Effects of Sevoflurane with or without Nitrous Oxide on Cardiac Contractility and Sinoatrial Node Rate

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Cardiac effects of sevoflurane (SE) with or without nitrous oxide were examined in the canine blood-perfused papillalry muscle and sinoatrial node preparations. Although SE depressed developed tension (DT), mean arterial pressure (MAP) and heart rate of the donor dog (DHR) dose dependently, sinoatrial rate (SAR) was not changed significantly. No significant chanages in MAP, DHR and SAR were observed with the addition of nitrous oxide to SE. However, the addition of nitrous oxide to SE resulted in significant decrease of DT.

These results suggest that SE depresses BP and cardiac contractility dose dependently, but dose not change heart rate. The combination of nitrous oxide and SE may produce less cardiovascular depressant effect at a given MAC level than SE given alone. (Key words: sevoflurane, nitrous oxide, cardiac effects)

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Sevoflurane (SE) is a newly developed inhalational anesthetic. The addition of nitrous oxide to halothane[1] or enflurane[2] produced less cardiovascular depressant effect at a given MAC level than halothane or enflurane given alone. There have been few reports examined effects of the addition of nitrous oxide to SE[3]. Then to examine the cardiac effects of SE with or without nitrous oxide, we used a method in which an isolated papillary muscle and a sinoatrial node were perfused by the other donor dog.

Methods

Experiments were carried out on six papillary muscle[4] and sinoatrial node preparations[5] perfused by the circulating blood of anesthetized donor dogs through the cannulated anterior septal artery (ASA) and right coronary artery (RCA). The technique of the methods has been described in detaile else where[6]. Six donor dogs of either sex, weighnig 12–20 kg, were obtained as follows: General anesthesia (thiamylal, 15 mg/kg i.v. for induction and SE, 3.0% for maintenance) was given for placement of Tygon catheters in the carotid artery (for supplying arterial blood to the preparations) and the jugular vein (for returning venous blood), and of a polyethylene catheter in the femoral artery (for monitoring blood pressure). As soon as SE was stopped, donor dogs were injected with intramuscular droperidol 0.5 mg/kg and fentanyl 0.04 mg/kg, and with intravenously vecuronium 0.2 mg/kg. Anesthesia was maintained by continuous i.v. infusions of pentobarbital (1 mg/kg/h) and fentanyl (10 μg/kg/h). Controlled ventilation with a Shinano constant volume ventilator (Shinano Apparatus) was facilitated by a continuous i.v. infusion

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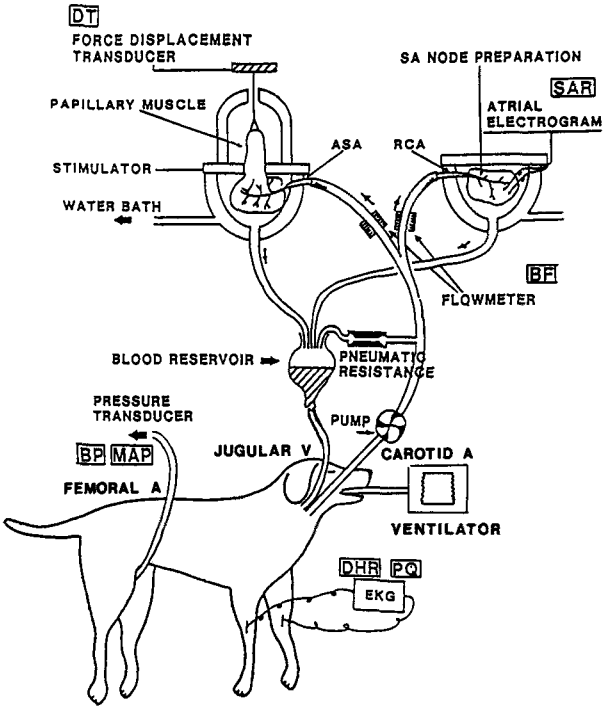

Fig. 1. A schematic representation of cross-circulation diagram of the isolated papillary muscle and sinoatrial node preparations. DT: developed tension of the papillary muscle, SAR: sinoatrial rate of the sinoatrial node preparation, ASA: the anterior septal artery, RCA: the right coronary artery.

