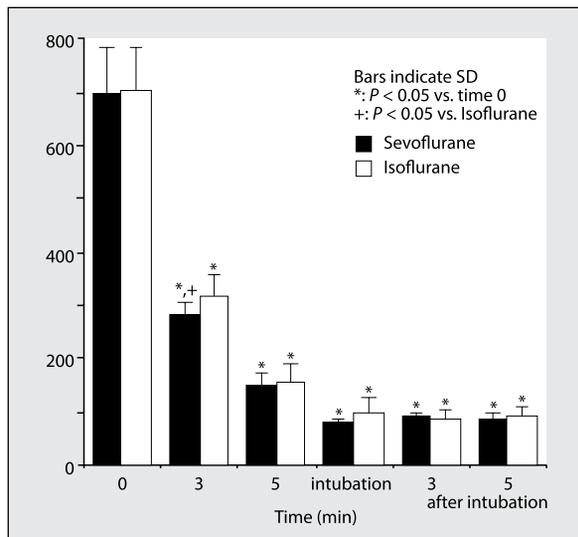


Figure 4. Low frequency component of heart rate variability

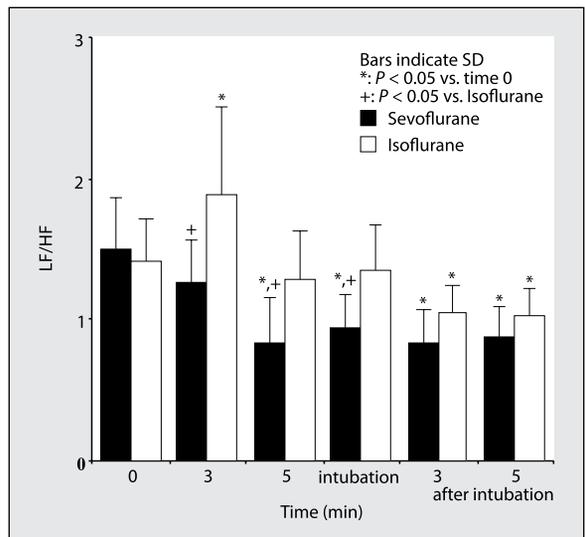


Figure 6. Low frequency component/high frequency component ratio of heart rate variability

of HRV. Although the heart rate increased under isoflurane, it decreased during sevoflurane anaesthesia. The decrease in blood pressure was larger in sevoflurane anaesthesia. The decreases in total power and LF were larger in sevoflurane anaesthesia than those in isoflurane anaesthesia, while that in HF was larger in isoflurane anaesthesia. In isoflurane anaesthesia, LF/HF transiently increased after induction, then decreased, while this decreased in sevoflurane anaesthesia.

In previous studies, isoflurane decreased total power, LF [4], and HF [2]. In isoflurane anaesthesia, HF decreased with an increase in isoflurane concentration, whereas LF and total power showed a biphasic response downward with a second peak at 1.5 MAC of isoflurane [2]. Our pre-

sent results showed a transient increase of LF/HF before intubation during isoflurane anaesthesia. These showed isoflurane increases cardiac sympathetic activity transiently. In a dog study [3], isoflurane resulted in high LF and low HF in a dose dependent manner, which shows high cardiac sympathetic activity.

Sevoflurane is reported to decrease both HF and LF [6, 8, 9]. These results are consistent with our present study. However, our previous study showed that although rapid inhalation induction with 7% sevoflurane with nitrous oxide increased HF before intubation, then decreased, it did not change LF/HF [5]. In the present study, sevoflurane concentration increased gradually, while in the previous study [5],

sevoflurane increased at once to a high concentration. Therefore, it might stimulate cardiac parasympathetic activity during induction. Sevoflurane decreased LF, but not HF and LF/HF, except for at the lower bispectral index (BIS) values (BIS 40) where LF/HF decreased in a study by Kanaya *et al.* [10]. Therefore, in deep sevoflurane anaesthesia, as also shown in other studies [6, 7], both cardiac sympathetic and parasympathetic activity decreased, although the decrease was larger in parasympathetic activity [7].

In our previous study [11], the induction of anaesthesia with sevoflurane-nitrous oxide showed a transient increase in HF without significant changes in LF/HF, while induction with thiopental-isoflurane-nitrous oxide decreased HF and transiently increased LF/HF. While the induction method of our previous study was almost the same as our present study in the sevoflurane group, we did not find a transient increase in HF this time. The only difference between the two studies was that the previous study used atropine as a premedication in addition to midazolam. This might have provoked the decrease in HF values. We did not know the reason for this discrepancy. In a study by Ishida *et al.*, isoflurane decreased HF and LF, and increased LF/HF, while sevoflurane decreased LF, HF, and LF/HF. Moreover, Ishida *et al.* [12] studied the changes not in the induction of anaesthesia, but during the maintenance phase after induction with intravenous anaesthetics. Therefore, their results included the effects of intravenous anaesthetics, and were almost consistent with our results.

It has been documented that the plasma epinephrine concentration is higher in isoflurane anaesthesia than that in sevoflurane anaesthesia [13], which is similar to our results showing higher cardiac sympathetic activity in isoflurane anaesthesia. Picker *et al.* showed that sevoflurane and isoflurane decreased both vagal tone and HRV in dog experiments [14]. Indeed, their experiments may display similar results with our clinical results.

In conclusion, we may state that anaesthesia induction with isoflurane-nitrous oxide transiently increased cardiac sympathetic activity, while sevoflurane-nitrous oxide decreased both cardiac sympathetic and parasympathetic activities. Moreover, the balance of cardiac parasympathetic/sympathetic activity was higher in sevoflurane anaesthesia.

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