A Review of Recent Advancements in the Surgical Treatment of Equine Recurrent Uveitis

Brian C. Gilger, DVM, MS, and Janice B. Allen, PhD

Intravitreal cyclosporine devices (IVCsA) and core vitrectomy (CV) are relatively new treatments for long-term control of equine recurrent uveitis (ERU). IVCsA are indicated for eyes with progressive ERU but minimal ocular changes. CV is indicated for predominantly posterior ERU or in eyes with significant ocular changes in advanced stage ERU. Author's address: Departments of Clinical Sciences (Gilger) and Anatomy, Physiology and Radiology (Allen), College of Veterinary Medicine, North Carolina State University, 4700 Hillsborough Street, Raleigh, North Carolina 27606, USA. © 2001 AAEP.

1. Introduction

Equine recurrent uveitis (ERU) is a recurrent, painful ocular disease that is the leading cause of blindness in horses worldwide. In the United States, 8–25% of horses are affected with ERU. ERU is characterized by episodes of intraocular inflammation that develop weeks to months after an initial uveitis episode subsides. In active, recurrent bouts of ERU, a breakdown of the blood–ocular barrier occurs, with infiltration of inflammatory cells and protein, miosis, iris hyperemia, corneal edema, and ocular discomfort. These active bouts may last days or weeks, then gradually resolve, resulting usually in a relatively comfortable quiescent period. Each recurrent episode imparts permanent damage to the eye. Ultimately, even with aggressive treatment, many horses develop a chronically painful eye and blindness as a result of secondary cataract, synechia, scarring, and development of phthisis bulbi.

Eyes from horses with chronic ERU have infiltration of mononuclear cells consisting predominantly of CD4+ T-lymphocytes, exhibiting an elevated interleukin-2 (IL-2) and gamma interferon and low IL-2 cytokine profile (Th1-like response). This suggests that in chronic ERU, the inflammation is non-specific and immune-mediated and that the reaction is not in response to specific microorganisms.

Traditional treatments used for ERU (i.e., corticosteroids and non-steroidal anti-inflammatory medications) are aimed at reducing inflammation and minimizing permanent ocular damage at each active episode. They are not effective in preventing recurrence of disease. Other medications used to prevent or decrease severity of recurrent episodes, such as aspirin, phenylbutazone, and various herbal treatments, have limited efficacy and potential detrimental effects on the gastrointestinal and hematologic systems when used chronically in the horse.

Two recently described surgical procedures are aimed at preventing the recurrence of uveitis and therefore provide long-term control of the disease. Intravitreal cyclosporine devices (IVCsA) release locally a constant low level of cyclosporine A, a potent immunosuppressant, into the vitreous. The
placement of the device into the vitreous overcomes the fact that CsA is hydrophobic and penetrates into the eye minimally when applied topically. Core vitrectomy (CV) is another recent surgical advancement for the treatment of ERU and it is used to replace diseased, inflamed vitreous in eyes with ERU with saline. This technique is used widely in Europe and is beginning to be used in the U.S.

The purpose of this review article is to describe these two new surgical techniques for ERU and to compare their indications, surgical technique, complications, and long-term results.

2. Literature Review

Intravitreal cyclosporine A

A polyvinyl alcohol/silicone-coated intravitreal CsA sustained-delivery device that has been shown previously to produce a sustained level of CsA in ocular tissues (rabbit) was evaluated for use in horses. A CsA device was implanted into normal horse eyes for up to 1 yr and was not associated with ocular inflammation or complications. In equine eyes with experimentally-induced uveitis, the IVCsA decreased the duration and severity of inflammation, cellular infiltration, tissue destruction, and level of transcription of pro-inflammatory cytokines. The 2 × 3 mm device releasing 4 μg/day of CsA is placed into the vitreous through a full-thickness scleral and pars plana incision, and anchored into place by suturing the stem of the device into the scleral incision. The estimated time that the device will continue to deliver medication is 5 yr.

In a recent study using IVCsA in horses with naturally-occurring ERU, horses with frequent recurrence of uveitis without vision threatening ocular changes (i.e., cataracts, retinal degeneration) or systemic illnesses were selected to receive the device. Few complications occurred during and after surgery. Only 2 of 16 horses had severe complications after surgery resulting in vision loss: one horse with retinal detachment and one with a mature cataract formation. Few recurrent episodes of uveitis were noted with only 3 (19%) developing any evidence of uveitis after device implantation and vision was judged to be normal in 14 of 16 horses (88%) at a mean follow up of 13.8 months (range 6–24 months).

Core vitrectomy

There have been few English publications describing this surgical technique, but there have been several abstracts and articles in German veterinary journals describing this surgery. This surgery uses a single-port, nearly total vitrectomy, in which an incision is made 1 cm posterior to the dorsolateral limbus, through the pars plana, and into the vitreous. The vitreous is removed and replaced by saline or balanced salt solution. Removal of T cells or organisms from the vitreous is the goal and this is thought to decrease the recurrent episodes of uveitis. In fact, the surgery reportedly decreases ERU recurrence by 92%.

