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INTRAVITREAL INJECTION OF GENTAMICIN IN DROMEDARY CAMEL WITH UVEITIS

Turke Shawaf
Department of Clinical Sciences, College of Veterinary Medicine and
Animal Resources, King Faisal University, Al Hasa, Saudi Arabia

ABSTRACT

This study was aimed to evaluate intravitreal injection of gentamicin in cases of uveitis in camels. Eighteen camels that suffered from anterior, posterior or panuveitis were included in the present study. Complete ophthalmic examinations were performed before and following the treatments and these were treated with a 4 mg gentamicin which was injected intravitreally together with topical antibiotics for one week, and topical nonsteroidal anti-inflammatory drugs over the course of 2-6 weeks based on each camel's individual response to therapy. One third camels (33%) affected with uveitis had poor vision before the treatments, while vision was not improved by 10% after six months improvement of vision was seen from 41-75% after one year of intraocular injection of gentamicin. The results of this study showed that the intravitreal gentamlcin injection in camel affected with anterior uveitis, posterior uveitis and panuveitis help in healing and improved the vision.

Key words: Camel, gentamicin, intravitreal, ophthalmology, uveitis

Ocular affections in camels, like in most other livestock, can cause a debilitating condition that can severely affect animal productivity (Bishnoi and Gahlot, 2004; Fahmy *et al,* 2003; Kumar *et al,* 2016). However, camels are prone to eye injuries while browsing from trees and thorny weeds and it results into corneal wounds and injuries to the outer parts of the eye (Abdella *et al,* 2018; Bishnoi and Gahlot, 2004). Moreover, camels suffer from a wide range of ophthalmic affections, which causes anterior and posterior eyes infection (Abdella *et al,* 2018; Fahmy *et al,* 2003; Gebreyohanes and Assen, 2017). Occasionally, damage to the eye can be severe enough and may lead to blindness (Abdella *et al,* 2018).

Uveitis is characterised by exceptionally wide heterogeneity, regarding both oetiology and symptoms (Laven and Lawrence, 2006; Malalana *et al,* 2017). The pathophysiology and course of the disease are complex and multifactorial associated with various symptoms (Rojas-Carabali *et al,* 2021). The classic signs of uveitis are episcleral congestion, epiphora, corneal oedema, blepharospasm, aqueous flare and fibrin in the anterior chamber (Fingerhut *et al,* 2019; Rojas-Carabali *et al,* 2021). The chronic from of uveitis may lead to irreversible complications (Fischer *et al,* 2019; Rojas-Carabali *et al,* 2021). Few reports described uveitis in camels (Abdella *et al,* 2018; Fahmy *et al,* 2003; Gahlot, 2000; Madany *et al,* 2006) and there are no specific treatments reported for uveitis in camels except local and systemic anti-inflammatory treatment (Bishnoi and Gahlot, 2004; Madany *et al,* 2006). Recently, uveitis is being treated in veterinary medicine in many surgical procedures like pars plana vitrectomy in horses, dogs and non-human primates (Fingerhut *et al,* 2019; Fruhauf *et al,* 1998; Hirashima *et al,* 2022; Hopster *et al,* 2013; Tshilenge *et al,* 2016). However, intravitreal injection of gentamicin in horses (Fischer *et al,* 2019), suprachoroidal injection of triamcinolone in horses (Gagnon *et al,* 2021) and cidofovir injection in dogs with chromic glaucoma (Low *et al,* 2014) has been reported.

Several recent studies indicated the good efficacy of gentamicin in equine recurrent uveitis (ERU) (Fischer *et al,* 2019; Kleinpeter *et al,* 2019; Launois *et al,* 2019).

This study was, therefore, aimed to evaluate the efficacy of single-dose intravitreal injections of gentamicin in cases of uveitis of camels.

Materials and Methods

Ethical approval

The study was approved for research purposes by the Ethics Committee at King Faisal University in Saudi Arabia (Approval number: KFU-REC-2021-OCT-EA00010).

