Use of a combination of propofol and fentanyl, alfentanil, or sufentanil for total intravenous anesthesia in cats

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Objective—To determine the cardiorespiratory effects of an IV infusion of propofol alone or in association with fentanyl, alfentanil, or sufentanil in cats and, for each combination, the minimal infusion rate of propofol that would inhibit a response to noxious stimuli.

Design—Randomized crossover study.

Animals—6 cats.

Procedure—Cats were anesthetized 4 times in random order. After IV administration of fentanyl, alfentanil, sufentanil, or saline (0.9% NaCl) solution, anesthesia was induced with propofol (7 mg/kg [3.2 mg/lb], IV) and maintained for 90 minutes with a continuous infusion of propofol in conjunction with fentanyl (0.1 µg/kg/min [0.045 µg/lb/min]), alfentanil (0.5 µg/kg/min [0.23 µg/lb/min]), sufentanil (0.01 µg/kg/min [0.004 µg/lb/min]), or saline solution (0.08 mL/kg/min [0.036 mL/lb/min]).

Results—Minimal infusion rate of propofol required to prevent a response to a noxious stimulus was higher when cats received saline solution. After 70 minutes, minimal infusion rate of propofol was significantly higher with fentanyl than with sufentanil. Decreases in heart rate, systolic blood pressure, rectal temperature, and respiratory rate were detected with all treatments. Oxygen saturation did not change significantly, but end-tidal partial pressure of carbon dioxide increased with all treatments. There were no significant differences in recovery times or sedation and recovery scores among treatments.

Conclusions and Clinical Relevance—Results suggest that infusion of propofol in combination with fentanyl, alfentanil, or sufentanil results in satisfactory anesthesia in cats. (*J Am Vet Med Assoc* 2003;223:1608–1613)

Propofol is a highly lipophilic anesthetic agent notable for its rapid onset of action and brief duration of effects.[1,2] It has gained popularity in **total intravenous anesthesia (TIVA)** protocols in humans[3,4]; however, propofol does not block autonomic responses to noxious stimuli, causes substantial respiratory depression, and must be administered at high infusion rates to induce a surgical plane of anesthesia in animals.[1,5-7] Studies[4,7] suggest that infusion of opioids in conjunction with propofol reduces the infusion dose of propofol, improves cardiovascular function, and enhances the quality of anesthesia and recovery. Thus, infusion of fentanyl or 1 of its derivatives (ie, alfentanil and sufentanil) with propofol has proven to be a suitable technique for TIVA in humans.[4,8]

Sufentanil is approximately 10 times as potent as fentanyl,[9,10] whereas alfentanil is approximately a fifth as potent as fentanyl, but has a very short elimination half-life.[11,12] All 3 agents have been shown to induce analgesia and to have a sparing effect when administered with inhalant anesthetic agents.[11-13]

Studies[5-7] of the pharmacokinetics of propofol and its use for TIVA in dogs have been published. However, there are few reports of the clinical use of propofol in cats[2,14] and of the effects of TIVA protocols including propofol in cats.[15,a] In addition, to our knowledge, there are no reports of the clinical effects of an infusion of propofol in combination with fentanyl, alfentanil, or sufentanil in cats.

The purposes of the study reported here, therefore, were to determine the cardiorespiratory effects of an IV infusion of propofol alone or in association with fentanyl, alfentanil, or sufentanil in cats and to determine, for each combination, the minimal infusion rate of propofol that would inhibit a response to noxious stimuli.

Materials and Methods

Animals—Six healthy neutered adult domestic shorthair cats (2 males and 4 females) between 2 and 5 years old (mean ± SD, 3.2 ± 2.6 years) were used in the study. Mean ± SD weight was 3.6 ± 0.43 kg (7.92 ± 0.9 lb). Cats were housed in approved facilities, fed a standard commercial diet,[b] and given water ad libitum. All cats were considered to be in good physical condition on the basis of results of a physical examination, CBC, and serum biochemical analyses. The study protocol was approved by the Universidade de Brasília's Animal Care and Use Committee. Food, but not water, was withheld for 12 hours before each anesthetic episode.

Study design—A randomized crossover design was used. A single individual who did not know which drugs each cat received during any individual anesthetic episode evaluated the plane of anesthesia and responses to noxious stimuli throughout the study.

