# Use of orally administered carfentanil prior to isoflurane-induced anesthesia in a Kodiak brown bear

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- A combination of carfentanil and isoflurane may be used to safely induce and maintain anesthesia in Kodiak brown bears.
- Response to oral administration of carfentanil may vary.
- Despite the large size of bears, instrumentation such as venous and arterial catheterization may prove challenging.

WILDLIFE

A captive 590-kg (1,298-lb [scale weight]) 22-year-old castrated male Kodiak brown bear was referred to the **Colorado State University Veterinary Teaching Hospital (CSU-VTH)** in October 1998 for evaluation of a soft-tissue mass in the region of the right carpus and antebrachium. After visual examination of the affected site, radiographic evaluation of the affected limb and the thorax (to determine possible metastasis) as well as biopsy of the mass under general anesthesia, were recommended. Prior to development of the mass, the bear had no history of serious medical or surgical conditions. A combination of injectable (tiletamine-zolazepam) and inhalation (halothane) agents had been used during a prior anesthetic procedure performed when the bear weighed 177 kg (389 lb).

Although the owners and handler of the bear were able to partially restrain and handle the bear if an injection was necessary, there was a strong desire not to create a situation during anesthetic induction that might compromise the bear's trust in them. Therefore, after food was withheld for 16 hours, the bear was administered carfentanil[a] (8 µg/kg [3.6 µg/lb] of body weight) orally in approximately 10 ml of honey; the bear willingly licked the honey off a large metal spoon while in the transport trailer. The bear became partially recumbent (sternal posture) in 7 to 10 minutes, and a mouth gag was placed to facilitate manual endotracheal intubation 15 minutes after carfentanil administration. **Heart rate (HR)** at this time was 30 beats/min, and **respiratory rate (RR)** was 10 breaths/min. Because of a gag reflex and head movement during an attempt to palpate the arytenoid cartilages, tiletamine-zolazepam[b] (3 mg/kg [1.36 mg/lb], IM) and atropine[c] (0.02 mg/kg [0.009 mg/lb], IM) were administered. Oxygen was insufflated at 10 L/min until the trachea was intubated. Intubation was challenging because of difficulty palpating or viewing the arytenoid cartilages as a result of the bear's position (not quite lateral) in the trailer but was accomplished with a 22-mm endotracheal tube 20 minutes after tiletamine-zolazepam administration. The bear was then manually moved onto a lightly padded transport cart; body position varied throughout the procedure.

Anesthesia was maintained by administration of isoflurane[d] (vaporizer setting gradually decreased from 1.25 to 0.6%) in oxygen (4 L/min) for 2 hours and 15 minutes. This was administered via a standard large-animal anesthetic breathing circle, using an out-of-circuit vaporizer. The HR fluctuated between 55 and 65 beats/min; RR was spontaneous at 1 to 2 breaths/min. Analysis of a lingual venous blood sample[e] obtained 1 hour after intubation indicated that respiratory and metabolic acidosis contributed to moderate acidemia (blood pH, 7.17; $P_{CO_2}$, 63.3 mm Hg; $P_{O_2}$, 165.1 mm Hg; $HCO_3^-$, 21.7 mmol/L; base balance, –8.1 mmol/L [values not corrected for temperature]). Nasal temperature at the time of sample collection and for the duration of anesthesia was 36.2 C (97.2 F). Despite an easily palpated arterial pulse, cannulation of the auricular artery proved to be more challenging than anticipated, likely because of difficulty immobilizing the vessel within the surrounding tissue. A 20-gauge 5-cm arterial catheter[f] was successfully placed in the lingual artery during the latter half of the anesthetic period. Mean arterial pressure remained between 75 and 90 mm Hg. Oxygen saturation[g] determined via lingual probe[h] was ≥ 95% during the entire procedure. A 20-gauge 5-cm venous catheter placed in the lingual vein was used to administer a balanced electrolyte solution and to maintain intravenous access (for additional drug administration, if necessary) during maintenance of anesthesia.

