Effects of intravenous administration of perzinfotel, fentanyl, and a combination of both drugs on the minimum alveolar concentration of isoflurane in dogs

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Objective—To determine the effects of IV administration of perzinfotel and a perzinfotel-fentanyl combination on the minimum alveolar concentration (MAC) of isoflurane in dogs.

Animals—6 healthy sexually intact Beagles (3 males and 3 females).

Procedures—All dogs were instrumented with a telemetry device for continuous monitoring of heart rate, arterial blood pressure, and core body temperature (at a femoral artery). Dogs were anesthetized with propofol (6 mg/kg, IV) and isoflurane. Isoflurane MAC values were determined in 3 experiments in each dog, separated by at least 7 days, before (baseline) and after the following treatments: no treatment (anesthetic only), perzinfotel (20 mg/kg, IV), fentanyl (5 µg/kg bolus, IV, followed by a continuous IV infusion at 0.15 µg/kg/min), and a fentanyl-perzinfotel combination (20 mg of perzinfotel/kg, IV, plus the fentanyl infusion). Bispectral index and oxygen saturation as measured by pulse oximetry were also monitored throughout anesthesia.

Results—Without treatment, the mean ± SD isoflurane MAC for all 6 dogs was 1.41 ± 0.10%. Baseline MAC was 1.42 ± 0.08%. Intravenous administration of perzinfotel, fentanyl, and the perzinfotel-fentanyl combination significantly decreased the MAC by 39%, 35%, and 66%, respectively. Perzinfotel and perzinfotel-fentanyl administration yielded significant increases in the bispectral index. Mean, systolic, and diastolic arterial blood pressures significantly increased from baseline values when perzinfotel was administered. Systolic arterial blood pressure significantly increased from the baseline value when perzinfotel-fentanyl was administered. No adverse effects were detected.

Conclusions and Clinical Relevance—IV administration of perzinfotel, fentanyl, or a perzinfotel-fentanyl combination reduced isoflurane MAC in dogs and increased arterial blood pressure. (*Am J Vet Res* 2009;70:1459–1464)

Potential benefits of administering sedative, hypnotic, or analgesic drugs prior to or during surgery are a reduction in the MAC of volatile anesthetic required to maintain a surgical plane of anesthesia and improvement in cardiovascular or respiratory function. For example, fentanyl (a potent and short-acting opioid µ-receptor agonist), ketamine (a dissociative anesthetic), and dexmedetomidine (a potent α_2-adrenoceptor agonist) are routinely administered to dogs to decrease the amount of inhalant anesthetic required for surgery.[1–5] An arguable benefit of combining drugs that act at multiple sites is their potential to act additively or synergistically, thereby reducing the total amount of drug needed to yield an anesthetic effect and the potential for adverse effects.[6] Intravenous infusion of a combination of morphine, lidocaine, and ketamine, for example, decreases the isoflurane MAC in dogs without resulting in adverse hemodynamic effects.[7] Additive or synergistic drug actions, however, can be associated with severe adverse effects, including but not limited to bradycardia, hypotension, ventilatory depression, and apnea.[8,9] Coadministration of fentanyl and midazolam can cause hypoxemia and apnea in humans, and IV infusion of opioids or α_2-adrenoceptor agonists can cause bradycardia and arrhythmia in dogs and cats.[9–12] Antagonistic

Abbreviations

BIS	Bispectral index
EEG	Electroencephalography
ETISO	End-tidal concentration of isoflurane
MAC	Minimum alveolar concentration of anesthetic that results in immobility in 50% of animals to a painful stimulus
NMDA	*N*-methyl-D-aspartate
P_{ETCO_2}	End-tidal partial pressure of carbon dioxide
Spo_2	Oxygen saturation as measured by pulse oximetry

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effects of drug combinations evaluated for anesthetic uses have also been reported.[6]

Perzinfotel is a novel, selective, and competitive NMDA-receptor antagonist with a potency of at least 10 times that reported for the nonselective NMDA-receptor antagonist ketamine.[13–15] In another study,[16] we found that IV administration of perzinfotel results in a dose-dependent decrease in isoflurane MAC, with attendant increases in arterial blood pressure, without causing clinically relevant adverse effects. The purpose of the study reported here was to determine the effect of IV administration of perzinfotel in conjunction with fentanyl on isoflurane MAC in dogs as well as on heart rate, arterial blood pressure, and core body temperature.