Each cat was anesthetized 4 times, with an interval of at least 2 weeks between each anesthetic episode. Anesthetic combinations consisted of IV infusion of fentanyl[c] (0.1 µg/kg/min [0.045 µg/lb/min]) and propofol,[d] IV infusion of alfentanil[e] (0.5 µg/kg/min [0.23 µg/lb/min]) and propofol, IV infusion of sufentanil[f] (0.01 µg/kg/min [0.004 µg/lb/min]) and propofol, and IV infusion of saline (0.9% NaCl) solution (0.08 mL/kg/min [0.036 mL/lb/min]) and propofol. In each cat, anesthetic combinations were administered in random order. For IV infusion, fentanyl, alfentanil, and sufentanil were diluted with saline solution as needed to allow an infusion rate of 0.08 mL/kg/min.

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At the beginning of each anesthetic episode, baseline data were collected, and a 24-gauge, 19-mm catheter[g] was inserted in a cephalic vein. Cats were initially given fentanyl (1 µg/kg [0.45 µg/lb], IV), alfentanil (5 µg/kg [2.3 µg/lb], IV), sufentanil (0.1 µg/kg, IV), or saline solution (0.8 mL, IV). Five minutes later, anesthesia was induced by administration of propofol (7 mg/kg [3.2 mg/lb], IV) over 30 seconds. Anesthesia was maintained with an infusion of propofol (0.2 mg/kg/min [0.09 mg/lb/min], IV). Propofol was diluted in 5% glucose solution to a final concentration of 0.5%. All drugs were administered with infusion pumps.[h]

After induction of anesthesia, cats were positioned in right lateral recumbency, and a tight-fitting mask with an oxygen flow rate of 2 L/min was placed. Breathing was spontaneous throughout the anesthetic period.

Infusion of fentanyl, alfentanil, sufentanil, or saline solution was started 20 minutes after induction of anesthesia and maintained throughout the anesthetic period. A 24-gauge, 19-mm catheter was inserted in a femoral vein for this purpose after anesthetic induction. The rate of propofol infusion was increased by 0.01 mg/kg/min when movement was detected after application of a noxious stimulus and was decreased by 0.01 mg/kg/min when movement was not detected within 30 seconds after application of a noxious stimulus or when depth of anesthesia was considered to be too deep, as judged by commonly accepted standards for cats during inhalation anesthesia.[16] When a cat moved spontaneously, the depth of anesthesia was increased by administration of a bolus of propofol (0.3 mg/kg [0.135 mg/lb], IV). Anesthesia was maintained for 90 minutes. At the end of the anesthetic period, infusions of propofol and the selected drug (opioid or saline solution) were discontinued simultaneously.

Data collection—The quality of sedation and anesthetic recovery were scored (**Appendix**). The individual assessing quality of sedation and recovery was unaware of which drugs cats had received.

The minimum infusion rate of propofol was determined by pinching the interdigital skin of a hind limb while it was being stretched.[17] To avoid unnecessary pain, pinching was initiated lightly with the fingernails and stopped immediately after withdrawal of the limb was induced or after 30 seconds of noxious stimulation. For consistency in stimulus intensity, the same trained person always evaluated responses to noxious stimulation. The infusion rate of propofol was recorded every 5 minutes, along with the number of boluses of propofol (ie, total volume needed) required to maintain an adequate depth of anesthesia.

Cardiorespiratory variables were recorded before sedation and at 5-minute intervals during anesthesia. **Heart rate (HR)** was obtained before sedation from a 1-minute lead-II ECG recording[i] and was evaluated continuously during anesthesia. **Systolic blood pressure (SBP)**, **diastolic blood pressure (DBP)**, and **mean blood pressure (MBP)** were measured noninvasively by use of an oscillometric technique[j] with the cuff placed around the antebrachium; cuff width was approximately 40% of the circumference of the limb. **Oxygen saturation (Spo_2)** was estimated with a pulse oximeter[j] with the infrared sensor attached to the cat's lips. **Respiratory rate (RR)** and **end-tidal partial pressure of carbon dioxide (P_{ETCO_2})** were measured with a sensor[k] attached to the tight-fitting mask. **Rectal temperature (RT)** was measured with a digital thermometer. All values were recorded immediately before each application of the noxious stimulus.

Variables used to clinically judge depth of anesthesia (eg, position of the eyes, nystagmus, eyelid reflex, blinking, and ear flick reflex) were recorded. An experienced anesthetist who was unaware of which drugs the cat was receiving evaluated the anesthetic depth of the cats. During recovery, time to lifting of the head and time to standing were recorded.

Statistical analyses—Cardiorespiratory variables and infusion rates of propofol were compared among treatments by means of ANOVA for repeated measures[l] followed by the Student-Newman-Keuls test to compare values within and between treatments. Time to lifting of the head and time to standing were compared with Student *t* tests. Proportion of cats requiring boluses of propofol was calculated for the 4 treatments with the Kaplan-Meier technique and compared among treatments with the log-rank test. For all analyses, values of $P < 0.05$ were considered significant. Data are given as mean ± SD.

