Effects of nitrous oxide on mask induction of anesthesia with sevoflurane or isoflurane in dogs

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Objective—To determine the effects of nitrous oxide (N_2O) on the speed and quality of mask induction with sevoflurane or isoflurane in dogs.

Animals—7 healthy Beagles.

Procedure—Anesthesia was induced with sevoflurane or isoflurane delivered in 100% oxygen or in a 2:1 mixture of N_2O and oxygen via a face mask. Each dog received all treatments with at least 1 week between treatments. Initial vaporizer settings were 0.8% for sevoflurane and 0.5% for isoflurane (0.4 times the minimum alveolar concentration [MAC]). Vaporizer settings were increased by 0.4 MAC at 15-second intervals until settings were 4.8% for sevoflurane and 3.0% for isoflurane (2.4 MAC). Times to onset and cessation of involuntary movements, loss of the palpebral reflex, negative response to tail-clamp stimulation, and endotracheal intubation were recorded, and cardiopulmonary variables were measured.

Results—Administration of sevoflurane resulted in a more rapid induction, compared with isoflurane. However, N_2O had no effect on induction time for either agent. Heart rate, mean arterial blood pressure, cardiac output, and respiratory rate significantly increased and tidal volume significantly decreased from baseline values immediately after onset of induction in all groups. Again, concomitant administration of N_2O had no effect on cardiopulmonary variables.

Conclusions and Clinical Relevance—Administration of N_2O did not improve the rate or quality of mask induction with sevoflurane or isoflurane. The benefits provided by N_2O attributable to concentrating and second gas effects appear minimal in healthy dogs when low solubility inhalation agents such as isoflurane and sevoflurane are used for mask induction. (*Am J Vet Res* 2001;62:1727–1733).

Administration of inhalation anesthetics via a face mask is a good choice for induction of anesthesia in small animals,[1-3] because it results in a smooth and rapid onset of anesthesia. Moreover, mask induction provides the veterinarian with greater control of anesthetic depth, compared with IV administration of induction agents. Induction of anesthesia with inhalation anesthetics appears to be appropriate for outpatients receiving general anesthesia prior to computed tomography or magnetic resonance imaging, patients undergoing minor surgery that require rapid recovery from anesthesia, or high-risk patients with hepatic failure whose recovery period would be prolonged if anesthetics were administered intravenously.

Mask induction is most efficient when agents with a high potency and low blood solubility are administered. Recent introduction of new halogenated volatile anesthetics such as isoflurane and sevoflurane has made mask induction a more attractive option for veterinarians. Isoflurane is one of the safest and most effective volatile anesthetics available for human and veterinary patients.[4] Sevoflurane has emerged as the most promising agent after isoflurane for mask induction in humans. The blood-gas partition coefficient of sevoflurane (0.65 at 37 C) is approximately half that of isoflurane (1.40 at 37 C).[5] The mean (± SD) **minimum alveolar concentration (MAC)** for sevoflurane is 2.09 ± 0.13% in dogs, indicating that sevoflurane is less potent than halothane (MAC, 0.94 ± 0.09%) or isoflurane (1.30 ± 0.12%).[6] Sevoflurane induces cardiopulmonary changes similar to those induced by isoflurane, and the arrhythmogenic dose of epinephrine in dogs during sevoflurane anesthesia (8.6 µg/kg of body weight/min) is higher than that during halothane anesthesia (2.2 µg/kg/min) but similar to that during isoflurane anesthesia (9.8 µg/kg/min).[7,8]

Mask induction with sevoflurane is reported to be faster and better in dogs than isoflurane, enflurane, or halothane.[6,9] Although mask induction is sometimes associated with pronounced cardiovascular responses characterized by an increase in heart rate and arterial blood pressure,[10,11] these changes are similar to or less severe than those caused by IV administration of induction agents such as thiobarbiturates and propofol.[12] Induction of anesthesia with sevoflurane or isoflurane has been determined to be useful and safe in a clinical study[13] of 124 small- to medium-sized dogs (body weight, approx 14 kg) undergoing surgery at our institute.

