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Evaluation of acute and chronic ophthalmic pain

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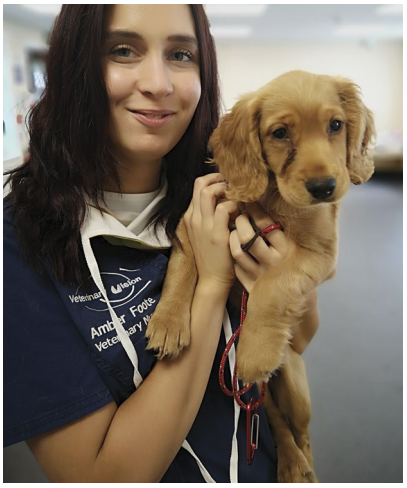
ABSTRACT: Pain management of veterinary patients is an important role for Registered Veterinary Nurses (RVN); pain has been described as the fourth vital sign and knowledge of the nociceptive mechanisms involved in pain has advanced significantly. Ophthalmic pain is often overlooked by both veterinary professionals and pet owners; the demonstration of ocular pain is species and patient specific and can often be difficult to assess. This article uses two cases studies to discuss pain management options for both acute and chronic ophthalmic pain in canine and feline patients.

Keywords: pain management; ophthalmic nursing; acute and chronic pain



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Supplementary files for this article can be found here: https://doi.org/10.1080/17415349.2021.1905574

DOI: 10.1080/17415349.2021.1905574

Introduction

Registered Veterinary Nurses (RVN) play a vital role in the recognition and management of pain in ophthalmic patients; as veterinary patients are unable to verbalise the amount of pain they are experiencing, it is the responsibility of veterinary professionals to recognise and act upon the signs of pain (Bloor & Allan, 2017). Ophthalmic pain is often overlooked by both veterinary professionals and pet owners; the demonstration of ocular pain is species and patient specific and can often be difficult to assess (Knott, 2020). Patients with ophthalmic disease are commonly presented in first opinion practice due to a variety of acute and progressive diseases or trauma. The adnexa and orbit of the canine and feline eye are heavily innervated with sensory neurons therefore, ophthalmic disease and surgery is thought to cause moderate to severe pain (Mathews et al., 2014).

Knowledge of the physiology of pain and the nociceptive mechanisms involved in pain has increased significantly and the negative consequences of untreated pain is now widely accepted amongst veterinary professionals (Tabor, 2016). This increase in knowledge is emphasised by the recent development of pain scoring systems, quality of life tools and the availability of veterinary analgesia. Veterinary professionals must understand the physiology, pathophysiology and the consequences of pain to be able to assess pain successfully and to ensure that good health and welfare standards are maintained (Grubb et al. 2018, Bloor & Allan, 2017). Once signs of pain are recognised, veterinary professionals should determine the type of pain the patient is suffering such as, neuropathic, acute or chronic and create an individual analgesic treatment plan (Balakrishnan & Benasutti, 2012).

Pain serves a protective role that alerts an individual to injury; The International Association for the Study of Pain has defined pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" (International Association for the Study of Pain [IASP], 2020). Pain can be classified as mild, moderate or substantial and depending on the duration of the pain it may be described as acute or chronic. For an animal to experience pain, nociceptive information must be transmitted from afferent neurons to the central nervous system (CNS) to be integrated, modulated and interpreted (Mathews et al., 2014). The pain pathway consists of four elements: transduction of a noxious input, transmission of the signal, modulation of sensory information and the perception of pain (Flaherty, 2013, Table 1). Analgesic drugs work at various levels of the pain pathway to interrupt the signal transmission to the brain; the use of multi-modal analgesia has been shown to target different levels of the pain pathway leading to superior pain management (Mathews et al., 2014, Melis, 2020). Epstein et al. (2015) recommended a multimodal approach as the synergistic effect of multiple drug combinations targets various sites of the pain pathway, potentially allowing for lower doses of each drug and minimising the potential for side effects associated with any single drug. Traditional methods encompass pharmacological treatments such as pure or partial opioids, non-steroidal anti-inflammatory

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Table 1. The four elements of the pain pathway.

