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# Diagnostic and therapeutic management of deep corneal ulcers in dogs

**Arukontham Deepika, P Nagaraj, VVV Amruth Kumar, M Usha Rani and K Satish Kumar**

**Abstract**
Corneal ulcers or ulcerative keratitis is one of the most common eye diseases in dogs. During the present investigation 1850 dogs were presented to ophthalmic ward of these 52 dogs were detected with corneal ulcers of which 20 dogs were detected as Deep corneal ulcers based on ophthalmic examination, Fluorescein stain test (FST) and Ocular Surface Test. These were divided into two groups and treated with two different treatment regimens. Group I were treated with 0.1% Tacrolimus, 0.5% moxifloxacin and Oral Doxycycline and dietary nutrient supplements. Group II were treated with 0.1% cyclosporine, 0.5% moxifloxacin and Oral doxycycline and dietary nutrient supplements for a period of 1 month. After 1 month of therapy in both the groups, group I showed significant improvement in clinical findings and ulcer healing than group II.

**Keywords:** Deep corneal ulcer, tacrolimus, cyclosporine, slit lamp examination and fluorescein stain test

## Introduction
The cornea is transparent structure and is a part of the outer layer of eye which plays a vital role in vision. It refracts the light and protects content of the eye. Corneal ulcers or ulcerative keratitis is one of the not common eye diseases in domestic dogs (Gilger 2007) [2]. A corneal ulcer is present when there is break in the corneal epithelium that exposes the underlying corneal stroma (Nassisse, 1985) [6]. Corneal ulcers are very commonly encountered in veterinary practice. It is common disease encountered in domestic animals, especially in dogs. Although corneal ulcer is usually traumatic in origin, it may rapidly become contaminated with bacteria. Depending of the number of affected cornel layers, they can be superficial corneal ulcers which are characterized by loss of corneal epithelium and exposure of corneal stroma without stromal loss (Gelatt *et al*., 2013) [7] and Deep corneal ulcers involve stromal layers and Descement's membrane. A detailed ophthalmic examination with direct and indirect ophthalmoscope revealed involvement of stroma which was detected with the help of fluorescein stain test and slit lamp examination.

## Materials and Methods
The study was carried out from December 2020 to August 2021 at veterinary Clinical Complex, Veterinary Hospital, Bhoiguda and Campus veterinary Hospital, College of Veterinary Science, Rajendranagar, Hyderabad.
A total of 52 cases were identified with corneal ulcers based on ophthalmic examination and conducting fluorescein stain test on 1850 dogs presented to the ophthalmology ward formed the material for the present study. Among them 20 were detected with Deep corneal ulcers.
During the study, Ophthalmic examination using direct and indirect ophthalmoscope and slit lamp were employed for detection of corneal ulcers as per the procedure outlined by Ollivier *et al.*, 2007 Heine DO Mini 3000 Ophthalmoscope was used for direct ophthalmocopy in dogs during the present study under dark settings. The sequence of examination was optic nerve/optic disc, tapetal fundus, non-tapetal fundus, fundic periphery, retinal vascualture, vitreous body, lens, pupil, iris, anterior chamber and cornea.
Ocular surface test which include Schirmer tear test (STT-I), Ocular ferning test and Tear film break up time (TFBT).
Fluorescein stain test was conducted as described by Ollivier *et al*., 2007 [2]. Fluorescein stain test (FST) was conducted in the dogs to detect the corneal ulcers in the eye using sodium fluorescein dye impregnated sterile paper strips.

20 dogs detected with deep corneal ulcers were divided into 2 different groups and treated with 2 different therapeutic regimens of which group 1 were treated with 0.1% Tacrolimus, 0.5% Moxifloxacin and Oral Doxycycline and dietary nutrient supplements. Group II were treated with 0.1% cyclosporine, 0.5% moxifloxacin and Oral doxycycline and dietary nutrient supplements for a period of 1 month.

**Fig 1:** Instrument used for conducting direct ophthalmoscopy


**Fig 2:** Instrument used for conducting indirect ophthalmoscopy

**Fig 3:** Measuring tear wetting

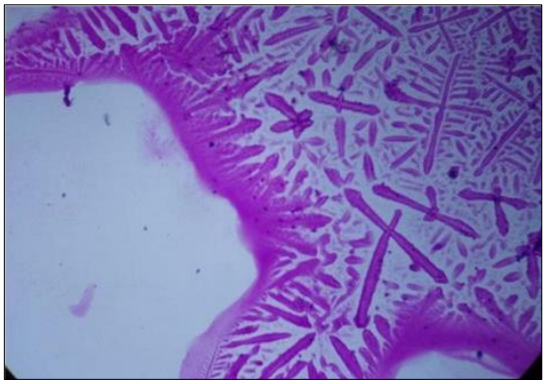

**Fig 4:** Appearance of normal tear film on Ocular Ferning Test with good uniformity, integrity, ferning with few cells.

