Case report

Neuromuscular blockade as part of an anaesthetic protocol for cataract surgery in an alpaca

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Abstract

A six-month-old alpaca was presented to the veterinary teaching hospital of the University of Liège (Belgium) with a bilateral cataract. A decision was made to perform bilateral cataract surgery after an ocular ultrasound and electroretinogram were performed to assess the posterior segment and retinal function, respectively. As a premedication, the alpaca received xylazine, butorphanol and midazolam intramuscularly. Anaesthesia was induced subsequently with ketamine and midazolam intravenously and maintained with isoflurane on oxygen/air mixture. The alpaca was mechanically ventilated during surgery. Neuromuscular blockade was induced and maintained with cis-atracurium intravenously. The dose of cis-atracurium was permanently adapted using a peripheral nerve stimulator. This case report brings new knowledge regarding the use and dosage of cis-atracurium in alpacas.

Keywords: alpaca, cataract, cis-atracurium, phacoemulsification

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Introduction

Alpacas (*Vicugna pacos*) are domesticated camelids originating from South America. They are mainly bred for their fibre. However, recently alpacas are kept as companion animals. Cataract is the most frequent disorder of the lens in alpacas and can lead to complete blindness (Gelatt et al., 1995). In contrast to alpacas, phacoemulsification has been successfully described in other camelids (Gionfriddo and Blair, 2002; Powell et al., 2002). As in any other species, general anaesthesia and neuromuscular blockade (NMB) are highly recommended to prevent eye movement and external pressure on the eye during cataract surgery. Different anaesthetic protocols have been used for alpacas, with good results. Atracurium has been previously used in camelids other than alpacas (Gionfriddo and Blair, 2002; Powell et al., 2002). To the authors' knowledge, the use of cis-atracurium in alpacas has not been reported before.

Case

A six-month-old intact female alpaca, weighing 30 kg, was presented to the veterinary teaching hospital of the University of Liège for a white opacity in both eyes. This had been noticed three weeks before by the owner. The alpaca was bumping into objects and had difficulties to follow its mother. The animal did not receive any ocular or systemic treatment beforehand and had been well vaccinated.

On ocular examination no menace response was present on either eye. Pupillary light reflexes and dazzle responses were present bilaterally. No signs of blepharospasm were noted, however there was a mild bilateral mucous ocular discharge. A marked palpebral and bulbar conjunctival hyperaemia was present on both eyes. On slit lamp biomicroscopy a bilateral mature cataract was diagnosed. The fundus was not visible due to the maturity of the cataract.

The intraocular pressure (Tonopen, Medtronic, USA) was 11 mmHg and 13 mmHg for the right and left eye respectively. Fluorescein staining was negative on both eyes. Following ocular examination, the alpaca was sedated intramuscularly using 0.2 mg/kg xylazine (Proxylaz, Prodivet Pharmaceuticals, Belgium) and 0.15 mg/kg butorphanol (Dolorex, Intervet International B.V., Belgium)) for ocular ultrasound. Both globes were symmetric in size (anteroposterior length 24.5 mm for the left eye and 24.8 mm for the right eye). No abnormalities in the posterior eye segment were noticed on ultrasound.

An electroretinogram was performed under general anaesthesia to assess retinal function, which revealed normal functioning of both retinas. Based on the results of the ocular ultrasound and the electroretinogram, a decision was made to perform bilateral cataract surgery. The patient was fasted for twelve hours and water withheld for six hours. A preoperative clinical examination was performed and data recorded (Table 1).

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| Heart rate (beats minute ⁻¹) | 60 |
|--|----|
| Respiratory rate (breaths minute ⁻¹) | 20 |
| Temperature (°C) | 39 |
| Capillary refill time (seconds) | 1 |

Table 1. Preoperative clinical examination results.