At the conclusion of the diagnostic procedures (radiography and tissue biopsy), instrumentation was discontinued, and the bear was moved back into the transport trailer. Oxygen was administered by use of a demand valve.[i] Naltrexone[j] (0.25 mg/kg [0.11 mg/lb], IV, and 0.59 mg/kg [0.27 mg/lb], IM) was administered, and the bear was allowed to recover from anesthesia. Within 7 minutes, the bear's lips were moving, and a brisk palpebral reflex was evident. The bear was extubated 12 minutes after anesthesia when a strong swallowing reflex and head movements were apparent. The bear then made many uncoordinated attempts to attain sternal recumbency but was unsuccessful. A second dose of naltrexone (0.42 mg/kg [0.19 mg/lb], IM) was administered. The bear's attempts to attain sternal recumbency continued and gradually became more

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The authors thank Dr. Terry Campbell, Lucien Brevard, and Denise Parker for technical assistance.

coordinated. Approximately 40 minutes after anesthesia was discontinued, the bear was able to sit in sternal recumbency and drink fruit juice; the bear stood approximately 30 minutes later.

On the basis of results of examination of a tissue biopsy specimen, myxofibrosarcoma was diagnosed, and surgical debulking of the mass was attempted in January 1999. The decision was made to perform this procedure at a location closer to the bear's normal residence. Carfentanil (8 µg/kg) was administered orally in honey, applesauce, and a fruit muffin. Atropine (0.02 mg/kg, IM) was administered as the bear became recumbent. Twenty minutes after carfentanil administration, endotracheal intubation (20-mm tube) was accomplished manually with the bear hoisted in dorsal recumbency. The endotracheal tube was then connected to the large-animal breathing circuit, and the bear was allowed to breath oxygen (4 to 6 L/min) during positioning (left lateral recumbency on a 12-in foam pad) and instrumentation. The isoflurane vaporizer was turned on approximately 20 minutes later, and the dial setting was maintained between 0.0 and 1.0% for the duration of the procedure; anesthetic duration from intubation to discontinuation of isoflurane was 3 hours. Respiration was spontaneous and ranged from 1 to 4 breaths/min. Tidal volume was approximately 25 L.

A 20-gauge 5-cm venous catheter was placed in the lingual vein, and a 14-gauge 13.75-cm catheter[k] was placed in the medial saphenous vein. The medial saphenous vein was located by use of a 22-gauge 2.5-cm needle, and a relief incision was made prior to cannulation. Venous catheters were used to administer a balanced electrolyte solution, antimicrobials, anesthetic agents, and sympathomimetic drugs. Oxygen saturation was recorded continuously and remained ≥ 98%. A 22-gauge 2.5-cm catheter[l] was placed in the auricular artery to record systolic, diastolic, and mean blood pressure and obtain samples for determination of blood pH, blood gas values,[m] blood glucose concentration, BUN, serum electrolyte values, PCV, and serum total protein concentration. Mean values of 3 samples for arterial pH (7.21), $P_{CO_2}$ (54.6 mm Hg), $P_{O_2}$ (328 mm Hg), $HCO_3^-$ (21.5 mmol/L), and base balance (–6.2 mmol/L) were determined. Electrolyte values were within reference ranges determined for dogs and cats at the CSU-VTH. Nasal temperature was recorded continuously during the procedure and ranged from 36.5 to 36.8 C (97.7 to 98.2 F).

The HR gradually increased from 40 beats/min at intubation to approximately 70 beats/min within the first hour of anesthesia, remained at this rate for the next hour and 45 minutes, and then increased to a peak value of approximately 100 beats/min during a hemorrhagic episode before gradually returning to approximately 70 beats/min. Mean arterial pressure, which ranged from 120 to 180 mm Hg, decreased to a low value of 65 mm Hg during hemorrhage. It was estimated that the bear lost 8 L of blood during the surgical procedure, with most blood loss occurring toward the end of the procedure.

During the procedure, the bear received 8 L of balanced electrolyte solution, carfentanil (200 µg, IV), and potassium penicillin[n] ($20 \times 10^6$ units, IV). Infusions of norepinephrine[o] (16 µg/ml) and dobutamine[p] (0.25 mg/ml) were administered IV briefly during the hemorrhagic period to maintain mean arterial pressure > 70 mm Hg. The norepinephrine infusion was discontinued upon observation of ventricular dysrhythmias, indicating the need for caution during the administration of sympathomimetic drugs in species in which knowledge of the effects of these drugs is limited. The PCV and serum total protein concentrations prior to acute hemorrhage were 40% and 8.4 g/dl, respectively; further assessments were not possible.

The surgical site was closed, and a pressure bandage was placed around the site. The bear was transported to a trailer where naltrexone (0.42 mg/kg, IV and IM) was administered. Within minutes, the bear had increased RR, swallowed, and was extubated. The bear rolled to sternal recumbency, and 25 minutes after naltrexone administration, the bear was drinking an electrolyte solution given by the owners.