Regardless of the advantages of mask induction, delivery of inhalation anesthetics via a face mask can be difficult in some patients. Difficulties include struggling, apnea, breath-holding, vocalization, ataxia, and excitement.[1-3,10,11,13] **Nitrous oxide (N_2O)** is the least plasma soluble of the commonly used inhalation anesthetics (blood-gas partition coefficient, 0.47 at 37 C).[4] Thus, its onset of action is rapid. Although the anesthetic potency of N_2O in dogs (MAC, 222%) is approximately half that in humans (104%),[4] N_2O can still be of value in veterinary practice, particularly when adminis-

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tered at high concentrations (50 to 70%) concomitantly with other more potent volatile anesthetics. Administered this way, N_2O exerts a second gas effect, which results from an increased inspiratory volume of the more potent agent secondary to the large volume of N_2O inspired. In addition, the second gas (ie, the more potent agent) is concentrated in a smaller volume. This has the advantage of decreasing the time of mask induction by augmenting the alveolar concentration of the more potent and soluble agent. Nitrous oxide has been recommended as an adjunct agent for mask induction with halothane or methoxyflurane in dogs.[1-3]

We hypothesized that administration of N_2O would also improve the speed and quality of mask induction with sevoflurane or isoflurane. Thus, the purpose of the study reported here was to determine the effects of N_2O on the speed and quality of mask induction with sevoflurane or isoflurane in dogs. We elected to use a conventional incremental mask induction protocol, because this method has an advantage over rapid mask induction in terms of avoiding induction-related complications such as struggling and breath-holding, which may occur in response to rapid administration of high concentrations of inhalation anesthetics.[1-3]

Materials and Methods

Animals—Seven Beagles (4 females and 3 males) were used. Their mean age was 15 months (range, 12 to 18 months), and their mean body weight was 9.8 kg (range, 8.5 to 11.4 kg). Dogs were housed in individual runs maintained at constant temperature and humidity and fed a commercial dry food once daily; water was available ad libitum. Food was withheld for 12 hours before each experiment. All experimental procedures were reviewed and approved by the Animal Care Committee of the Graduate School of Agricultural and Life Sciences and were performed in accordance with the *Guidelines for Animal Experimentation* established by the Japanese Association for Laboratory Animal Science.

Animal preparation—At least 7 days before the study, a 14-gauge heparin-coated polyvinyl chloride catheter[a] was implanted into the left common carotid artery of each dog for measurement of arterial blood pressure as described.[8,10,14] Butorphanol (0.2 mg/kg of body weight, IM) was administered every 6 hours for 24 hours after catheter placement for postoperative analgesia. The catheter was tunneled subcutaneously and covered with an elastic adhesive bandage around the neck to prevent the dogs from dislodging the catheter. Dogs received cephalexin (25 mg/kg, PO, q 12 h) for at least 10 days after surgery. Blood samples were obtained daily for CBC and serum biochemical analyses to confirm that dogs were in good health.

Drugs and anesthesia equipment—Sevoflurane, isoflurane, and N_2O were the anesthetic agents used. Minimum alveolar concentrations for sevoflurane, isoflurane, and N_2O in dogs are 2.09, 1.30, and 222%, respectively.[4,6] A semiclosed circle anesthetic system[b] with an out-of-circle agent-specific vaporizer was used for induction. The sampling head from an anesthetic gas analyzer[c] was inserted into the anesthetic circuit between the face mask[d] and the Y-piece connector to monitor inspired and expired gases. Data were simultaneously downloaded to a computer, and anesthetic concentrations were calculated every 15 seconds. All experiments were performed in an operating room equipped with central vacuum systems so that waste gases from the breathing system were vented through the pop-off valve and discharged into a scavenging system through corrugated tubing (outer diameter, 30 mm).

Experimental protocol—Each dog received sevoflurane in oxygen, isoflurane in oxygen, sevoflurane in 66% N_2O, or isoflurane in 66% N_2O in a randomized cross-over design with at least 7 days between treatments. All 7 dogs were assigned to receive each treatment once. Immediately prior to each treatment, dogs were positioned in sternal recumbency on a restraining table.[e] A 6-F 10-cm introducer[f] was implanted percutaneously into the right jugular vein. A 5-F Swan-Ganz catheter[g] was then positioned at the proximal portion of the right atrium and at the distal portion of the pulmonary artery. An IV catheter was placed in the cephalic vein, and lactated Ringer's solution (10 ml/kg/h) was infused. Anesthesia was induced by use of a face mask connected to the anesthetic system. To acclimate dogs to the mask, dogs were allowed to breathe 100% oxygen through the mask at a flow rate of 4 L/min for at least 1 minute before induction. Baseline rectal temperature and cardiopulmonary variables were measured. The anesthetic vaporizer was then turned to a setting of 0.8% for sevoflurane or 0.5% for isoflurane (0.4 MAC) in 100% oxygen or a 2:1 mixture of N_2O and oxygen at a flow rate of 4 L/min. Vaporizer settings were increased by 0.4 MAC at 15-second intervals until setting were 4.8% for sevoflurane or 3.0% for isoflurane (2.4 MAC). These settings were maintained until no response was elicited to application of a noxious stimulus to the tail (negative tail-clamp response). Intubation was attempted. If the mouth could not be opened, then anesthetic induction was continued at the same setting (ie, 2.4 MAC), and intubation was attempted at the next minute interval. At the completion of the induction period, the vaporizer was set to 0%, and dogs were allowed to recover. No other medications were administered during the study.