Mode of Action	Description
Transduction	A painful (noxious) stimulus is converted into an electrical signal at the pain receptor (nociceptor)
Transmission	A nerve impulse moves along nerve fibers to the dorsal horn of the spinal cord
Modulation	Adaptation of pain information at various sites of the nervous system
Perception	Awareness and sensation of the pain.

Figure 1. Feline corneal sequestrum.

drugs (NSAIDs) and local anaesthetic drugs. Epstein et al. (2015) also noted that to have a truly multi-modal approach, the use of complementary and non-pharmacological interventions should be considered for each individual patient, for example, thermal therapies, acupuncture and environmental modifications.

Case study 1: acute surgical case – sequestrum removal by keratectomy (feline)

A 4-Year-old Persian was referred with blepharospasm, epiphora, and the presence of a dark lesion in the centre of the cornea; the patient was diagnosed with a corneal sequestrum of the left eye (Figure 1). Sandmeyer et al. (2015) described corneal sequestrum as the development of dark necrotic tissue which acts as a foreign body within the cornea and often results in inflammation and ulceration. Spontaneous healing of the sequestered stoma is unlikely with topical medication, so surgical intervention is recommended to reduce the risk of corneal perforation, prolonged pain and excessive scarring (Stiles, 2013). The patient underwent removal of the sequestered stroma by lamella keratectomy under general anaesthesia, and the pharmacological agents used can be found in Table 2. Keratectomy is the surgical excision of necrotic corneal tissue including epithelium and variable amounts of stroma, the depth of the keratectomy is determined by the extensivity of the corneal sequestrum. It is recommended that if more than 50% of the corneal stroma is removed, either a conjunctival or corneo-conjunctival transposition graft is performed.

Analgesia and treatment plan

Corneal sequestrum is thought to cause moderate to severe pain, and Mathews et al. (2014) suggested the use of opioids for their efficacious analgesic effect when moderate to severe pain is predicted. Drozdzynska and Pelligand (2016) expanded upon this and suggested the use of pure μ-opioid agonists rather than partial μ-opioid agonists to provide the most efficacious level of analgesia. Buprenorphine (Buprecare®) is a synthetic partial μ-opioid agonist which binds avidly to, and dissociates slowly from opioid receptors, but does not elicit a maximal clinical response as opposed to a full μ-opioid agonist (Steagall et al., 2014). Furthermore, Steagall et al.'s study showed that individual variability in response to buprenorphine indicates that it may not provide sufficient analgesia in some cats. Conversely, methadone is a synthetic pure μ-opioid agonist and it elicits a maximal response at the receptor bind sites of the CNS (Inturrisi 2002). Steagall et al. (2006) study found that methadone provided a superior level of analgesia to that provided by buprenorphine in cats. Opioids are often avoided in cats due to CNS side effects such as mydriasis, tachycardia and hyperkinesis (Shelby, 2018). However, the use of opioids may lower the requirements of other anaesthetic agents and their mode of action can be dosed to effect with minimal side effects (Shah et al., 2018). Flaherty (2013) stated that two or more drug groups should be used in combination as part of a multimodal approach.

Alongside the intramuscular pre-medication of buprenorphine and acepromazine, the patient was provided with intravenous meloxicam. The pre-emptive analgesia was administered one hour prior to induction to allow metabolism of the drugs providing a full analgesic affect (Epstein et al. 2015). NSAIDs are indicated for peri-operative ophthalmic pain as they exert their action both peripherally, at the site of the tissue damage and have a component of central analgesic activity (Delgado et al., 2014, Montefiori and Flaherty, 2014). The patient was provided with oral meloxicam for seven days post-operatively, the owner reported that the patient was comfortable and without ocular discomfort. Epstein et al. (2015) stated that local anaesthetics (LA) are the only class of drugs which render complete analgesia through the inhibition of peripheral nerve impulses; the cornea contains a high density of nociceptors which can be targeted by LA for rapid onset analgesia (Mathews et al., 2014). The patient was provided with topical proxymetacaine prior to surgical incision and post-operatively however, it is important to note that the number of applications should be limited as repetitive application can cause keratitis (Giuliano 2008). To reduce the risk of keratitis and provide a relieving effect, topical lubrication was administered intermittently during the peri-operative period (Mathews et al., 2014). Complementary therapies for ophthalmology are generally very limited however, in this case the use of cold compression could have been implemented to reduce pain and inflammation (Mathews et al., 2014).

