The Comparative Cardiovascular Effects of Sevoflurane with Halothane and Isoflurane

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Using closed chest dogs, the cardiovascular effects of sevoflurane were compared with those of halothane and isoflurane in equipotent doses of 1.0, 1.5, 2.0, 2.5 and 3.0 MAC. They were evaluated by the changes of arterial blood pressure, central venous pressure, pulmonary artery pressure, maximum rate of left ventricular pressure rise (LV dp/dt), cardiac output and coronary sinus blood flow. The suppression of left cardiac function by sevoflurane was less than that of halothane, but was greater than that of isoflurane. Heart rate, systemic vascular resistance with sevoflurane were slightly lower than that of isoflurane. The coronary sinus blood flows with sevoflurane and isoflurane were significantly ($P<0.05$ at 1.0 MAC, $P<0.005$ at 2.0 MAC) higher than halothane. There was no significant difference on coronary sinus flow between sevoflurane and isoflurane. The depth of anesthesia could be quickly changed by adjustment of inspired sevoflurane concentration in comparison with the other two anesthetics. (Key words: sevoflurane, halothane, isoflurane, myocardial function, coronary blood flow)

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The suppression of cardiac function and coronary blood flow during anesthesia is of critical importance in all patients. As the newest major inhalational agent, sevoflurane must be compared in this respect with the other two potent inhalational anesthetics, isoflurane and halothane. Gelman et al. reported in the dog that myocardial blood flow increased with isoflurane[1]. Moffitt et al. reported the effects on cardiac function and coronary sinus blood flow of halothane anesthesia[2]. Bruckner and colleagues compared the cardiovascular effect of sevoflurane with that of halothane on the same volume percent (0.5–3.0%)[3]. However the comparison of cardiovascular effects by inhalational anesthetics must be done on the equipotent dose. We reported MAC (minimum alveolar concentration) of sevoflurane as 2.36%, about 2.5 times that of halothane[4]. It is used for comparison of the pharmacological properties of inhalational anesthetics. The present study attempted to compare sevoflurane with halothane and isoflurane with respect to the cardiovascular effects and coronary sinus blood flow on the equipotent dose of MAC (0.5–3.0 MAC).

Materials and Methods

A total of 23 mongrel dogs of either sex were used. Fifteen dogs, weight 7.5–15.0 kg, were used for measurements of cardiovascular effects. They were anesthetized on two or three occasions, more than two weeks apart with each of the anesthetics of sevoflurane,

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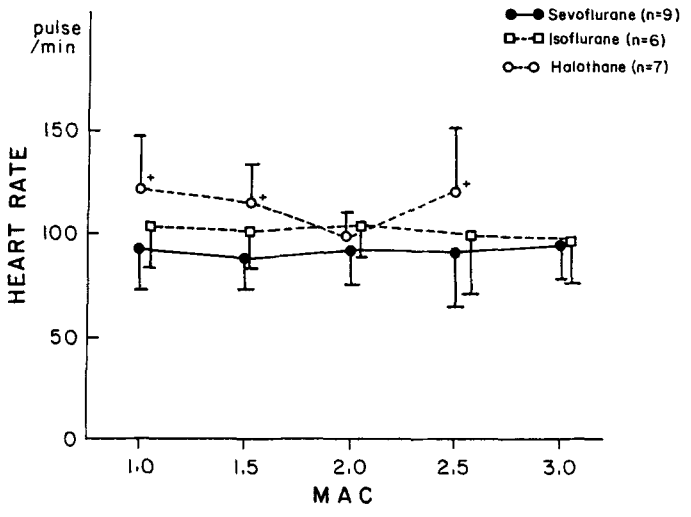

Fig. 1. +: Significant difference from sevoflurane ($P<0.05$).