Materials and Methods

Animals and instrumentation—Six healthy sexually intact Beagles (3 males and 3 females) with a mean ± SD body weight of 11.7 ± 0.86 kg (range, 10.4 to 13.1 kg) were used. Each dog was equipped with a telemetry device that had been surgically implanted at least 3 months before beginning the study. The telemetry device permitted the simultaneous and continuous monitoring of respiration and ECG activity as well as arterial blood pressure and body temperature as measured at a femoral artery. The study protocol was approved by the Institutional Animal Care and Use Committee of The Ohio State University.

Experimental procedures—Food was withheld for 12 hours and water for 2 hours before each experiment began. A cephalic vein was catheterized, and anesthesia was induced with propofol[a] (4 to 6 mg/kg, IV), administered to effect. Each dog was orotracheally intubated and positioned in right lateral recumbency. Anesthesia was maintained with isoflurane[b] in oxygen delivered through an out-of-circle, agent-specific vaporizer,[c] by means of a semiclosed anesthetic circle rebreathing system.[d] The oxygen flow rate was 2 L/min, and the ETISO was initially maintained at approximately 2.0%. Respiration was controlled (respiratory rate, approx 6 breaths/min; volume, approx 15 mL/kg) to maintain the P_{ETCO_2} between 35 and 45 mm Hg.[e] Inspired and expired concentrations of isoflurane and carbon dioxide were continuously monitored.[f] The anesthetic analyzer was calibrated before after each experiment by use of 3 standard concentrations of isoflurane.[g] The following variables were continuously monitored and periodically recorded: ECG activity; heart rate[h]; systolic, mean, and diastolic direct arterial blood pressures[h]; ETISO[f]; P_{ETCO_2}; Spo_2[f]; and body temperature (as measured[h] at a femoral artery). Body temperatures were maintained between 37.5° and 38.5°C throughout anesthesia by positioning each dog on a hot water circulating heating pad[i] and covering it with a blanket.

Determination of isoflurane MAC—Isoflurane MAC was determined by delivering a supramaximal electrical stimulus to the buccal mucosa of each dog.[2,7] Two 24-gauge, 10-mm insulated stimulating electrodes[j] were inserted 1 cm apart into the buccal mucosa at a location dorsal and caudal to the incisors. The opposite ends of the electrodes were connected to an electrical stimulator[k] that delivered a predetermined stimulus (50 V, 5 Hz, and 10-millisecond duration). Stimulation continued for 1 minute unless the dog had signs of gross purposeful movement (lifting of the head and repeated movement of the limbs) before completion of the 1-minute stimulation. Slight paw movement, arching of the back, chewing, swallowing, blinking, opening of the eyes, and nystagmus were not considered gross purposeful movement and were therefore considered a negative response.

The ETISO was initially set at 1.5% during the first MAC determination (anesthesia only; control treatment) and at 1.2 × the dog-specific control MAC during subsequent days when experimental treatments were administered. When there was a negative response to the electrical stimulus, the ETISO was decreased by 20% and allowed to equilibrate for at least 15 minutes before the stimulus was reapplied. This process was continued until the dog responded with gross purposeful movement. The ETISO was then increased in increments of 10% until the dog failed to have signs of gross purposeful movement. The MAC was defined as the mean of the lowest ETISO value that did not result in gross purposeful movement and the highest ETISO value that did result in gross purposeful movement.[2,7]