Pain assessment

In order to assess the traditional and complementary therapies implemented, a modified ophthalmic pain score was used (Appendix A1, in Supplementary Materials.). The demonstration of ocular pain is species and patient specific and can often be difficult to assess (Knott, 2020). Weise (2018) recommended the use of validated pain scoring systems to optimise pain detection, reduce bias and assess therapeutic interventions. However, in this

Table 2. Pharmacological agents used for patient 1.

Drug	Description
Buprenorphine (Buprecare®)	A centrally acting partial μ-opioid agonist
Acepromazine (Acecare®)	Phenothiazine Derivative
Propofol (Propomitor®)	Intravenous sedative hypnotic agent for use in the induction and maintenance of anaesthesia
Meloxicam (Metacam®)	Non-steroidal anti-inflammatory drug
Proxymetacaine	Topical ocular local anaesthetic

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case a non-validated and modified ophthalmic pain score was used due to the limited availability of ophthalmic-specific pain scoring systems. The modified ophthalmic pain score was based on the Glasgow Feline Composite Measure Pain Scale (CMPS) which is validated for use in measuring acute pain (Mathews et al., 2014); the modified part of this pain score focussed on signs of ophthalmic pain including photophobia, blepharospasm and lacrimation. This system proved effective in the management of this case and allowed for timely pain management. It is vital, whichever pain assessment tool is used, that patients are regularly assessed to provide effective pain management and increase standards of care (Epstein et al., 2015, Bloor & Allan, 2017).

Evaluation

The pain scores revealed that the patient was provided with effective multimodal analgesia and remained relatively stable throughout the peri-operative period. The use of a pure μ-opioid agonist could have been provided for superior pain relief, to further lower the requirements of other anaesthetic agents and potentially minimise side effects (Epstein et al., 2015). The multimodal approach proved beneficial in this case as the individual drug doses, the anaesthetic induction and maintenance agents were lowered; potentially lowering the risk of individual side-effects (Epstein et al., 2015). The multimodal approach targeted various sites of the pain pathway and provided a synergistic effect. To achieve a truly multimodal approach, the use of complementary therapies could have been implemented; there is very limited veterinary research in ophthalmic complementary therapies. Though, in this case the use of cold compression could have been implemented to reduce pain and inflammation post-operatively (Mathews et al., 2014). The use of topical lubrication also provided a cooling and soothing effect during the peri-operative period.

Summary

The outcome of this case was successful; the anaesthetic period was uneventful, and the patient was discharged later that day. As corneal sequestrum is thought to be a painful condition, this anaesthetic and surgery was necessary to remove the necrotic corneal tissue and prevent chronic ophthalmic pain. The pain management for this case provided sufficient analgesia; ideally a pure μ-opioid agonist and further complementary therapies could have been implemented for a truly multi-modal and holistic approach.

Case study 2: chronic medical case – canine glaucoma

A notable disease that RVNs may have significant involvement in is glaucoma (Figure 2); canine glaucoma is characterised by the elevation of intraocular pressure (IOP) with associated optic neuropathy and retinal damage (Figure 2) (Turner, 2010, Komáromy & Petersen-Jones, 2015). A 10-year-old Jack Russel Terrier was referred with blepharospasm, bupthalmos and episcleral congestion; the patient was diagnosed with chronic glaucoma and right lens subluxation. The right eye was enucleated due to uncontrollable intraocular pressure (IOP), lens subluxation and suspected retinal damage. Ocular histopathology of the enucleated globe confirmed open-angle glaucoma. Emergency anterior chamber paracentesis was performed on the remaining left eye to reduce the intraocular pressure and a treatment plan was prescribed.

