Balanced anesthesia and ventilation strategies for an alpaca *(Lama pacos)* with an increased anesthetic-risk

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Summary

We report the use of a balanced anesthetic technique in a three-year-old, female Huacaya alpaca with an increased anesthetic risk that underwent an extensive dental surgery. Anesthesia was provided with an infusion of midazolam, fentanyl, S-ketamine and low concentrations of isoflurane in oxygen. The mandibular alveolar nerve was desensitized with a lidocaine-bupivacaine combination. The alpaca showed signs of hypoxemia fifteen minutes after anesthesia induction and arterial blood gases confirmed severe venous admixture. Application of positive end expiratory pressure (PEEP) of 6–9 cm H_2O improved the arterial oxygenation. Other cardiopulmonary variables remained within the normal range. At the end of surgery, sarmazenil was administered to antagonize the effects of midazolam and emergence from anesthesia was smooth and uneventful. Flunixine meglumine and a transdermal delivery system for fentanyl were administered for post-operative analgesia. This method of balanced anesthesia allowed for an adequate anesthetic plane and a safe recovery, however, special ventilation strategies (PEEP) had to be applied.

Keywords: South American camelids, Alpaca, anesthetic risk, positive end expiratory pressure (PEEP) ventilation

Ausgewogene Anästhesie und Ventilationsstrategien bei einem Alpaka *(Lama pacos)* mit erhöhtem Anästhesierisiko

Zusammenfassung

Dieser Fallbericht beschreibt die Technik der ausgewogenen Anästhesie bei einem 3 Jahre alten weiblichen Huacaya Alpaka mit erhöhtem Anästhesierisiko. Das Alpaka wurde wegen eines Zahnwurzelabszesses operiert. Die Anästhesie wurde mittels einer Infusion von Midazolam, Fentanyl, S-Ketamin und einer Inhalationsnarkose mit einer niedrigen Isofluran-Konzentration durchgeführt. Der Nervus alveolaris mandibularis wurde mit einem Lidocaïn-Bupivacaïn-Gemisch anästhesiert. Das Alpaka zeigte eine Hypoxämie 15 Minuten nach Anästhesiebeginn. Die arteriellen Blutgaswerte bestätigten eine ernsthafte venöse Vermischung. Die Anwendung eines positiven endexspiratorischen Druckes (PEEP) von 6–9 cm H_2O verbesserte die arterielle Oxygenierung des Tieres. Andere kardiopulmonäre Variablen blieben während der Operation in der Norm. Am Ende des chirurgischen Eingriffes wurde Sarmazenil verabreicht, vor allem um den Midazolameffekt zu antagonisieren. Die Aufwachphase erfolgte sanft und komplikationslos. Flunixin meglumine und ein transdermaler Fentanylpatch wurden zur postoperativen Schmerzbekämpfung eingesetzt. Diese Methode der ausgewogenen Anästhesie erlaubte eine sichere Narkose mit sanfter Aufwachphase, wobei eine spezielle Ventilationsstrategie (PEEP) angewendet werden musste.

Schlüsselwörter: Neuweltkameliden, Alpaka, Anästhesierisiko, positiver endexspiratorischer Ventilationsdruck (PEEP)

Introduction

The anesthetic procedures of patients with an increased anesthetic risk must be tailored to their individual circumstances and careful consideration should be given to the choice of drugs. Balanced or multimodal anesthesia aims to improve the anesthetic technique by combining specific drugs with additive or synergistic effects and with different modes of action or administered via different routes (Bettschart-Wolfensberger and Larenza, 2007). Short-acting, non-cumulative injectable agents are usually associated with low concentrations of inhaled agents, allowing for the reduction of their individual doses, thereby reducing the incidence and severity of adverse effects. Balanced anesthetic techniques might be especially preferred for moderate to high anesthetic risk patients. Compared with other domesticated species, few reports exist about the effects of anesthetic agents in compromised South American camelids. We report a case of an alpaca *(Lama pacos)* anaesthetized with a midazolam, fentanyl and S-ketamine combination supplemental to isoflurane in O_2, which underwent an extensive dental surgery. To our knowledge, there are no reports regarding the administration of this drug combination in South American camelids.

History

A three-year-old, 43 kg, female Huacaya alpaca, with a two-month-old cria and a recent history of weight loss, was scheduled for surgical removal of the fourth premolar of the right mandible, which had a root abscess and osteomyelitis. Apart from the facial swelling, preanesthetic physical examination showed moderate emaciation. Blood results revealed a low-degree anemia (hemoglobin concentration: 6.8 mmol/L; normal ranges: 6.9–9.2 mmol/L) (Hengrave Burri et al., 2005). Based on the hematological and clinical examination findings the patient was classified as *"ASA III"* which according to the American Society of Anesthesiologists' rank of health status indicates a moderate anesthetic risk (*ASA I* = low anesthetic risk; *ASA V* = high anesthetic risk) (Keats, 1978).

