Anaesthetic management of a cheetah (*Acinonyx jubatus*) for caesarean section

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ABSTRACT

After delivering a single stillborn cub, a 4-year-old, semi-feral, captive cheetah (*Acinonyx jubatus*) presented at full-term pregnancy with either suspension of labour or uterine inertia and a caesarean section was performed. The cheetah was sedated with 0.0357 mg/kg medetomidine intramuscularly, followed by intravenous induction with propofol to effect and maintenance on isoflurane inhalational anaesthesia. Each cub was administered a total of 0.15 mg atipamezole intramuscularly, in 0.05 mg increments, after delivery. The anaesthetic management of the cheetah focused on selecting anaesthetic drugs that would minimise neonatal drug exposure and ultimately maximise the chances of neonatal viability. Additionally, the drugs administered had to also provide sufficient sedation to ensure personnel safety. Finally, the anaesthesia of the cheetah had to be considered in context of the physiological changes that occur during pregnancy.

BACKGROUND

Cheetahs (*Acinonyx jubatus*) are listed as vulnerable by the International Union for Conservation of Nature (IUCN)[1] and face continued threat by habitat destruction, population fragmentation, genetic bottlenecking, and human–wildlife conflict.[2-4] Thus, effective reproductive management of captive populations is imperative in ensuring species survival.[2, 5]

Caesarean section (CS) is a common intervention in domestic species, with 60%–80% of canine dystocias resolved surgically.[6, 7] Ideally, the anaesthetic plan for CS should provide adequate narcosis and muscle relaxation for surgery, while simultaneously providing analgesia and limiting compromise to the dam, and still culminating in the delivery of vigorous neonates.[8, 9] Common recommendations are minimal to no preanaesthetic medication prior to intravenous induction with propofol or alfaxalone and subsequent maintenance on inhalation drugs, with emphasis on administering opioid receptor agonists for analgesia after delivery of neonates.[8, 10-12] Chemical immobilisation is routinely employed in both wild and semi-feral captive cheetahs.[13] However, in pregnant animals, immobilisation drugs might result in preoperative iatrogenic compromise to both the dam and neonates.

The aim of this case report was to detail the considerations surrounding the anaesthetic management of a captive semi-feral cheetah undergoing CS.

CASE PRESENTATION

A 4-year-old, 40 kg, primiparous cheetah from a breeding sanctuary was presented awake in a transport crate for examination after delivering a stillborn cub 3 days prior. The sanctuary was in the process of moving premises and had subjected their animals to a disturbed routine. Prior to arrival at the hospital, the keeper observed transabdominal movement and suspected that live fetuses remained within the uterus. The gestation period of the cheetah has been described as 90−98 days from mating,[14] although the breeding dates of this individual were unknown and the stillborn fetus was not available for examination. Therefore, it was unknown whether the animal was intrapartum or had undergone an incomplete abortion.

The cheetah was sedated with 0.0375 mg/kg medetomidine (Domitor, Zoetis) administered intramuscularly by hand injection. Twenty minutes later, a sufficient level of sedation was attained for a 20G, over-the-needle, intravenous catheter (Jelco; Smiths Medical) to be inserted into the left medial saphenous vein. Anaesthesia was induced with propofol (Fresenius Propoven 1%; Fresenius-Kabi) intravenously to effect, to facilitate endotracheal intubation with a cuffed, polyvinyl chloride tube (10 mm internal diameter; Ho-Lee Tube, JC Medical) with the aid of an illuminated laryngoscope. Anaesthesia was maintained with isoflurane (Isofor; Safeline Pharmaceuticals) in 100% oxygen delivered via a circle rebreathing system (Minicare Anaesthesia System; Crest Healthcare Technology) to facilitate an obstetric examination.

INVESTIGATIONS

On clinical examination, no abnormalities were detected on thoracic auscultation (respiratory rate of 30 breaths/min), peripheral pulses were regular and of good quality (pulse rate of 90 beats/min) and the cheetah was in good body condition (BCS 5/9), with no external injuries noted. Colostrum could be easily expressed from all mammae. The abdomen was distended, fetal movement could be palpated and fetal heartbeats could be auscultated.

Manual vaginal palpation and vaginoscopy was performed using a Perspex tube speculum of 12 mm internal diameter. The birth canal was subjectively relaxed, and a mucoid vaginal discharge was present with no smell. No fetal membranes or fetus was visible in the birth canal. Right lateral and ventrodorsal radiographs were exposed, revealing three fetuses, all with well mineralised caudal vertebrae, teeth and phalanges. On ultrasonographic examination, all fetuses had regular heartbeats of between 170 and 200 beats per minute. Fetal intestinal peristalsis could not be visualised.

