Effects of anesthetic induction with a benzodiazepine plus ketamine hydrochloride or propofol on hypothermia in dogs undergoing ovariohysterectomy

Jennifer L. Bornkamp DVM, MS
Sheilah Robertson BVMS, PhD
Natalie M. Isaza DVM
Kelly Harrison DVM, MS
Brian A. DiGangi DVM, MS
Luisito Pablo DVM, MS

Received February 27, 2015.
Accepted June 9, 2015.

From the Departments of Large Animal Clinical Sciences (Bornkamp, Pablo) and Small Animal Clinical Sciences (Isaza, Harrison, DiGangi), College of Veterinary Medicine, University of Florida, Gainesville, FL 32611; and the Department of Small Animal Clinical Sciences, College of Veterinary Medicine, Michigan State University, East Lansing, MI 48824 (Robertson). Dr. Bornkamp's present address is Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Iowa State University, Ames, IA 50011. Dr. Pablo's present address is Department of Clinical Sciences, College of Veterinary Medicine, Auburn University, Auburn, AL 36849.

Address correspondence to Dr. Bornkamp (bornkamp@iastate.edu).

OBJECTIVE
To assess the effect of anesthetic induction with a benzodiazepine plus ketamine or propofol on hypothermia in dogs undergoing ovariohysterectomy without heat support.

ANIMALS
23 adult sexually intact female dogs undergoing ovariohysterectomy.

PROCEDURES
Baseline rectal temperature, heart rate, and respiratory rate were recorded prior to premedication with buprenorphine (0.02 mg/kg, IM) and acepromazine (0.05 mg/kg, IM). Anesthesia was induced with midazolam or diazepam (0.25 mg/kg, IV) plus ketamine (5 mg/kg, IV; n = 11) or propofol (4 mg/kg, IV; 12) and maintained with isoflurane in oxygen. Rectal temperature was measured at hospital intake, prior to premedication, immediately after anesthetic induction, and every 5 minutes after anesthetic induction. Esophageal temperature was measured every 5 minutes during anesthesia, beginning 30 minutes after anesthetic induction. After anesthesia, dogs were covered with a warm-air blanket and rectal temperature was measured every 10 minutes until normothermia (37°C) was achieved.

RESULTS
Dogs in both treatment groups had lower rectal temperatures within 5 minutes after anesthetic induction and throughout anesthesia. Compared with dogs that received a benzodiazepine plus ketamine, dogs that received a benzodiazepine plus propofol had significantly lower rectal temperatures and the interval from discontinuation of anesthesia to achievement of normothermia was significantly longer.

CONCLUSIONS AND CLINICAL RELEVANCE
Dogs in which anesthesia was induced with a benzodiazepine plus propofol or ketamine became hypothermic; the extent of hypothermia was more profound for the propofol combination. Dogs should be provided with adequate heat support after induction of anesthesia, particularly when a propofol-benzodiazepine combination is administered. (*Am J Vet Res* 2016;77:351–357)

Hypothermia is a common complication of general anesthesia in small animal practice. The incidence of postanesthetic hypothermia in dogs[1] and cats[2] that do not receive heat support during general anesthesia is reportedly 83.6% and 97.5%, respectively. Compared with normothermia, hypothermia has been associated with several complications, including decreased drug metabolism, increased myocardial oxygen consumption from shivering, increased incisional pain from shivering, cardiac arrhythmias, increased bleeding, and increased probability of postoperative wound infections.[3–6] Furthermore, hypothermia (vs normothermia) has been associated with an increased interval to regaining consciousness after anesthesia,[7] which may be a result of decreased drug metabolism, decreased inhalant anesthetic requirements, and increased solubility of inhalant agents at lower body temperatures.[8,9] Additionally, hypothermia may contribute to anesthetic-related death in cats weighing < 2 kg and dogs weighing < 5 kg.[10]

Redistribution hypothermia is the primary process responsible for heat loss in anesthetized patients.[5] Mammalian bodies can be considered as being comprised of 2 thermal compartments: the core and the periphery or shell.[5] The core compartment contains organs with high metabolic rates, is warmer than the periphery, and consists of the brain, heart, lung, liver, and kidneys.[5] The peripheral compartment acts as a thermoregulatory buffer between the body and the environment and is comprised mainly of blood vessels and arteriovenous shunts.[11]