Besides the ocular lesions, the patient clinically healthy prior was to intervention. However, no complete The alpaca received xylazine 0.3 mg/kg, butorphanol 0.2 mg/kg and midazolam 0.1 mg/kg (Dormicum, Roche, Belgium) intramuscularly. Thirty minutes after premedication, a 16 G venous catheter was introduced in the right jugular vein and anaesthesia was induced with ketamine 5 mg/kg (Ketamidor, Richter Pharma, Belgium) and midazolam 0.25 mg/kg intravenously, both mixed in the same syringe. The larynx was visualised with a long Miller blade laryngoscope and trachea was intubated with a 6.5 mm internal diameter endotracheal tube using a guide wire and the cuff was inflated. Lidocaine 10% (Linisol, B. Braun. Germany) was used to desensitize the larynx prior to intubation. The endotracheal tube was connected to a rebreathing circuit.

General anaesthesia was maintained with isoflurane on oxygen/air mixture

blood count or serum biochemistry were performed before anaesthesia.

with the patient in dorsal recumbency. Heart rate, respiratory rate, invasive blood pressure, temperature, F_E 'CO₂ and isoflurane were continuously monitored and recorded every five minutes. Hartmann's solution (Ringer Lactate Hartmann, B. Braun Vet Care, Belgium) was continuously infused during surgical procedure at a rate of 10 ml/kg/h.

Soon after intubation the volume controlled ventilation was provided at a tidal volume of 240 ml and respiratory rate of 20 breaths minute⁻¹. Ventilation was adapted during anaesthesia in order to maintain a F_E 'CO₂ close to the normal limits (35-45 mmHg).

Cardiovascular and respiratory parameters did not vary during anaesthesia (Table 2). However, heart rate was significantly higher during anaesthesia compared to the base values. Neuromuscular blockade was monitored by a peripheral nerve stimulator (TOFwatch S; Organon Ltd, Ireland) using a train of four (TOF) stimulation pattern set by default at 50mA and 200µs. Needle electrodes were placed subcutaneously over the superficial Neuromuscular blockade was induced with cis-atracurium (0.2)mg/kg) (Nimbex, GSK, Belgium) administered intravenously prior to surgery. Neuromuscular blockade was maintained with a constant rate infusion (CRI) and additional boluses of cisatracurium adapted to keep the TOF count under three. Cis-atracurium CRI lasted for 125 minutes. The total dose needed to maintain TOF count under three was 14 µg/kg/min, counting the additional boluses.

peroneal nerve of the left hind limb with a distance of 3 cm between the two electrodes. The TOF count and rate were objectively assessed with an acceleromyograph, which was attached on the dorsal face of the hoof and seconds. recorded 15 every The TOF ratio exceeded 90% 35 minutes after cis-atracurium CRI was interrupted. The patient return to spontaneous breathing by this time and general anaesthesia was interrupted. The patient was placed in sternal recumbency with the head lifted and was extubated when trachea the endotracheal tube started to produce discomfort to the patient. Recovery went uneventful and no signs of residual NMB were noticed.

| V_{T} (mL) | 244 ± 4.8 |
|--|----------------|
| f_R (breaths minute ⁻¹) | 19 ± 3.8 |
| F _E 'CO ₂ (mmHg) | 45 ± 2.9 |
| F_E 'ISO (%) | 1.6 ± 0.1 |
| HR (beats minute ⁻¹) | 110 ± 14.3 |
| MAP (mm Hg) | 84 ± 10 |
| Temperature (°C) | 37.6 ± 0.6 |

Table 2. Cardiovascular and respiratory parameters during general anaesthesia (mean±SD).

 $V_{T,}$ tidal volume; f_{R} , respiratory rate; F_{E} 'CO₂, fraction of expired CO₂; F_{E} 'ISO, fraction of expired isoflurane; HR, heart rate; MAP, mean arterial pressure.

Bilateral phacoemulsification with irrigation/aspiration of the lens was performed two-handed using а technique. А large posterior capsulorrhexis and a partial anterior performed. vitrectomy were No intraocular lens was placed.