DIFFERENTIAL DIAGNOSIS

Incomplete abortion of the litter was considered; however, clinical, radiographic and ultrasonographic findings supported the diagnosis of a full-term pregnancy with either stress-associated suspension of labour or uterine inertia with a full-term litter.

TREATMENT

A decision was taken to perform a CS to allow greater control over parturition and postpartum care of the neonates and increase the chances of survival of potentially compromised cubs in the event of maternal rejection.

The abdomen was clipped from xiphoid to pubis and surgically prepared for a midline celiotomy, after which it was transferred to a operation theatre for CS.

Anaesthesia

Isoflurane in oxygen and air (fraction of inspired oxygen [FiO_2] 0.75) was delivered via a circle rebreathing system (Datex Ohmeda 9100; GE Medical Systems). Fresh gas flow rate was set at 3 L/min with the vapouriser setting between 1.5% and 2.5% to achieve a fractional expired isoflurane tension of 1.6%−2.2%. A balanced isotonic electrolyte solution (Lactated Ringers' Solution; Fresenius-Kabi) was administered at 5 ml/kg/h for perioperative fluid therapy and perioperative antimicrobial therapy (20 mg/kg cefazolin; Zefkol, GlaxoSmithKline) was administered intravenously. The cheetah was positioned in dorsal recumbency after which a 20G, over-the-needle, intravenous catheter (Jelco) was inserted into the right dorsal pedal artery to measure invasive blood pressure and facilitate intermittent arterial blood sampling. A forced-air warming device (Bair-Hugger, 3 M) and warming blanket (Hot Dog Patient Warming System; Augustine Surgical) were used to maintain the body temperature at 36−37°C.

A multiparametric monitor (S/5 Anaesthesia Monitor; GE Healthcare) was used to obtain side-stream sampling of respiratory gases to measure end-tidal carbon dioxide partial pressure ($PE'CO_2$) and anaesthetic agent concentration. A three-lead electrocardiogram (limb leads) was used to detect cardiac electrical activity, and invasive blood pressure was monitored via a strain-gauge transducer (BD TDX, Becton Dickinson) zeroed to atmospheric pressure at the right atrial level. A thermistor probe was inserted into the oesophagus up to the level of the scapulae to monitor temperature. Anaesthetic depth was assessed based on the reactivity of the palpebral reflexes (lateral and medial) and masseter muscle tone.

LEARNING POINTS/TAKE-HOME MESSAGES

- Medetomidine may be used as an effective premedication for caesarean section (CS) in semi-feral, captive cheetah.
- Atipamezole at a dose of 0.15 mg per cub was effective in resuscitating neonates when medetomidine was used as part of a CS anaesthetic regimen, administered at 0.0375 mg/kg to the dam.
- The cardiopulmonary effects of pregnancy may be altered by anaesthetic drugs; recognition and intervention are necessary to prevent morbidity and mortality in both the dam and neonates.

Arterial blood gas analysis was performed twice, 20 minutes prior to the start of surgery (75 minutes after induction of anaesthesia) and again 35 minutes after the commencement of surgery (140 minutes after induction). Samples were drawn anaerobically into a heparinised syringe (BD A-Line; Becton Dickinson) and immediately analysed on a bench-top analyser (RAPIDPoint 500; Siemens Healthineers) using the alpha-stat method (Table 1). The first blood gas analysis indicated moderate respiratory acidosis with a widened partial pressure of

arterial carbon dioxide to end-tidal carbon dioxide tension (P[a-E']CO_2) gradient (normal in dogs: 2−4 mm Hg[15]). Intermittent positive pressure ventilation was instituted (FiO_2 1.0, peak inspiratory pressure 14 cmH_2O, respiratory rate 14 breaths/min, positive end expiratory pressure [PEEP] 4 cmH_2O). The respiratory rate was further adjusted during the course of the anaesthesia as required in order to maintain the PE'CO_2 between 35 and 45 mmHg. An expiratory tidal volume of 410 ml was achieved with these settings; this value was obtained together with a pressure–volume loop via a pitot tube (D-Lite Spirometry Sensor; GE Healthcare). The second blood gas analysis indicated a resolution of the respiratory acidosis and a normal P(a-E')CO_2 gradient.

