PAIN IN THE EYE:
AN EVIDENCE-BASED APPROACH TO OCULAR/PERIOCULAR ANESTHESIA & ANALGESIA

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Background

Today's veterinary practitioner is perhaps more aware than ever of the need to effectively recognize the need for peri- and postoperative analgesia in dogs and cats, and to be able to determine an appropriate pain management plan. This increased awareness and growing need to proactively identify effective and safe analgesic protocols is also likely a primary contributor to the rapid development and marketing of analgesic medications in the veterinary market. Kohn et al have defined animal pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, and should be expected in an animal subjected to any procedure or disease model that would be likely to cause pain in a human".[1] Despite the apparent simplicity of this definition, however, it still proves exquisitely challenging for practitioners and investigators to make objective assessments of pain or the potential for pain in non-verbal patients. Furthermore, many of the species we treat have evolved to mask "expected" pain in order to avoid predation.[2] This, in combination with other species-specific factors, heavily influence behavioral manifestations of pain in the clinical setting.[3]

Historically, many of the published behavior-based pain scoring systems were developed for use in laboratory species, but more recently objective scoring systems are becoming more commonly reported for companion animals.[4-7] However, studies specifically addressing the assessment and management of ocular pain in animals remain infrequently published. In fact, the eye has been identified by the American Animal Hospital Association and American Association of Feline Practitioners as a common source of overlooked pain in veterinary medicine.[8] Several clinical studies in dogs have assessed corneal/ocular pain, or pain following enucleation (eye removal) using different behavior-based systems[9-14]. In some of those studies[9, 10, 14], the Melbourne Pain Scale[5] was amended to include a category for blepharospasm. Two studies[9, 14] utilized a control group with strongly identified placebo-treated dogs, confirming those systems' sensitivities for detecting moderate or severe pain. Interestingly, a review of the literature in dogs has indicated that blepharospasm is widely considered the strongest and most consistent indicator of corneal pain. Despite these reports, however, a system for assessing topical ocular pain in animals has not been validated.

While ophthalmic surgical procedures are a routine aspect of practice for many small animal practitioners, local anesthetic techniques are often underutilized. For such procedures, however, local anesthesia may minimize or obviate the need for heavy sedation or general anesthesia, mitigate postoperative discomfort, and expedite recovery. Currently, most topical and injectable local anesthetics utilized in veterinary ophthalmology (i.e. lidocaine, bupivacaine, proparacaine, tetracaine) act by inhibiting conduction of pain-sensing nerves. What follows is a review of recent veterinary literature with possible applicability to ocular surgeries and procedures performed in general small animal practice.

General Indications for Ocular Anesthesia/Analgesia in General Practice

Given the dense sensory innervation of the adnexal and ocular structures, anesthesia is indicated for most diagnostic and surgical procedures. Topical anesthesia of the ocular surface facilitates many commonly performed procedures including: applanation tonometry; collection of corneal and conjunctival samples for culture and/or cytology; corneal debridement and grid/diamond burr

keratotomy; excisional biopsies of the conjunctiva and third eyelid; placement of third eyelid flaps; removal of conjunctival or corneal foreign bodies; and diagnostic alleviation of spastic entropion. The primary indications for anesthesia of the eyelids include: curettage and cryotherapy of benign eyelid tumors; placement of tacking staples or sutures for temporary management of entropion; and perioperative analgesia for entropion surgery or excisional biopsies. In general practice, retrobulbar/peribulbar anesthesia/analgesia is principally indicated for routine enucleation.

Anesthesia of the Ocular Surface

Most practitioners are familiar with topical ophthalmic analgesics such as 0.5% proparacaine or tetracaine. These agents are capable of penetrating the superficial cornea, inhibiting the nociceptive nerve endings concentrated within the anterior corneal stroma. One drop of topical 0.5% proparacaine produces corneal anesthesia within one minute of application, lasting approximately 45 minutes in dogs (maximal effect up to 15 minutes) and 25 minutes (maximal effect up to 5 minutes) in cats.[15, 16] Administration of 2 drops, 10 minutes apart in dogs extends maximal effect to up to 25 minutes.[16] **It should be noted, however, that topical proparacaine or tetracaine never be dispensed to pet owners as topical pain management for corneal ulcerations or other ocular surface pain**. Frequent sequential application of topical anesthetics has been shown to significantly delay wound healing, and toxicity to the corneal epithelium may exacerbate existing ulcerations and even incite corneal malacia or "melting".[17]

Conjunctival sensory nerves, unlike those in the cornea, are less superficial and located within the deeper stromal (substantia propria) of the bulbar conjunctiva. As proparacaine does not penetrate very deep into the cornea and conjunctiva, topical proparacaine may not achieve sufficient levels of conjunctival anesthesia, particularly for incisional procedures or biopsies. Furthermore, aqueous proparacaine or tetracaine drops likely do not remain in contact with the conjunctiva long enough to induce sufficient analgesia. Therefore for conjunctival procedures, this author advocates that surgeon's consider local application of 2% lidocaine viscous gel to the intended surgical/procedural site for at least 2 minutes, using a cotton-tipped applicator.

