VETERINARSKI ARHIV 79 (4), 421-428, 2009

Balanced anesthesia in the Capuchin monkey (*Cebus capucinus*) - a case report

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VNUK, D., A. MUSULIN, M. KRESZINGER, M. PEĆIN, I. BATA, D. ŽUBČIĆ, N. LEMO: Balanced anesthesia in the Capuchin monkey (*Cebus capucinus*) - a case report. Vet. arhiv 79, 421-428, 2009.

ABSTRACT

A balanced anesthetic technique was achieved in a monkey undergoing surgery for tibial osteosynthesis. The patient was hostile so a combination of ketamine, diazepam and atropine was administered prior to anesthesia to immobilize it. Propofol was administered for anesthetic induction. Fentanyl citrate was administered as an intravenous bolus and maintained as a continuous rate infusion. An endotracheal cuffed tube was placed. A mixture of oxygen and isoflurane was administered through a non-rebreathing system. Spontaneous breathing ceased after pancuronium bromide administration and manual ventilation with a balloon was started. Surgery lasted 90 minutes. Spontaneous breathing started 10 minutes after skin closure, and the patient was extubated 10 minutes later, when swallowing was observed. Butorphanol tartrate was given by an intramuscular route at 4-hour intervals during the first twelve hours after the surgery. A fentanyl transdermal patch was administered on the medial thigh at the end of the surgery.

Key words: anesthesia, capuchin monkey, fentanyl

Introduction

When anesthetizing primates, the greatest challenge is to restrain the patients during the induction because of their agility, strength and defensive nature. Different drugs and combinations for immobilizing and anesthetizing primates are recommended. The use of dissociatives for restraint, as preanesthetics and as anesthetics has revolutionized the handling of primates. Inhalation anesthesia produces surgical anesthesia and prevents

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ISSN 0372-5480
Printed in Croatia

involuntary movements observed when administering ketamine alone (SCHUMACHER, 1998).

The purpose of this case is to describe a new method of balanced anesthesia in a Capuchin monkey and the cardiopulmonary effects of this anesthesia and to test analgesia with a transdermal fentanyl patch.

Materials and methods

A seven year old female monkey (capuchin) from the zoo, weighing 2.2 kg was presented with a history of right hind-limb lameness lasting for 2 days. The monkey had been bitten by another monkey. The first obvious signs were hemorrhage in the right stifle area and lameness. The zoo veterinarian examined the monkey by palpation and found crepitation and abnormal movement in the stifle joint. The monkey was referred to the surgery clinic. On admission, the monkey had a rectal temperature of 38.9 ^{O}C, pulse was 140 beats per minute and respiratory rate was 25 breaths per minute. On lateral and anterio-posterior radiographs of the right hind limb, a proximal epiphyseal fracture of the tibia was observed. It was decided that osteosynthesis would be performed.

Food was withheld for 18 hours and water for 6 hours before anesthesia. For premedication, a combination of ketamine hydrochlorid 15 mg/kg i.m. (Narketan®, Vetoquinol, Switzerland), diazepam 1 mg/kg i.m. (Apaurin®, Krka, Slovenia) and atropin 0,04 mg/kg i.m. (Atropin®, Belupo, Croatia) were administered. After 10 minutes, an intravenous canula was placed in the antebrachial vein. Blood samples were taken for hemogram, coagulation and biochemical profile. Creatinine was 57 µmol/L (reference range 70,7-205), alkaline phosphatase 55 IU/L (reference range 43-120), AST 72 IU/L (reference range 13-37) and ALT 23 IU/L (reference range 0-82), GGT 52 IU/L, glucose 11.3 mmol/L (reference range 4.72-7.27), creatine kinase 3503 IU/L, LDH 988 IU/L (reference range 173-275), amylase 191 IU/L, total bilirubin 1.8 µmol/L (reference range 1.71-8.55), cholesterol 5.65 mmol/L, HDL cholesterol 2.34 mmol/L, albumin 29 g/L (reference range 31.3-53), calcium 2,00 mmol/L (reference range 2.28-2.95), phosphorus 1.63 mmol/L (reference range 1.42-1.78), sodium 142 mmol/L (reference range 142-160), potassium 5.1 mmol/L (reference range 3.5-6.5), chloride 113 mmol/L (reference range 97.5-113.5), triglycerides 0.65mmol/L (reference range 0.75±0.58), urea 5.0 mmol/L, uric acid 122 µmol/L, magnesium 1.08 mmol/L (reference range 0.68±0.13), iron 6.3 mmol/L (reference range 12.5-25). Reference ranges for primates were taken from KANEKO et al. (1997). Also an HIV test was performed and the result was negative. Prothrombin time was 0.64 INR, prothrombin time >147%, APTT 46 seconds, thrombin time 24 seconds, D-dimers 1.60 µg/mL, fibrinogen 3.3 g/L, antithrombin III 78 %, and protein C 50%.