The mean values (±SD) for heart rate are shown for the three groups, sevoflurane, isoflurane and halothane. Hart rate did not change significantly as the anesthetic concentration increased.

halothane and isoflurane. All dogs fasted for 12 hours. Sevoflurane, 5% in oxygen, was delivered through a dog mask. Isoflurane and halothane, both 4% in oxygen, were administered in a sealed box, 600 liter in volume, since the animals did not accept these anesthetics when they were given by mask. When the dogs became unconscious, the trachea was intubated. The end tidal carbon dioxide was maintained at 30–35 mmHg with the aid of Datex® end tidal CO_2 monitor (CD-300®). The end tidal anesthetic concentration was measured with the Engstrome EMMA®, pre-calibrated with mass spectrometer and gas chromatograph. The rectal temperature was maintained at 36.5°C–38.0°C. The electrocardiogram (lead II) was monitored. A Swan-Ganz thermodilution catheter (5 Fr. or 6 Fr.) was inserted via the external jugular vein. A 20 gauge flexible catheter was passed into the right ventricle and withdrawn under pressure monitoring to the right atrium for pressure recording and injection of cold saline for measurement of cardiac output. The femoral artery was cannulated for recording blood pressure. All catheters for pressure recording were connected to Hewlet-Packard® (HP 7404A®) transducers positioned midway between the front and back of the chest. Left ventricular pressure was measured with Millar Micro-Tip® catheter pressure transducer (MPC-500®). Heart rate, mean arterial pressure, cardiac output, systemic vascular resistance, LV dp/dt max, pulmonary artery pressure and central venous pressure were measured at 1.0, 1.5, 2.0, 2.5, 3.0 MAC with three anesthetics. The statistical comparisons among the measurements of different exposure doses were performed using Student's paired t-test and those among the measurements of different inhalational anesthetics were performed using Student-Newman-Keuls test.

The remaining 8 dogs, weight 8.5–15.5 kg, were used to study the drug effects on the coronary sinus blood flow. The anesthesia was induced and the trachea was intubated in the same way as in the previous study. All surgical procedures were performed under 2 MAC anesthesia with one of the anesthetics studied. The coronary blood flow was measured using 2 channel-thermodilution catheter, CCS-7U-90B® (Webster Laboratories®), which was introduced in the coronary sinus via the jugular vein. The catheter was guided under fluoroscopy and positioned by confirming with a radiopaque material, Angiographin®. The cardiac output was measured with a Swan-Ganz catheter introduced via the remaining jugular vein and connected

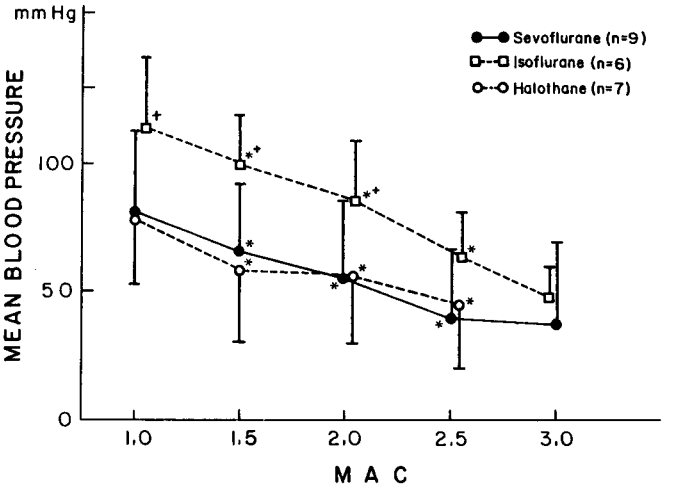

Fig. 2. +: Significant difference from sevoflurane ($P<0.05$). *: Significant difference from 1.0 MAC ($P<0.05$).

The mean values (±SD) for mean blood pressure are shown for the three groups. Blood pressure decreased significantly as the anesthetic concentration increased.