TABLE 1. Arterial blood gas variables, ventilation characteristics and physiological variables for a cheetah anaesthetised for caesarean section

Time of analysis		**20 Minutes before commencing surgery**	**35 Minutes after commencing surgery**
Parameter	Unit	Value	Value
pH		7.094	7.236
$PaCO_2$	mm Hg	81.3	48.3
PaO_2	mm Hg	147.2	199.3
HCO_3^- (actual)	mmol/L	24.3	20.0
Base excess (ECF)	mmol/L	−5.4	−7.5
SaO_2*	%	97.9%	99.2%
PaO_2/FiO_2		196	199
PE'CO_2	mm Hg	64	43
P(a-E')CO_2 gradient	mm Hg	17.3	5.3
Na^+	mmol/L	156.5	152.4
K^+	mmol/L	3.45	3.92
Ca^{++}	mmol/L	1.38	1.32
Cl^-	mmol/L	120	118
Anion Gap	mmol/L	15.6	18.3
Lactate	mmol/L	0.36	0.69
FiO_2		0.75	1.0
Body temperature	°C	36.7	35.2
Heart rate	beats/min	95	55
Blood pressure†	mm Hg	100/68 (79)	90/40 (57)
Respiratory rate	breaths/min	22‡	10§

*Saturation of haemoglobin with oxygen.
†Blood pressure is expressed as systolic/diastolic (mean).
‡Spontaneous ventilation.
§Intermittent positive pressure ventilation (IPPV).

Surgery

A midline celiotomy was performed, with skin incision from approximately 4 cm cranial to 10 cm caudal to the umbilicus. Haemostasis was achieved by electrocautery (ValleyLab Force 2; Covidien). After incision of the linea alba, the gravid uterus was exteriorised. An incision was made at the base of each uterine horn, through which three cubs were delivered (approximately 10 minutes after the commencement of surgery). The uterus was closed with a size 2/0 polydiaxanone suture (MonoPlus; BBraun) in a Cushing pattern, the linea alba was closed with size 0 polydiaxanone suture (MonoPlus; BBraun) in a continuous pattern, the subcutaneous tissue was closed with size 4/0 polyglycolic acid (Viamac; Gabler Medical

Group) in a continuous pattern and the skin was closed with size 2/0 poliglecaprone 25 suture (Monosyn; BBraun) in a simple interrupted pattern.

Neonatal resuscitation

Immediately after delivery, the cubs were vigorously towel dried and administered 0.05 mg atipamezole (Antisedan; Zoetis) intramuscularly. At this point, the Apgar scores (adapted from puppy Apgar scores[16]) of all the cubs was 3 (Table 2). Oxygen was provided to the cubs via face mask at 3 L/min and warmth was provided via a forced air warmer (3 M Bair-Hugger System; 3 M US). The atipamezole dose was repeated twice in all the cubs approximately 8 minutes apart (total of 0.15 mg per cub), after which the Apgar scores of all the cubs improved to 10 approximately 25 minutes after delivery (Table 2).

TABLE 2. The puppy Apgar scoring system (adapted from Veronesi et al.[16]) as applied to the cheetah cubs at different time points after delivery

Variable	Score			Cub scores at delivery	Cub scores 25 minutes after delivery
	0	1	2		
Heart rate (beats/min)	<180	180–220	>220	1	2
Respiratory effort (breaths/min)	<6, no crying	6–15, some crying	>15, crying	0	2
Reflex irritability	Absent	Grimace	Vigorous	1	2
Motility	Absent	Some flexions	Vigorous	1	2
Mucus membrane colour	Cyanotic	Pale	Pink	0	2
Total				3	10

Scores above 7 indicate vigorous pups.

Once the cubs were delivered, the cheetah was administered 500 IU oxytocin (Fentocin; Virbac) intravenously. Analgesia was provided by administering 0.015 mg/kg buprenorphine (Temgsic; Schering Plough) intravenously and 0.3 mg/kg meloxicam (Petcam; Ascendis Animal Health) subcutaneously.

Once the skin had been sutured and cleaned, the cubs were allowed to suckle for approximately 10 minutes. Total anaesthetic time, including all preoperative clinical assessments, was 160 minutes and surgical time was 50 minutes. Ten minutes after the cessation of the inhalation anaesthesia, the cheetah was placed into a transport crate in right lateral recumbency and administered 0.19 mg/kg atipamezole intramuscularly. Ten minutes later, the swallowing reflex returned and the cheetah was extubated and the crate closed. The cheetah stood up calmly approximately 10 minutes after extubation after which the cheetah and cubs were transported back to the sanctuary.