Assessment of induction speed—Time to onset and cessation of involuntary movements, loss of the palpebral reflex, a negative tail-clamp response, and successful intubation were recorded. The palpebral reflex was assessed by gently brushing the eyelashes of 1 eyelid with a finger every 10 seconds after the onset of induction. The tail-clamp response was monitored by applying a large noncrushing intestinal forceps to the tail for 3 seconds at 1-minute intervals.

Determination of cardiopulmonary variables—Heart rate was recorded on a cardiotachometer[h] that was triggered by a lead-II ECG. **Mean arterial blood pressure (MAP)** was measured by use of a pressure transducer[i] connected to the arterial catheter. **Right atrial pressure (RAP)** and **mean pulmonary arterial pressure (MPAP)** were measured by use of the Swan-Ganz catheter. Respiratory rate, tidal volume (V_T), and expired volume per unit time ($\dot{V}_E$) were recorded by use of a respirometer[j] attached to the face mask. From tracings of the respiratory airflow, changes in ventilatory pattern during mask induction were characterized for each dog. Breath-holding was defined as the prolongation of inspiration time, and apnea was defined as the absence of breathing for a period corresponding to the duration of 3 control-breathing cycles.[15,16] Rectal temperature was measured by use of a thermometric probe connected to the multifunction electrocardiograph. Cardiopulmonary variables and rectal temperature were recorded throughout the induction period at 1-minute intervals. **Cardiac output (CO)** was determined every 2 minutes after the onset of induction by use of the thermodilution technique; 3 ml of ice-cold (0 C) saline (0.9% NaCl) solution was injected into the right atrium during end expiration.

Cardiac index (CI), **stroke index (SI)**, and **systemic vascular resistance (SVR)** were calculated according to the following formulas:

CI (ml/min/kg) = CO/body weight
SI (ml/kg) = CI/heart rate
SVR (dynes · s/cm^5) = (MAP – RAP)/CO × 79.9

Arterial blood samples were also collected in heparinized syringes and placed on iced water for determination of pHa, Pa_{O_2}, and Pa_{CO_2}, using a blood-gas analyzer with temperature correction.[k]

Statistical analyses—Results were expressed as mean ± SD. Cardiopulmonary variables and time to events were compared over time (events) and treatments (induction groups) by use of a 2-way ANOVA for repeated measures. When the interaction was significant, mean values were compared by use of a Tukey post-hoc test. Values of $P < 0.05$ were considered significant.

Results

Characteristics of mask induction—Mask induction with sevoflurane resulted in significantly less time to onset and cessation of involuntary movements, loss of the palpebral reflex, negative tail-clamp response, and intubation, compared with induction with isoflurane (**Table 1**). However, N_2O did not have a significant effect on induction characteristics in dogs induced with either sevoflurane or isoflurane. Intubation was successful on the first attempt in all dogs regardless of treatment. With the exception of involuntary movements, no dog displayed induction-related complications such as struggling, swallowing, salivation, vocalization, ataxia, or excitement throughout the induction period.

Table 1—Induction characteristics associated with administration of sevoflurane (Sevo) or isoflurane (Iso) delivered in 100% oxygen (O_2) or a 2:1 mixture of nitrous oxide (N_2O) and O_2 in 7 healthy dogs

	O_2		N_2O	
Time (s)	**Sevo**	**Iso**	**Sevo**	**Iso**
To onset of involuntary movements	72 ±17*†	106 ± 16	64 ± 19*†	98 ± 9
To end of involuntary movements	141 ± 20*	195 ± 27	136 ± 22*	186 ± 28
To loss of palpebral reflex	157 ± 18*	259 ± 23	182 ± 21*	227 ± 23
To negative tail-clamp response	310 ± 34*†	424 ± 29	261 ± 22*†	406 ± 24
To intubation	340 ± 38*	452 ± 35	296 ± 18*†	428 ± 27

Data are reported as mean ± SD.
*Significantly ($P < 0.05$) different from value determined for dogs induced with Iso in O_2. †Significantly ($P < 0.05$) different from value determined for dogs induced with Iso in N_2O.