Arteriovenous shunts may receive up to 80% of cutaneous blood flow and play an important role in hypothermia during general anesthesia.[12,13] The

amount of heat lost to the environment can be regulated in conscious animals via constriction of peripheral blood vessels and dilation of peripheral arteriovenous shunts, which are controlled by the hypothalamus, resulting in a core temperature that fluctuates by only 0.5°C.[14]

During general anesthesia, hypothalamic activity becomes depressed and constriction of arteriovenous shunts does not occur until body temperature has decreased by 1.5°C, resulting in an increase in the amount of heat lost to the environment.[5,14] The vasodilatory effects of most anesthetic agents increase blood flow to the extremities, which release heat into the environment from arteriovenous shunts via radiation and conduction. Blood in the extremities cools and mixes with warmer blood in the core compartment, thereby decreasing overall core temperature.[5] This process continues, unless the immediate environment surrounding the patient becomes warmer than the patient (eg, through the use of supplemental heat sources or triggering of arteriovenous shunts causing vasoconstriction).[14]

Hypothermia induced by general anesthesia can be considered to have 3 phases.[1,2,5] Phase I or redistribution hypothermia generally occurs during the first hour of anesthesia and is attributed to rapid redistribution of heat from the core to the peripheral compartment. Additionally, radiative and conductive heat loss occurs when the environmental temperature is lower than an animal's body temperature. During phase I, the animal's skin is typically being shaved of hair and prepared for surgery; therefore, evaporative and convective heat losses are likely occurring. Phase II or continual loss of heat occurs as heat is lost to the environment via radiation, convection, evaporation, and conduction. Warming devices can increase the environmental temperature close to the animal and prevent additional heat loss during this phase.[5,15] Phase III or the plateau occurs when either hypothalamic-induced vasoconstriction occurs to prevent further heat loss or the patient gains heat from warming devices so that heat loss and gain are equal.

Ketamine hydrochloride, a dissociative anesthetic, is widely used in combination with a benzodiazepine for induction of anesthesia in small animal practice.[16] Ketamine administration decreases the extent of redistribution hypothermia in humans, likely because it leads to an increase in the amount of circulating norepinephrine, causing an increase in peripheral arteriolar resistance and muscle activity.[17,18] Additionally, propofol (2,6-diisopropylphenol) is routinely used for anesthetic induction and maintenance in dogs and cats.[19] Propofol causes a dose-related decrease in arterial blood pressure and vasodilation that has been associated with an increase in heat loss through arteriovenous shunts.[18]

The purpose of the study reported here was to compare the influence of induction of general anesthesia with a benzodiazepine plus ketamine or propofol on intraoperative rectal and esophageal temperatures and postoperative rectal temperature in dogs undergoing routine ovariohysterectomy. Our hypothesis was that anesthetic induction with the ketamine-benzodiazepine combination would result in higher core and rectal temperatures than would induction with the propofol-benzodiazepine combination.

Materials and Methods

Animals

Twenty-five adult sexually intact female dogs brought to the veterinary teaching hospital at the University of Florida for routine ovariohysterectomy were used in this study. Ages ranged from 8 months to 5 years (mean ± SD, 1.8 ± 1.2 years), and body weight ranged from 4 to 27.3 kg (mean, 16.4 ± 6.6 kg). All dogs were patients of the university's Veterinary Community Outreach Program, and managers of The Humane Society and other animal shelters consented to the use of the dogs in this study. Dogs were transported from their foster home or shelter the morning of ovariohysterectomy. All were deemed clinically normal on the basis of physical examination findings, a body condition score between 4 to 6 on a 9-point scale,[a] and an initial rectal temperature[b,c] between 37.9° and 40.1°C and were classified as American Society of Anesthesiologists category I.[20] The study protocol was approved by the Institutional Animal Care and Use Committee at the University of Florida. No animals were euthanized as a result of the study.

Environmental monitoring

The study environment included the housing areas for cages and runs, anesthesia preparation room, operating room, and recovery room. In each room, room temperature and relative humidity were recorded by use of a thermal environmental monitor[d] within 15 minutes after the entry of each dog. Room temperatures ranged from 18.5° to 22.5°C (mean, 19.2 ± 0.5°C), and relative humidity ranged from 41% to 71% (mean, 61.6 ± 3.5%).