Results

During all anesthetic episodes, cats lost the righting reflex soon after administration of propofol, and sedation scores for all cats, regardless of treatment, were 1 or 2. There were no significant differences among treatments in regard to sedation quality (**Table 1**). Following induction of anesthesia with propofol, cats appeared to be in a light plane of anesthesia. The palpebral reflex was fairly brisk, and ventral rotation of the eye was maintained during the anesthetic period. The ear flick reflex was absent or barely detectable. Nystagmus occurred in 3 cats 30 minutes after induction during infusion of propofol and saline solution. After each painful stimulation, increases in HR and RR were observed in some cats in all treatment groups.

From 45 to 90 minutes, mean infusion rate of propofol was significantly lower when cats were treated with fentanyl, alfentanil, or sufentanil than when cats were treated with propofol alone (**Fig 1**). In 1 cat, when

Table 1—Recovery times and quality of sedation and recovery in 6 cats anesthetized with a continuous infusion of propofol in combination with saline (0.9% NaCl) solution (0.08 mL/kg/min [0.036 mL/lb/min]), fentanyl (0.1 µg/kg/min [0.045 µg/lb/min]), alfentanil (0.5 µg/kg/min [0.23 µg/lb/min]), or sufentanil (0.01 µg/kg/min [0.004 µg/lb/min])

Variable	Saline solution	Fentanyl	Alfentanil	Sufentanil
Lifting of the head (min)	10.8 ± 4.3 (6.3–14.5)	10.0 ± 4.1 (5.7–15.0)	9.2 ± 3.7 (5.0–13.6)	6.8 ± 1.4 (5.3–7.0)
Standing (min)	14.7 ± 3.2 (12.6–18.3)	18.6 ± 5.3 (10.5–22.7)	14.0 ± 4.5 (10.3–19.8)	13.6 ± 2.5 (11.4–16.6)
Sedation score	1.0 ± 0.0 (1)	1.0 ± 0.0 (1)	1.0 ± 0.0 (1)	1.2 ± 0.4 (1–2)
Recovery score	1.2 ± 0.4 (1–2)	1.4 ± 0.4 (1–2)	1.4 ± 0.5 (1–2)	1.4 ± 0.4 (1–2)

Values are given as mean ± SD (range).

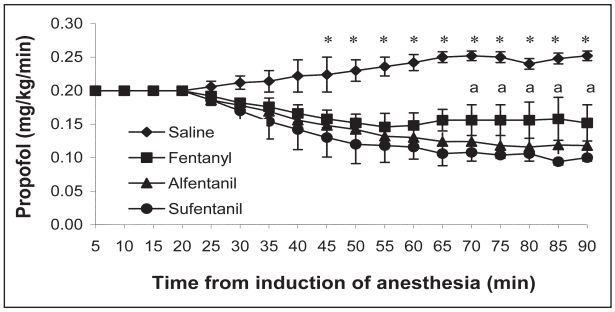

Figure 1—Mean ± SD propofol infusion rates in 6 cats anesthetized with propofol in combination with saline (0.9% NaCl) solution (saline; 0.08 mL/kg/min [0.036 mL/lb/min]), fentanyl (0.1 µg/kg/min [0.045 µg/lb/min]), alfentanil (0.5 µg/kg/min [0.23 µg/lb/min]), or sufentanil (0.01 µg/kg/min [0.004 µg/lb/min]). *Significantly ($P < 0.05$) different from values for infusion in combination with fentanyl, alfentanil, or sufentanil. [a]Significantly ($P < 0.05$) different from values for infusion in combination with sufentanil.

it was anesthetized with sufentanil and propofol, the initial infusion rate of propofol was reduced by 0.03 mg/kg/min before application of the first noxious stimulus, because RR was < 8 breaths/min. From 70 to 90 minutes, mean infusion rate of propofol was significantly lower when cats were treated with sufentanil than when they were treated with fentanyl. During infusion with propofol and saline solution, 1 cat required an additional bolus of propofol to maintain an acceptable plane of anesthesia, and during infusion of propofol with each of the opioids, 2 cats required additional boluses of propofol. However, the percentage of cats that required additional propofol boluses was not significantly different among treatments. Movements after noxious stimulation were always slow and gentle. All spontaneous movements were controlled by administration of a single bolus of propofol (0.3 mg/kg) followed by an increase (0.01 mg/kg/min) in the infusion rate. Recovery was fast, and no adverse reactions developed in any cat. Mean times to lifting of the head, times to standing, and recovery scores were not significantly different among drug treatments (Table 1).