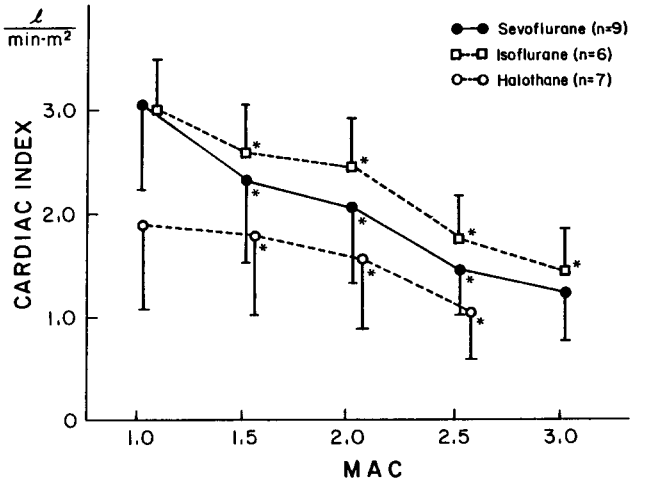

Fig. 3. *: Significant difference from 1.0 MAC ($P<0.01$).

The mean values (±SD) for cardiac index are shown for the three groups. Cardiac index decreased significantly in all groups as anesthetic concentration increased.

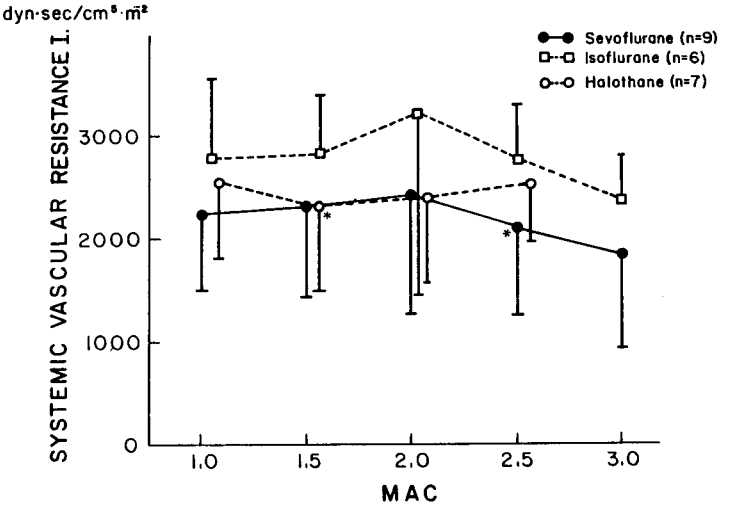

Fig. 4. *: Significant difference from 1.0 MAC ($P<0.05$).

The mean values (±SD) for systemic vascular resistance index are shown for the three groups.

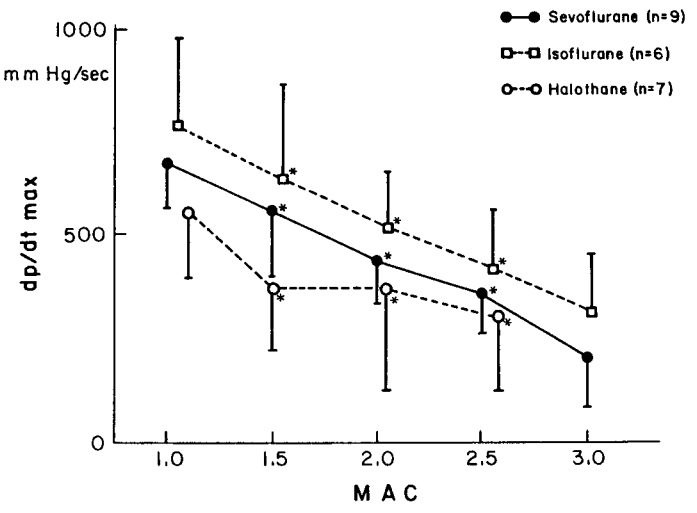

Fig. 5. *: Significant difference from 1.0 MAC ($P<0.05$).

The mean values (±SD) for LV dp/dt max are shown for the three groups. LV dp/dt max decreased significantly as anesthetic concentration increased.