Determination of BIS values—Bispectral index values were derived from continuously monitored EEG activity. The EEG was obtained by use of platinum subdermal needle electrodes with a 3-lead referential montage, arranged in a bifrontal configuration with the reference electrode positioned on the midline of the head rostral to the medial canthus of the eyes. The ground electrode was positioned on the midline in the atlanto-occipital region.[7,16] The EEG and BIS values were continuously acquired and displayed by use of a proprietary BIS monitor[l] with the high-frequency filter set at 70 Hz and the low-frequency filter set at 2 Hz. The BIS number was automatically calculated and digitally displayed every 5 seconds and represented the EEG activity during the previous 60 seconds. Eight BIS values were recorded during a 2-minute period before and after buccal mucosal stimulation.

Experimental design—Isoflurane MAC and other experimental variables were repeatedly determined for each dog on 3 experimental days separated by a minimum washout period of 7 days. The investigator was aware of all treatments administered.

On the first experimental day, the isoflurane MAC for each dog was determined (control MAC). This was done to establish the isoflurane concentration (1.2 × control MAC) to be used in later experiments and to identify any changes in isoflurane MAC during anesthesia. To obtain control MAC values, isoflurane was initially administered at 1.5% in each dog. The first control MAC measurement was made approximately 1.5 hours after anesthetic induction, and the second control MAC measurement was made approximately 5.5 hours after induction.

On the second experimental day, the effects of perzinfotel[m] administration on isoflurane MAC were measured. The dose of perzinfotel was selected on the basis

of the findings in another study[16] in dogs. Isoflurane anesthesia was induced at 1.2 × the control MAC value for each dog. A bolus IV injection of saline (0.9% NaCl) solution (5 mL) was administered 1 to 6 minutes after anesthetic induction, and isoflurane baseline MAC was determined approximately 1.5 hours after induction. Perzinfotel (20 mg/kg, IV) was administered 3 to 5 minutes later, and posttreatment isoflurane MACs were measured approximately 2 and 3.5 hours afterward.

On the third experimental day, the effects of fentanyl and fentanyl-perzinfotel administration on isoflurane MAC were measured. Isoflurane anesthesia was induced at 1.2 × the control MAC value for each dog. A bolus IV injection of saline solution (5 mL) was administered 1 to 6 minutes after anesthetic induction, and isoflurane baseline MAC value was determined approximately 0.5 hours after induction. Fentanyl[n] (5 µg/kg initial bolus, IV, followed immediately by a continuous IV infusion at 0.15 µg/kg/min) was administered 3 to 5 minutes later, and the posttreatment MAC for fentanyl alone was measured approximately 1.5 hours after administration. Three to 5 minutes afterward, while the fentanyl infusion was maintained, perzinfotel (20 mg/kg, IV) was administered, and posttreatment MACs for the fentanyl-perzinfotel combination were measured approximately 1 and 3 hours after administration.

Statistical analysis—All analyses were performed with commercial statistical software.[o] Data are reported as mean ± SD. Values of variables for dog responses at each measurement point after each treatment were compared with each other, with control values (anesthetic-only treatment), and with baseline values (obtained after administration of saline solution). Responses at the 2 posttreatment measurement points were also compared with each other. Repeated-measures ANOVA was used for comparisons, and least square means of each variable were calculated for all treatments. Least square means for the various treatments were compared with each other by use of the 2-sided Student *t* test, with Bonferroni adjustment for multiple comparisons. A value of $P < 0.05$ was considered significant.

Results

Isoflurane MAC values in anesthetized dogs when they received no additional treatment (control values) or saline solution (baseline values) varied only slightly with time (**Table 1**). Without treatment, the mean ± SD isoflurane MAC for all dogs was 1.41 ± 0.10%. Administration of perzinfotel alone significantly decreased the isoflurane MAC from a mean baseline value of 1.42 ± 0.08% to 0.87 ± 0.12% and 0.87 ± 0.10% at 1.8 ± 0.3 hours and 3.7 ± 0.4 hours after administration, respectively (3.3 ± 0.7 hours and 5.2 ± 0.8 hours after anesthetic induction). This represented a reduction in MAC of approximately 39%.