Expired concentrations of sevoflurane and isoflurane increased with vaporizer setting and time (**Fig 1**). For the first 2 minutes after onset of induction, the increase in expired sevoflurane concentration in dogs that received sevoflurane in oxygen was greater than in dogs that received sevoflurane in N_2O. However, concentration changes became similar in these groups after 3 minutes. The increase in expired isoflurane concentration was not different between dogs that received isoflurane in oxygen or N_2O. Mean (± SD) expired concentrations of sevoflurane or isoflurane at intubation were 3.09 ± 0.29% and 1.94 ± 0.18%, respectively, in dogs that received these agents delivered in oxygen, whereas concentrations in dogs that received sevoflurane or isoflurane in N_2O were 2.96 ± 0.26% and 1.89 ± 0.21%, respectively. When these concentrations were expressed as percentage of MAC for each agent (sevoflurane, 2.09%; isoflurane, 1.30%[6]), we did not detect significant differences among groups.

Cardiopulmonary changes associated with mask induction—Baseline values for each variable were not significantly different among induction groups. However, in all groups, heart rate increased significantly from baseline values within 1 to 2 minutes after the

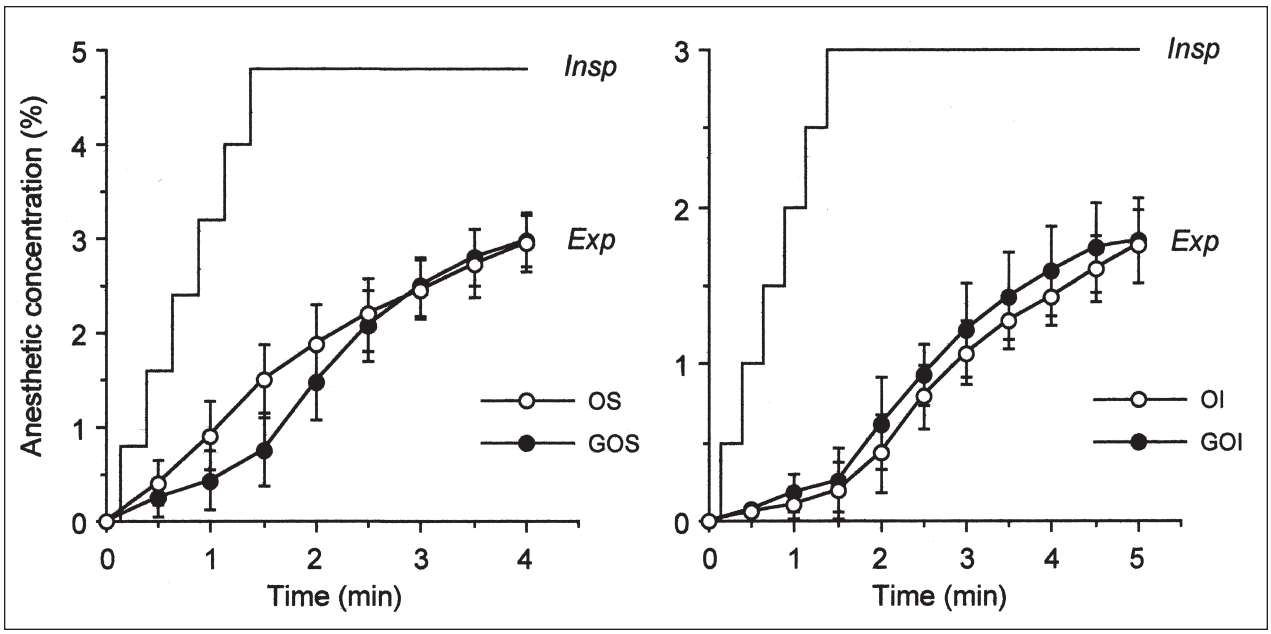

Figure 1—Mean (± SD) expired anesthetic concentrations during mask induction with sevoflurane (left) or isoflurane (right) in 100% oxygen (OS and OI, respectively) or a 2:1 mixture of nitrous oxide and oxygen (GOS and GOI, respectively) in 7 healthy dogs. The solid line in each panel (Insp) represents the vaporizer settings of sevoflurane (left) or isoflurane (right). Vaporizer settings were increased every 15 seconds by 0.4 times the minimum alveolar concentration (MAC) of each agent until settings corresponded to 2.4 MAC.