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Animals

Camels (aged 2-18 years) with uveitis (n=18; male=7, females=11) brought to the Veterinary Teaching Hospital, College of Veterinary Medicine, King Faisal University were selected. The uveitis was unilateral (n=9) and bilateral (n=9). Further clinical examination revealed panuveitis (n=12), anterior uveitis (n=2) and posterior uveitis (n=4). Complete history, clinical examination, ocular examinations using ophthalmoscope and ultrasound were performed in Veterinary Teaching Hospital. The clinical signs of uveitis were conjunctival congestion, miosis, epiphora, blepharoedema or blepharospasm, aqueous flare, photophobia, fibrin in the anterior chamber, equatorial vesicular cataracts, capsule adhesions, lens vitreous body opacifications, and retinal detachment. This study was conducted from March 2020 to January 2022.

Ocular examination

After history and clinical examination, complete ophthalmic examinations were performed to differentiate between anterior (Fig 1B) and posterior and panuveitis (Fig 1A) by evaluation (dazzle, and pupillary light reflexes (PLR)), slit-lamp biomicroscope (Kowa SL-15) (Kowa Company Ltd., Tokyo, Japan) and a subjective clinical vision assessment (menace response) and neuro-ophthalmic indirect ophthalmoscopy (Heine Beta 200 and Heine Omega 500; Heine Optotechnik, Herrsching, Germany). Aqueous flare was graded as follows: 0 (none), 1 (faint), 2 (moderate), 3 (severe) or 4 (blood