OUTCOME AND FOLLOW-UP

The initial suckling attempts of the cubs during recovery of the cheetah were suboptimal. Colostrum was, therefore, collected from the cheetah as a precaution, should the cubs continue to suckle poorly. The colostrum was syringe fed to the cubs during transportation back to the sanctuary. Two cubs received adequate amounts of colostrum but the third failed to drink enough. After numerous failed attempts for the cheetah to accept the cubs, the decision was made to hand raise the cubs. The cubs were bottle fed with milk replacer (Babycat milk; Royal Canin) and gradually weaned over to venison (antelope meat) at 6 weeks old. All three cubs presented with diarrhoea at 7 weeks of age. The cub that initially

failed to consume sufficient colostrum was the most severely affected, presenting with vomiting and severe lethargy in addition to the diarrhoea. Clinical signs correlated with feline panleukopenia, which was confirmed using a rapid test (SNAP Parvo Test; Idexx Laboratories[17]) on the most severely affected cub only. Despite intensive treatment, the most severely affected cub succumbed to the disease, while the other two made a full recovery.

DISCUSSION

This case highlights three learning points. Firstly, despite administering medetomidine as preanaesthetic medication, three healthy cubs were delivered. Secondly, atipamezole as a medetomidine antagonist, at a dose of 0.15 mg per cub, effectively offset the sedative and cardiovascular effects of medetomidine. Finally, considerations and interventions to optimise cardiopulmonary functioning during CS in light of the physiological adaptations that occur during pregnancy.

Wild cheetahs are immobilised with sedative or anaesthetic drugs prior to any intervention to maintain safety of both personnel and the animal.[13] Immobilisation produces mental obtundation and physical restraint and in cheetahs, protocols comprise varying combinations of cyclohexylamines (ketamine or tiletamine), α_2-adrenoceptor agonists (xylazine, medetomidine or dexmedetomidine), benzodiazepines (midazolam or zolazepam) and opioids (butorphanol) prior to anaesthesia.[2, 13] In the present case, the rationale behind using medetomidine alone was to limit drug exposure to the cubs and to use drugs that are reversible, providing the best chance for successful resuscitation of the cubs. Moreover, medetomidine has been successfully used as a preanaesthetic medication during canine CS,[8] although xylazine has been associated with reduced puppy vigour and increased mortality.[9] Benzodiazepines or opioids were not included in the premedication due to their respiratory depressant effects.[9-11] Furthermore, the use of cyclohexylamines was avoided as ketamine has also been shown to be associated with reduced puppy vigour at birth and increased puppy mortality during canine CS,[9, 17] speculated to be due to profound respiratory depression in the neonate.[18, 19]

Most observed clinical effects of medetomidine, a highly selective α_2-adrenoceptor agonist, stem from its effects on the central nervous and cardiovascular systems.[20] Medetomidine exerts its sedative and anxiolytic effects by interrupting neural transmission within the forebrain, limbic system and reticular activating system.[10, 20] Furthermore, association between central α_2-adrenoceptors and opioid receptors give rise to the analgesic effects of medetomidine.[10, 20] Consequent to the sedation, anxiolysis and analgesia produced by medetomidine, it displays a drug-sparing effect on both intravenous induction and inhalation anaesthetic drugs – up to a 70% reduction in isoflurane requirement.[10, 11] The cardiovascular effects of medetomidine are biphasic. An initial hypertensive phase due to activation of peripheral extra- and postsynaptic α_2-adrenoceptors, causing vasoconstriction,[10] precedes a baroreceptor-mediated reduction in heart rate and cardiac output that follows.[11] The subsequent reduction blood pressure to presedation values[19] is due to activation of presynaptic α_2-adrenoceptors, which decreases the release of noradrenaline.[10, 11] The reduced heart rate may still persist due to a reduction in central sympathetic outflow.[11]

During pregnancy, the developing fetoplacental units increase maternal metabolic demands and oxygen consumption.[9, 12] These demands are met by an increase in maternal blood volume by relative plasma expansion, an increased cardiac output and a reduction in systemic vascular resistance to ensure adequate perfusion to the developing fetoplacental units and

mammary glands.[9, 12] Uterine blood flow is not controlled by intrinsic autoregulation; rather, it is directly proportional to maternal systemic blood pressure and myometrial vascular resistance.[9] Thus, considering the cardiovascular effects of medetomidine and the fact that it crosses the placenta,[10] it is seemingly counterintuitive to use medetomidine as part of the anaesthetic regimen for caesarean section. However, De Cramer et al.[8] investigated the use of medetomidine 0.007 mg/kg intravenously as a premedication, followed by propofol induction and sevoflurane maintenance, for planned CS in female dogs to exploit the clinical effects of medetomidine. Immediately after delivery, each puppy received 0.05 mg of atipamezole subcutaneously. The puppy survival rate was 96% at 2 hours with an average Apgar score of 9.66 when evaluated 15 minutes after delivery. The neonatal Apgar scores and survival rates and maternal survival rates obtained by De Cramer et al.[8] were better, compared to other studies evaluating these variables, irrespective of anaesthetic protocol or mode of delivery.