Table 2—Cardiovascular effects of mask induction with Sevo or Iso delivered in 100% O_2 or in a 2:1 mixture of N_2O and O_2 in 7 healthy dogs

		Time after induction (min)					
Variable	**Baseline**	**1**	**2**	**3**	**4**	**5**	**Intubation**
Heart rate (beats/min)							
Sevo in O_2	97 ± 13	119 ± 14	158 ± 11*	140 ± 8*	126 ± 9*†‡	ND	119 ± 10*†‡
Iso in O_2	100 ± 10	135 ± 13*	169 ± 16*	154 ± 13*	147 ± 11*	140 ± 11*	134 ± 14*
Sevo in N_2O	98 ± 9	125 ± 12*	149 ± 15*	131 ± 16*	122 ± 9*†	ND	116 ± 12*†‡
Iso in N_2O	97 ± 6	130 ± 10*	161 ± 19*	150 ± 12*	145 ± 12*	134 ± 14*	130 ± 16*
MAP (mm Hg)							
Sevo in O_2	113 ± 13	127 ± 12*	126 ± 12*	112 ± 13	99 ± 6*	ND	94 ± 7*
Iso in O_2	108 ± 9	128 ± 9*	131 ± 9*	117 ± 12	105 ± 14	97 ± 8*	90 ± 7*
Sevo in N_2O	111 ± 8	126 ± 9*	127 ± 8*	118 ± 7	102 ± 8	ND	96 ± 8*
Iso in N_2O	112 ± 9	124 ± 10*	128 ± 9*	120 ± 8	111 ± 12	99 ± 5*	92 ± 7*
CI (ml/min/kg)							
Sevo in O_2	218 ± 26	ND	274 ± 18*	ND	248 ± 26	ND	228 ± 29
Iso in O_2	204 ± 28	ND	294 ± 29*	ND	269 ± 36	ND	248 ± 22
Sevo in N_2O	211 ± 23	ND	269 ± 23*	ND	240 ± 23	ND	226 ± 28
Iso in N_2O	207 ± 19	ND	286 ± 31*	ND	260 ± 27	ND	240 ± 25
SI (ml/kg)							
Sevo in O_2	2.05 ± 0.15	ND	1.74 ± 0.18*	ND	1.98 ± 0.19	ND	1.92 ± 0.18
Iso in O_2	2.04 ± 0.16	ND	1.72 ± 0.21*	ND	1.83 ± 0.18	ND	1.87 ± 0.20
Sevo in N_2O	2.05 ± 0.19	ND	1.79 ± 0.21*	ND	1.97 ± 0.19	ND	1.95 ± 0.21
Iso in N_2O	2.03 ± 0.22	ND	1.77 ± 0.25*	ND	1.80 ± 0.18	ND	1.86 ± 0.20
SVR (dynes · s/cm^5)							
Sevo in O_2	4,086 ± 476	ND	3,616 ± 547	ND	3,125 ± 588	ND	3,220 ± 481*
Iso in O_2	4,152 ± 489	ND	3,532 ± 590	ND	3,238 ± 594	ND	2,837 ± 507*
Sevo in N_2O	4,163 ± 495	ND	3,712 ± 573	ND	3,330 ± 579	ND	3,321 ± 416*
Iso in N_2O	4,279 ± 478	ND	3,548 ± 604	ND	3,349 ± 556	ND	2,998 ± 510*

Data are reported as mean ± SD.
*Significantly ($P < 0.05$) different from baseline value. †Significantly ($P < 0.05$) different from value for dogs induced with Iso in O_2. ‡Significantly ($P < 0.05$) different from value for dogs induced with Iso in N_2O.
ND = Not determined. MAP = Mean arterial pressure. CI = Cardiac index. SI = Stroke index. SVR = Systemic vascular resistance.

Table 3—Respiratory effects of mask induction with Sevo or Iso delivered in 100% O_2 or in a 2:1 mixture of N_2O and O_2 in 7 healthy dogs