Prior to induction of anesthesia, there were no significant differences among drug treatments for any variable. During the first 15 minutes after anesthetic induction, mean HR was not significantly different from mean baseline HR, regardless of treatment, but after 30 minutes of anesthesia, HR was significantly lower than baseline HR with all treatments (**Table 2**). When cats were given alfentanil, the decrease in HR was significantly greater 30 minutes after anesthetic induction than when cats were given the other treatments. No significant differences in SBP, DBP, and MBP were detected among treatments, although when cats were treated with alfentanil, DBP and MBP were significantly decreased, compared with baseline values, from 30 through 90 and from 15 through 90 minutes after induction, respectively.

Although no significant differences in RR were found among treatments (**Table 3**), mean P_{ETCO_2} was significantly increased, compared with baseline values, after administration of propofol in all treatment groups. Significant changes in Sp_{O_2} were not detected, regardless of treatment. Rectal temperature decreased significantly after 60 minutes of anesthesia when cats were given fentanyl, alfentanil, or sufentanil.

Table 2—Cardiorespiratory variables in 6 cats anesthetized with a continuous infusion of propofol in combination with saline solution, fentanyl, alfentanil, or sufentanil

		Time from induction of anesthesia (min)						
Variable	**Group**	**0 (Baseline)**	**15**	**30**	**45**	**60**	**75**	**90**
Heart rate (beats/min)								
	Saline solution	165.6 ± 4.5 (160–172)	156.2 ± 6.9 (145–162)	138.8 ± 26.1[a] (105–167)	131.1 ± 14.7* (112–136)	130.4 ± 12.0* (119–149)	128.8 ± 10.0* (120–144)	130.6 ± 10.5* (122–144)
	Fentanyl	165.6 ± 6.6 (160–172)	145.0 ± 21.4 (121–160)	118.8 ± 11.4*[a] (133–107)	112.4 ± 8.7* (101–123)	111.6 ± 10.6* (103–130)	113.0 ± 7.0* (107–122)	113.2 ± 12.1* (100–133)
	Alfentanil	164.0 ± 4.8 (160–172)	160.4 ± 3.5 (156–166)	91.8 ± 15.4* (76–112)	96.6 ± 10.5* (82–107)	95.8 ± 11.6* (83–110)	103.4 ± 10.6* (85–112)	102.4 ± 7.9* (92–114)
	Sufentanil	166.8 ± 5.9 (116–122)	146.0 ± 15.7 (122–164)	116.8 ± 24.0*[a] (95–143)	116.2 ± 28.2* (90–146)	109.0 ± 19.0* (86–137)	110.8 ± 19.5* (116–135)	118.4 ± 7.8* (112–127)
Systolic blood pressure (mm Hg)								
	Saline solution	118.8 ± 2.2 (116–122)	105.4 ± 5.7* (98–114)	100.6 ± 2.5* (99–102)	104.2 ± 6.0* (102–105)	102.0 ± 6.6* (98–105)	103.8 ± 4.8* (101–105)	106.8 ± 3.5* (104–113)
	Fentanyl	118.4 ± 7.6 (110–128)	107.4 ± 3.7* (102–112)	101.8 ± 2.6* (101–103)	105.4 ± 4.3* (98–107)	105.0 ± 7.4* (103–118)	102.6 ± 3.5* (90–104)	105.6 ± 2.9* (102–108)
	Alfentanil	120.2 ± 5.8 (113–128)	109.0 ± 6.1* (107–112)	102.2 ± 4.0* (99–104)	105.0 ± 3.7* (102–108)	100.2 ± 3.9* (95–106)	104.2 ± 5.4* (98–107)	102.0 ± 2.3* (100–106)
	Sufentanil	123.2 ± 5.0 (118–128)	110.0 ± 3.7* (108–112)	103.0 ± 4.0* (102–104)	103.0 ± 3.3* (98–107)	103.2 ± 8.7* (118–95)	103.4 ± 4.9* (101–106)	104.6 ± 5.1 (102–112)
Diastolic blood pressure (mm Hg)								
	Saline solution	83.8 ± 3.6 (80–89)	78.4 ± 5.8 (72–88)	77.2 ± 6.14 (73–89)	77.8 ± 6.1 (72–85)	77.2 ± 4.7 (72–85)	76.6 ± 5.9 (72–80)	81.8 ± 5.4 (89–97)
	Fentanyl	84.4 ± 3.6 (82–86)	77.4 ± 4.2 (71–79)	76.2 ± 5.3 (72–80)	79.0 ± 5.1 (74–87)	80.2 ± 7.9 (73–92)	76.6 ± 4.7 (71–84)	80.8 ± 3.6 (76–86)
	Alfentanil	86.8 ± 3.1 (84–89)	82.8 ± 4.6 (79–83)	75.4 ± 5.2* (70–79)	75.8 ± 5.4* (73–80)	74.4 ± 2.7* (71–78)	78.0 ± 4.0* (73–86)	74.2 ± 5.0* (72–81)
	Sufentanil	85.4 ± 4.6 (82–89)	78.0 ± 4.8 (72–83)	78.0 ± 4.6 (72–80)	79.0 ± 7.2 (73–80)	76.4 ± 6.5 (71–92)	78.4 ± 5.4 (73–86)	79.4 ± 5.0 (72–86)
Mean blood pressure (mm Hg)								
	Saline solution	94.2 ± 3.4 (94–96)	91.6 ± 5.5 (91–95)	91.6 ± 3.6 (82–91)	91.0 ± 3.8 (88–95)	93.2 ± 5.5 (80–95)	90.2 ± 3.6 (86–94)	93.8 ± 2.7 (91–97)
	Fentanyl	96.8 ± 2.0 (95–99)	91.6 ± 4.8 (90–93)	91.8 ± 3.0 (89–94)	87.6 ± 5.1 (82–89)	88.0 ± 4.3 (82–90)	89.6 ± 3.9 (84–93)	87.9 ± 3.2 (86–89)
	Alfentanil	96.8 ± 2.3 (93–99)	92.0 ± 2.1* (90–94)	87.6 ± 4.9* (80–92)	81.6 ± 2.8* (88–93)	89.0 ± 6.5* (80–95)	86.6 ± 4.9* (81–93)	86.8 ± 3.6* (81–90)
	Sufentanil	97.0 ± 2.5 (93–99)	91.6 ± 2.8 (90–94)	92.6 ± 2.4 (90–96)	90.0 ± 2.8 (87–93)	91.6 ± 8.3 (89–105)	91.6 ± 2.0 (90–93)	88.4 ± 2.3 (86–90)