Administration of fentanyl alone significantly decreased the isoflurane MAC from a baseline value of 1.42 ± 0.08% (1.4 ± 0.5 hours after anesthetic induction) to 0.93 ± 0.04% 1.7 ± 0.1 hours later (3.2 ± 0.3 hours after anesthetic induction). This represented a reduction in MAC of approximately 35%. Subsequent administration of perzinfotel, with continued IV infusion of fentanyl, significantly decreased the MAC to 0.50 ± 0.05% and 0.47 ± 0.10% at 1.0 ± 0.7 hours and 3.0 ± 0.3 hours after administration, respectively (4.3 ± 0.7 hours and 6.2 ± 0.5 hours after anesthetic induction). The mean of these 2 determinations, 0.49 ± 0.08% isoflurane, represented a 66% decrease in the MAC relative to the baseline value, which was equivalent, within experimental error, to the sum of the separate percentage decreases associated with administration of fentanyl or perzinfotel alone (39% + 35% = 74%).

Mean BIS values for the control and baseline conditions were also similar over time and among dogs, and some increases were evident after perzinfotel treatment (Table 1). The second BIS value measured approximately 3.5 hours after administration of perzinfotel alone

Table 1—Mean ± SD values for isoflurane MAC and BIS at various measurement points in 6 isoflurane-anesthetized Beagles in 2 experiments involving IV administration of saline (0.9% NaCl) solution (baseline values) followed by IV administration of perzinfotel (20 mg/kg) or fentanyl (5 µg/kg initial bolus followed immediately by continuous IV infusion at 0.15 µg/kg/min) followed by perzinfotel (20 mg/kg, IV).

Variable	Baseline	First measurement	Second measurement
MAC (% isoflurane)			
Anesthesia only	ND	1.38 ± 0.11[a]	1.44 ± 0.08[a]
Perzinfotel alone	1.42 ± 0.08	0.87 ± 0.12[b,c]*	0.87 ± 0.10[b]*
Fentanyl alone	1.42 ± 0.08	0.93 ± 0.04[b]*	ND
Fentanyl and perzinfotel	NA	0.50 ± 0.05[d]*	0.47 ± 0.10[d]*
BIS			
Anesthesia only	ND	68 ± 18[b]	68 ± 12[b]
Perzinfotel alone	69 ± 7	74 ± 7[a,b]†	84 ± 6[a]*†
Fentanyl alone	70 ± 15	76 ± 6[a,b]	ND
Fentanyl and perzinfotel	NA	83 ± 7[a]	89 ± 6[a]*

*Value is significantly ($P < 0.05$) different from the baseline value for the indicated treatment. †Values are significantly ($P < 0.05$) different between posttreatment measurement points for the indicated treatment.

NA = Not applicable. ND = Not done.

[a–d]Within a column, values with different superscript letters are significantly ($P < 0.05$) different.

Baseline, first, and second measurements were made at various points as follows: anesthesia only, 1.5 and 5.5 hours after anesthetic induction (first and second measurements); saline solution (baseline treatment), 1.5 hours after anesthetic induction; perzinfotel alone, 2 and 3.5 hours after administration (3.5 and 5 hours after anesthetic induction); fentanyl alone, 1.5 hours after administration (3 hours after anesthetic induction); and fentanyl followed by perzinfotel, 1 and 3 hours after perzinfotel administration (4 and 6 hours after anesthetic induction). Saline solution was not administered during the anesthesia-only treatment.

Table 2—Mean ± SD values for heart rate and arterial blood pressure at various measurement points in 6 isoflurane-anesthetized Beagles in 2 experiments involving IV administration of saline solution (baseline values) followed by IV administration of perzinfotel (20 mg/kg) or fentanyl (5 µg/kg initial bolus followed immediately by continuous IV infusion at 0.15 µg/kg/min) followed by perzinfotel (20 mg/kg, IV).