Analgesia and treatment plan

The treatment plan included the use of two topical medications including, topical latanoprost (Xalatan, Pfizer) and topical brinzolamide (Azopt, Novartis). Latanoprost is a prostaglandin analogue which improves the outflow of aqueous humour (Reinstein, 2019). Brinzolamide is a carbonic anhydrase inhibiter which lowers the intraocular pressure by reducing the production of aqueous humour at the ciliary body (Dower et al., 2018). The aims of glaucoma treatment are to prevent further vision loss and control the pain caused by increased IOP (Ofri, 2019). Mathews et al. (2014) stated that although analgesia is one of the primary interventions used in the management of chronic pain, treatment options for chronic pain are complex and require a multimodal approach, tailored treatment plans and effective pain recognition. NSAIDs are indicated in glaucoma cases to reduce pain and inflammation by blocking prostaglandin production through Cyclooxygenase (COX) enzyme inhibition. NSAIDs treat the inflammation at the posterior segment of the eye which often occurs during an acute intraocular pressure spike (Reinstein, 2019). On that note, topical corticosteroids such as dexamethasone 0.1%, could have been indicated to treat anterior segment inflammation, however topical corticosteroids are generally avoided as they can reduce the efficacy of latanoprost and exacerbate intraocular pressure elevation (Reinstein, 2019).

Figure 2. Glaumatous eye of a pug.

Following the initial diagnosis and right enucleation, the patient had a follow-up nurse clinic to discuss how to monitor for signs of ocular pain and to allow the owner to raise any concerns. An RVN provided thorough information in layman's terms to allow the owner to understand that the aim of medical or surgical therapy is to stabilise the IOP. Although there is no cure for glaucoma, owner compliance with medical management can prevent further vision loss and control pain. Poor compliance or poor understanding of the condition prior to a treatment plan can lead to inadequate IOP control and enucleation of blind, painful eyes (Ofri, 2019). However, in cases of primary glaucoma, medications become less effective over time and the IOP will continue to rise (Reinstein, 2019).

Furthermore, the patient had monthly nurse appointments for intra-ocular pressure monitoring and assessment of ocular pain (Figure 3). Ophthalmic pain can be difficult to assess and often dogs do not show obvious discomfort (Ofri, 2019). The patient remained relatively stable and pain-free however, the owner did report reduced appetite and lethargy in the later stages of glaucoma in the remaining left eye. As the topical medications had become less effective in this case, the treatments were not altered as there is limited evidence to show that increasing the dose rate of latanoprost or brinzolamide will decrease the IOP. However, as the owner reported signs of chronic pain (reduced appetite/lethargy), the systemic analgesia could have been altered. Mathews et al. (2014) suggested that the alleviation of chronic pain will require drugs with a long duration of action and a range of adjunct drug therapies. Although the patient was reasonably controlled on long-term NSAIDs (Meloxicam, Metacam®), the introduction of Paracetamol (Acetaminophen) could have provided superior pain relief as part of a multimodal approach (Mathews et al., 2014). Moreover, Reinstein (2019) suggested the use of traditional opiates, such

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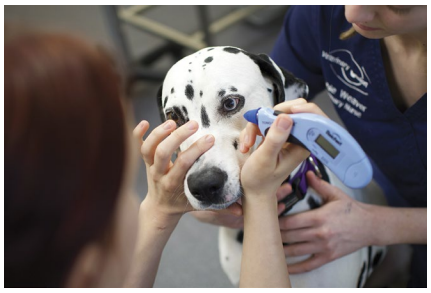

Figure 3. Registered Veterinary Nurse (RVN) performing tonometry (measurement of intraocular pressure).

as methadone or tramadol, during acute glaucoma spikes.