Values are given as mean ± SD (range).
*Significantly ($P < 0.05$) different from baseline value.
[a]Significantly ($P < 0.05$) different from value obtained during infusion with alfentanil.

Table 3—Respiratory variables and rectal temperature in 6 cats anesthetized with a continuous infusion of propofol in combination with saline solution, fentanyl, alfentanil, or sufentanil

Variable	Group	Time from induction of anesthesia (min)						
		0 (Baseline)	15	30	45	60	75	90
Respiratory rate (breaths/min)								
	Saline solution	36.0 ± 3.7 (32–42)	20.8 ± 3.3* (16–24)	16.8 ± 3.3* (12–20)	16.0 ± 2.8* (12–20)	16.8 ± 4.3* (12–24)	15.2 ± 1.7* (16–12)	16.0 ± 2.3* (20–12)
	Fentanyl	36.8 ± 4.3 (32–44)	22.3 ± 2.6* (30–36)	14.4 ± 2.1* (12–16)	17.6 ± 4.5* (12–24)	18.4 ± 5.2* (14–24)	14.2 ± 4.3* (12–18)	13.4 ± 6.0* (12–28)
	Alfentanil	35.6 ± 6.4 (32–44)	25.2 ± 3.8* (20–30)	15.6 ± 8.9* (8–20)	16.8 ± 7.6* (8–20)	19.2 ± 7.6* (8–20)	21.6 ± 7.2* (12–28)	16.0 ± 3.1* (12–20)
	Sufentanil	36.8 ± 3.3 (32–40)	25.6 ± 5.1* (20–30)	12.4 ± 6.0* (4–16)	12.8 ± 1.7* (12–16)	14.4 ± 3.5* (12–20)	16.8 ± 5.2* (12–24)	17.6 ± 4.5* (12–24)
Oxygen saturation (%)								
	Saline solution	97.2 ± 0.8 (96–98)	98.8 ± 0.8 (98–100)	98.8 ± 1.3 (97–99)	98.7 ± 1.8 (97–100)	98.0 ± 0.7 (97–99)	98.0 ± 0.7 (97–99)	98.2 ± 0.8 (97–99)
	Fentanyl	97.4 ± 1.5 (96–99)	98.6 ± 1.5 (97–100)	99.0 ± 0.7 (98–100)	99.0 ± 0.7 (98–100)	98.6 ± 0.5 (98–100)	98.2 ± 0.5 (98–99)	97.8 ± 0.8 (97–99)
	Alfentanil	97.6 ± 1.1 (96–99)	99.0 ± 0.7 (98–100)	99.4 ± 0.5 (98–100)	98.0 ± 1.0 (96–99)	98.8 ± 0.4 (97–99)	98.8 ± 0.8 (97–99)	98.4 ± 1.1 (97–100)
	Sufentanil	97.6 ± 1.1 (96–99)	99.0 ± 1.2 (98–100)	99.4 ± 0.5 (97–98)	98.0 ± 1.0 (97–99)	98.8 ± 0.4 (98–100)	96.2 ± 0.8 (98–99)	98.4 ± 1.3 (98–100)
End-tidal partial pressure of CO_2 (mm Hg)								
	Saline solution	36.8 ± 5.3 (30–44)	54.6 ± 4.5* (48–54)	53.0 ± 5.3* (43–65)	50.0 ± 5.8 (45–59)	59.4 ± 8.4* (49–69)	55.8 ± 6.1 (50–65)	40.8 ± 6.2[a] (30–45)