Discussions

For more than 60 years, NMB have been used in human medicine to increase surgical comfort in cataract surgeries. Neuromuscular blockade is essential in this type of intervention by returning the eye to central position, avoiding involuntary movements of the head and the eye, abolishing corneal reflex and decreasing intraocular pressure (Dahlene and Mckinney, 1955). The first case report of the use of neuromuscular blocking agents (NMBA) in camelids was in 1992 and describes the use of atracurium to ensure immobilization of the eye for intraocular surgery in a llama (Donaldson et al., 1992). Rocuronium was used in an alpaca to produce NMB for an ophthalmic surgery (Yamaoka and Auckburally, 2015). Sub-Tenons injection of lidocaine has been described alternative to an obtain eye as immobilisation during phacoemulsification in dogs (Ahn et al., 2013). Compared to the NMB technique, Sub-Tenons injection of lidocaine has

the advantage to produce local analgesic effect. However, to the authors' knowledge this technique has not been described in camelids before.

There are possible side effects to the use of NMBA. The most frequent side effects in humans include accidental awareness during general anaesthesia (AAGA), residual NMB, seizures and anaphylactic reaction. In humans, the incidence of AAGA is reported to be very low (0.005%). However, the use of NMBA is estimated to increase the incidence of AAGA by twelve fold (Pandit et al., 2014). The "5th National Audit Project" strongly recommends the use of expiratory fraction of volatile agent monitoring along with NMB monitoring to minimise the risk of AAGA (Pandit et al., 2014). In veterinary practice it is difficult to assess the incidence of AAGA.

To the authors' knowledge, there are no reports on the minimal alveolar concentration (MAC) of isoflurane in alpacas. However, the reported MAC of sevoflurane and desflurane in llamas and alpacas (Grubb et al., 2003, 2006) and the MAC of isoflurane in llamas have been reported to be similar, even lower, compared to other species ($1.05 \pm 0.17\%$ at sea level) (Mama et al., 1999). Yet, the MAC of isoflurane may be influenced by age. Young patients have an increase of MAC of isoflurane of more than 25 % (Nickalls, 2003).We limited the risk for AAGA to a minimum by increasing the F_E 'ISO to $1.6 \pm 0.1\%$. However, a high F_E 'ISO may lead to hypotension. This might be the reason why our patient had an increased heart rate during general anaesthesia to maintain a normal arterial blood pressure.

The heart rate of the alpaca gradually increased at the beginning of anaesthesia and reached a plateau before cisatracurium was injected. By this time the F_E 'ISO reached a constant value of 1.6%. Another reason that may explain an increase in heart rate is an augmentation of the sympathetic tone due to pain or light plane of anaesthesia. However, both are unlikely. Heart rate increased and reached a constant level before surgery was started and at F_E 'ISO of 1.6% superficial anaesthesia is unlikely.

Fast administration of high doses of atracurium can produce histamine release leading to a possible life threatening situation (Scott et al., 1986). In addition, Hofmann elimination process of atracurium and cis-atracurium results in laudanosine production, a central nervous system stimulant which may induce seizures (Katz et al., 1994). In this case report, none of these side effects were observed during and after NMB. Cis-atracurium is approximately four times as potent as atracurium, so a smaller dose is needed to obtain the same NMB effect. This dose reduction leads to a risk reduction of histamine release and less production of laudanosine (Sparr et al., 2001).

Residual NMB. also known as postoperative residual curarization, is the most frequent postoperative side effect of the NMBA. It has been reported to have an incidence of up to 62% in human patients in case NMB was not objectively monitored and when NMB was not reversed at the end of the surgery (Baillard et al., 2005). Residual NMB may cause postoperative hypoxia, tracheal aspiration and skeletal muscle weakness (Murphy et al., 2008). The use of endrophonium or neostigmine in association with anticholinergic drugs, such as atropine or glycopyrrolate, to antagonise the effect of NMBA, was not an option in this case because it is proven in dogs that atropine may have a direct detrimental effect on intraocular pressure (Kovalcuka et al., 2015). However to compensate, isoflurane was ended only after the TOF ratio exceeded 90% and the patient return to a normal

spontaneous breathing. Also, the patient was closely monitored for 24 hours after surgery and no signs of muscular weakness or hypoxia were noticed. With the safety measurements that were taken, we considered that the risk of residual NMB was limited to a minimum. Double burst stimulation pattern is specifically design to detect residual NMB. The first tetanic stimulation consumes the acetylcholine from the neuromuscular synaptic cleft and exacerbates the sensibility of the second burst. A fade in the second burst is correlated to a TOF rate of less than 60% (Fuchs-Buder et al., 2009). Unfortunately, even if available, we did not use this type of stimulation pattern to detect traces of residual NMB.