The bear recovered without complications until approximately 4 months after surgery when the owners observed a slight gait abnormality that was followed by a recurrence of tumor growth. The bear was readmitted to the teaching hospital in June 1999 for palliative treatment with a single dose of radiation (10 Gy via parallel apposed portals by use of source-to-axis distance geometry) followed by surgical debulking of the mass and local placement of sustained-release cisplatin.[1]

With the bear in a transport trailer, carfentanil (8 µg/kg) was administered orally in a mixture of honey, applesauce, and muffin. Although the bear appeared sedated, he still responded to any attempts at handling during the next 40 minutes. This necessitated the administration of 2 additional doses of carfentanil (4 µg/kg [1.82 µg/lb], IM) given 10 minutes apart. Atropine (0.02 mg/kg, SC) was also administered during this time. Although the bear's reactivity decreased, the bear was not relaxed sufficiently to allow endotracheal intubation. Isoflurane (5%) in 10 L of oxygen was administered by facemask for approximately 5 minutes, after which endotracheal intubation with a 22-mm endotracheal tube was successfully performed with the bear in sternal recumbency.

Oxygen (5 L/min) was administered by use of a large-animal anesthetic breathing circle during instrumentation and positioning in the radiation therapy unit. The isoflurane vaporizer was turned on 40 minutes later; dial setting ranged from 0.3 to 1.25% for the duration of the procedure except for approximately 20 minutes when the bear was transported from the radiation therapy unit to the surgical suite where it was positioned in left lateral recumbency on a water bed. Ketamine (100 mg, IV), diazepam (10 mg, IV), and oxygen (demand valve) were administered during transport. The time from endotracheal intubation until discontinuation of isoflurane administration was 4 hours; surgical time was 2 hours.

The HR ranged from 60 to 80 beats/min during the entire procedure. Respiration was spontaneous and ranged from 3 to 6 breaths/min. Mean arterial pressure recorded from an arterial catheter placed in the lingual artery ranged from 169 to 211 mm Hg until the end of

the procedure when it decreased to a low value of 98 mm Hg during an episode of blood loss estimated at 4 to 6 L. Oxygen saturation was ≥ 96% throughout the procedure. A fluid pump was used to facilitate IV administration of 30 L of a balanced electrolyte solution; catheters were placed in the medial saphenous and lingual veins. Nasal temperature ranged from 36.4 to 36.8 C (97.5 to 98.2 F). Blood was obtained at various times during the procedure for measurement of pH, blood gases, and electrolyte concentrations. Mean values of 2 samples for arterial pH (7.362), $P_{CO_2}$ (37.5 mm Hg), $P_{O_2}$ (429 mm Hg), $HCO_3^-$ (20.7 mmol/L), and base balance (–3.7 mmol/L) were determined. Serum electrolyte values were within reference ranges. The PCV and serum total protein concentration were 43% and 5.6 g/dl, respectively, at the beginning of surgery and 39% and 5.7 g/dl, respectively, 1 hour after surgery was begun. Potassium penicillin ($20 \times 10^6$ units, IV and by infiltration at the surgical site), flunixin meglumine[q] (600 mg, IV), carfentanil (300 µg, IV), and bupivacaine[r] (150 mg, by infiltration at the surgical site) were also administered during the surgical procedure.

At the conclusion of the surgical procedure, instrumentation was discontinued, and the bear was moved to a trailer where naltrexone (0.5 mg/kg [0.23 mg/lb], IV and 0.84 mg/kg [0.38 mg/lb], IM) was administered. A demand valve was used to provide oxygen until extubation 7 minutes after naltrexone administration. Although the bear recovered in a similar time frame as that described for the first 2 anesthetic periods, certain aspects of recovery were qualitatively different at this time. The bear appeared distressed and uncomfortable and reacted violently to any approach, even from the owners and trainer. Interventions (including repeat carfentanil administration via dart) were discussed, but after consideration of all factors, it was felt that the best decision was to leave the bear in a quiet, cool environment under observation. The bear's distressed behavior lasted approximately 2 hours, after which the bear's temperament gradually improved but did not return to normal until the next morning when orally administered medications, including phenylbutazone, were administered. Six months after the last intervention, there was no evidence of a mass at the treated site, and the bear appeared pain free and was fully weight-bearing on the limb.