Anesthetic protocol

Food and water were withheld from all dogs for a minimum of 12 hours prior to surgery. Dogs were placed in unheated cages or runs and allowed to acclimate to the hospital for at least 30 minutes prior to premedication. Prior to surgery, dogs were randomly assigned to receive a benzodiazepine plus propofol or a benzodiazepine plus ketamine by use of a computer-generated random numbers chart.[e] All dogs were given firocoxib[f] (5 mg/kg, PO) or carprofen[g] (2.2 mg/kg, PO) as an analgesic and were then given buprenorphine hydrochloride[h] (0.02 mg/kg, IM) and acepromazine maleate[i] (0.05 mg/kg, IM) as premedication. Dogs were allowed to move freely in their cages or kennels after premedication.

Twenty minutes after premedication, dogs were moved to the anesthetic induction area and positioned on a stainless steel table covered with a blanket; then,

IV catheterization was performed by a veterinary student or technician. Dogs assigned to receive a benzodiazepine with ketamine were given the entire volume of midazolam hydrochloride[j] or diazepam[k] (0.25 mg/kg, IV) combined with ketamine hydrochloride[l] (5 mg/kg, IV), and orotracheal intubation was performed when the dog appeared relaxed with no evidence of jaw tone or gag reflex. Dogs assigned to receive a benzodiazepine with propofol were given midazolam hydrochloride or diazepam (0.25 mg/kg, IV) followed by a third of the propofol[m] dose (total dose, 4 mg/kg, IV). If muscle relaxation was not achieved or jaw tone was detected, additional propofol was administered until the dog appeared relaxed with no evidence of jaw tone or gag reflex and orotracheal intubation was performed.

Anesthesia was maintained with isoflurane[n] in oxygen delivered via a circle system with an oxygen flow rate of 30 mL/kg/min and vaporizer setting of 2%. Oxygen saturation as measured by pulse oximetry,[o] pulse rate, and respiratory rate were recorded every 5 minutes after anesthetic induction until the end of anesthesia (vaporizer turned off). Pulse rate was measured by manual palpation of the distal aspect of the median artery or major palatine artery, and respiratory rate was recorded by observation of the reservoir bag or chest movement. When the anesthetic plane was deemed too deep because of an absence of jaw tone or withdrawal reflex, low respiratory rate, or low heart rate, the isoflurane setting was decreased.

An inactivated circulating water blanket[p] covered with fleece was placed on top of the stainless steel surgical table. Dogs were positioned on the fleece on the surgical table for the procedure and did not have direct contact with any area of the table. The circulating warm water blanket was turned on when the rectal or esophageal temperature reached 35°C. Ovariohysterectomy was performed by a veterinary student under the supervision of a veterinarian.

The end of anesthesia was recorded as the time the vaporizer was turned off. The breathing circuit was disconnected, flushed with oxygen, and reattached to the endotracheal tube, at which point dogs were allowed to breathe 100% oxygen for 10 minutes before transfer to the recovery area. All dogs were covered with a warm-air blanket[q] until normothermic. Veterinary students performed extubation when the dogs' coughing and swallowing reflexes had returned.

Recording and measurement of study variables

Timings were recorded for administration of premedications, induction of anesthesia (point induction agent was administered), start of surgery, end of surgery, initiation of intraoperative heat support, end of anesthesia, and subsequent achievement of normothermia. Timing of orotracheal extubation was not recorded.

Measurement of rectal and esophageal temperature was performed by use of 2 thermistor probes.[c,r] Accuracy of both probes was verified within 0.1°C by use of a water bath of known temperature prior to use each day. Water bath temperatures were validated by use of a thermometer[s] with certified accuracy between −20° and 110°C. Rectal temperatures were measured by inserting the rectal thermistor probe 6 cm into the rectum[21] and were recorded at initial hospital intake, prior to premedication (baseline), and immediately after anesthetic induction (0 minutes) and every 5 minutes for 90 minutes after anesthetic induction. Rectal temperature was recorded every 10 minutes after the end of anesthesia until normothermia was achieved. Once each dog had been moved into the operating room and positioned on the surgical table, esophageal temperature was measured by placement of an esophageal thermistor probe in the caudal fourth of the esophagus.[21] Measurements were made every 5 minutes beginning 30 minutes and ending 90 minutes after anesthetic induction. The esophageal probe was removed at the end of anesthesia. The same investigator (JLB) performed all physical examinations, thermistor probe verification, temperature measurements, and anesthetic monitoring during this study. This investigator was not present during anesthetic induction and was blinded to treatment group assignment until all dogs were discharged from the hospital.