Quality of life assessment

The use of a quality-of-life (QOL) scale could have been implemented during these nurse clinics to assess if the patient was showing signs of chronic pain at home. The HHHHHMM scale is a quantitative QoL scale which stands for hurt, hunger, hydration, hygiene, happiness, mobility, and more good days than bad (Villalobos, 2011; Table 3). The HHHHHMM scale is easy to implement and provides useful guidelines for owners to follow and understand their dog's QoL. A score of above 35 points is an acceptable quality of life for pets, however, when using this QoL scale to assess a dog with glaucoma and visual impairment it is also important to focus on individual factors such as happiness and mobility. If the dog is displaying depressed, anxious or aggressive behaviours which are significantly impacting the dog and owner's lifestyle then the scale may not be relevant for that patient. In these cases, it may be more relevant to focus on how behaviour is affecting both the patient's and owner's lifestyle and the impact of the treatment plan; many ophthalmic conditions require multiple topical medications applied daily, which may cause significant distress and changes in behaviour in nervous dogs. The use of a QOL scale in this case may have shown an obvious trend of a reduced score, allowing for timelier intervention.

The patient remained comfortable with the left eye for three months after the initial presentation and right enucleation. In the latter month the owner reported inappetence, lethargy and ocular discomfort; in the nurse intra-ocular pressure checks the IOP had increased to 30 mmHg. The patient was referred back to the veterinary surgeon and anterior chamber paracentesis was performed as a salvation attempt. Unfortunately, the following week the patient presented as an emergency re-examination with signs of ocular hypertension and pain. The IOP was 70 mmHg which resulted with enucleation of the remaining hypertensive and painful eye. Unfortunately, the glaucomas share a unified final pathway of characteristic optic neuropathy and retinal damage resulting in loss of vision (McLellan & Miller, 2011; Komaromy et al., 2019).

Table 3. The HHHHHMM scale.

Quality of Life Scale: The HHHHHMM Scale Adapted from: Villalobos A, E. (2011). Quality-of-life assessment techniques for veterinarians, Veterinary Clinics of North America: Small Animal Practice 41(3): 519-529	
Criterion	Score (1 – 10, 10 being the highest quality of life)
Hurt: Adequate pain control, including breathing ability, is first and foremost on the scale. Is the pet's pain successfully managed?	
Hunger: Is the patient eating enough? Does the patient require assisted feeding?	
Hydration: Is the patient dehydrated? Does the patient require fluid therapy?	
Hygiene: Is the patient able to maintain hygiene and groom themselves? {Avoiding pressure sores and keeping wounds clean}	
Happiness: Does the pet express joy and interest? Is the pet responsive to things around him or her (family, toys, etc.)? Is the pet depressed, lonely, anxious, bored or afraid? Can the pet's bed be close to the family activities and not be isolated?	
Mobility: Can the patient get up without assistance? Does the pet need human or mechanical help? Does the pet feel like going for a walk?	
More good days than bad: When bad days outnumber good days, quality of life might be compromised. When a healthy human-animal bond is no longer possible, the owner must be made aware the end is near. The decision needs to be made if the pet is suffering and if euthanasia should be cosidered	
*A total over 35 points represents acceptable life quality	

Evaluation

There are a number of traditional and complementary therapies that could have been implemented in this case and the use of QOL scale could have been implemented throughout. The use of a QOL scale may have revealed the more subtle signs of chronic pain including inappetence and lethargy in a timelier manner. On a positive note, the monthly nurse clinics allowed the early recognition of ocular hypertension and increased client and practice rapport. Long-term NSAIDs are often used and recommended in cases of chronic pain, though to achieve a truly multimodal approach, various traditional and complementary therapies could have been implemented. Under veterinary direction, the introduction of paracetamol or traditional opiates such as tramadol, could have provided superior pain relief in this case.