		Time after induction (min)					
Variable	**Baseline**	**1**	**2**	**3**	**4**	**5**	**Intubation**
RR (breaths/min)							
Sevo in O_2	18 ± 1	18 ± 2	23 ± 2*	20 ± 3	17 ± 2	ND	13 ± 1*
Iso in O_2	16 ± 1	19 ± 2*	27 ± 3*	23 ± 2*	20 ± 2	16 ± 2	12 ± 2*
Sevo in N_2O	17 ± 2	18 ± 2	22 ± 2*	20 ± 3	19 ± 2	ND	14 ± 1*
Iso in N_2O	17 ± 1	19 ± 3	26 ± 3*	22 ± 2*	18 ± 3	16 ± 2	13 ± 2*
Tidal volume (ml)							
Sevo in O_2	161 ± 17	ND	117 ± 20*	ND	164 ± 19	ND	185 ± 21
Iso in O_2	177 ± 21	ND	97 ± 29*	ND	137 ± 28	ND	191 ± 27
Sevo in N_2O	170 ± 19	ND	124 ± 24*	ND	148 ± 22	ND	179 ± 19
Iso in N_2O	168 ± 23	ND	103 ± 27*	ND	155 ± 25	ND	182 ± 24
EV (L/min)							
Sevo in O_2	2.89 ± 0.22	ND	2.68 ± 0.39	ND	2.78 ± 0.26	ND	2.41 ± 0.20*
Iso in O_2	2.84 ± 0.26	ND	2.60 ± 0.50	ND	2.74 ± 0.33	ND	2.30 ± 0.24*
Sevo in N_2O	2.92 ± 0.24	ND	2.71 ± 0.35	ND	2.81 ± 0.28	ND	2.52 ± 0.18*
Iso in N_2O	2.85 ± 0.26	ND	2.69 ± 0.43	ND	2.78 ± 0.30	ND	2.35 ± 0.22*
Pa_{O_2} (Torr)							
Sevo in O_2	102 ± 13	ND	378 ± 16*†‡	ND	415 ± 19*†‡	ND	468 ± 29*†‡
Iso in O_2	100 ± 15	ND	354 ± 19*†‡	ND	431 ± 24*†‡	ND	484 ± 23*†‡
Sevo in N_2O	106 ± 14	ND	134 ± 15*	ND	142 ± 18*	ND	163 ± 18*
Iso in N_2O	102 ± 13	ND	123 ± 12*	ND	139 ± 20*	ND	160 ± 16*
Pa_{CO_2} (Torr)							
Sevo in O_2	35.6 ± 3.0	ND	38.6 ± 3.4	ND	41.1 ± 3.8	ND	42.8 ± 2.8*
Iso in O_2	36.7 ± 2.2	ND	39.5 ± 3.6	ND	41.6 ± 4.2	ND	43.2 ± 3.3*
Sevo in N_2O	36.3 ± 2.5	ND	38.8 ± 3.8	ND	40.9 ± 4.1	ND	42.5 ± 2.9*
Iso in N_2O	35.1 ± 2.9	ND	38.2 ± 3.0	ND	40.1 ± 3.4	ND	42.6 ± 3.1*
pHa							
Sevo in O_2	7.38 ± 0.02	ND	7.35 ± 0.04	ND	7.32 ± 0.03	ND	7.30 ± 0.03*
Iso in O_2	7.37 ± 0.02	ND	7.34 ± 0.04	ND	7.31 ± 0.04	ND	7.28 ± 0.04*
Sevo in N_2O	7.37 ± 0.02	ND	7.36 ± 0.03	ND	7.33 ± 0.03	ND	7.31 ± 0.03*
Iso in N_2O	7.38 ± 0.02	ND	7.36 ± 0.03	ND	7.32 ± 0.05	ND	7.29 ± 0.03*

Data are reported as mean ± SD.
RR = Respiratory rate. EV = Expiratory volume.
See Table 2 for key.

onset of induction, peaked at 2 minutes, and then decreased but remained slightly but significantly greater than baseline values thereafter (**Table 2**). Four minutes after induction, heart rates in dogs that received isoflurane in either oxygen or N_2O were significantly greater than those in dogs that received sevoflurane. Cardiac arrhythmias were not detected in any group during the induction period.

After reaching peak values at 2 minutes in all groups, MAP decreased gradually and significantly until intubation, compared with baseline values (Table 2). Systemic vascular resistance did not change significantly in any group after the onset of induction, but did decrease significantly in all groups at intubation. Stroke index decreased slightly but significantly in all groups 2 minutes after the onset of induction. Because of the increase in heart rate and decrease in SI, CI increased significantly 2 minutes after the onset of induction, compared with baseline values. After that CI decreased to baseline values and remained constant until intubation. Stroke index and CI were not significantly different among the 4 induction groups. Right arterial pressure and MPAP did not change significantly during mask induction with any inhalation agent.

Immediate respiratory responses to mask induction were variable. In 14 of 28 (50%) inductions, baseline breathing patterns did not change, but in the remainder either breath-holding (10/28 [36%]) or apnea (4/28 [14%]) was detected. These responses ceased within 1 minute after the onset of induction. Respiratory rate increased significantly from baseline values 2 and 3 minutes after the onset of induction in all groups then gradually decreased (**Table 3**). At intubation, respiratory rate was significantly decreased from baseline values in all groups. Tidal volume decreased significantly 2 minutes after the onset of induction but returned to baseline 3 to 4 minutes after induction and remained constant thereafter. Because of the changes in respiratory rate and V_T, $\dot{V}_E$ remained constant until 4 minutes after the onset of induction in all groups, after which these variables gradually but significantly decreased from baseline values.