Statistical analysis

Commercially available statistical software[t] was used for statistical analysis. Descriptive statistics were computed to confirm that values for the interval between premedication and induction, total duration of anesthesia (from anesthetic induction to disconnection from the anesthetic circuit), total duration of surgery, and interval from discontinuation of anesthesia to achievement of normothermia were normally distributed for each treatment group. Descriptive statistics were computed to confirm that values for rectal and esophageal temperature were normally distributed. Rectal temperature at each measurement point for each treatment was compared by use of 2-way ANOVA for repeated measures, followed by Bonferroni adjustment. Within-treatment changes were examined by means of 1-way ANOVA for repeated measures, with post hoc comparisons against baseline values. Rectal and esophageal temperatures at 30 and 90 minutes for each treatment were compared by means of 2-way ANOVA for repeated measures. The within-treatment differences were examined by means of 1-way ANOVA for repeated measures. Summary data are reported as mean ± SD; values of $P \leq 0.05$ were considered significant.

Results

Animals

Twenty-three dogs completed the study, including 11 that received the ketamine-benzodiazepine combination and 12 that received the propofol-benzodiazepine combination for anesthetic induction. For the benzodiazepine, 3 dogs received diazepam (1 with

ketamine and 2 with propofol) and 20 received midazolam (10 with ketamine and 10 with propofol). Twenty dogs were mixed breeds, and 3 were purebred (1 each of Border Collie, Shiba Inu, and Chihuahua). One dog inadvertently received only propofol. For another dog, frank blood was detected on the rectal thermometer used during anesthesia; therefore, rectal temperature measurements were discontinued. Neither of these dogs was included in the analysis. All dogs (including the excluded dogs) recovered from anesthesia without complication and were discharged from the hospital on the same day of surgery.

Durations of procedures

The interval from premedication to anesthetic induction and total durations of anesthesia and surgery did not vary significantly between treatment groups. For dogs in the propofol-benzodiazepine group, mean ± SD values were 42 ± 12 minutes, 134 ± 25 minutes, and 102 ± 20 minutes, respectively. For dogs in the ketamine-benzodiazepine group, mean values were 38 ± 5 minutes, 125 ± 19 minutes, and 93 ± 17 minutes, respectively.

Rectal and esophageal temperatures

No difference in baseline rectal temperature (recorded at hospital intake) was identified between treatment groups. Mean baseline rectal temperature was 39.0 ± 0.4°C and 38.8 ± 0.7°C for the ketamine-benzodiazepine and propofol-benzodiazepine groups, respectively. Immediately after anesthetic induction (0 minutes), rectal temperature in each group was significantly lower than at baseline (mean temperature for ketamine-propofol at 0 minutes, 37.8 ± 0.4°C; mean temperature for propofol-benzodiazepine, 37.3 ± 0.5°C; **Figure 1**). Rectal temperature in each group continued to be significantly lower from 0 to 90 minutes, compared with the temperature at baseline, and throughout that period, dogs in the propofol-benzodiazepine group had significantly lower temperatures than did dogs in the ketamine-benzodiazepine group.