Atipamezole, a highly selective α_2-adrenoceptor antagonist, is routinely employed to reverse medetomidine-induced sedation.[20] The atipamezole dosing recommendation in dogs is an atipamezole to medetomidine ratio of 5:1.[21] However, the dosing recommendation in cats is 2.5:1, due to the risk of excitement at higher doses. After administration, arousal is usually apparent after 3−5 minutes in dogs and cats, with complete reversal of the sedative effects within 15 minutes.[20-22] This timeline is in agreement the study by De Cramer et al.,[8] where Apgar scores indicating vigorous neonates were obtained 15 minutes after delivery (and administration of atipamezole). In our case, however, Apgar scores of 10 were only obtained approximately 25 minutes after delivery and administration of 0.15 mg of atipamezole per cub. The dose of atipamezole administered to each cub during this case was extrapolated from the study by De Cramer et al. (0.05 mg at a time per cub); additional doses were administered until clinical effect was achieved. The higher dose of atipamezole required by the cubs in this case is likely related to the high dose of medetomidine received by the dam, 5.4 times greater than the dose received by the female dogs in the study by De Cramer et al.[8] However, the cubs only required three times greater dose of atipamezole before successful resuscitation, when compared to the dose administered to the puppies by De Cramer et al.[8] Furthermore, the longer duration to successful resuscitation of the neonates may be explained by the fact that the onset of action of atipamezole is shorter in dogs as compared to cats, especially when a lower atipamezole to medetomidine dose ratio is used.[21-23] In addition, the longer duration of isoflurane anaesthesia in the present case, contrasted to a shorter duration of sevoflurane anaesthesia by De Cramer et al.,[8] affected a greater uptake of inhalation anaesthetic drug by the cubs. Moreover, the hypercapnia in the dam together with the isoflurane resulted in a longer time to successful resuscitation. Finally, at the time of delivery, the body temperature of the cheetah was 35°C; thus, warming the cubs to physiological temperature further elongated the recovery.

Prior to initiation of ventilation, the cheetah was severely hypercapnic, with a $PaCO_2$ of 81.3 mmHg (normal in cats: 25−37 mmHg[10]). While this is likely the result of anaesthetic-mediated respiratory depression and hypoventilation, the elevated $P(a\text{-}E')CO_2$ gradient also suggested mismatching of alveolar ventilation to pulmonary perfusion (*V*/*Q*) as a contributing factor.[15] Anatomical deadspace ventilation produces a *V*/*Q* ratio of 0.8, resulting in a $P(a\text{-}E')CO_2$ gradient of 2−5 mmHg,[15] in healthy individuals. An increase in cardiac output together with a reduction in tidal volume, as occurs during pregnancy, increases the *V*/*Q* ratio and therefore a reduction in the $P(a\text{-}E')CO_2$ gradient may be observed (a negative $P(a\text{-}E')CO_2$ gradient is commonly seen in pregnant women).[15] During pregnancy, the functional residual capacity (FRC) of the lungs is reduced due to cranial displacement of the diaphragm by the expanding uterus.[10, 12] This reduction in FRC makes pregnant animals prone to atelectasis

under anaesthesia, especially when positioned in dorsal recumbency.[24] During the present case, the increased P(a-E')CO_2 gradient is suggestive of a large intrapulmonary shunt (areas of lung with $V/Q = 0$), as indicated by the PaO_2/FiO_2 ratio below 200,[25] likely secondary to atelectasis. Furthermore, the poor response of the PaO_2 to an increase in the FiO_2 (0.75–1.0) is also suggestive of a shunt. The degree of intrapulmonary shunting required to reduce the PaO_2/FiO_2 ratio is less than that required to increase the P(a-E')CO_2 gradient.[25] Thus, the application of mechanical ventilation with PEEP, which recruits and stabilises collapsed alveoli,[26] improved *V*/*Q* matching enough to normalise the P(a-E')CO_2 gradient, but not the PaO_2/FiO_2 ratio.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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