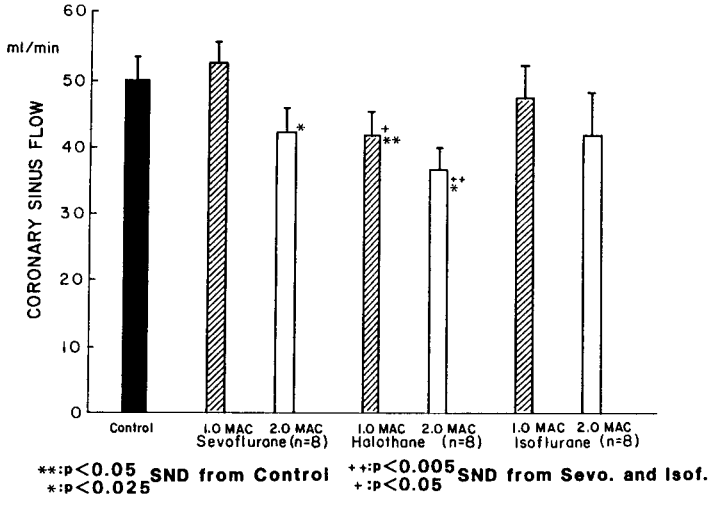

Fig. 6. SND: Significant difference. Sevo.: Sevoflurane. Isof.: Isoflurane.

The mean values (±SE) for coronary sinus flow are shown for the three groups. The coronary sinus flows for sevoflurane were significantly higher than those of halothane.

to the Hewlet Packard® transducer (HP 7404A®). The concentration of anesthetics studied were 2.0 and 1.0 MAC. Approximately 40 min after discontinuation of the first test anesthetic, when its endtidal concentration became less than 0.05%, the next test anesthetic was administered. The control measurements were done at this end tidal anesthetic level, and the study of the thired anesthetic was done in succession. We numbered the three anesthetics randomly in each experiment. The results were tested with student-Newman-Keuls test in comparison among the measurements of different inhalational anesthetics. Student's paired t-test was used in comparison among the measurements of different exposure doses.

Results

Heart rate did not change significantly as the anesthetic concentration increased (fig. 1). Arterial pressure decreased significantly in response to decreased cardiac index (fig. 2). As the anesthetic concentration increased, cardiac index and dp/dt max. decreased significantly in all anesthetics (fig. 3, 5). Arterial pressure at 2.0 and 3.0 MAC sevoflurane decreased significantly to 69.1 and 47.8% of that at 1.0 MAC. Although the arterial pressure of sevoflurane was significantly lower than that of isoflurane, cardiac index of sevoflurane was sustained

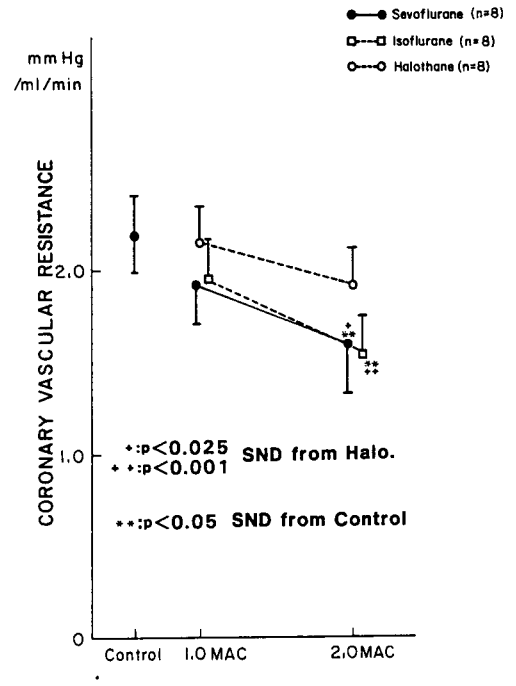

Fig. 7. SND: Significant difference. Halo.: Halothane.

