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TITLE OF CASE ***Do not include "a case report"***

Pain management of a mandibular fracture in an alpaca (Vicygna pacos) via epidural catheter placement in the mandibular foramen.

SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

A 9-year-old, female alpaca, with a history of a recurrent tooth root abscess presented for further investigation of a swelling of the left mandible and possible tooth extraction. During the manipulation of the mandible in surgery, the mandibular body fractured and, due to active infection, it was left to heal by secondary intention. After surgery, the alpaca became dull and inappetent. Analgesic drugs included buprenorphine and meloxicam, which were ineffective according to the alpaca's clinical appearance. An inferior alveolar nerve block was achieved by repeated administration of local anaesthetic (ropivacaine 0.75%) every 6 h via an epidural catheter placed in the mandibular foramen under CT guidance.

Despite the adequate level of comfort achieved, discharge from surgical site resumed and

owner elected euthanasia.

In conclusion, the placement of an epidural catheter in the mandibular canal, under CT guidance, was proven to successfully provide analgesia to an alpaca suffering from mandibular fractures.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Alpacas are one of the camelid species originating from South America. Camelids are not ruminants; however, they do share, some common characteristics regarding their behavioural response to pain with ruminants(1). In general, outward signs of pain in ruminants are subtle and experience in interpreting their responses to pain is essential. As herd animals, the relative lack of pain behaviour can be regarded as 'a survival strategy' against potential predators(2). In addition, ruminants and camelids as food-producing animals face several restrictions regarding analgesic agents that can be used (3). Although alpacas are often considered fibre animals and can also be classified as pets, they need to be signed off the food chain before administering any medication in order to minimise the concerns over drug residues and drug withdrawal times. An additional challenge is introduced with the use of some analgesics, such as opioids, in order to differentiate whether some clinical signs (i.e. gut stasis) are related to pain or to the side effects of the drug itself; the use of opioids is often linked in ruminants with signs of ileus(4) caused by the activation of the opioid receptors in the gastrointestinal tract that inhibit gut motility(5).

The use of systemic analgesics, including opioids (3, 6-9) non-steroidal anti-inflammatory agents (NSAIDs) (10-12), ketamine(13) and lidocaine(14) has been well described in alpacas. Local anaesthesia techniques have also been incorporated extensively in their analgesia plans, depending on the procedure (15). Local anaesthetic techniques, such as mental, mandibular and maxillary nerve blocks, are commonly used for dental trimming and tooth extractions, procedures

often encountered in practice(16, 17).

Dental disease is common in alpacas and can be linked to genetic, dietary and husbandry factors(18). Periodontitis, malocclusion, tooth root abscesses and fractures are some of the most common manifestations of dental disease requiring surgical intervention. Using local anaesthetic drugs to block dental nerves is an effective method to provide analgesia and to decrease the use of opioids and their systemic side effects, such as reduced gastrointestinal mobility and faecal output(19), as well as to improve and accelerate full recovery. Maxillary and inferior alveolar nerve blocks are the most common; they are inexpensive and easily performed using a needle of appropriate gauge and a local anaesthetic of choice(15). Local anaesthetics reversibly block neuronal voltage-gated sodium channels and reduce the excitability of neuronal and central nervous system tissue. Thus, the conduction of noxious stimuli to the spinal cord and brain is prevented, providing perioperative analgesia(20).

The use of epidural catheters has been previously described in sheep and cattle in order to provide epidural analgesia(21) in the thoracic and the dorsolumbar spine. In dogs, epidural catheters have been also used to provide continuous brachial plexus block(22) and to achieve opioid free anaesthesia(23).

This case report describes the placement of an epidural catheter in the mandibular foramen, under CT guidance, in order to provide long-term analgesia for an alpaca that suffered a mandibular fracture during a dental procedure and in which systemic analgesia was insufficient.

CASE PRESENTATION *Presenting features, clinical and environmental history*

A nine-year-old, female huacaya alpaca, weighing 59 kg, was referred for further investigation of a swelling on the left mandible and history of decreased food intake. The swelling had been present for the previous three years and was reported to have a purulent

discharge that intermittently resolved after repeated courses of florfenicol (20 mg kg^{-1} subcutaneously, three times a day). The alpaca was kept as a pet on a farm and was signed out of the food chain.