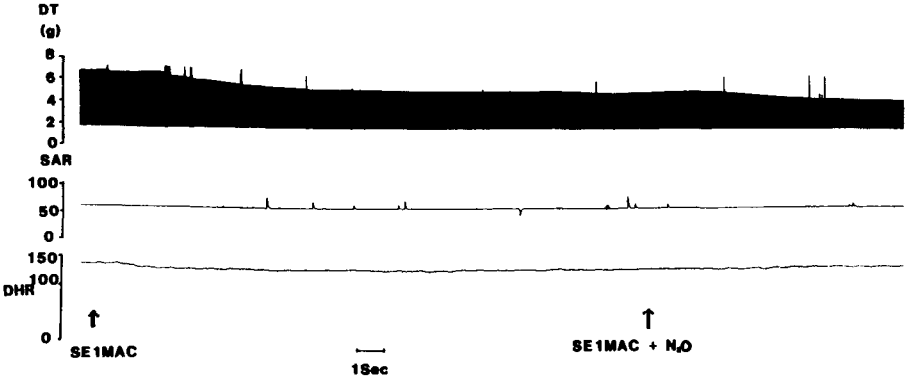

Fig. 2. Effects of SE with or without nitrous oxide on DT, SAR and DHR.

of vecuronium (0.04 mg/kg/h). Tidal volume was set at 20 ml/kg. Respiratory rate was adjusted to maintain the arterial carbon dioxide tension (Pa_{CO_2}) between 30 and 40 mmHg. All animals received 5 ml/kg/h of normal saline. After an initial 60 min stabilization period, each donor dog was studied during the following conditions: 1) control, 2) 60% nitrous oxide, 3) 1.18% end-tidal sevoflurane, 4) 1.18% end-tidal sevoflurane + 60% nitrous oxide, 5) 2.36% end-tidal sevoflurane, 6) 2.36% end-tidal sevoflurane + 60% nitrous oxide, 7) 3.54% end-tidal sevoflurane and 8) 3,54% end-tidal sevoflurane + 60% nitrous oxide anesthesia. The order of steps 1), 3), 5) and 7) was randomized for every dog and the steps 2), 4), 6) and 8) followed steps 1), 3), 5) and 7) respectively. End-tidal sevoflurane concentration was monitored continuously during the equilibration period (about 30 min) using a calibrated infrared medical gas analyzer (anesthetic agent monitor, ACOMA). $F_{I_{O_2}}$ was kept 0.4 with nitrogen and oxygen in

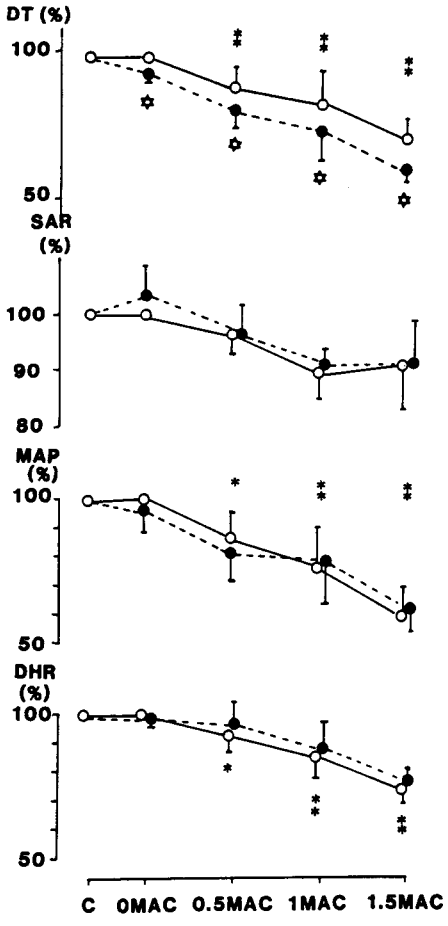

Fig. 3. Summarized results of SE with (solid circles) or without nitrous oxide (open circles) on DT, SAR, MAP and DHR.

Asterisks (*) mean that values were significantly different from the values of control (C) at each stage (*:$P < 0.05$, **:$P < 0.01$). Another asterisks (✡) mean that values of SE with nitrous oxide group were significantly different from the values of SE group at each stage (✡:$P < 0.05$).

steps 1), 3), 5) and 7). Tension developed (DT) by the papillary muscle, the sinoatrial rate (SAR) of the sinoatrial node preparation, mean arterial pressure (MAP) of the donor dog and heart rate of the donor dog (DHR) were monitored[6]. For determination of the effects of inhaled gas, Student's t-test (dependent) was used. When P-values are smaller than 0.05, it is decided that a satistical significant difference exists between two mean values.

Results

Although SE depressed DT, MAP and DHR dose-dependently, SAR did not change significantly. No significant changes in MAP, DHR and SAR were observed with the addition of nitrous oxide to any concentrations of SE. However, the addition of nitrous oxide to SE resulted in significant decrease of DT in any concentrations of SE (table 1).