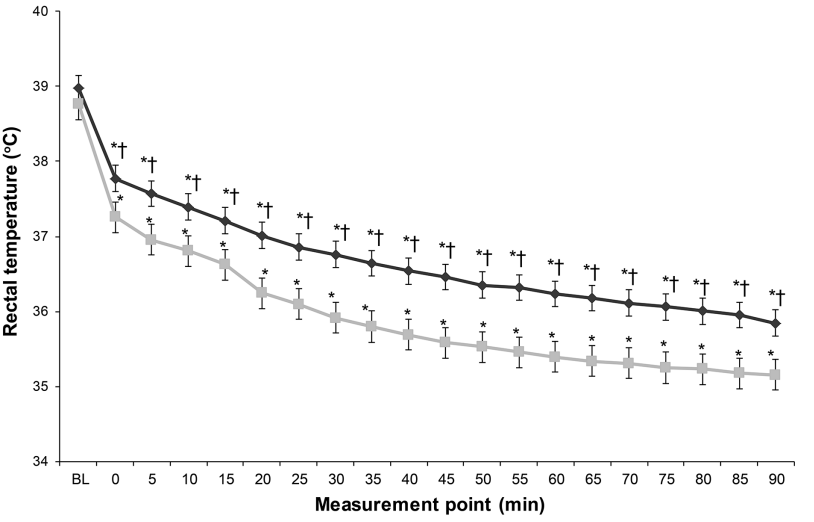

Figure 1—Mean rectal temperatures recorded at hospital intake (baseline [BL]) and prior to (0 minutes) and every 5 minutes after anesthetic induction for 23 adult dogs undergoing routine ovariohysterectomy. All dogs were premedicated with buprenorphine and acepromazine. Anesthesia was induced with midazolam or diazepam (0.25 mg/kg, IV) plus ketamine hydrochloride (5 mg/kg, IV; diamonds [n = 11]) or propofol (4 mg/kg, IV; squares [12]). Error bars represent SD. *Value differs significantly ($P \leq 0.05$) from respective BL value. †Value differs significantly ($P \leq 0.05$) between groups at the indicated measurement point.

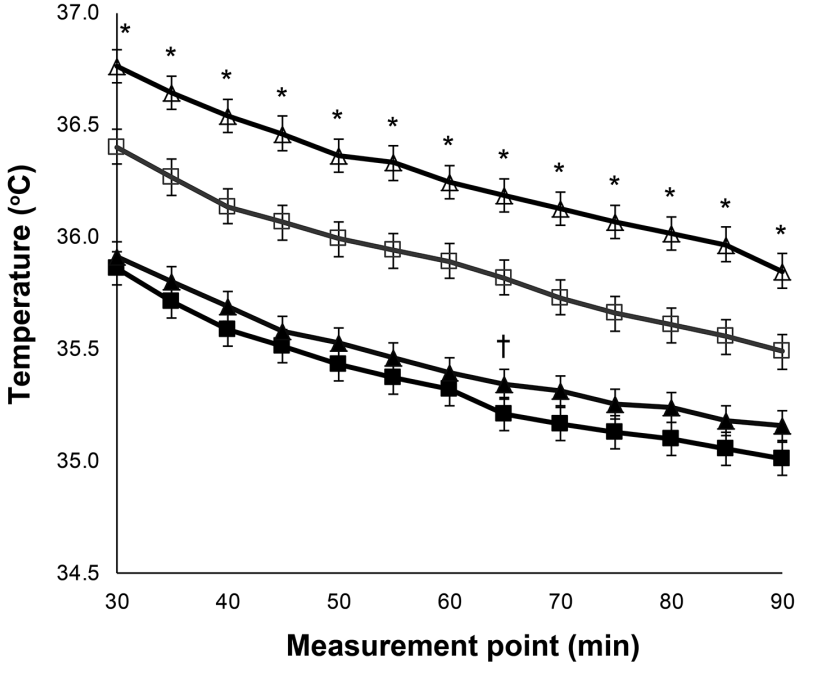

Figure 2—Mean rectal (triangles) and esophageal (squares) temperatures recorded at various points from 30 to 90 minutes after anesthetic induction with a combination of ketamine-and-benzodiazepine (white symbols) or propofol-benzodiazepine (black symbols) for the dogs in Figure 1. *Value differs significantly ($P \leq 0.05$) from the esophageal value at the same measurement point in the same treatment group. †Esophageal temperature differs significantly ($P = 0.04$) between groups at the indicated measurement point.

Esophageal and rectal temperatures decreased from 30 to 90 minutes after anesthetic induction in both treatment groups **(Figure 2)**. No difference between groups in esophageal temperatures at the various measurement points was identified, except at 65 minutes after anesthetic induction ($P = 0.04$). For dogs

in the propofol-benzodiazepine group, esophageal and rectal temperatures did not vary significantly from 30 minutes (when esophageal temperature recording began) to 90 minutes after anesthetic induction. However, for dogs in the ketamine-benzodiazepine group, rectal temperatures were significantly higher than esophageal temperatures at each measurement point from 30 to 90 minutes after anesthetic induction. No significant difference in mean values of temperatures recorded from 30 to 90 minutes was identified between rectal temperature (35.4 ± 0.3°C) and esophageal temperature (35.3 ± 0.3°C) for dogs in the propofol-benzodiazepine group. For dogs in the ketamine-benzodiazepine group, the mean for all rectal temperatures recorded from 30 to 90 minutes (36.3 ± 0.4°C) was significantly higher than the mean for esophageal temperatures recorded during the same period (35.9 ± 0.4°C).

During anesthesia, 11 dogs in the propofol-benzodiazepine group and 6 dogs in the ketamine-benzodiazepine group required intraoperative heat support (esophageal or rectal temperature, 35°C). Mean interval from discontinuation of anesthesia to achievement of normothermia was significantly longer for dogs in the propofol-benzodiazepine group (86 ± 29 minutes) than for dogs in the ketamine-benzodiazepine group (54 ± 25 minutes).