On presentation, all physiological variables were within normal limits. There was a 5 cm diameter swelling on the caudal third of ventral aspect of the left mandible with some purulent discharge and the body condition score was 3/5. A CT scan was performed under sedation to re-evaluate the extension of the lesion and revealed periapical infection and fragmentation of the left first mandibular tooth. The infection also extended through the mandible to an external draining tract. Based on the recurrent clinical signs and the severity of the CT findings, extraction of the fractured molar tooth and debridement of the surrounding area was carried out. Unfortunately, the alveolar medial portion of the infected part of the mandible was fractured during extraction. The surgeon decided that the best course of action was to allow the fracture to heal by secondary intention, as the presence of active infection made the option of implant use unviable. After obtaining a sample from the mandibular lesion for culture and sensitivity, the animal was allowed to recover form anaesthesia, with provision of adequate analgesia and antimicrobials until the complete healing of the fracture.

The analgesia plan included meloxicam 0.5 mg kg^{-1} administered intravenously once daily and buprenorphine 0.01 mg kg^{-1} intravenously every 8 hours. To reduce the risk of third gastric compartment ulceration, pantoprazole 1 mg kg^{-1} was administered intravenously once daily and ceftiofur 2.2 mg kg^{-1} intravenously every 12 hours was started as an antimicrobial. However, over the five days following surgery, the animal became dull, inappetent and lethargic. In an attempt to increase food intake, the appetite stimulant diazepam (0.05 mg kg^{-1}) was given intravenously but was not effective. Physical examination and further haematology and biochemistry results showed no abnormalities that could explain the profound lethargy, inappetence or lack of faecal output and it was assumed that the pain relief plan was inadequate. On that basis, medetomidine at a dose of 2 μg kg^{-1} was given intravenously, aiming for a synergistic analgesic effect when

combined with opioids. However, the administration of medetomidine resulted only in profound sedation rather than improving the animal's comfort and appetite. A second CT scan performed under sedation to re-evaluate the extent of the lesion. It revealed that the left first mandibular molar tooth was successfully removed during surgery but that a left mandibular defect was present with large amounts of absent bone. The lateral cortex of the left mandible was still intact but there were no signs of further bone healing, which was attributed at the time to the presence of profound inflammation.

With the aim to provide analgesia with minimal systemic effects, an inferior alveolar nerve block was regarded as the most appropriate treatment. Due to the need for repeated administration of local anaesthetic, an epidural catheter was placed in the mandibular foramen, under CT guidance. In order to place the catheter, the alpaca was sedated with xylazine 0.2mg kg^{-1} IV followed by ketamine 2mg kg^{-1} intravenously 10 minutes later. She was placed in right lateral recumbency in the CT scanner and oxygen was provided via face mask at a flow of 4 L min^{-1}. On the CT image, two lines, perpendicular to each other, were drawn to measure the distance from the mandibular foramen to both the largest part of the angular process of the mandible and the lower part of the angular process. The distances were measured as 3.3 cm and 4.1 cm, respectively *(Fig. 1, 2)*. A 22 G × 720 mm Tuohy needle was inserted medial to the body of the mandible and advanced in a caudal and rostral direction to the aforementioned distance from the largest part of the angular process. Needle position was confirmed with CT, with the tip of the Tuohy needle at the mandibular foramen (*Fig. 3*). The epidural catheter was advanced through the needle into the mandibular canal and its position was again confirmed with CT; the catheter was advanced 2.5 cm in the mandibular canal as estimated by the CT image. The proximal part of the epidural catheter was then tunnelled under the skin and sutured between the ears, after the addition of an antibacterial filter (*Fig. 4*). The catheter and antibacterial filter were preloaded with 1 ml of ropivacaine 0.75% and there was no need for flushing through after each injection. Before recovery, 1 mL of ropivacaine 0.75% was injected into the mandibular catheter

and the animal moved back to its pen.