Anesthesia

Food was withheld for 12 hours and one hour before anesthesia ceftiofur (1 mg/kg BW; Excenel 1g®, Pharmacia & Upjohn-Pfizer, Zürich) was administered subcutaneously. The left jugular vein was catheterised with a 16-gauge catheter and midazolam (0.4 mg/kg BW; Dormicum®, Roche-Pharma, Reinach) was administered intravenously for sedation. Anesthesia was induced with a combination of intravenous fentanyl (0.002 mg/kg BW; Fentanyl-Janssen®, Janssen-Cilag, Baar) and S-ketamine (3 mg/kg BW; Ketanest S®, Parke-Davis/Goedecke, Berlin). Within

one minute after induction a cuffed 9.5-mm inner-diameter tube was placed into the trachea and connected to the anesthesia machine via a circle breathing system. The animal was placed in left lateral recumbency and allowed to breathe spontaneously. Physiologic saline solution was infused (10 ml/kg BW/hour). Anaesthesia was maintained with intravenous midazolam (0.4 mg/kg BW/hour), fentanyl (0.011 mg/kg BW/hour) and S-ketamine (2.1 mg/kg BW/hour) and low end-tidal concentrations of isoflurane (range: 0.6-0.8 %, IsoFlo®, Abbott, Bern) in O_2 (1 to 2 L/min). The mandibular alveolar nerve of the diseased side was desensitized with lidocaine (15 mg; Xylesin 2%®, Amino, Neuenhof) and bupivacaine (11.25 mg; Bucain 0.75%®; Curasan Pharma, Klinostheim).

Anesthetic depth was evaluated by assessing eye positioning, reflexes and the occurrence of swallowing and regurgitation. A lead II electrocardiogram, heart rate (HR), pulsoximetry and hemoglobin O_2 saturation (SpO_2), esophageal temperature (T), respiratory rate (Rf), inspired O_2 concentrations ($FI'O_2$), capnogram and end-tidal carbon dioxide partial pressure ($PE'CO_2$), tidal volume (V_T), peak inspiratory (PIP) and positive end-expiratory pressures (PEEP) and continuous spirometry curves were monitored (S/5™ Compact Anesthesia Monitor® and D-lite flow sensor®, Datex-Ohmeda, Helsinki). An 18-gauge catheter was placed percutaneously in the left femoral artery for direct arterial blood pressure measurement using a calibrated pressure transducer (Angiokard®, Medizintechnik GmbH & Co.KG, Friedeburg) placed at the sternum level and for arterial blood gases analysis (Table 1; pH/Blutgas-System® series 840-Ciba, Corning Diagnostic, Dietikon). The alveolar to arterial oxygen partial pressure difference ($P(A–a)O_2$) was calculated as follows:

$P(A–a)O_2 = [FiO_2 (Pb–PH_2O)–1.2 (PaCO_2)]–PaO_2$

where Pb is the barometric pressure in mm Hg and PH_2O is the partial pressure of water in mm Hg at 37°C.

Surgery consisted in lateral mandible osteotomy with removal of the diseased tooth and the alveolar plate. Fifteen minutes after anaesthesia induction, the HR decreased from 85 to 50 beats/min and SpO_2 decreased from 94 to 88%. Arterial blood gas analysis showed a decreased PaO_2 and an increased $P(A–a)O_2$ (Tab. 1). Heart rate restored to base line values after intravenous glycopyrrolate (0.007 mg/kg BW; Rubinol®, AHP, Zug) administration. Intermittent positive pressure ventilation (IPPV) with a volume-controlled pressure-limited ventilator (Roche 3100 electronic respirator®, Carba, Bern) was initiated by setting the Rf at 18 breath/min and the minute volume at 8 L/min. Additional changes of the ventilator settings were made according to the spirometry pressure-volume curves and are summarized in Table 1. Thirty minutes after, the analysis of arterial blood gases showed no evident improvement of the oxygenation parameters. Both, V_T and PIP were subsequently increased and PEEP (6–9 cm H_2O) was started. Further arterial blood gas analysis at 90 and 120 minutes after anesthesia induction revealed an improvement of the oxygenation parameters (Tab. 1).

