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Ocular pain model and pain scoring in the horse: a pilot study

Introduction

Corneal sensitivity
The eye, the adnexa of the eye, and the orbit are richly innervated, thus creating the potential for substantial discomfort when a pathologic eye problem occurs. The cornea is densely innervated by the ophthalmic branch of the trigeminal nerve (CN V) which makes it one of the most sensitive tissues in the body. Ciliary nerve trunks enter the middle stromal layer of the cornea at the limbus and, collateral fibers arise from the anterior stromal and subepithelial plexi as they travel superficially toward the center of the cornea. These fibers continue to branch and penetrate the epithelium with terminal enlargements at the wing cell level. Corneal sensitivity can be evaluated by the corneal touch threshold (CTT – threshold of the stimulus that results in a corneal reflex) using a Cochet-Bonnet esthesiometer. Similar to other species, the central area of the cornea, was found to be the most sensitive and the dorsal region the least sensitive in healthy horses (1, 3).

Pain model
Standardized pain stimulus is necessary to compare the effect of different analgesic treatment on ocular pain. Our goal is to use a model which provokes long lasting (min 48 hours) pain stimulus so we could assess the response to analgesic therapy, without severe long term consequences like intraocular inflammation, significant corneal scarring or permanent visual impairment. According to personal clinical experiences the signs of inflammation and discomfort associated with simple aqueous paracentesis in horses are short lasting and mild and the intraocular injection of irritant substances can lead to severe consequences. However, pain from anterior uveitis can be different that from an ulcerative keratitis, standardized corneal injury seems to be a less invasive model of ocular pain. However superficial keratotomy may also be considered, but keratectomy may simulate corneal epithelial loss better and may carry less risk for deep corneal infection than keratotomy. Therefore, superficial keratectomy performed with an Algerbrush II (corneal rust ring remover) was chosen as model of experimentally induced acute ocular pain.

Pain scoring
Due to animal welfare reason the treatment of pain became one of the most important tasks of the veterinarians. However, proper pain assessment is crucial for successful analgesic management, unfortunately, there is no „gold standard” to evaluate ocular pain in horses under clinical conditions. Recently, multifactorial pain scales are the favoured methods to evaluate pain in clinical patients as they provide consistent results even if applied by unexperienced observers but they need validation for reliable use. Ideal pain scales enable the recognition of different levels of pain and the follow up and documentation of the response to the treatment (7). As behavioural parameters have been found to be the most reliable indicators of pain in animals, we modified the composite pain scale published by Bussieres et al in 2008 (8) by replacing lameness-related indices with eye-related factors and omitting the insensitive physiological parameters.
The aims of this study are the followings:

1. To detect clinical signs that are associated with ocular pain/inflammation. Another aim is to construct and validate a multifactorial ocular pain scale which enables reliable documentation of progress or deterioration through the treatment.

2. To develop a pain model of acute ocular pain by superficial keratectomy performed with an Algerbrush II (corneal rust ring remover). This method has been selected because it does not cause severe intraocular inflammation, significant corneal scarring or permanent visual impairment.

3. To evaluate the effectiveness of intravenous flunixin meglumine ameliorating the induced ocular pain as there are no established guidelines regarding to its dose reducing ocular discomfort/pain.

**Materials and methods**

**Animals** - Four Hungarian half-breed horses with healthy eyes owned by the Szent Istvan University are included in the study after complete ophthalmic examinations using slit lamp and direct ophthalmoscope. The age of the horses ranges from 3 to 19 years. This study is performed with the approval of the institutional Animal Care and Use Committee of the Szent Istvan University in compliance with the guidelines of the Hungarian Animal Care Act.

**Procedures**

Experimental design: prospective, randomized, cross-over, blinded, placebo-controlled study using the superficial keratectomy as acute ocular pain model.

**Phase I**: All horses are medicated according to their weight with detomidine (0.02 mg/kg IV) to provide strong sedation. Frontal and auriculopalpebral nerve blocks (1 ml of 2% lidocaine at each site) and topical anaesthesia with oxybupracaine (Humacain eyedrop) are performed on the first eye. A 6 mm central corneal epithelial and superficial stromal round lesion is created by using an Algerbrush II corneal rust ring remover while supporting the head and holding the upper eyelid manually. After the procedure, clinical signs such as blepharospasm, swelling of the eyelids, miosis, corneal edema or opacification, epiphora, comfort, behaviour are recorded by clinical observation and taking photographs at 0, 1, 2, 4, and 6h, than every 6h until corneal wound is healed. The modified multifactorial acute ocular pain scale is also completed every time point by a blinded observer. Randomly selected 2 horses receive 1.1 mg/kg flunixin meglumine intravenously q24h right after the procedure (treatment group), the other 2 horses receive the same volume of sterile saline IV q24h (placebo-control group). The intensity of tearing and blepharospasm are scored from 0 to 3 (most severe tearing: 3 scores, no tearing: 0 score) as the part of the pain scale. Heart rate and respiratory rate are recorded as they were found to be the only sensitive physiological parameters when orthopaedic pain was evaluated in horses. The photos are evaluated by a board certified ophthalmologist blinded to
the treatment. The clinical pain scales are used to assess the analgesic effects of flunixin. All horses receive topical antibiotic ophthalmic ointment (oxytetracycline, Tetran eye ointment) q8h until healing (approx. for 1-2 weeks), but other analgetics are not administered. The healing of the corneal lesion is monitored regularly and checked by Fluorescein staining. If more than 30% of the total pain scores are allocated, 0.1 mg/kg morphine IM will be given to the horse as rescue analgesia.

**Statistical analysis:** Pain scores between groups are compared with the Mann-Whitney U test to compare the effect of treatment with control on ocular pain.

Results are presented and discussed on the lecture.

**References**