Variable	Baseline	First measurement	Second measurement
Heart rate (beats/min)			
Anesthesia only	ND	96 ± 12[a]†	118 ± 13[a]†
Perzinfotel alone	88 ± 4	111 ± 33[a]	122 ± 30[a]*
Fentanyl alone	114 ± 29	106 ± 21[a]	ND
Fentanyl and perzinfotel	NA	97 ± 24[a]	119 ± 33[a]
SAP (mm Hg)			
Anesthesia only	ND	86 ± 3[b]	91 ± 9[c]
Perzinfotel alone	81 ± 10	120 ± 26[a]*	120 ± 13[a,b]*
Fentanyl alone	92 ± 14	106 ± 20[a]	ND
Fentanyl and perzinfotel	NA	116 ± 18[a]*	112 ± 10[b]*
DAP (mm Hg)			
Anesthesia only	ND	49 ± 5[b]	54 ± 9[c]
Perzinfotel alone	45 ± 7	71 ± 20[a]*	76 ± 15[a,b]*
Fentanyl alone	55 ± 13	61 ± 17[a,b]	ND
Fentanyl and perzinfotel	NA	63 ± 13[a,b]	61 ± 12[b,c]
MAP (mm Hg)			
Anesthesia only	ND	62 ± 4[b]	67 ± 9[c]
Perzinfotel alone	57 ± 7	85 ± 24[a]*	91 ± 14[a,b]*
Fentanyl alone	68 ± 14	77 ± 18[a,b]	ND
Fentanyl and perzinfotel	NA	81 ± 16[a,b]	79 ± 12[b,c]

DAP = Diastolic arterial blood pressure. MAP = Mean arterial blood pressure. SAP = Systolic arterial blood pressure.
See Table 1 for remainder of key.

was significantly higher than baseline (saline solution) and control values and was also higher than the first BIS value measured approximately 1.5 hours after perzinfotel administration. These increases ranged from 14% to 24%. Administration of fentanyl alone did not result in significant changes in BIS values. However, at the second measurement point after subsequent administration of the perzinfotel-fentanyl combination (approx 3 hours after perzinfotel had been administered), the BIS was significantly higher than control and baseline values (31% and 27% higher, respectively).

Administration of perzinfotel alone also yielded significant increases in systolic and diastolic arterial blood pressures at both posttreatment measurement points relative to control and baseline values (**Table 2**). A significant increase in heart rate relative to the baseline value was detected at the second measurement after perzinfotel administration. Systolic arterial blood pressure significantly increased after administration of fentanyl relative to the first control value but not relative to the baseline value. Systolic arterial blood pressure significantly increased after administration of the perzinfotel-fentanyl combination at both posttreatment measurement points, compared with control and baseline values.

Body temperature and Spo_2 did not change after administration of perzinfotel, fentanyl, or the perzinfotel-fentanyl combination. No adverse effects were detected as dogs recovered from anesthesia.

Discussion

Results of the present study confirmed and extended the findings of other studies[1,2,16] in which the anesthetic-sparing effects of perzinfotel and fentanyl administration were investigated in isoflurane-anesthetized dogs. Administration of fentanyl followed by perzinfotel had cumulative effects and reduced the mean MAC by 66%, a value that was approximately equal and within experimental error of the sum of the effects of each drug alone (74%).