Arterial pH decreased and Pa_{CO_2} increased 4 minutes after the onset of induction in all groups, but values were not significantly different among groups. In all inductions, Pa_{O_2} was significantly higher in dogs induced with sevoflurane or isoflurane in oxygen, compared with the same agents in N_2O.

Discussion

In this study, we compared the speed and quality of mask induction with sevoflurane with that with isoflurane delivered in oxygen or N_2O. Speed of induction, determined as the time to a negative tail-clamp response, was less in dogs treated with sevoflurane regardless of whether the agent was delivered in oxygen or N_2O. Quality of induction was similar, with significant differences only in the duration of involuntary movements and time to loss of the palpebral reflex. Involuntary movements and loss of the palpebral reflex are usually associated with stage II of induction, which is the stage of delirium or involuntary movement.[17] The time course of induction in the present study was similar to that reported in dogs that underwent rapid mask induction with 2.5 MAC of sevoflurane or isoflurane.[10] Time to negative tail-clamp response (ie, speed of induction), however, was less than that reported in another study[9] that used 2 MAC of sevoflurane or isoflurane in a conventional incremental mask induction protocol. The precise mechanism of the more rapid mask induction with sevoflurane, compared with isoflurane, is unclear. Our study was designed to compare mask induction with sevoflurane and isoflurane delivered at the same potency (2.4 MAC; vaporizer setting of 4.8% for sevoflurane and 3.0% for isoflurane); MAC is the standard for comparison of anesthetic potencies between inhalation anesthetics.[18] Moreover, inhalation anesthetics are conventionally used in clinical practice at a 3 to 5% concentration to speed the rate of equilibration in the alveoli.[1-3,10,13,14] Because sevoflurane has a lower blood-gas partition coefficient and less of a respiratory depressive effect than isoflurane, the rate at which delivery of 4.8% sevoflurane resulted in an increase in MAC may have been less than that for delivery of 3% isoflurane.[19-21] This would result in speeding the rate of equilibration of sevoflurane between alveolar (end-tidal) and inspired concentrations. However, we found that both agents induced similar respiratory changes during mask induction.

Theoretically, the addition of 50 to 70% N_2O may facilitate the speed of induction by decreasing the MAC of the inhalation anesthetics (concentrating effect).[4] Unexpectedly, the addition of 66% N_2O to sevoflurane or isoflurane did not speed induction, nor did it decrease induction-related complications, as had been demonstrated in children undergoing mask induction with 7% sevoflurane in 66% N_2O.[22] In the present study, 66% N_2O did not exert a significant effect on expired anesthetic concentrations, suggesting that N_2O minimally, if at all, reduced the MAC of sevoflurane and isoflurane. The mechanisms that determine the apparent lack of N_2O-induced effects on MAC are not fully understood. However, results of a recent study[23] in children indicate that the MAC-sparing effects of N_2O may be attenuated when N_2O is used for mask induction with less soluble inhalation agents such as sevoflurane. Furthermore, several investigators have speculated a relationship between the addition of N_2O and the incidence of airway reflexes.[22-24] In other reports,[25,26] the addition of N_2O decreased the maximum deliverable inspired sevoflurane concentration, which may, in part, be attributable to the fact that N_2O dissolves in the liquid anesthetic within the vaporizer. Further studies are warranted to confirm these preliminary observations.

Mask induction with either sevoflurane or isoflurane caused a transient increase in heart rate, MAP, and CI immediately after the onset of induction. These responses occurred in stage I or II of induction. During these stages, a fast strong heartbeat and hypertension can develop as a result of the initial administration of each inhalation agent. A regular pattern of breathing typically returns approximately 4 minutes after initial administration, which is attributable to anesthetic-induced CNS depression and continued catecholamine release.[17] Our findings in the present study coincide

with results of previous studies[10,13] from our laboratory that evaluated dogs undergoing rapid mask induction with sevoflurane or isoflurane. However, the cardiovascular responses to incremental administration of each anesthetic agent were less pronounced, compared with responses after rapid mask induction.