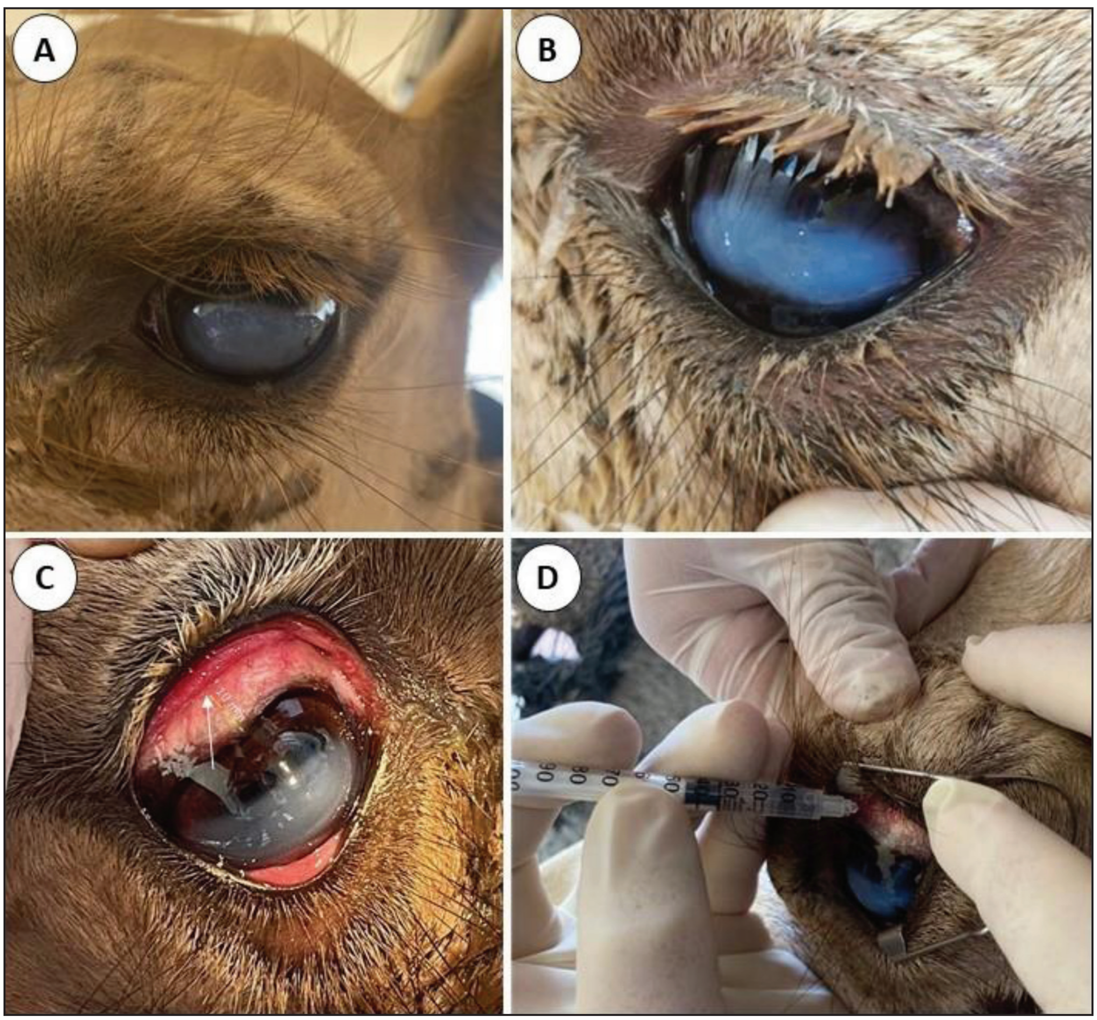

Fig 1. (**A**) Five-year old camel presented for a persistent chronic panuveitis of the left eye with an accumulation of fibrin in the anterior and posterior chamber, blepharospasm and miosis were present. (**B**) Twelve-year old camel affected with anterior uveitis with epiphora, corneal oedema, and blepharospasm. (**C**) This image shows the place of intravitreal injection, where the yellow dashed line indicates the distance between the upper part of the cornea and the place of injection (10 mm); the white arrow showed the position of injection. (**D**) This image shows the intravitreal injection after opening the eye using a Barraquer eyelid speculum; the injection is done using a 30-gauge needle/syringe combination.