Discussion

For adult dogs undergoing ovariohysterectomy, induction of general anesthesia with a ketamine-benzodiazepine combination resulted in higher rectal temperatures throughout a 90-minute anesthetic period than did induction with a propofol-benzodiazepine combination. In the first hour of anesthesia, mean rectal temperature of dogs in the ketamine-benzodiazepine group decreased by 1.5°C and that of dogs in the propofol-benzodiazepine group decreased by 1.9°C. The extent of this heat loss was similar to that reported for other studies[1,2,5] involving dogs and was consistent with redistribution hypothermia (ie, phase I of anesthesia-induced hypothermia). However, the significant difference in rectal temperatures between the 2 induction agents has not been previously reported for dogs.

Ketamine administration minimizes the incidence of redistribution hypothermia in humans, likely as a result of the peripheral vasoconstriction that results from an increase in blood norepinephrine concentration and peripheral vasoconstriction.[17,18,22] Vasoconstriction limits blood flow to the extremities, minimizing the amount of heat lost to the environment and decreasing the extent of redistribution hypothermia.[18] Propofol administration, on the other hand, has been associated with peripheral arterial and venous vasodilation, resulting in an increase in blood flow to the extremities and loss of heat to the environment via radiation and convection.[18] Propofol undergoes rapid redistribution and clearance from the body, but the heat loss to the environment associated with its administration cannot be reversed without supplemental heat sources. In the present study, we attempted to measure heat loss from the peripheral compartment in dogs by use of skin thermistor probes (data not shown), similar to methods used in human studies.[11,18,23] However, we had difficulty maintaining adequate contact between the probes and skin, indicating that this technique requires further refinement prior to use in the quantification of peripheral heat loss.

During anesthesia in the present study, 11 of the 12 dogs in the propofol-benzodiazepine group and 6 of the 11 dogs in the ketamine-benzodiazepine group required rewarming. Circulating warm water blankets can be used to minimize heat loss by prevention of conductive losses to cold surgical tables and blankets.[24] However, such blankets are not as effective as warm-air blankets or resistive warming systems for maintaining normothermia.[15,24,25] The effects of warm-air blankets or resistive warming systems on the incidence of hypothermia in the dogs in the present study would have been interesting to investigate and may have provided valuable information regarding appropriate measures for provision of intraoperative thermal support.

Rectal temperatures at the end of anesthesia were significantly lower and the interval to achieving normothermia was significantly longer in dogs in the propofol-benzodiazepine group than in dogs in the ketamine-benzodiazepine group. One possibility is that dogs in the propofol-benzodiazepine group were at a deeper plane of anesthesia because of altered enzyme activity, decreased drug metabolism, and increased inhalant anesthetic solubility at temperatures < 37°C.[4,9] Propofol clearance decreases in hypothermic states secondary to decreases in hepatic blood flow and metabolism.[26] However, all dogs in the present study were assessed by an experienced anesthetist, who made adjustments to the vaporizer setting on the basis of physical findings that included jaw tone, withdrawal reflexes, and monitored values (eg, pulse rate, respiratory rate, and oxygen saturation as measured by pulse oximetry).

Dogs in the ketamine-benzodiazepine group had esophageal temperatures that were significantly lower than their rectal temperatures; however, this phenomenon was not observed for dogs in the propofol-benzodiazepine group. The reason for this difference between groups could not be explained by the study data, but we suspect it was attributable to decreased heat loss from the peripheral compartment caused by greater peripheral vasoconstriction in dogs that received ketamine rather than propofol, resulting in less heat returning from the periphery to the central compartment. The techniques that we used to measure peripheral compartment temperatures require further refinement. Another way to evaluate temperature in the core and peripheral compartments would be with infrared thermography, which is a noninvasive, real-time technique that generates a 2-D image of the intensity of infrared radiation emitted by an object.[27]

However, the associated equipment is expensive, interpretation of images requires specialized software and training, and results can be influenced by the environment or use of heating devices.[27]