Heart rate peaked 2 minutes after initiation of induction and remained higher than baseline in all groups. In addition, heart rates were greater 4 minutes after induction in dogs that received isoflurane, compared with dogs that received sevoflurane. Nonetheless, heart rates remained within reference range for dogs in a maintenance plane of anesthesia (1 to 2 MAC).[8] Inhalation of 1 to 4% isoflurane increases heart rate in rabbits as a result of sympathetic stimulation rather than as a result of the baroreflex elicited by a decrease in arterial blood pressure.[27] It is possible that the baroreflex was attenuated in these dogs, because isoflurane and sevoflurane are known to depress this reflex in response to changing blood pressure.[19] In fact, the decrease in MAP was similar among groups despite detection of higher heart rates in dogs that received isoflurane. However the gradual decrease in MAP 3 minutes after the onset of mask induction was primarily attributable to systemic vasodilation, as represented by a decrease in SVR, because CI at this time was not decreased. A similar vasodilatory effect caused by sevoflurane and isoflurane is associated with both controlled and spontaneous ventilation,[8,28] suggesting a direct action of these agents on the smooth muscle of peripheral blood vessels. In the present study, CI peaked 2 minutes after onset of induction, then decreased and remained near baseline values until intubation, because SI and heart rate were adequately maintained close to the expected values for dogs at a maintenance plane of anesthesia.[8]

Incremental mask induction with sevoflurane or isoflurane induced mild respiratory depression that was qualitatively similar to that detected in previous studies[10,13] of rapid mask induction in dogs. The respiratory depressant effects, characterized by an increase in $Paco_2$, were associated with ventilatory depression characterized by a decrease in respiratory rate. It is possible that both respiratory reflexes and effects of the inhalation anesthetics caused slowing of breathing during induction. We recently demonstrated that inhalation of 3 to 5% isoflurane or halothane into isolated upper airways of dogs induced respiratory depression as a result of prolongation in expiration; sevoflurane caused no changes in breathing patterns.[21,29,30] Reflex-evoked inhibition of breathing resulting from stimulation or inhibition of airway sensory receptors[31-36] could have a potential role in triggering respiratory impairment via CNS-mediated mechanisms[37,38] during mask induction in dogs.

In the present study, the addition of 66% N_2O to sevoflurane or isoflurane did not modify cardiopulmonary responses during induction. Effects of N_2O on circulation and respiration are small, compared with effects of other inhalation anesthetics, because although N_2O depresses myocardial function directly, it also has sympathetic stimulatory properties that counteract these direct effects.[4] We did not detect additive or synergistic effects of N_2O, which raises questions regarding the usefulness of this agent for mask induction. The advantages and disadvantages of N_2O use should be weighed on an individual basis. We have shown that the use of 50% N_2O for rapid mask induction with 5% isoflurane or sevoflurane improved the rate of induction by approximately 50 seconds without improving cardiopulmonary effects.[14] The use of preinduction sedatives rather than N_2O may better decrease the adverse cardiopulmonary effects (eg, increased heart rate and MAP and respiratory reflexes) of sevoflurane and isoflurane during the initial phase of mask induction. Intravenous administration of midazolam (0.1 mg/kg) and butorphanol (0.2 mg/kg) prior to mask induction reduces induction-related complications and cardiopulmonary responses in dogs.[20]

Our results indicate that the use of N_2O did not improve the speed or quality of mask induction with sevoflurane or isoflurane in healthy dogs. On the basis of these results, the benefits provided by concomitant administration of N_2O owing to concentrating or second gas effects appear to be minimal in dogs when low solubility inhalation agents are used. Because of the potential risks of N_2O associated with transfer to the closed-gas space, which may result in an increase in volume of the gastrointestinal tract, pneumothorax, blood embolus, and damage to the cuff of the endotracheal tube, as well as risks associated with occupational or abusive exposure to operating room personnel,[4] the use of N_2O for mask induction in dogs should not be considered.

[a]Anthron, Toray Medical Co, Tokyo, Japan.
[b]Model KA-3020, Kimura Medical Co, Tokyo, Japan.
[c]AGM-103 Capnomac, Datex, Helsinki, Finland.
[d]Face mask for animals, Kimura Medical Co, Tokyo, Japan.
[e]Takeda-style canine restraining table, Clea Japan Inc, Osaka, Japan.
[f]SI-5600, Arrow International Inc, Reading, Pa.
[g]Model 93-132-5 F, Baxter Healthcare Co, Santa Ana, Calif.
[h]CMO-104 Cardiocap, Datex, Helsinki, Finland.
[i]DX-300, Nihon Kohden, Tokyo, Japan.
[j]NVM-1, Bear Medical Systems Inc, Riverside, Calif.
[k]IL-1303, Instrumentation Laboratory Inc, Lexington, Mass.

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