This case report indicates that safe management of a bear is possible by use of a balanced anesthetic technique consisting of an opioid (eg, carfentanil) and an inhalation anesthetic agent (eg, isoflurane). Given the right clinical circumstances, orally administered carfentanil is efficacious, but the potential for variable effects must be considered. Because of high magnitude and severity of complications when high doses of carfentanil are administered orally to bears, and because the age and medical condition of this bear were unknown, a dose at the lower end of the reported dose range[2] was selected. The variability in the observed effect, which ranged from mild sedation to conditions appropriate for intubation, could be attributed to small differences in the bear's body weight (the bear was weighed only prior to the first anesthetic procedure), anxiety prior to drug administration, or differences in drug absorption. Bears are considered pseudohibernators, and given that this bear was anesthetized in 3 seasons, fall (when metabolism begins to slow down), winter (peak of the slow down), and summer (just prior to a phase where activity and appetite increase [hyperphagia]), it is possible (although we have no direct evidence) that the drug dose requirements to reach the same end point could vary with season.

In each instance, naltrexone was used to reverse the effects of carfentanil by use of a dose in the range recommended by the manufacturer; this dose is based on the dose of carfentanil received by the animal. The decision to use naltrexone was based on the potential for adverse effects (eg, hypoventilation or hypoxemia) if the bear remained under the narcotic effects of carfentanil. In retrospect, it may have been more appropriate in this circumstance (in which long-term patient support and monitoring was possible and the bear underwent a potentially painful procedure) to let the bear recover more gradually and maintain the analgesic benefit of carfentanil.

Given our previous experiences with anesthetizing bears and in discussing their anesthetic management with others, problems with instrumentation of this bear were somewhat surprising. The remarkable size and mass of this bear may have contributed to these problems. For example, palpation of the medial saphenous vein, which is easily accomplished in a smaller bear, was extremely difficult in this bear, and cannulation of the auricular artery was also difficult. Indirect blood pressure monitoring (Doppler) was also unsuccessful because of difficulty identifying a peripheral artery in the distal portion of the limbs and because an occlusive cuff large enough to encircle the limb was not available. Intubation was greatly facilitated by positioning the bear in a sternal or dorsal position.

Blood pressure during the second and third anesthetic periods was in the range reported in bears anesthetized with medetomidine and tiletamine-zolazepam[s,3] and in elephants in which an opioid plus inhalation anesthetic technique[4] was used. A lower value recorded during the first anesthetic procedure was likely attributable to the combined effects of isoflurane, carfentanil, tiletamine-zolazepam, and lack of surgical stimulation. Although there was some variability, nasal temperature, HR, RR, oxygen saturation, $P_{O_2}$, and $P_{CO_2}$ values were in a clinically acceptable range during all 3 anesthetic procedures. The coordinated efforts of the bear's owners, trainer, veterinary and human medical specialists, and veterinary technicians was an important factor in the successful management of anesthesia in this bear, because knowledge of anesthetic protocols for this species is scarce.

[a]Carfentanil citrate, Wildlife Laboratories Inc, Fort Collins, Colo.
[b]Telazol, Fort Dodge Animal Health, Fort Dodge, Iowa.
[c]Atropine sulfate, The Butler Co, Columbus, Ohio.
[d]Isoflo, Abbott Laboratories, North Chicago, Ill.
[e]ABL 505, Radiometer America Inc, Westlake, Ohio.
[f]Insyte, Becton-Dickinson, Sandy, Utah.
[g]Medical Data Electronics, Arleta, Calif.
[h]VetSat probes, Nellcor, Pleasanton, Calif.
[i]Equine demand valve, JD Medical Inc, Phoenix, Ariz.
[j]Trexonil, Wildlife Laboratories Inc, Fort Collins, Colo.

[k] Abbocath-T, Abbott Laboratories, North Chicago, Ill.
[l] Insyte, Becton-Dickinson, Sandy, Utah.
[m] IRMA SL series 2000, Diametrics Medical Inc, St Paul, Minn.
[n] Marsam Pharmaceuticals Inc, Cherry Hill, NJ.
[o] Levophed, Abbott Laboratories, North Chicago, Ill.
[p] Dobutamine, Abbott Laboratories, North Chicago, Ill.
[q] Flunixamine, Fort Dodge Animal Health, Fort Dodge, Iowa.
[r] Bupivacaine hydrochloride USP, Abbott Laboratories, North Chicago, Ill.
[s] Caulkett NA, Cattet MRL, Caulkett JM, et al. Comparative cardiopulmonary effects of medetomidine-telazol in polar bears (abstr), in *Proceedings*. Annu Meet Am Coll Vet Anesth, 1998;28.

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