One limitation to the present study was the small number of dogs (23) used. An additional limitation was the need to substitute midazolam for diazepam because of drug availability. Three dogs received diazepam (1 with ketamine and 2 with propofol) as the benzodiazepine, and the rest received midazolam. No clinical differences related to the quality of anesthetic induction were detected between the drugs; however, because of the uneven and small sample sizes, the study may have lacked power to identify such differences. The mechanism of action of diazepam and midazolam is similar, with major differences relating to water solubility and elimination half-lives. Diazepam is water insoluble and is prepared with organic solvents such as propylene glycol.[19] The elimination half-lives of diazepam and nordiazepam, its active metabolite, after IV administration of a high dose are 3.2 hours and 21 hours, respectively.[15,16] Midazolam is water soluble, and its elimination half-life in dogs is 28 minutes, leading to rapid redistribution and hepatic clearance.[15,16]

In the study reported here, IV administration of a ketamine-benzodiazepine or propofol-benzodiazepine combination to dogs undergoing routine ovariohysterectomy resulted in hypothermia within 5 minutes after anesthetic induction. However, dogs that received the propofol-benzodiazepine combination had a greater temperature decrease and a longer interval to restoration of normothermia than did dogs that received the ketamine-benzodiazepine combination. On the basis of these findings, we recommend that all dogs be provided adequate heat support after induction of general anesthesia, particularly when a propofol-benzodiazepine combination is used for induction.

Acknowledgments

Supported in part by the Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, Fla.

Presented as a poster at the American College of Veterinary Anesthesia and Analgesia Meeting, Washington, DC, September 2015.

The authors thank Nicole Bengyel and Daniela Isaza for technical assistance.

Footnotes

a. Body condition score chart for dogs. World Small Animal Veterinary Association Global Nutrition Committee, Dundas, ON, Canada. Available at: www.wsava.org/sites/default/files/Body%20condition%20score%20chart%20dogs.pdf. Accessed Jun 1, 2015.
b. Adult reusable tubular oral or rectal thermometer (REF403), Measurement Specialties Inc, Dayton, Ohio.
c. Precision thermometer 4600, Measurement Specialties Inc, Dayton, Ohio.
d. QUESTemp 32 thermal environment monitor. Quest Technologies, Oconomowoc, Wis.
e. Random Integer Generator, Randomness and Integrity Services Ltd, Dublin, Ireland.
f. Previcox, Merial LLC, Duluth, Ga.
g. Rimadyl, Pfizer Animal Health, Exton, Penn.
h. Buprenex, Reckett Benckiser Pharmaceuticals, Richmond, Va.
i. Acepromazine maleate, Boehringer Ingelheim Vetmedica, St Joseph, Mo.
j. Midazolam injection USP, West-Ward, Eatontown, NJ.
k. Diazepam injection USP, Hospira Inc, Lake Forest, Ill.
l. Ketaset, Fort Dodge Animal Health, Fort Dodge, Iowa.
m. Propoflo, Abbott Animal Health, Chicago, Ill.
n. Isoflo, Abbott Laboratories, Chicago, Ill.
o. Pulse oximeter N20-PAV, VetEquip Inc, Pleasanton, Calif.
p. Gaymar T/Pump, Gaymar Industries Inc, Orchard Park, NY.
q. Bair Hugger Patient Warmer 500, 3M Health Care, Saint Paul, Minn.
r. Reusable esophageal/rectal adult temperature probe (REF401AC), Measurement Specialties Inc, Dayton, Ohio.
s. Durac Plus certified partial immersion thermometer, H-B Instrument, Collegeville, Pa.
t. SAS, version 9.3, SAS Institute Inc, Cary, NC.