Discussion

The model used in the present experiments is very suitable for determining the cardiovascular effects of anesthetics[7,8], either intravenous or inhalation anesthetics. In the canine isolated, blood-perfused heart preparations the direct effects of the agents which were given even into the donor dog could be observed, while in the donor animal the systemic effects of the agents which would be modified by neurohumoral compensatory reflex mechanisms could be observed.

In the present study, DT, MAP and DHR were decreased dose dependently by SE, however SAR was not decreased significantly. These results, except on DHR and

Table 1. Effects of SE with or without nitrous oxide

	addition of N_2O	C	1/2MAC	1MAC	3/2MAC
DT (%)	−	100	91 ± 6.2	79 ± 12	67 ± 14
	+	95 ± 2.7	87 ± 10	72 ± 15	62 ± 13
SAR (beats/min)	−	74 ± 8	72 ± 7	71 ± 5	65 ± 14
	+	75 ± 12	71 ± 9	70 ± 5	65 ± 4
DHR (beats/min)	−	137 ± 25	123 ± 22	120 ± 27	109 ± 25
	+	130 ± 27	130 ± 28	123 ± 24	107 ± 29
MAP (mmHg)	−	105 ± 13	85 ± 19	81 ± 16	71 ± 13
	+	102 ± 17	85 ± 24	74 ± 10	68 ± 10

SAR, are generally consistent with previous reports by Manohar et al[3]. The difference in DHR may be attributed to the higher DHR resulting from the hyperhemodynamic state in the control state in our study. Iwatsuki et al.[9] and Akazawa et al.[10] reported that SE produced dose-dependent decrease in heart rate. These reports are consistent with our present study. The direct effect of SE to HR can be observed in SAR in the present study, because sinoatrial node preparation is free from the influence of neurohumoral response. In the present experiment, nitrous oxide plus SE more depressed DT than SE alone. Nitrous oxide have sympathetic effect and may have cardiac depressant effects. By sympathetic and cardiac depressant effects, MAP didn't change significantly, but in the papillary muscle the direct depressive effects of the combination of nitrous oxide plus SE may be observed.

Our results suggest that SE depresses BP and cardiac contractility dose dependently, but dose not change HR. The combination of nitrous oxide and SE may appear to produce less depression at a given MAC level than SE given alone.

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References

1. Smith NT, Eger II EI, Stoelting RK, Whayne TF, Cullen D, Kadis LB: The cardiovascular and sympathomimetic responses to the addition of nitrous oxide to halothane in man. Anesthesiology 32:410–421, 1970
2. Smith NT, Calverley RK, Pryo-Roberts C, Eger II EI, Jones CW: Impact of nitrous oxide on the circulation during enflurane anesthesia in man. Anesthesiology 48:345–349, 1978
3. Manohar M, Parks CM: Porine systemic and regional organ blood flow during 1.0 and 1.5 minimum alveolar concentration of sevoflurane anesthesia without and with 50% nitrous oxide. J Pharmacol Exp Ther 231:640–648, 1984
4. Endoh M, Hashimoto K: Pharmacological evidence of autonomic nerve activities in canine papillary muscle. Am J Physiol 218:1459–1463, 1970
5. Kubota K, Hashimoto K: Selective stimulation of the parasympathetic preganglionic nerve fibres in the excised and blood-perfused SA node preparation of the dog. Naunyn-Schmiedeberg's Arch Pharmacol 278:135–150, 1973
6. Manabe M, Motomura S, Kumazawa T, Ookawa I, Oguchi T: Positive inotropic and chronotropic effects of pancuronium and vecronium in the canine blood-pefused papillary muscle and sinoatrial node preparations. J Anesth 2:202–206, 1988
7. Motomura S, Kissin I, Aultman DF, Reves JG: Effects of fentanyl and nitrous oxide on contractility of blood-perfused papillary muscle of the dog. Anesth Analg 63:47–50, 1984
8. Manabe M, Motomura S, Hashimoto K: Interaction between diltiazem and halothane or enflurane in the canine blood-perfused papillary muscle and sinoatrial node preparations cross-circulated by chronically instrumented conscious donor dog. J Anesth 2:50–62, 1988
9. Iwatsuki N, Kaise A, Koga Y, Ishii H: Cardiovascular interaction between sevoflurane and nicardipine in open chest dogs. J Anesth 2:146–153, 1988
10. Akazawa S, Shimizu R, Kasuda H, Nemoto K, Yoshizawa Y, Inoue S: Effects of sevoflurane on cardiovascular dynamics, coronary circulation and myocardial metabolism in dogs. J Anesth 2:227–241, 1988