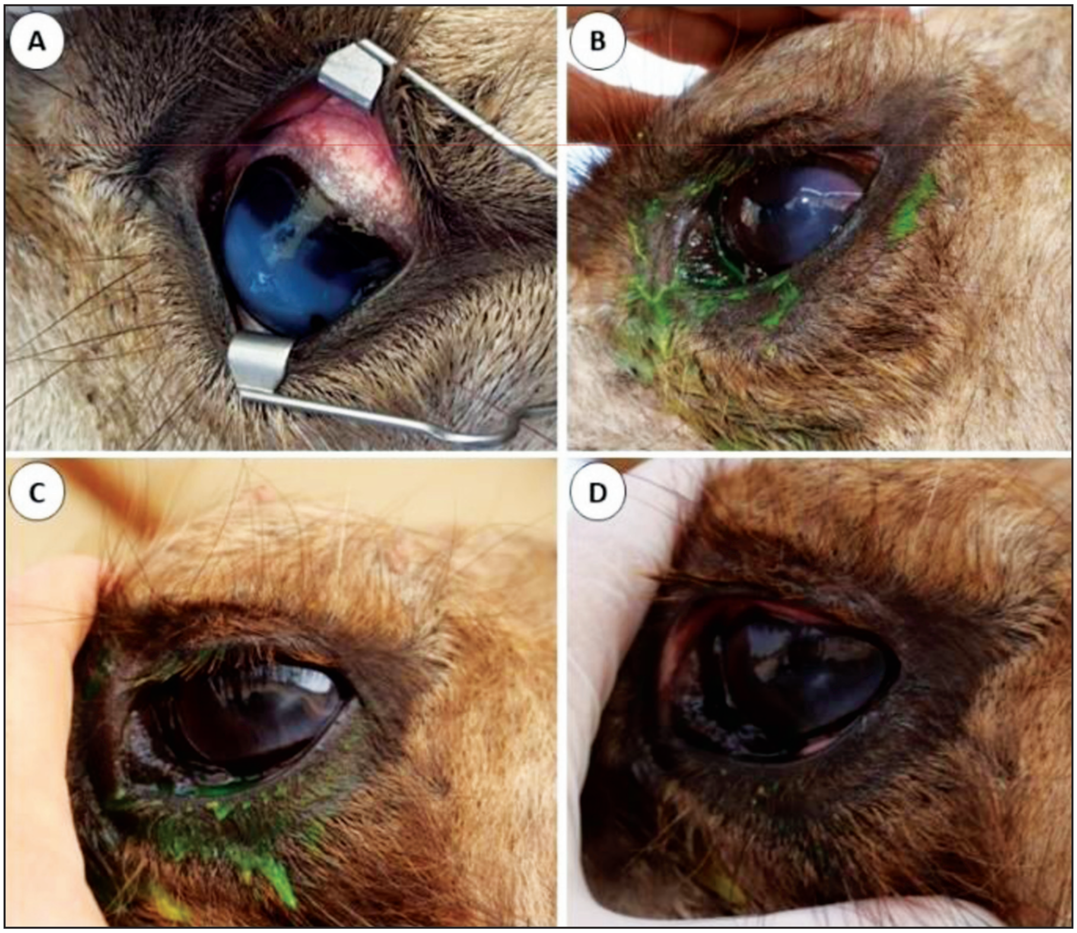

Fig 2. (**A**) Twelve-year old camel before the intravitreal injection presented with anterior uveitis with corneal oedema and overall cloudiness. (**B**) Four weeks after injection: Slight reduction in cloudiness and fibrin in the anterior chamber. (**C**) Six months after injection: reduced corneal oedema (by 50%), cloudiness with improved vision. (**D**) One year after injection: more reduced cloudiness than six months ago; the vision was restored to a moderate degree.

or fibrin present in the anterior chamber) (Lam *et al,* 2015). Fundus images were obtained by Kowa Genesis (Kowa Company Ltd., Tokyo, Japan) in camels with posterior segment abnormalities, whenever possible.

Sedation and intravitreal gentamicin injection

Each camel was sedated with intravenous injection of xylazine 2% (0.1 mg/kg bodyweight; Rompun, Bayer Health Care), and an auriculopalpebral nerve block (1.5 mL lidocaine SC, 2% Lidocain inj., Teva) was performed on the respective eye. Topical oxybuprocaine (Novesine 0.4% eyedrops, OmniVision) was used for topical corneal analgesia. However, eyelids were held open manually. The ocular surface was first irrigated with 0.5% povidone-iodine solution (Betadine, Egis) and then rinsed with saline. Following sedation, the camel's head was positioned atop a pair of pads placed on a ground to increase stability. The conjunctival fornices were irrigated with 1.0 ml of baby shampoo solution (0.1% dilute in saline solution), 1.0 ml of a 1.0% dilute iodine solution, and 1.0 ml of balanced saline solution (Brooks *et al,* 2017). Dorsal globe exposure was facilitated with prototype eyelid retractor, and further enhanced by rotating the camel's head away from the examiner to exaggerate ventral globe rotation. Camels were treated with a 4 mg injectable gentamicin solution containing preservatives (Genta80; 80 mg/ml) which was drawn up in a 30- gauge needle/syringe combination (12mm length, 1.0 ml insulin syringe) (Fig 1D). The injection site was 10 mm posterior to the limbus at 12 o'clock (Fig 1C). Due to the difficulty of accurately measuring and determining the injection point with calipers, the injection point was roughly estimated by the examiner immediately before the injection. The injection was facilitated by applying gentle but steady pressure while slowly and deliberately rotating the needle in a clockwise manner with the needle directed toward the optic nerve head to avoid inadvertent contact