Complementary therapies

There is no cure for glaucoma and complementary therapies are generally very limited; there are however several human complementary therapies that could be researched further for veterinary use. One of the most widely cited complementary therapy for glaucoma is the use of medical marijuana; the intraocular pressure lowering effects of marijuana were first reported in 1971 by Hepler and Frank. Several studies have shown that medical marijuana can produce hypotensive effects within 60 to 90 minutes with a duration of action of 3 – 4 hours (Merritt et al., 1980, Flach, 2002). Novack (2016) agreed that marijuana is an effective ocular hypotensive agent however, the cardiovascular and neurological effects may reduce the beneficial effect of lowering IOP by reducing ocular blood flow. Several ophthalmological societies also agree that the short duration of action and side effects make it a poor treatment option for glaucoma therapy (Jampel 2010, Buys & Rafuse, 2010). Given the lack of evidence for the use of medical marijuana in the human field and the similar negative side effects in canines, the use of medical marijuana should be discouraged as further research for veterinary use is required (Smither & Prendergast, 2016). Furthermore, in the human field, medical grade marijuana is used limitedly for rare forms of epilepsy, chemotherapy and multiple sclerosis (MS) and is not widely available for veterinary use.

A recent human study by Chen et al. (2020) showed that acupuncture can be beneficial for reducing the intraocular pressure in glaucoma patients. The study showed that acupuncture reduces IOP within 60 minutes

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Figure 4. Canine following Bilateral Enucleation due to Glaucoma.

of treatment and that repeated acupuncture sessions were beneficial for lowering IOP in glaucoma patients (Chen et al., 2020). An earlier study in monkeys by Brooks et al. (2007) showed similar results as their IOP reduced to less than half the baseline IOP when compared to the group not receiving acupuncture. The study also showed that the IOP of glaucomatous eyes receiving acupuncture was also significantly lower at 24- and 48-hours post-treatment (Brooks et al., 2007. Studies on canine acupuncture for glaucoma is limited and is an area in need of further research to broaden the scope of complementary treatment for glaucoma.

Summary

Canine glaucoma is a leading cause of irreversible vision loss and can be classified by the underlying cause of impaired aqueous humor drainage and the duration of glaucoma (Reinstein, 2019). Despite advancements in medical and surgical treatments, there is no known cure and unfortunately, as the with the patient in this case, affected dogs often have eyes enucleated because of painfully high, uncontrollable IOP (Komaromy et al., 2019). Therefore, advanced surgical procedures such as ciliary body laser ablation or anterior chamber shunts should be considered for visual patients, while blind patients may eventually require enucleation (Figure 4).

Conclusion

Pain management is vital as veterinary patients are unable to verbalise the amount of pain they are experiencing; RVNs are well within the remits of their role to recognise and act upon signs of pain by notifying and working with the veterinary surgeons in adjusting analgesia protocols.

Ophthalmic pain is often overlooked and difficult to assess in both canine and feline patients; the use of pain scoring systems and QOL tools are highly recommended. Pain scoring systems prove useful in acute ophthalmic cases and for use peri-operatively. Whereas, QOL tools can be used by veterinary professionals and owners for assessment of chronic pain and recognition of subtle signs. It is clear through discussing these cases that there are improvements, additional therapeutic and complementary treatments that could be implemented. Although, it is also evident that ophthalmic complementary treatments are very limited and further research throughout this field is required to provide superior pain management.

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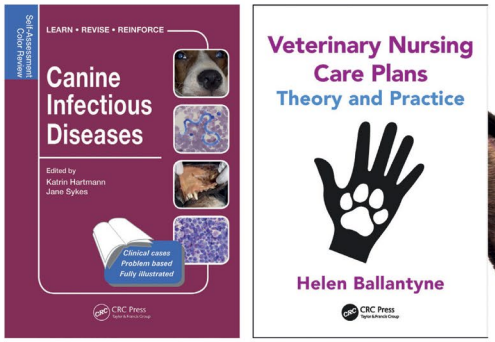

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