Table 1. Hemogram, blood gas analysis, pH and total protein of the capuchin recorded after premedication, after induction, 1 h after induction and after extubation.

Parameter	After premedication	After induction	1 h After induction	After extubation
Red blood cells×10^{12}/L	4.3	3.2	2.7	2.7
Hemoglobin (g/L)	97	75	63	64
Packed cell volume	31	23	20	20
MCV	72	72	72	72
MCH	23	23	23	23
MCHC	313	325	318	327
White blood cells×10^{9}/L	21	21.4	17.7	15.9
Platelets×10^{12}/L	234	232	219	217
pH	7.37	7.20	7.23	7.31
pCO_2 (mm Hg)	32	52	45	36
HCO_3^- (mmol/L)	18	19	17	17
Base excess (mmol/L)	-6	-10	-10	-8
Total protein (g/L)	66	64	59	56

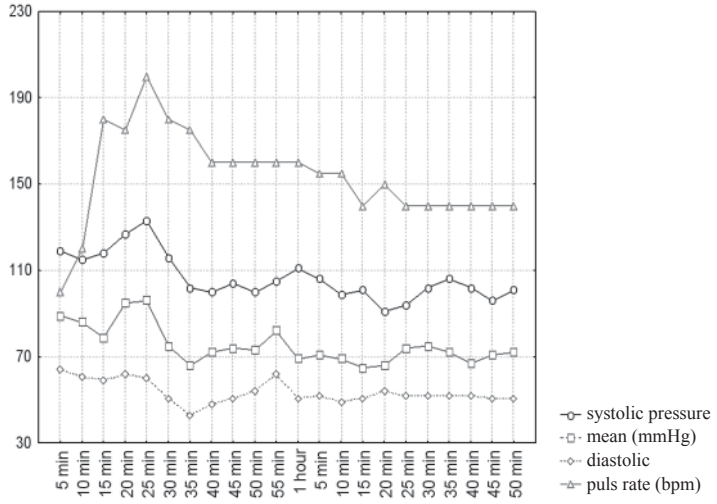

Fig. 1. Systolic, mean and diastolic blood pressure and pulse rate during surgery