Fig 3. (**A**) Three-year old camel before the intravitreal injection presented with chronic panuveitis with secondary keratitis. (**B**) Six months after injection: Uveitis remained controlled without medical treatment; the keratitis was reduced. (**C**) This image shows the intravitreal fluid withdrawn from the right eye at 1:00 o'clock after opening the eye using a Barraquer eyelid speculum; the aspiration was done slowly using a 23-gauge needle/ syringe combination.

with the lens. Same fluid quantity from vitreous was withdrawn using a second insulin syringe with 23-gauge needle at either the 11:00 o'clock (left eye) or 1:00 o'clock (right eye) positions in order to keep the same fluid pressure in the ocular and this fluid was used for more investigations (Fig 3C).

Post-injection therapy and Follow-up examination

Post intravitreal injection, a medical therapy consisting of topical antibiotics (Oxytetracyclin) q12h for one week, and topical nonsteroidal anti-inflammatory drugs (NSAIDs) that were gradually tapered over the course of 2-6 weeks based on each camel's individual response to therapy. Systemic Flunixin-meglumine @ 1.1mg/kg, q24h was also administered intravenously for 7 days. Camels were monitored weekly for the first month. Subsequent follow-up examinations were spaced further apart based on the camel's individual response to treatment. Inflammation was markedly reduced which was evident by absence of signs of uveitis (Fig 2A, B, C, D and Fig 3A, B).

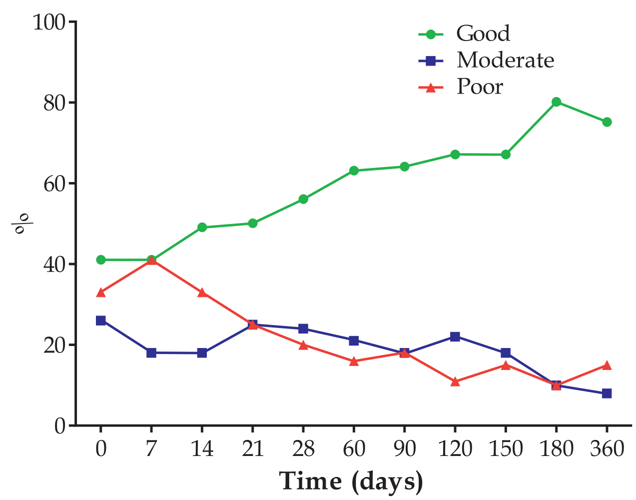

Fig 4. Changes in vision after intravitreal gentamlcin injection.

Statistical analysis

The obtained data was recorded in Excel spreadsheets and imported into Graph Pad Prism 7 (GraphPad Software, San Diego, CA, USA) software for further analysis. Graphs, calculations, and

Table 1. Subjective visual assessment pre- and post-intravitreal gentamicin injection (days).

Time (days)	Camels	Eyes	Unilateral/ bilateral	Improvements eyes (%)		
				Good	*Moderate*	*Poor*
Pre-injection (0 days)	18	27	9/9	11 (41%)	7 (26%)	9 (33%)
Post-injection (7 days)	18	27	9/9	11 (41%)	5 (18%)	11 (41%)
Post-injection (14 days)	18	27	9/9	13 (49%)	5 (18%)	9 (33%)
Post-injection (21days)	18	27	9/9	13 (50%)	7 (25%)	7 (25%)
Post-injection (28 days)	18	25	9/8	14 (56%)	6 (24%)	5 (20%)
Post-injection (60 days)	16	24	8/8	15 (63%)	5 (21%)	4 (16%)
Post-injection (90 days)	15	22	8/7	14 (64%)	4 (18%)	4 (18%)
Post-injection (120 days)	15	22	8/7	15 (67%)	5 (22%)	2 (11%)
Post-injection (150 days)	15	22	8/7	15 (67%)	4 (18%)	3 (15%)
Post-injection (180 days)	14	20	8/6	16 (80%)	(10%)2	2 (10%)
Post-injection (360 days)	8	12	4/4	9 (75%)	1 (8%)	2 (15%)

statistical analyses were performed using GraphPad Prism software.