A few hours later, the alpaca started eating and seemed brighter and more responsive. Analgesia was subsequently provided only by repeated administration of 1 mL of ropivacaine 0.75% every 6 hours; buprenorphine and meloxicam were discontinued.

INVESTIGATIONS ***If relevant***

DIFFERENTIAL DIAGNOSIS ***If relevant***

TREATMENT ***If relevant***

OUTCOME AND FOLLOW-UP

Over the following ten days, the animal continued eating normally with no signs of irritation over the catheter site. The dose and frequency of administration of ropivacaine remained unchanged. However, due to the presence of discharge from the previous surgical site on the ventral aspect of the mandible, further wound debridement was carried out under sedation. Upon recovery, the patient became distressed and dysphagic with suspected, although not confirmed, aspiration pneumonia. Due to the guarded prognosis of the case, the owner elected humanitary euthanasia.

Post mortem evaluation revealed absence of healing process in the mandibular fracture site. Histopathology was performed on both the right and left mandibular nerves, which demonstrated no obvious lesions attributable to ropivacaine administration.

DISCUSSION ***Include a very brief review of similar published cases***

In this case report, the placement of an epidural catheter in the mandibular canal, under CT guidance, was proven to successfully provide analgesia to an alpaca suffering from a mandibular fracture; no complications were encountered.

Analgesia can be challenging in camelids due to their stoic nature and their tendency to hide any manifestation of pain(2). The lack of a validated pain scale to facilitate early recognition of signs of pain and to evaluate the response to analgesic drugs(19) constitutes an additional difficulty. In this case, the severity of the injury and the clinical demonstration of decrease in food intake and lethargy suggested that buprenorphine and meloxicam were providing inadequate analgesia. The aim of the mandibular catheter was to provide analgesia for a sufficient period, in

order to allow the fracture to heal while maintaining an acceptable body condition. A further increase in buprenorphine dose could have been attempted in case the analgesia from the local anaesthesia technique was inadequate.

In human medicine, the use of indwelling catheters for continuous block of the mandibular nerve in a patient with intractable orofacial cancer pain, trigeminal neuralgia or mandibular fractures have been described (24-26). A neurolytic block was also utilised in one of the aforementioned cases after the block with local anaesthetic - an option that could be considered more appropriate in cases related to cancer pain. (27). In our case, the use of chemical neurolysis could not have been a viable option since the intention was to provide analgesia until the healing of the fracture was completed.

The placement of the mandibular catheter was performed under CT guidance, as CT images are superior to radiographs for the examination of the skull and dental structures in camelids(28). This superiority is attributed to better resolution, lack of common radiographic artefacts and the possibility of multidimensional image processing and reconstruction that CT offers. In addition, it should also be considered that the mandibular foramen in camelids, in contrast to other species, is not palpable. The above characteristic, in combination with the fact that placement of the mandibular catheter could not be facilitated with ultrasound guidance, led to the utilisation of advanced imaging (CT). Using this technology, it was possible to measure the exact distance to insert the Tuohy needle so that it was positioned at the mandibular foramen, and to confirm the correct position of the epidural catheter that was advanced through the needle.

Peripheral nerve blocks and catheters have proven a vital component of a multimodal analgesia approach. In humans, they demonstrate numerous benefits such as reduced opioid use, fewer opioid-related side effects, reduced length of hospital stay, faster rehabilitation and patient satisfaction(29, 30). In this case, placement of a mandibular catheter and the administration of local anaesthetic was indeed the most appropriate way to provide adequate pain relief, compared to systemic analgesics.

In camelids, opioids can have serious side effects, including decreased gastrointestinal tract motility and inappetence, both of which are detrimental for this species (7, 19, 31). The presence of pain and stress itself is also linked with the above undesirable gastrointestinal side effects and poor quality of life(32). In addition, the use NSAIDs in camelids has been linked with decreased contractility of the gastrointestinal tract and third compartment ulcers. (33)

In this case, administration of systemic analgesics was discontinued after mandibular catheter placement, as the analgesia provided by the local anaesthetic delivered with this device was considered to provide adequate pain relief.