	Fentanyl	38.0 ± 4.4 (33–44)	57.2 ± 9.7* (45–69)	60.0 ± 6.2* (53–70)	59.4 ± 7.2* (49–69)	55.6 ± 10.7* (45–70)	56.4 ± 2.3* (54–59)	60.4 ± 11.0* (49–72)
	Alfentanil	40.8 ± 5.9 (30–45)	54.2 ± 7.6* (45–66)	55.4 ± 4.0* (52–62)	59.0 ± 4.6* (52–63)	54.6 ± 8.2* (42–64)	48.4 ± 12.4 (30–59)	43.6 ± 3.5[a] (40–49)
	Sufentanil	34.4 ± 4.3 (30–40)	53.2 ± 6.9* (42–60)	54.0 ± 7.2* (42–60)	55.8 ± 10.1* (45–70)	56.4 ± 7.6* (49–69)	43.8 ± 11.2 (30–60)	42.0 ± 6.7[a] (30–45)
Rectal temperature (°C)								
	Saline solution	38.5 ± 0.4 (37.9–38.9)	38.2 ± 0.3 (38.4–38.8)	38.3 ± 0.2 (38.1–38.5)	38.2 ± 0.2 (38.5–38.0)	38.1 ± 0.2 (37.9–38.5)	37.9 ± 0.1 (37.7–38.1)	37.7 ± 0.1 (37.6–37.9)
	Fentanyl	38.7 ± 0.1 (38.3–38.9)	38.6 ± 0.1 (38.5–38.9)	38.3 ± 0.3 (38.0–38.7)	37.7 ± 0.5 (37.1–38.4)	37.3 ± 0.4* (37.0–37.7)	37.3 ± 0.4* (37.0–37.8)	37.0 ± 0.3* (36.5–37.2)
	Alfentanil	38.6 ± 0.2 (38.3–38.9)	38.6 ± 0.1 (38.5–38.9)	38.2 ± 0.5 (37.6–38.6)	38.0 ± 0.1 (37.7–38.2)	37.2 ± 0.5* (36.8–37.7)	37.1 ± 0.5* (36.8–37.7)	37.0 ± 0.4* (36.7–37.7)
	Sufentanil	38.6 ± 0.2 (38.3–38.9)	38.3 ± 0.1 (38.3–38.5)	38.0 ± 0.5 (37.5–38.3)	37.8 ± 0.3 (37.4–38.0)	37.5 ± 0.3* (37.2–37.7)	37.6 ± 0.3* (37.4–38.0)	37.6 ± 0.5* (37.0–38.0)

See Table 2 for key.

Discussion

Total IV anesthesia gained widespread acceptance in human medicine after the development of computer-controlled infusion devices that allow the depth of anesthesia to be altered the same way it is altered during inhalation anesthesia.[3,7] Although several propofol infusion protocols have been described for dogs,[5,6] only recently have optimal target concentrations and pharmacokinetic data for dogs been identified,[7] because blood concentrations of propofol are dependent on many factors, such as other medications used, patient status, and type of procedure.[3,5,7] However, published pharmacokinetics studies[2,18,19] of propofol in cats do not provide sufficient pharmacokinetic data for establishment of optimum target concentrations during anesthetic induction and maintenance in cats.