To the authors' knowledge, the use of cis-atracurium in alpaca has not been reported before. Cis-atracurium dose used to induce and maintain NMB in this case was adapted from the dose for recommended dogs (Duke-Novakovski and Seymour, 2007). Cisatracurium 0.2 mg/kg was sufficient to induce a complete NMB (TOF count 0). However, the initial CRI of 5.5 µg/kg/min was insufficient to maintain a TOF count under three and supplementary cis-atracurium boluses were needed along to an increase the CRI to 11 µg/kg/min. The total dose of cis-atracurium needed to maintain the TOF below three was 14 µg/kg/min and was calculated as the sum of the additional boluses and quantity of drug used in the CRI per unit of time. This maintenance dose is almost twice as high compared to dogs and five times higher compared to the leaflet of Nimbex[®] in humans. In contrast, compared to humans and dogs, sheep are much more sensitive to vecuronium and extrapolating doses from other species may result in overdosing (Martin-Flores et al., 2012).

Many factors may influence the potency of a NMBA. Volatile anaesthetic agents, ketamine and in particular, antibiotics (aminoglycosides and polymyxin) may potentiate the effect of NMBA (Silverman and Mirakhur, 1994; Sokoll and Gergis, 1981). Other factors that may enhance the effect of NMBA are respiratory acidosis (Crul-Sluijter and Crul, 1974), electrolyte disturbances (Waud and Waud. 1980) and hypothermia. Neither hypercapnia, nor electrolyte disturbances were recorded or suspected during NMB. However, the use of ketamine and isoflurane to induce and maintain anaesthesia respectively might have potentiated the effect of cisatracurium.

Weaning in alpacas occurs around the age of 4 to 7 months and a female alpaca is considered to reach puberty when she passes 50% of the adult body weight, which is around 48-84 kg (Sumar, 1999). In our case, the six-month-old female alpaca was already weaned and was considered to be a young adult. Hypoglycaemia is a risk in paediatric patients if fasted, however blood glucose was not measured perioperatively in this case.

The drugs and doses used to premedicate and induce anaesthesia in this alpaca have been reported before for alpacas (Abrahamsen, 2009). The patient lost standing position thirty minutes after intramuscular injection of premedication. This was expected since the mixture of butorphanol and benzodiazepines already proved to produce such effect for short period of time in camelids (Abrahamsen, 2009). Also xylazine alone may produce recumbency but at higher doses than those used in this case (Abrahamsen, 2009). Jugular vein cannulation in camelids is not as easy as in other ruminants. The skin of the South American camelids is thicker and a cannula can be accidentally placed into the carotid artery (Amsel et al., 1987). However, the strong sedation facilitated

a fast and accessible cannulation of the vein. Ketamine/midazolam jugular produced an uneventful deep anaesthetic induction that allowed a good relaxation the larynx and easy tracheal of intubation. Deep anaesthetic induction prevented active regurgitation also during intubation. With the head extended to almost 180° and with the help of a Miller blade laryngoscope the larynx was visualised and the trachea was intubated with a 6.5 mm internal diameter endotracheal tube. Other straight blade laryngoscopes that can be used for this purpose include: Cranwall, Jackson, Janeway, Magill, Phillips, Robertshaw, Seward, Soper, Wis-Hipple and Wisconsin.

In conclusion, this case report brings new knowledge regarding the use of NMB in alpacas. To the authors' knowledge, the use of cis-atracurium in alpacas has not been reported before. Adapting the doses of cis-atracurium reported for dogs, combined with NMB monitoring proved feasible in this case. However, this was not without risk since some ruminants proved to be more sensible to NMBA compared to other (Martin-Flores species et al., 2012). Therefore, close monitoring is essential in alpacas which receive NMBA as part of a balanced anaesthetic protocol.

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