References

1. Redondo JI, Suesta P, Serra I, et al. Retrospective study of the prevalence of postanesthetic hypothermia in dogs. *Vet Rec* 2012;171:374–379.
2. Redondo JI, Suesta P, Gil L, et al. Retrospective study of the prevalence of postanesthetic hypothermia in cats. *Vet Rec* 2012;170:206–211.
3. Sessler DI. Complications and treatment of mild hypothermia. *Anesthesiology* 2001;95:531–543.
4. Doufas AG. Consequences of inadvertent perioperative hypothermia. *Best Pract Res Clin Anaesthesiol* 2003;17:535–549.
5. Armstrong SR, Roberts BK, Aronsohn M. Perioperative hypothermia. *J Vet Emerg Crit Care* 2005;15:32–37.
6. Taggart R, Austin B, Hans E, et al. In vitro evaluation of the effect of hypothermia on coagulation in dogs via thromboelastography. *J Vet Emerg Crit Care (San Antonio)* 2012;22:219–224.
7. Pottie RG, Dart CM, Perkins NR, et al. Effect of hypothermia on recovery from general anaesthesia in the dog. *Aust Vet J* 2007;85:158–162.
8. Haskins SC. Monitoring anesthetized patients. In: Tranquilli WJ, Thurmon JC, Grim KA, eds. *Lumb & Jones' veterinary anesthesia and analgesia*. 4th ed. Ames, Iowa: Blackwell Publishing, 2007;552–553.
9. Lockwood GG, Sapsed-Byrne SM, Smith MA. Effect of temperature on the solubility of desflurane, sevoflurane, enflurane, and halothane in blood. *Br J Anaesth* 1997;79:517–520.
10. Brodbelt DC, Pfeiffer DU, Young LE, et al. Risk factors for anaesthetic-related death in cats: results from the confidential enquiry into perioperative small animal fatalities (CEPSAF). *Br J Anaesth* 2007;99:617–623.
11. Matsukawa T, Sessler DI, Sessler AM, et al. Heat flow and distribution during induction of general anesthesia. *Anesthesiology* 1995;82:662–673.
12. Rubinstein EH, Sessler DI. Skin surface temperature gradients correlate with fingertip blood flow in humans. *Anesthesiology* 1990;73:541–545.
13. Shitara T, Wajima Z, Ogawa R. Dobutamine infusion modifies thermoregulation during GA. *Anesth Analg* 1996;83:1154–1159.
14. Leslie K, Sessler DI. Perioperative hypothermia in high-risk surgical patient. *Best Pract Res Clin Anaesthsiol* 200;17:485–498.
15. Röder G, Sessler DI, Roth G, et al. Intra-operative rewarming with Hot Dog resistive heating and forced-air heating: a trial of lower-body warming. *Anaesthesia* 2011;66:667–674.
16. Lemke KA. Anticholinergics and sedatives. In: Tranquilli WJ, Thurmon JC, Grim KA, eds. *Lumb & Jones' Veterinary anesthesia and analgesia*. 4th ed. Ames, Iowa: Blackwell Publishing, 2007;203–239.
17. Kinoshita T, Suzuki M, Shimada Y, et al. Effect of low-dose ketamine on redistribution hypothermia during spinal anesthesia sedated by propofol. *J Nippon Med Sch* 2004:71:92–98.
18. Ikeda T, Kazama T, Sessler DI, et al. Induction of anesthesia with ketamine reduces the magnitude of redistribution hypothermia. *Anesth Analg* 2001;93:934–938.

19. Branson KR, Booth NH. Injectable anesthetics. In: Adams H, ed. *Veterinary pharmacology and therapeutics.* 7th ed. Ames, Iowa: Iowa State University Press, 1995;209–273.
20. Muir WW. Considerations for general anesthesia. In: Tranquilli WJ, Thurmon JC, Grim KA, eds. *Lumb & Jones' veterinary anesthesia and analgesia*. 4th ed. Ames, Iowa: Blackwell Publishing, 2007;17–29.
21. Machon RG, Raffe MR, Robinson EP. Warming with a forced air warming blanket minimizes anesthetic-induced hypothermia in cats. *Vet Surg* 1999;28:301–310.
22. Riccó CH, Henao-Guerrero N. Cardiovascular effects of orotracheal intubation following anesthetic induction with propofol, ketamine-propofol, or ketamine-diazepam in premedicated dogs. *J Am Vet Med Assoc* 2014;244:934–939.
23. Sessler DI, McGuire J, Hunson J, et al. Thermoregulatory vasoconstriction during isoflurane anesthesia minimally decreases cutaneous loss. *Anesthesiology* 1992;76:670–675.
24. Cabell LW, Perkowski SZ, Gregor T, et al. The effects of active peripheral skin warming on perioperative hypothermia in dogs. *Vet Surg* 1997;26:79–85.
25. Kibanda JO, Gurney M. Comparison of two methods for the management of intraoperative hypothermia in dogs. *Vet Rec* 2012;170:392.
26. Bjelland TW, Klepstad P, Haugen BO, et al. Effects of hypothermia on the disposition of morphine, midazolam, fentanyl, and propofol in intensive care unit patients. *Drug Metab Dispos* 2013;41:214–223.
27. Usamehtiaga R, Venegas P, Guerediaga J, et al. Infrared thermography for temperature measurement and non-destructive testing. *Sensors (Basel)* 2014;13:12305–12348.