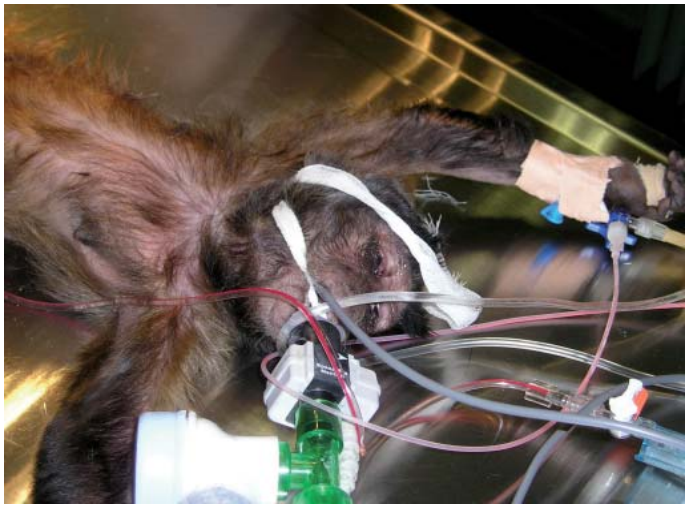

Fig. 2. Patient during anesthesia

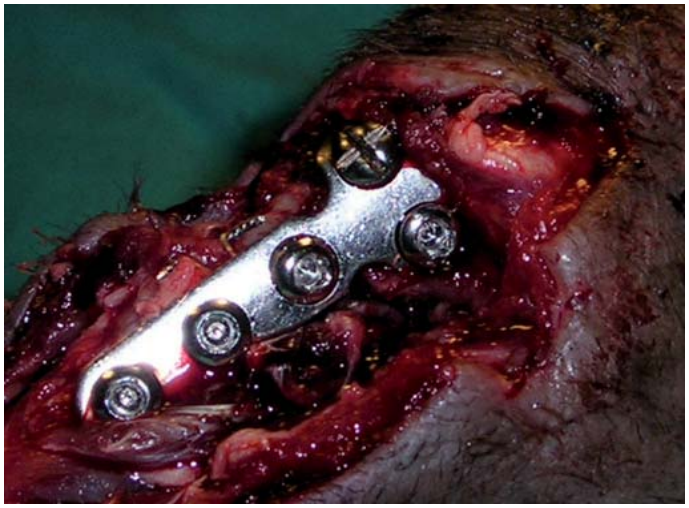

Fig. 3. Tibial osteosynthesis

Lactated Ringer solution was infused at the rate of 20 mL/kg/h for the first hour and later at the rate of 10 mL/kg/h. The rate was controlled by an infusion pump (BIOF 3000®, Biotron CO, South Korea). Cefuroxim 22 mg/kg IV (Ketocef®, Pliva, Croatia) was administered before and immediately after the surgery. An intraarterial canula was inserted in the left femoral artery. Blood samples were taken from the canula for pH and blood gas analysis. The intraarterial canula served for blood sampling and continuous invasive blood pressure measurement (Ultraview® 1050, anesthesia monitor, Spacelabs Medical Inc, USA). During the anesthesia, the ECG, pulse oxymetry and capnography (mainstream system) were performed. For induction, propofol 4 mg/kg i.v. (Propofol Abbott®, Abbott Laboratories, Spain) was administered. Blood samples were taken from the intraarterial canula for pH and blood gas analysis and from the intravenous canula for hemogram. Fentanyl citrate (Fentanyl-Jannsen®, Jannsen Pharmaceutica, Belgium) was administered as a bolus of 10 μg/kg i.v. and maintained at 0.2 μg/kg/min i.v. continuous rate infusion by syringe pump (Single syringe pump SEP 11S®, Ascor, Poland). Endotracheal cuffed tube (i.d. 3 mm) was placed. The mixture of oxygen (6 l/min) and isoflurane (first five minutes 2.5%, later 1%) was administered using the non-rebreathing Mapleson F pediatric system. Spontaneous breathing ceased after the administration of pancuronium bromide 0.02 mg/kg i.v. (Pavulon®, Hoechst, Germany) and manual ventilation with a balloon was started. One hour after the induction of anesthesia and immediately after extubation, blood samples were taken from the intraarterial canula for pH and blood gas analysis and from the intravenous canula for hemogram. A blood sample was taken for coagulation after extubation.

Surgery lasted 90 minutes. A T-plate was applied to the proximal tibia. Spontaneous breathing started 10 minutes after skin closure, and the patient was extubated 10 minutes later, when swallowing was observed.

Butorphanol tartrate (Torbugesic®, Fort Dodge, USA) was given at the dose of 0.35 mg/kg by intramuscular route at 4-hour intervals during the first twelve hours after the surgery. Fentanyl transdermal patch (Durogesic™® 25 μg/h, Jannsen Pharmaceutica, Beerse, Belgium) was administered on the medial thigh at the end of the surgery. Hyperventilation, vocalization, restlessness and decreased appetite were not noticed postoperatively.

Discussion

Less co-operative monkeys may need sedation by intramuscular injection before an attempt is made to induce anesthesia. The use of projectile syringes is not recommended because monkeys are adept at dodging or deflecting the projectile with their hands. Intravenous injections are rarely possible because of the defensive nature of these animals. Ketamine is the agent of choice in non-human primates. Exceptions are squirrel

monkeys and marmosets, where Saffan is the drug of choice (HALL et al., 2001b). VIE et al. (1998) used combination of medetomidine and ketamine in Wild red howler monkeys (*Alouatta seniculus*). Medetomidine (150 μg/kg) associated with ketamine (4 mg/kg) gave the best results. The injection rapidly resulted in complete immobilization with good to excellent myorelaxation and provided considerably shortened immobilization duration. The induction stage was quiet, with the absence of both corneal and pedal withdrawal reflexes. Rectal temperature and respiratory and heart rates decreased during anesthesia, whereas relative oxyhemoglobin saturation increased. One death occurred during anesthesia. One abortion and one death also occurred the day following anesthesia but were more probably a result of capture stress. Atipamezole given i.m. at a dose of five times the medetomidine dose led rapidly to standing recovery. Spontaneous recovery occurred in 17 animals before the atipamezole injection. Total recovery time was shorter in young animals.

KARESH et al. (1999) used 8 free-ranging black spider monkeys (*Ateles paniscus chamek*) for immobilization with Telazol® (tiletamine/zolazepam) for the purpose of radio-collaring. The authors were satisfied with results of immobilization.

In our case, because of the hostility of the patient, a combination of ketamine hydrochloride and diazepam administered by intramuscular injection was used for immobilization. After immobilization, intraarterial and intravenous canulas were placed without any resistance from the patient.