Determination of minimal infusion rates allows comparison of the cardiopulmonary effects of equipotent doses of injectables agents[20,21] and has proved to be a practical approach to TIVA in cats and horses.[20,a] Minimal infusion rate is comparable to the **minimum alveolar concentration (MAC)**, a standard measure of the potency of inhalant anesthetics.[20,21] Significant differences between manually controlled and target-controlled infusion systems have not been identified in humans.[8] Although target-controlled anesthesia is more expensive than manually controlled anesthesia,[8] the use of computer-assisted target-controlled infusion systems for propofol has gained popularity in human anesthesia, as target-controlled systems are easier to handle than manually controlled systems.[4,8]

Our results and previous data[2,15,a] show that cats require lower propofol infusion rates to achieve anesthesia than do dogs[5-7] and horses.[20] This difference is probably related to differences in the rate of biotransformation and conjugation of propofol, as cats have a deficiency in the ability to conjugate phenol compounds.[1,2,19] Minimal infusion rates of propofol in association with fentanyl, alfentanil, and sufentanil in cats in the present study were similar to those reported for cats given ketamine and propofol.[a] In that study,[a] the minimal infusion rate for propofol decreased from 0.22 mg/kg/min (0.01 mg/lb/min) to 0.14 and 0.13 mg/kg/min (0.063 and 0.058 mg/lb/min) with simultaneous infusion of ketamine at a rate of 46 and 23 µg/kg/min (20.7 and 10.3 µg/lb/min), IV, respectively. The significant reduction in minimal infusion rate of propofol associated with opioid administration in the present study may be related to the fact that propofol uptake and elimination by the lungs is significantly reduced after fentanyl administration in cats.[18] Thus, the infusion rate of propofol necessary to achieve a

given depth of anesthesia may be lower in cats given fentanyl, alfentanil, or sufentanil irrespective of the contribution of these opioids to the level of hypnosis.

The pharmacokinetics of fentanyl and alfentanil, but not of sufentanil, have been studied in cats.[14,22] Doses of opioids administered in the present study were selected on the basis of previous studies indicating that ratios for equipotent doses of alfentanil, fentanyl, and sufentanil are approximately 5:1:0.1 in dogs[11] and humans.[4,10] The similar reduction in infusion rate of propofol when cats received alfentanil and fentanyl suggests that doses used in our study were equipotent, permitting comparisons with respect to clinical anesthetic potency and recovery characteristics. The significant difference in minimal infusion rates of propofol when cats were given fentanyl versus sufentanil may indicate that in cats, sufentanil is more potent than expected, in comparison with fentanyl.

The absence of significant differences in recovery times among treatments in the present study was in good agreement with a study[4] in humans anesthetized with continuous infusions of propofol and fentanyl, alfentanil, or sufentanil at equipotent doses.

Propofol induces a significant reduction in arterial blood pressure through a decrease in cardiac output and systemic vascular resistance in dogs.[23] In cats, propofol causes reductions in arterial blood pressure similar to those observed in dogs and humans,[15] although some authors have proposed that depression of arterial pressure after propofol administration could be minimized by titrating the dose to a suitable endpoint.[1]

Unlike morphine, which is associated with a decrease in arterial blood pressure during IV administration secondary to histamine-induced peripheral vasodilatation,[9] fentanyl and its analogs do not alter blood pressure and systemic vascular resistance,[10,12] which could explain the lack of differences in arterial blood pressure in cats given propofol alone or in combination with fentanyl or sufentanil in the present study. Alfentanil does not induce hemodynamic depression in cats anesthetized with isoflurane, and in 1 study,[13] alfentanil infusion in isoflurane-anesthetized cats increased HR and **mean arterial pressure (MAP)** as a result of a direct cardiovascular effect or a decrease in cardiovascular depression as the concentration of isoflurane was reduced. Conversely, in another study[12] with isoflurane-anesthetized cats receiving an alfentanil infusion, MAP and HR did not change as the concentration of isoflurane was kept constant. However, as observed in cats in the present study, studies in dogs[11] and humans[10] anesthetized with halothane revealed that alfentanil administration is associated with greater arterial hypotension, compared with fentanyl and sufentanil administration at equipotent doses. Although differences in DBP and MBP were not observed among treatment groups in this study, the decrease in DBP and MAP when cats received alfentanil could have resulted from a greater depressant effect of the drug, compared with the other opioids used in this study, when combined with propofol. Hemodynamic studies evaluating these drug combinations in cats are warranted to better determine the mechanism by which hypotension could result.

Previous data suggest that following administration of an induction dose of propofol, HR is stable or increases to counteract the vasodilatation and reduction of preload produced by this agent.[1,15,24] Studies in humans[24] and cats[25] demonstrated that depression of HR during propofol anesthesia is due to a resetting of the baroreceptor response despite the decrease in arterial blood pressure. Administration of fentanyl, alfentanil, and sufentanil has been associated with bradycardia in dogs.[11] This negative chronotropic action is believed to originate from the CNS and be mediated via the vagus nerve.[9,10] Previous studies[12,14] have indicated an increase in HR and arterial pressure after opioid administration in cats, and these cardiovascular effects could be attributable to either central sympathetic stimulatory effects or release of epinephrine.[26] In combination with inhalant anesthetics, the bradycardia induced by opioids decreases cardiac output in dogs,[9] whereas the increase in HR in cats contributes to the increase in cardiac output when opioids and inhalant anesthetics are administered.[12,13] The reduction in HR was similar when fentanyl, sufentanil, and saline solution were administered in the present study, which we believe suggests that concomitant infusion of these opioids had minimal effects on HR in cats anesthetized with a continuous infusion of propofol.