Table 1: Changes of respiratory parameters over time in relation to the ventilation mode in one alpaca anaesthetized with a constant rate infusion of midazolam, fentanyl and S-ketamine supplemental to isoflurane.

Time (min)	Ventilation mode	TV (mL)	Rf (breaths/min)	$PE'CO_2$ (mm Hg)	pH (units)	$PaCO_2$ (mm Hg)	$PaCO_2$ (mm Hg)	HCO_3 (mmol/L)	BE (mmol/L)	SaO_2 (%)	$P(A–a)O_2$ (mm Hg)
						Arterial blood gases values					
15	Spontaneous	390	14	32	7.4	42.8	65.0	26.2	1.2	92.8	540.1
45	IPPV PIP: 11 cmH2O PEEP: 0 cmH2O	460	18	39	7.37	53.0	66.7	30.3	4.2	92.5	528.2
90	IPPV PIP: 20 cmH2O PEEP: 6 cmH2O	540	20	41	7.34	53.5	236.8	28.2	1.7	99.5	343.9
120	IPPV PIP: 22 cmH2O PEEP: 9cmH2O	600	18	36	7.37	47.2	208.6	27.1	1.5	99.4	372.6

Time: minutes (min) after induction; IPPV: intermittent positive pressure ventilation; PIP: peak inspiratory pressure; PEEP: positive end-expiratory pressure; TV: tidal volume; Rf: respiratory rate; $PE'CO_2$: end-tidal carbon dioxide partial pressure; $PaCO_2$: arterial partial pressure of carbon dioxide, PaO_2: arterial partial pressure of oxygen, BE: base excess, SaO$_2$: arterial hemoglobin oxygen saturation, $P(A–a)O_2$: alveolar to arterial partial pressure of oxygen difference.

During surgery, T decreased slightly from an initial value of 38.2 to 37.5° C and mean arterial pressure (MAP) remained between 85 - 125 mm Hg during the whole procedure.

At the end of surgery the animal was weaned from the ventilator and anesthetic delivery was discontinued. General anesthesia lasted for 140 min. The alpaca was placed in sternal recumbency and O2 was insufflated through the endotracheal tube. Intranasal phenylephrine (5 mL, Phenylephrium 2%®, G. Streuli & Co, Uznach) and intravenous sarmazenil (0.025 mg/kg BW; Sarmasol®, Dr. E. Graeub, Bern), a benzodiazepine antagonist, were administered. Emergence from anaesthesia was calm and uneventful. One hour after the end of the surgery, O₂ delivery was discontinued and as values for SpO_2 remained above 97%, the endotracheal tube was removed. Postoperative analgesia was provided with intravenous flunixin meglumine (2.2 mg/kg BW; Fluniximin®, Berna Veterinaerprodukte, Bern) and fentanyl administered transdermally (Duragesic® 100 µg/hour system, Janssen-Cilag, Baar).

Discussion

Balanced anesthetic techniques are based on the concept that administration of a mixture of small amounts of several neuronal depressants would summate the advantages but not the disadvantages of the individual components of the mixture. In this alpaca, a balanced anesthetic technique combining regional, intravenous and inhaled anesthetics associated with mechanical ventilation applying PEEP permitted for a safe perioperative management.

To ensure adequate pulmonary gas exchange a secure patent airway is essential in compromised patients undergoing prolonged general anesthesia. Because the anatomy of South American camelids makes orotracheal intubation difficult, fast acting anesthetic agents are often required in order to minimize the risk of regurgitation and subsequent aspiration pneumonia. Doses of 4 to 8 mg/kg of racemic ketamine in combination with sedatives are usually necessary to accomplish a safe endotracheal intubation in such species (Neiger-Aeschbacher, 1999). The stereoisomer S-ketamine has been reported to produce an identical depth of anesthesia with only 50% of the necessary racemic dose (Kohrs and Durieux, 1998). In this case, only 3 mg/kg BW of S-ketamine in combination with fentanyl and midazolam provided excellent conditions for orotracheal tube placement.

Isoflurane has very poor analgesic properties and when is used as a sole agent high concentrations need to be provided before surgery can be tolerated. Unfortunately, high isoflurane concentratios can precipitate severe cardiorespiratory depression increasing the risk for perioperative mortality (Bettschart-Wolfensberger and Larenza, 2007). For this reason, isoflurane is generally not suitable as monoanesthetic without an analgesic supplement. In this alpaca, the mandibular nerve block added to the intravenous drug combination reduced the necessity of isoflurane administration to concentrations 20 to 40%

lower than those reported in previous studies (Mama et al., 1999) as the minimal alveolar concentration (MAC) for llamas ($FE'ISO = 1.05 +/- 0.17$ %). These low concentrations of isoflurane might have contributed to maintain MAP values above 85 mm Hg during anesthesia. In addition, an improvement in MAP has been observed when ketamine infusions are used compared with inhaled anaesthetics in goats (Larenza et al., 2005). In this alpaca S-ketamine was chosen instead of racemic ketamine because its stronger analgesic effects, better myocardial stability, and faster elimination time (Kohrs and Durieux, 1998). The intravenous agents doses were derived from studies performed in llamas and goats (Neiger-Aeschbacher, 1999; Larenza et al., 2005).