However, the goal of this surgery is to halt the progression and recurrent episodes of uveitis, not necessarily preserve vision. In one study, approximately one-third of the cases were deemed blind months after surgery and the authors observed a decrease in vision despite a decrease in recurrent episodes. This may be due to a high percent of cataract formation after surgery. In the only English publication of this surgical technique, of animals reexamined by the surgeons, 12 of 27 (45%) had “significant” cataract formation. This surgical technique was recommended to help preserve vision (but not to increase vision), decrease recurrent episodes, and to avoid enucleation. Studies of CV done in the United States indicate that there is a high percentage of cataract formation after surgery and most horses have decreased vision, however the episodes of uveitis seem decreased.

Both IVCsA and CV are being evaluated at several areas in the U.S. for long-term control of ERU. There are 6 sites across the United States that are currently performing the IVCsA procedure, but all ophthalmologists with facilities for equine ocular microsurgery could perform this surgery. Fewer locations are currently performing the CV in the U.S., including the University of Florida, and our University at North Carolina. A comparison of CV and IVCsA surgical techniques is provided in Table 1.

3. Discussion

Sustained-release IVCsA drug delivery devices and CV may be important tools for the long-term control of equine uveitis. Although the IVCsA device is expected to deliver 4 μg/day of CsA for approximately 5 years, if recurrent episodes recur after 5 years, a second device could be implanted. Control of uveitis after 5 years has not been reported with CV, but long-term results indicate that there is minimal recurrence of uveitis. With the IVCsA device, because it delivers medication constantly, reliance on the owner to treat a potentially painful eye is eliminated, thus increasing the likelihood of success in the long-term treatment of ERU.

Selection of appropriate horses to receive the IVCsA device or CV is very important for long-term success after surgery. Chronic uveitic changes in the eye, such as synechiae, corneal edema, glaucoma, vitreal degeneration, and retinal atrophy, will decrease vision in the eye and decrease the long-term success of the IVCsA because these changes cannot be reversed. Cataracts should be especially avoided when selecting patients for implantation. In a previous study using a CsA device releasing 2 μg/day in horses, cataracts involving approximately 25% of the lens or more continued to progress despite the fact that recurrent episodes of inflammation were largely eliminated. Cataract
formation is even more common after CV, with nearly 45% of cases that were followed developing significant cataract formation.13

The goal of both IVCsA and CV is to prevent further inflammatory episodes and thereby prevent additional chronic damage to eyes. Eyes with less chronic changes are better candidates for IVCsA surgery with a 4 μg/day device because these vision-threatening complications may be prevented. However, eyes with more chronic changes and significant cataract formation (>25% of the lens) may be better candidates for CV. With chronic changes in the eyes (i.e., cataract formation, posterior synechia, retinal degeneration, etc.), CV may not return or preserve vision, but it may decrease the number and severity of recurrent episodes of uveitis, thereby keeping the eye comfortable and eliminating the need for enucleation. However, use of CV for routine control of sighted ERU eyes is not recommended because of the high cataract formation rate.

IVCsA and CV are relatively new treatments for long-term control of ERU. IVCsA are indicated for eyes with progressive ERU but minimal ocular changes. CV is recommended for predominantly posterior ERU and in eyes with significant ocular changes (i.e., synchiae, cataract, vitreal degeneration, and retinal atrophy) in advanced stage ERU.

The authors acknowledge funding from the State of North Carolina, the Veterinary Equine Research Center Foundation, and the National Institutes of Health (grant #EY11364, JBA). The authors also acknowledge technical assistance provided by Patricia Rose, Elaine Smith, and Kelley Norris. The authors do not have financial interest in any of the products or procedures described in this article.

Table 1. Comparison of Surgical Techniques for Equine Recurrent Uveitis

<table>
<thead>
<tr>
<th>Stage of ERU</th>
<th>Core Vitrectomy</th>
<th>Intravitreal Cyclosporine A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General anesthesia?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Specialized surgical equipment?</td>
<td>Yes—vitrectomy unit modified for use in horses</td>
<td>No—Standard microsurgery/ophthalmic instrumentation</td>
</tr>
<tr>
<td>Length of procedure</td>
<td>Extensive, long</td>
<td>Simple, short</td>
</tr>
<tr>
<td>Number of horses treated</td>
<td>500–1000 in Europe</td>
<td>Less than 100</td>
</tr>
<tr>
<td>Long-term results</td>
<td>Good control of recurrent episodes, significant cataract formation in 40–45%</td>
<td>Excellent (88%)</td>
</tr>
<tr>
<td>Potential for blinding complications?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cost</td>
<td>Approximately $3000–4000</td>
<td>Approximately $1500</td>
</tr>
<tr>
<td>Availability</td>
<td>Not widely available in the U.S. (University of Florida and North Carolina State University currently performing procedure)</td>
<td>Limited, device not commercially available (approximately 6 sites performing procedure throughout U.S.)</td>
</tr>
</tbody>
</table>

References and Footnote


*Personal communication, Dr. Dennis Brooks, University of Florida, February 2001.