Propofol and opioids cause dose-related respiratory depression expressed by a decrease in tidal volume and RR that is strongly correlated with increases in Pa_{CO_2} values.[1,10,13,23] The infusion regimen in our study supports the hypothesis that infusion rates were close to minimal infusion rate and did not induce more respiratory depression than infusion of propofol alone, as observed in cats given a placebo or romifidine and anesthetized with the same dose of propofol.[18] The accuracy of our values for P_{ETCO_2} may be lower, because tidal breath of the cats could be diluted by the oxygen flow used,[16] despite the increase in P_{ETCO_2} during anesthesia with all 4 treatments. End-tidal partial pressure of CO_2 is likely to increase more profoundly after opioid premedication than without premedication,[1] but in the present study, this effect was not observed. Opioid-induced body and chest rigidity has been reported in humans[10,27] and cats.[13] However, we did not observe this adverse effect of opioids, probably because of the lower doses administered in this study.[9,13]

It is strongly recommended that oxygen always be administered during maintenance of anesthesia with propofol.[1,15,23] Although endotracheal intubation is the best method for administration of oxygen, a mask is an adequate alternative for short periods. In addition, endotracheal intubation may be difficult in cats because their well-developed protective reflexes make laryngeal spasms a common occurrence during light planes of anesthesia.[16,28] Furthermore, the minimum infusion rate of propofol that would permit endotracheal intubation in 50% of the cats in a previous study[a] was 0.22 mg/kg/min, which is higher than the infusion rate initially chosen in our study.

Corporal heat loss is an expected finding during anesthesia, especially in cats.[28] The increase in rectal temperature observed in cats given alfentanil and anes-

thetized with isoflurane[13] and in horses[29] anesthetized with alfentanil and halothane is probably a result of muscular rigidity induced by opioids.[27] This adverse effect was not observed in cats in the present study.

One major limitation of this study is that plasma propofol and opioid concentrations were not determined, so whether steady-state conditions of the drugs were achieved is not known.

In conclusion, concomitant infusion of propofol and fentanyl, alfentanil, or sufentanil resulted in a significant decrease in the infusion rate of propofol during TIVA in cats, without more substantial cardiovascular depression than that associated with infusion of propofol alone, although alfentanil infusion was associated with more profound decreases in HR and arterial blood pressure.

[a]Pascoe PJ, Ilkiw JE, Fisher LD. Dose response to propofol and propofol/ketamine infusion in cats (abstr), in *Proceedings*. Annu Meet Am Coll Vet Anesth 1996;4.
[b]Premier Fórmula Gatos Adultos, Premier Pet, São Paulo, Brazil.
[c]Fentanest, Cristália, São Paulo, Brazil.
[d]Propoabbott, Abbott Laboratories, North Chicago, Ill.
[e]Alfast, Cristália, São Paulo, Brazil.
[f]Fastfen, Cristália, São Paulo, Brazil.
[g]24-gauge Jelco, Johnson & Johnson, São José dos Campos, Brazil.
[h]Lifecare XL, Abbott Laboratories, North Chicago, Ill.
[i]ECGPC, TEB, São Paulo, Brazil.
[j]DX 2710, Dixtal, Manaus, Brazil.
[k]Digimax 5000 model ESFMN 2T, Digicare, Manaus, Brazil.
[l]SAS Institute Inc, Cary, NC.

Appendix

Criteria used to assess quality of sedation and recovery in cats anesthetized with propofol

Sedation score

Score	Description
1 (good)	Cat attained recumbency slowly and smoothly
2 (fair)	Cat attained recumbency slowly, with only slight paddling of limbs or shaking of head
3 (poor)	Cat attained recumbency slowly, with noticeable paddling of limbs or shaking of head
4 (very poor)	Cat attained recumbency unpredictably; vocalizing

Recovery score

Score	Description
1 (good)	Quiet; no thrashing, paddling, or vocalizing
2 (fair)	Some paddling or vocalizing
3 (poor)	Paddling, vocalizing, and ataxia
4 (very poor)	Paddling, vocalizing, thrashing, urinating, and defecating

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