Anesthesia of the Eyelids

For eyelid anesthesia, this author advocates administration of a combination of lidocaine and bupivacaine due to the rapid onset of anesthesia associated with lidocaine (within 1-2 minutes), and the comparatively longer duration of action associated with bupivacaine (approximately 4-6 hours). The technique for achieving eyelid anesthesia is relatively straightforward, typically requiring focal subcutaneous injection of the agent of choice adjacent to the intended surgical site, or alternatively as a line block at several locations along the eyelid(s) for more diffuse anesthesia. Fortunately, the small volumes required (typically 1-2 ml per eyelid, depending on the size of the animal) are not generally associated with systemic toxicity, but caution should be exercised in patients weighing less than 5 kg. For 2% lidocaine, the maximum canine dose of lidocaine to be safely administered is approximately 5 mg/kg (0.25 ml/kg); for 0.5% bupivacaine, the maximum dose is 1.5 mg/kg (0.3 mg/ml).[18] Local adverse reactions are also uncommon, but can be encountered if the agent is injected into a muscle or nerve.[18]

Perioperative Retrobulbar/Peribulbar Analgesia

In dogs, perioperative retrobulbar (RB) anesthesia is increasingly used as an adjunct to systemic analgesia in dogs undergoing routine orbital surgery. Retrobulbar injection with anesthetics such as lidocaine and/or bupivacaine has been shown to improve postoperative pain scores and recovery in canine patients undergoing enucleation.[13] The ideal RB injection technique is one that instills an anesthetic agent sufficiently into the RB muscle cone (intraconal diffusion), as this will produce a more rapid and consistent degree of analgesia. Additionally, the technique should carry a low complication rate and not adversely increase intraocular pressure (IOP). For dogs,

an inferotemporal (IT) approach has been described[19] that specifies use of a 22 gauge spinal (1 and 1⁄2") needle. In the original publication, the IT procedure was compared to two other techniques, proving effective, easy to perform, providing injectate diffusion into the intraconal space, and with low complication rate.[19] Furthermore, this technique did not increase IOP, and administration of 2 ml (total) of anesthetic into the orbits of all dogs adequately perfused the intraconal space while not increasing IOP and was clinically effective. However, a recent anatomical study of the canine skull has derived the formula "0.1 ml/cm of cranial length (approximately from occiput caudally to the midline bony depression between the eyes where the frontal and two nasal bones meet just below the glabella rostrally)" to calculate the suggested volume for intraconal anesthetic injection.[20] According to this study, therefore, volumes of greater than 2 ml may be necessary depending on a canine patient's skull conformation.

Other RB injection techniques have recently been reported for dogs including supero-temporal and peribulbar approaches[21, 22]. Both studies, however, only reported results for cadavers; efficacy and *in vivo* safety are currently unknown. While some practitioners may advocate for ultrasound (US) guidance when performing RB injections, a recent study has demonstrated that use of US had no effect on the quality and duration of RB sensory blockade.[23] Other recent studies have demonstrated comparable postoperative pain control to that achieved with IT injection using an intraoperative "splash" block at the surgical site[24], or implanting anesthetic-infused gelatin hemostatic sponges prior to surgical closure.[25] This author's currently preferred approach to RB anesthesia for routine enucleation in dogs is to: (1) determine total anesthetic volume to be injected using the formula of Klaumann et al (see above); and (2) inject that volume using the IT technique of Accola et al.

In cats, use of RB injections has been controversial, primarily due to concern about the species' small orbital volume and risk for optic traction and chiasmal damage following injection of a large injectate. However, recent investigations have shown the success of a ***peribulbar*** injection technique in achieving intraconal distribution and producing analgesia with low complication rates in cats.[26, 27] In the clinical arm of those studies, a volume of 1.5 ml 0.5% bupivacaine was mixed with 1 ml of sterile saline (and 0.5 ml of radiographic contrast agent) to increase the required volume of injectate which, according to the cadaveric arm, was approximately 3-4 ml. It is noteworthy, however, that these injections in cats do produce transient (~15 minutes) of elevated IOP.

In dogs or cats, transient and mild IOP elevation in an anesthetized animal undergoing routine enucleation is not necessarily a clinical concern. However, if the eye being enucleated is already ruptured or has structurally compromised cornea, transient IOP increase could rupture the globe during surgical preparation or intraoperatively which could increase the risk for infection or complication postoperatively. Therefore, these techniques should be used judiciously. Furthermore, RB injections are contraindicated in the presence of known, active ocular/orbital infection, or extensive ocular or orbital neoplasia.

Complications associated with the IT RB injection technique are uncommon. RB injection using any technique, however, can risk systemic reactions (arrhythmias, hypotension, seizures, death), particularly if the anesthetic is injected into the cerebrospinal fluid around the optic nerve, or into an orbital blood vessel. In healthy cats, systemic exposure to bupivacaine injected into the RB space was approximately 50% that of the dose reported to cause arrhythmia or convulsion, and approximately 17% of that required to produce systemic hypotension.[28]

Adjunctive Systemic Analgesia For Enucleation

Regardless of whether perioperative RB anesthesia is performed in a patient undergoing routine

enucleation, analgesia for the immediate postoperative period should be prescribed by the attending clinician. Historically, numerous mono- and multi-modal approaches using NSAIDs, opioids, synthetic opioids, and/or palliative cold and hot packing have been advocated. There is, however, little to no published evidence supporting the clinical superiority of one approach to another. A recent randomized, masked clinical trial, however, demonstrated evidence that NSAIDs like carprofen may provide more effective postoperative analgesia compared to tramadol.[29] In cats, NSAIDs should be used with caution postoperatively given the risks for renal or hepatic adverse effects. Alternatively, buccal (oral transmucosal) buprenorphine can be administered at 0.02 to 0.03 mg/kg q6h-q8h for 3-5 days postoperatively though no formal clinical studies have been performed to support this.

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