The mean values (±SE) for coronary vascular resistance are shown. The coronary vascular resistance with sevoflurane and isoflurane were significantly lower than that with halothane at 2.0 MAC.

and systemic vascular resistance was low (fig. 4). The central venous pressure and pulmonary artery pressure did not change significantly. In five of seven halothane cases, measurements were unobtainable at 3.0 MAC because of circulatory collapse. The change of coronary sinus blood flow and coronary vascular resistance at 1.0 and 2.0 MAC are shown in figure 6, 7. The coronary sinus blood flows of halothane were significantly ($P<0.05$ at 1.0 MAC, $P<0.005$ at 2.0 MAC) lower than those of sevoflurane and isoflurane. The coronary sinus blood flow at 2.0 MAC of sevoflurane was significantly ($P<0.025$) lower than control blood flow. The coronary vascular resistances with sevoflurane and isoflurane were significantly (sevoflurane: $P<0.025$, isoflurane: $P<0.001$) lower than halothane at 2.0 MAC. There was no significant difference on coronary vascular resistance between sevoflurane and isoflurane.

Discussion

The decrease of mean arterial pressure by sevoflurane was almost the same as that by halothane, but was greater than that by isoflurane. It must be emphasized that because of the small blood-gas partition coefficient of 0.6[5] which is smaller than that of other commonly available volatile anesthetics, the time required for the stabilization of blood pressure was short, only 1–2 minutes, compared with 30–40 minutes of halothane and 15–20 minutes of isoflurane. Nonetheless, the cardiac output during sevoflurane anesthesia was greater than that of halothane anesthesia and slightly smaller than that of isoflurane. Heart rate did not vary with different concentrations of sevoflurane. The F_A/F_I of sevoflurane (0.75 at 0.5 min.) rose more rapidly than that of halothane (0.25 at 0.5 min)[4]. The arrhythmogenicity of sevoflurane is lower than isoflurane and halothane[6]. Thus, sevoflurane has an advantage in the rapid control of depth of anesthesia by adjusting the inspired concentration. Gibbon and colleagues reported that the increase in the inspired concentration decreased the cardiac output and that the resulting decrease in uptake of anesthetics gave rise to the accelerated rise in the alveolar concentration in controlled ventilation[7]. In controlled ventilation with sevoflurane anesthesia, more attention will be necessary to avoid the decrease of blood pressure, because the depth of anesthesia changes more rapidly than that in spontaneous respiration.

Bruckner and colloeagues reported in the dog that cardiac functions were sustained better through all levels of sevoflurane anesthesia than the case of halothane[3]. They compared sevoflurane with halothane at the range of 0.5–3.0 percent (about 0–1.27 MAC in sevoflurane), and the results were consistent with our findings.

The measurement of coronary sinus blood flow requires stable position of catheter

in the coronary sinus to avoid admixture of the blood from right atrium[8,9]. These prerequisite conditions were satisfied in the present study. Tarnow and colleagues[10] reported that isoflurane decreased coronary vascular resistance but did not alter coronary blood flow. Gelman et al. reported in the dog that myocardial blood flow increased with isoflurane, despite reduction of blood pressure and cardiac output[1]. In the present study, isoflurane did not change the coronary blood flow significantly, but lowered the coronary vascular resistance (at 2.0 MAC isoflurane). In contrast halothane decreased coronary blood flow.

Reiz and colleagues suggested that the coronary vasodilatation produced by isoflurane in patients with coronary disease might cause a "steal" in the coronary circulation[11]. It is not clear that sevoflurane causes such a "steal" of coronary blood flow. Low cardiac work, moderate change of heart rate and decreased coronary vascular resistance produced by sevoflurane could be appraised by our experiments.

Measurement was not taken at 3.0 MAC halothane because of the circulatory collapse. The myocardial concentration of anesthetic which produces circulatory collapse may be divided by the concentration required for anesthesia (MAC value) to obtain a "cardiac anesthetic index." A larger ratio indicates a larger margin of safety. The ratio for isoflurane is 5.7 and halothane is 3.0 in rats[12]. That for sevoflurane would be greater than 3.0.

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