In the literature, we could not find any description of a balanced anesthesia technique used for non-human primates. FOWLER et al. (2001) used tiletamine/zolazepam and glycopirolate for premedication, propofol for induction and isoflurane and propofol for maintenance of anesthesia during MRI scanning in Rhesus macaques. It was a non-painful procedure and the authors did not use any opioid analgetic like fentanyl. In our case, the combination of a hypnotic drug (propofol and later isoflurane), an analgetic drug (fentanyl- bolus + constant rate infusion), a neuromuscular blocking agent (pancuronium) and an anticholinergic drug (atropine) was used. HALL et al. (2001b) and SCHUMACHER (1998) did not describe propofol for induction of anesthesia of non-human primates. In our case, propofol 4 mg/kg was administered by intravenous injection for induction of anesthesia. The dose was titrated to effect (the possibility of gentle intubation).

Fentanyl is a synthetic narcotic agonist, 100 to 150 times more potent than morphine (PADDLEFORD, 1999). In veterinary practice, fentanyl was initially used as a part of the neuroleptanalgetic mixture (droperidol + fentanyl). The use of this mixture is described in various works covering a variety of primates, from squirrel monkeys to a gorilla. The combination may be given intramuscularly or orally (MARSBOOM et al., 1963).

Fentanyl is now popular in balanced anesthesia techniques and for postoperative analgesia in intensive care. A recent development has been the availability of cutaneous

patches for the continuous, controlled, transdermal administration of fentanyl (HALL et al., 2001a).

In the case of primates, balanced anesthesia with fentanyl and postoperative analgesia with fentanyl transdermal patch have not yet been described in the available literature. In our case, fentanyl was used as an analgetic drug during anesthesia. We could not find the exact dose of fentanyl for a balanced anesthetic technique, so we used the canine dose (10 μg/kg bolus i.v., later a continuous rate infusion 0.2 μg/kg/min i.v.). Fentanyl did not change blood pressure, but it slowed the pulse rate. Occasional bradycardia was treated by administration of anticholinergics. In the first minutes after the administration of anticholinergics, tachycardia was noticed.

Morphine, meperidine, butorphanol, buprenorphine and aspirin were described in various works for postoperative analgesia in non-human primates (SCHUMACHER, 1998). In our case, butorphanol was used within the first twelve hours after surgery. After that time intramuscular administration of butorphanol was not possible because of the monkey's hostility. Fentanyl transdermal patch is a "fortunate" solution for postoperative analgesia of aggressive monkeys since it makes the intramuscular administration of opioids every 4 to 6 hours unnecessary. The problem with a fentanyl patch is that the patient can take it off. In our case, the patch was protected within a fiberglass bandage. The therapeutic plasma level of fentanyl is presumed to be reached 12 to 24 hours after fentanyl patch application (LAMONT, 2002). Hyperventilation, vocalization, restlessness and decreased appetite were not noticed after surgery, suggesting sufficient analgesia.

We can conclude that the balanced anesthetic technique can be used in capuchin monkeys. The use of propofol and fentanyl in the balanced anesthetic technique, and also transdermal fentanyl patch for postoperative analgesia, had not yet been described in the case of monkeys. Our case suggests that the balanced anesthetic techniques can be used in monkeys, with the specific difference only in immobilization before the induction of anesthesia, necessary because of the hostility of these animals. If protected with bandage, a transdermal patch can be used in monkeys, preventing the animal from taking the patch off. This type of balanced anesthesia caused minimal cardiopulmonary effects and therefore, we can conclude that it is an acceptable model of monkey anesthesia.

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Received: 31 March 2008
Accepted: 4 June 2009

VNUK, D., M. KRESZINGER, M. PEĆIN, A. MUSULIN, I. BATA, D. ŽUBČIĆ, N. LEMO: Balansirana anestezija u majmuna kapucina (*Cebus capucinus*) - prikaz slučaja. Vet. arhiv 79, 421-428, 2009.

SAŽETAK

Balansirana anestezija učinjena je u majmuna podvrgnutoga osteosintezi tibije. Zbog agresivnosti pacijent je prvo bio sediran kombinacijom ketamina, diazepama i atropina. Za indukciju anestezije primijenjen je propofol, a fentanil je primijenjen za analgeziju. Zatim je životinja intubirana, a anestezija je održavana smjesom izoflurana u kisiku. Spontano disanje prekinuto je primjenom pankuronija te je započeta ventilacija balonom. Operacija je trajala 90 minuta. Spontano disanje započelo je 10 minuta nakon završetka šivanja kože, a pacijent je ekstubiran 10 minuta nakon što je započeo gutati. Poslije operacije za analgeziju je dan butorfanol primijenjen intramuskularno svakih 4 sata prvih 12 sati nakon operacije. Fentanilski flaster postavljen je s medijalne strane bedra na kraju operacije.

Ključne riječi: anestezija, majmun, kapucin, fentanil