Results and Discussion

The information is limited about treatment of uveitis in camels; therefore. the main goal of this study was to conduct clinical trial of the intravitreal injection of gentamicin to treat the uveitis by minimising ocular inflammation and restoration of vision to a varying degree (Fischer *et al,* 2019; Gerding and Gilger, 2016; Wollanke *et al,* 2022). However, the pharmacodynamics of gentamicin in the all types or stages of uveitis remains enigmatic (Fischer *et al,* 2019; Gan *et al,* 2001; Kleinpeter *et al,* 2019; Wollanke *et al,* 2022). Romeike *et al* (1998) reported that the primary mechanism of action of gentamicin could suppress or block the activation of specific T-cell that are identified to play a significant role in autoimmune uveitis. While, many studies in recent years reported successful treatments of equine recurrent uveitis affected with Leptospira using intraocular gentamicin injection due to the direct effect of gentamicin on gram-negative bacteria and improvement was noticed within days of starting treatment (Fischer *et al,* 2019; Voelter *et al,* 2020; Wollanke *et al,* 2022).

In present study, no difficulties were found in intraocular injection in camels under sedation and local anesthesia except the posterior movement of the eye, which was more than described in horses or humans (Ganapathy *et al,* 2018; Jose-Vieira *et al,* 2021; Yi *et al,* 2008). In animals of present study, the eye was pushed and fixed it in the anterior part of the orbital cavity directly before the injection by applying pressure in medial side of the zygomatic process to expose the eye in order to facilitate the injection process. A difficulty was noticed in withdrawing the vitreous humor samples using the 30-gauge needle but fluid withdrawal was easy and safe with 23-gauge needle as in equine (Ackermann *et al,* 2021). One of the limitations of this study was the difficulty in follow up of the treatment with the owners, especially keeping the camel in the shade during the first days after treatment, which may have an impact on the results of the treatment.

In present study, 62% of eyes of affected camels had panuveitis, while the incidence of posterior and anterior uveitis were 27% and 11%, respectively. However, studies are scarce about the type of uveitis in camels (Kumar *et al,* 2016; Madany *et al,* 2006). A similar increased percentage of panuveitis type was recorded in horses (Ackermann *et al,* 2021; Fischer *et al,* 2019; Wollanke *et al,* 2022), while a higher percentage for anterior uveitis was reported in humans (Roche *et al,* 2021; Silvestri *et al,* 2020). The results of this study showed that the intravitreal gentamicin injection in camel affected with anterior uveitis, posterior uveitis and panuveitis helped in healing and improved the vision (Fig 2 and 3). On the other hand, three eyes in two camels developed cataracts, retinal degeneration and loss of vision after intraocular injection. Therefore, the risks of injection cannot be ignored, and must be discussed in detail with the owner before starting the treatment options (Fischer *et al,* 2019; Launois *et al,* 2019). In this study, nine eyes (Table 1 and Fig 5) (33%) affected with uveitis had poor vision before the treatments, while the vision decreased to 10% after six months of intraocular injection of gentamicin which was in agreement with result of Fischer *et al* (2019) and Kleinpeter *et al* (2019) for treatments of equine recurrent uveitis. The increased percentage of good vision improvement of eyes was from 41% to 75%

after one year of treatment indicated the effectiveness of intravitreal injections of gentamicin in animals of present study (Fig 2D). The stability of equine recurrent uveitis with reduction of ophthalmological symptoms and an improvement in vision after intravitreal injection with a single low dose of gentamicin was seen (Fischer *et al,* 2019; Kleinpeter *et al,* 2019; Wollanke *et al,* 2022). However, two camels of present study suffering from unilateral panuveitis continued to have poor vision even after one year of the treatment (Table 1).

In conclusion, intravitreal injection in camels affected with uveitis can be treated by intervitseal injection of gentamicin. However treatment and after care protocol needs more attention.

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