Fentanyl is commonly used as an adjunct during inhalant anesthesia in dogs and cats.[1,2,17–21] Its rapid onset of effect, short duration of action, and analgesic properties make it ideal for single injections and infusion.[22] Results of a study[23] conducted to evaluate plasma fentanyl concentrations after IV administration of the drug suggested that fentanyl pharmacokinetics in enflurane-anesthetized dogs are best described by a 3-compartment model. However, a more recent study[24] in conscious dogs revealed that fentanyl pharmacokinetics involve a short distribution half-life (4.5 minutes) and long elimination phase (approx 45 minutes) that can be attributed to a large volume of distribution, suggesting a 2-compartment model.[24] Data suggest that IV administration of 5 to 10 µg of fentanyl/kg followed by an IV fentanyl infusion of approximately 0.16 µg/kg/min (10 µg/kg/h) can be used to reduce the isoflurane MAC in dogs by approximately 50%.[2,24] In our study, plasma fentanyl concentrations were not measured. Therefore, we cannot exclude the possibility that plasma fentanyl concentrations increased with time during the fentanyl infusion, thereby contributing to a progressively increasing sparing effect on isoflurane MAC. The magnitude of this anesthetic-sparing effect remains speculative because the relationship between plasma fentanyl concentration and isoflurane MAC reduction in dogs has not been defined to our knowledge and may not be linear.

Similar to fentanyl, the distribution and elimination data for perzinfotel in dogs are best fitted by a 2-compartment model, but the elimination profile is consistent with moderate clearance (approx 6 mL/min/kg)

and volume of distribution (approx 2 L/kg), resulting in a longer biological half-life (approx 1.5 to 2 hours).[p] These data suggest that IV administration of only 1 dose should sustain an effect for several hours. Another study[16] conducted by our research group revealed that IV administration of one 20 mg/kg dose of perzinfotel decreases the isoflurane MAC in dogs by approximately 45% and that this effect is sustained for at least 5 hours. Findings of the present study confirmed data of other reports[16,17] in which the separate anesthetic-sparing effects of perzinfotel and fentanyl in dogs are described.[7] Coadministration of perzinfotel and fentanyl yielded a greater anesthetic-sparing effect than that of each drug administered alone, without resulting in adverse effects. We did not perform the type of experiment required to determine whether perzinfotel, fentanyl, or the fentanyl-perzinfotel combination was additive, synergistic, or antagonistic with isoflurane because the minimum effective doses for perzinfotel and fentanyl were not measured nor were isobolographic analyses performed.[25] However, our findings did suggest that the perzinfotel-fentanyl combination administered in conjunction with isoflurane reduced inhalant anesthetic requirements.

In another study,[16] our research group found that the IV administration of 5 to 20 mg of perzinfotel/kg in isoflurane-anesthetized dogs decreased the isoflurane MAC with associated increases in the BIS. The BIS is a dimensionless EEG variable ranging from 0 to 100. It is derived from Fourier and bispectral calculations performed on an artifact-free EEG and calculated from a proprietary algorithm relating the phase angle of the EEG waveforms (bicoherence), EEG power in the delta (1 to 4 Hz) versus beta (13 to 30 Hz) range (power spectrum), and percentage of the EEG that is isoelectric.[26–29] The EEG bicoherence increases with increasing anesthetic depth and is inversely related to the BIS.[27,29] Increases in BIS are generally indicative of a decrease in inhalant anesthetic concentration and a lightening of the anesthetic plane, even when animals do not overtly respond to a noxious stimulus. Values < 65 are generally considered to be indicative of adequate hypnosis, whereas values > 70 are associated with increased responsiveness.[27–29]

The relationship of the resting BIS to end-tidal concentration of inhalant anesthetics has been investigated in dogs,[30,31] pigs,[32] horses,[33] goats,[34] and cats.[35] Bispectral index values decrease as the concentration of administered inhalant anesthetic increases; the opposite also appears true. This correlation exists between BIS values and MAC multiples of isoflurane anesthesia in cats[35] and sevoflurane anesthesia in dogs.[29,36] In studies[7,16] involving isoflurane-anesthetized dogs, changes in BIS values have been used to evaluate anesthetic depth after administration of medetomidine, morphine, lidocaine, ketamine, and perzinfotel. To our knowledge, no studies have been conducted to evaluate the BIS or changes in BIS associated with administration of fentanyl in isoflurane-anesthetized dogs. In pigs, narcotic analgesics reduce the typical change in BIS values following surgical stimulation by depressing nociceptive signaling.[37] Opioid administration in dogs also results in a decrease in MAC values and, providing the dose of opioid analgesic is low, an increase in BIS values.[3]