Although intrapulmonary venous admixture is often observed in recumbent anaesthetized adult llamas (Neiger-Aeschbacher, 1999), in this alpaca the values for $P(A-a)O_2$ obtained at the beginning of anesthesia (Tab. 1; normal $P(A-a)O_2$ with a $FI'O_2 = 1 \leq 100$ mmHg) indicated a severe impairment of pulmonary O2 uptake, probably because of lung atelectasis (Wettstein et al., 2006). Compression and absorption are the two mechanisms most implicated in perioperative pulmonary atelectasis formation (Magnusson and Spahn, 2003). Compression atelectasis occurs normally in anesthetized large animals placed on dorsal recumbency as a result of increased abdominal pressure which is transmitted into the thoracic cavity and cannot be counterbalanced because the respiratory muscles have a reduced tone (Wettstein et al., 2006). Usually, this phenomenon can be minimized by fasting the patients before anesthesia. However, it might be possible that 12 hours of starvation were not enough despite of the alpaca›s recent history of low food intake. Absorption atelectasis occurs in some species when high $FI'O_2$ are given (Marntell et al., 2005). Oxygen is highly soluble in plasma and is removed from the alveoli along a concentration gradient by pulmonary capillaries in a faster way than it enters, leading to alveoli collapse. As nitrogen is absorbed in a slower fashion, addition of air to the inspiratory gases reduces absorption atelectasis (Marntell et al., 2005). However, it remains unclear whether the high $FI'O_2$ administered to this alpaca contributed to the hypoxemic event. Although horses and human patients do benefit from addition of air to the inspiratory gas mixture (Magnusson and Spahn, 2003; Marntell et al., 2005), normal $P(A-a)O_2$ values were reported for goats receiving only O_2 for 12–24 hours (Nash et al., 1971).

Prevention and treatment of intra-anaesthetic pulmonary venous admixture comprises the administration of bronchodilators and/or oxygen/air mixtures and/or application of special mechanical ventilation strategies, among others (Robertson and Bailey, 2002). In this case, IPPV without PEEP did not reverse the hypoxemic status of this alpaca. Instead, a slight respiratory acidosis was observed when IPPV was started. Institution of PEEP (6–9 cm H2O) partially reversed the venous admixture reflected in a decrease of $P(A-a)O_2$ and in an increase of PaO_2, which in turn allowed for an optimal SaO_2 (99%). Positive end expiratory pressure improves regional gas exchange within the affected lung lobes, probably by recruiting alveoli which were previously perfused but not ventilated (Wettstein et al., 2006). As reported for other species, administration of a higher PEEP could have reversed completely the venous admixture in this alpaca, but it was discouraged due to its possible detrimental impact over hemodynamics (Wettstein et al., 2006). Nevertheless, MAP values remained within the normal range with the institution of these PEEPs, suggesting an appropriate function of the cardiovascular system. Post-operative O_2 administration and placing the animal in sternal recumbency contributed to maintain an adequate oxygenation during the recovery period. Instillation of intranasal phenylephrine (Lukasik et al., 1997) efficiently prevented nasal obstruction due to edema and congestion and no signs of respiratory distress were observed after extubation.

Antagonization of benzodiazepine effects have been recommended in horses (Bettschart-Wolfensberger and Larenza, 2007). Sarmazenil, a partial inverse benzodiazepine agonist, was used to antagonize the effects of midazolam in this alpaca, which emerged quietly from anesthesia. Provision of adequate analgesia was ensured with both, flunixin meglumine IV and transdermally delivered fentanyl. This combination was tested in horses and appeared to provide superior analgesia than the administration of flunixin meglumine alone (Thomasy et al., 2004).

In conclusion, this report outlines the need for studying and validating alternative anesthetic protocols for South American camelids with a higher anesthetic-risk. In this case, fentanyl, midazolam and S-ketamine supplemental to low concentrations of isoflurane, provided an adequate anesthetic plane for an increased anesthetic risk alpaca. Special ventilation strategies had to be applied to overcome hypoxemia.

Acknowledgements

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