The most common complications of peripheral nerve catheters include dislocation, infection, catheter malfunction, improper catheter placement, neurologic complications and local anaesthetic toxicity(30, 34). Specific complications of mandibular catheters described in human medicine are rare and transient, these include diplopia, temporary loss of vision, ophthalmoplegia, ptosis, mydriasis and periorbital blanching(35, 36). None of these was observed in this alpaca.

Local anaesthetics have been found to have a beneficial action on the inflammatory response and haemostasis in addition to their well-described effect on the nervous system (37). Local anaesthetic-induced neurotoxicity, however, remains a concern and its mechanisms have not been completely clarified(20). The cellular mechanisms of local anaesthetic toxicity and cell death appear related to the concentration of the local anaesthetic, which initiates pathways leading to apoptosis(38). In this case, histopathological examination of the mandibular nerves demonstrated no lesions in the nerve receiving local anaesthetic, compared with the normal mandibular nerve of the contralateral side; this is a promising result for the long-term use of local anaesthetic for pain management in this species. There was also no evidence of mechanical damage or inflammation caused by the insertion of the catheter.

Ropivacaine was the local anaesthetic of choice for this case. The main benefit was the long duration of action, compared with procaine hydrochloride, the licenced local anaesthetic in farm animals. Ropivacaine was the preferred choice compared to bupivacaine which has a similar

duration of action, due to its increased safety profile with regards to cardiovascular and neuro-toxicity. Ropivacaine also has a greater degree of differential block and less potential for accumulation; both desirable characteristics when used in peripheral nerve catheters.(39)

Although the epidural catheter provided patient comfort without any complications, as confirmed by the post mortem examination, the alpaca was euthanised due to the non-healing fracture and possible aspiration pneumonia.

There is no evidence that the local anaesthetic could have affected the healing processes of the mandibular fracture. There are conflicting studies regarding local anaesthetic chondrotoxicity, with some demonstrating both *in vitro* and *in vivo* detrimental effects on articular cartilage(40), whilst others suggest that intermittent injections of intra-articular local anaesthetic may not have deleterious effects on chondrocytes(41). Regarding the effect of local anaesthetic on osteoblasts, however, there is only one *in vitro* study which demonstrated that they could affect negatively osteoblast proliferation and viability, but only after long periods and at high concentrations(42). In our case, the aim of the peripheral nerve catheter placement in the mandibular foramen was to block the afferent fibres of the mandibular nerve proximal to the fracture site. It is expected however, a small only amount of local anaesthetic to spread to the actual fracture site. The above makes the delay of bone healing less likely.

The low concentration and volume of the local anaesthetic may have also contributed to the absence of relevant complications. The effective analgesia provided, despite the low concentration and volume of the local anaesthetic may be a result of the accurate placement of the catheter, in close proximity with the mandibular nerve. (43)

In conclusion, peripheral nerve catheters may be used in alpacas for long-term administration of local anaesthetic drugs, as part of multimodal analgesia approach. Complications were not encountered, but normal precautions regarding technique and doses should be taken. Normal precautions could include accurate placement of the needle and aspiration before injecting local anaesthetic to avoid intravascular administration. Accurate

calculation of the local anaesthetic dose is also recommended to avoid toxicity.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

Local analgesia can be an important and valuable tool in alpaca analgesia regime.
Peripheral nerve catheters may be used for long term administration of local anaesthetic drugs
No abnormal histopathological findings found on the mandibular nerve after long term administration of local anaesthetic

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FIGURE/VIDEO CAPTIONS ***figures should NOT be embedded in this document***

Figure 1: CT image for positioning of the Tuohy needle. Red lines indicating distance from the mandibular foramen to both the largest part of the angular process of the mandible and the lower part of the angular process.

Figure 2: X-ray image indicating the red distance lines and the actual measurements in cm.

Figure 3: Image of the positioning of the Tyohy needle before advancing the epidural catheter.

Figure 4: The mandibular catheter was tunnelled under the skin and an antibacterial filter was attached at the proximal end of the catheter before securing it between the ears.

OWNER'S PERSPECTIVE *Optional*

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