In the present study, the BIS increased as the concentration of isoflurane decreased when dogs were treated with fentanyl, perzinfotel, or both. The decrease in isoflurane MAC and increase in BIS were greatest after administration of the perzinfotel-fentanyl combination. These data suggested that administration of perzinfotel or a perzinfotel-fentanyl combination provided sufficient analgesia to prevent mobility in response to a noxious stimulus in dogs that would otherwise have responded. Alternatively, this drug combination may have altered motor responses to noxious stimuli.

Administration of perzinfotel, fentanyl, or both did not yield depressant effects on heart rate, arterial blood pressure, or Spo_2 values in isoflurane-anesthetized dogs. No cardiac arrhythmias were detected in any dog at any time throughout the experiments. However, our study was not designed to provide a detailed evaluation of perzinfotel or fentanyl on cardiac electrical activity or load-independent indices of cardiac function, vessel tone, or reactivity. In dogs, plasma fentanyl concentrations within the clinical-dose range can cause bradycardia but have minimal to no effect on cardiac myoenergetics and baroreflex activity when administered at lower doses.[38,39] In isoflurane-anesthetized dogs, clinically relevant plasma concentrations of fentanyl are associated with dose-dependent decreases in heart rate and minimal changes in arterial blood pressure and indices of myocardial performance.[39] Fentanyl-induced bradycardia could partially offset any improvement in arterial blood pressure caused by a reduction in isoflurane concentration. In the present study, values of cardiovascular variables remained well within reference limits for isoflurane-anesthetized dogs and did not decrease when the perzinfotel-fentanyl combination was administered.

Fentanyl administration can reportedly cause respiratory depression when administered with benzodiazepines, α_2-adrenoceptor agonists, and propofol.[8,10] We could not evaluate drug effects on respiratory function in the present study because all dogs were ventilated. In our experience, ventilatory depressant effects are not a typical result of perzinfotel administration in conscious or isoflurane-anesthetized dogs. However, the effects on ventilatory function of perzinfotel administration when combined with other sedatives or injectable anesthetics has not been investigated. No adverse cardiovascular effects were detected at any time during our study. We concluded that fentanyl and perzinfotel and their combination yielded isoflurane anesthetic-sparing effects in dogs and did not produce adverse effects evident in the ECG, cardiac rate or rhythm, or arterial blood pressure.

a. PropoFlo, Abbott Laboratories, North Chicago, Ill.
b. IsoFlo, Abbott Laboratories, North Chicago, Ill.
c. Isotec 3, Ohmeda, Madison, Wis.
d. LEI Medical, Boring, Ore.
e. Veterinary Anesthesia Ventilator Model 2KIE, Hallowell Engineering and Manufacturing Corp, Pittsfield, Mass.
f. Passport 2, Datascope, Montvale, NJ.
g. Isoflurane gas standards, Scott Medical Products, Plumsteadville, Pa.
h. SI PhysioTel D70-PCT transmitter, Data Sciences International, Saint Paul, Minn.
i. T/Pump, Gaymar Industries Inc, Orchard Park, NY.

j. Genuine grass platinum subdermal needle electrodes, Astro-Med Inc, West Warwick, RI.
k. Grass SD9 Stimulator, Grass Medical Instruments, Quincy, Mass.
l. A-1000 EEG Monitor, Aspect Medical Systems Inc, Newton, Mass.
m. Fort Dodge Animal Health, Princeton, NJ.
n. Hospira, Lake Forest, Ill.
o. SAS, version 8.2, SAS Institute Inc, Cary, NC.
p. Adedoyin A, Wyeth, Madison, NJ: Unpublished data, 2006.

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