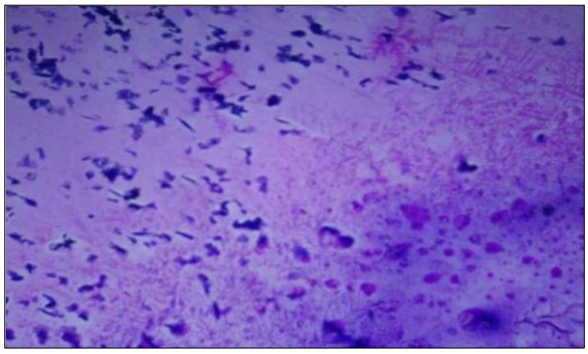

**Fig 5:** Appearance of abnormal tear film on Ocular Ferning Test with loss of uniformity, branching, ferning with keratinized cells

**Fig 6:** Appearance of dark spots in tear film on cornea in tear film breakup time (TFBT) estimation

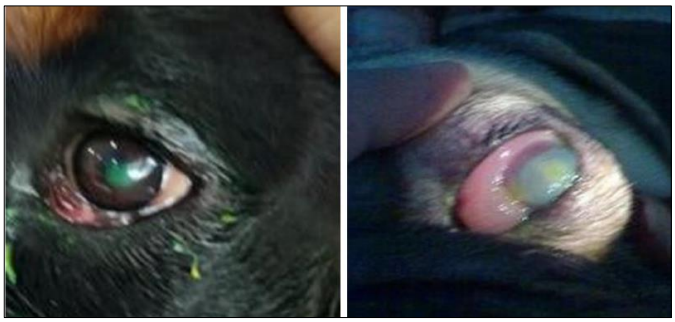

**Fig 7:** Retention of topically applied fluorescein dye by corneal ulcer on Fluorescein stain test (FST) Staining using (a) sodium fluorescein dye impregnated sterile paper strips (b) Superficial Corneal Ulcer (c) Deep Corneal Ulcer

## Results and Discussion

The dogs in the both the groups showed improvement in clinico-ophthalmic signs within 15 days of treatment. The regimen showed good therapeutic efficacy in all (100%) dogs. On comparison, the treatment efficacy between the drug regimens of the Groups, I and II in Deep corneal ulcers were found non-significant. Kaswan and Salisbury (1990) [8] reported Cyclosporine (CsA) as a naturally occurring fungal metabolite which exhibited lacrimostimulant and lacrimomimetic properties in Keratoconjunctivitis Sicca (KCS) affected dogs with significant improvement in tear wetting. Kaswan *et al.* (1989) [9] reported for the first time the immunosuppressive activity in ocular condition *viz*. KCS due to its binding of specific nuclear proteins that were required for initiating T-cell activation. They observed activation of the Tcells resulted in production of inflammatory cytokines *viz*. Interleukin-2 (IL-2), IL-4, primarily involved in immune-mediated processes. According to them, Cyclosporine formed

a complex with the cytosolic protein 'cyclophilin' and inhibited the phosphatase activity of calcineurin which was found activating the T-cells. Moore *et al.* (2001) [10] also reported the direct effects of Cyclosporine on the conjunctival goblet cells with improved mucus production in experimentally induced KCS dogs. Similar observations were made by Palmar *et al.* (1995) [11], Tilley and Smith (2007) [12], Hendrix *et al.* (2011) [17], Nagaraj (2011) [4] and Rani (2018) [14] in dogs affected with corneal ulcers. The good therapeutic results achieved during the present study supported the observations of the above authors.

Berdoulay *et al.* (2005) [15] reported Tacrolimus as a newer immunosuppressant agent used for the treatment of immune mediated KCS in dogs. Schreiber and Crabtree (1992) [16] reported Tacrolimus as a macrolide antibiotic isolated from *Streptomyces tsukubaensis* that shares a similar immunomodulatory action with Cyclosporine (CsA)**.** Tacrolimus acts as a calcineurin inhibitor that reversibily inhibits T-cell proliferation and prevents the release of proinflammatory cytokines. The calcineurin inhibitors bind to intracellular immunophillins and form complexes that subsequently bind to and inhibit calcineurin. On blocking calcineurin the translocation of the cytoplasmic components of the nucleus was thus prevented. The prevention of translocation impairs transcription of the genes encoding IL-2 and other cytokines, thereby suppressing T- cell proliferation and normal immune function. Hendrix *et al.* (2011) [17] reported Tacrolimus as a good lacrimomimetic and found effective in increasing the STT-I values in dogs which were nonresponsive to Cyclosporine. Similar observations were made by Radziejewski and Balicki (2016) [18] and Zulim *et al.* (2018) [19] in KCS affected dogs. The good therapeutic results achieved during the present study supported the observations of the above authors.

During the present study, 0.5% Moxifloxacin ophthalmic drops was preferred over Enrofloxacin and Gentamycin as it achieved good broad spectrum activity against Gram positive and Gram negative organisms in corneal ulcers affected dogs. Townsend (2007) [20] stated that topical fluoroquinolones can be effective in treating infected corneal ulcers. However, Lin *et al.* (2007) [21] and Nagaraj (2011) [4] have used ciprofloxacin in their treatments.

Gelatt (2014) [7] reported corneal epithelial cells, fibroblasts, polymorph nuclear leucocytes, and some microorganism produce proteases and collagenases which aid in removal of devitalized cells and debris from the cornea. In some cases these enzymes exceed more than which is essential for normal healing process and results in breakdown and rapid melting of corneal stroma. Similar observations were made by Nagaraj (2011) [4] and Chandler *et al.* (2010) [1] further advocated the use of Protease inhibitors like Doxycycline in the treatment of corneal ulcers. Gilger *et al.* (2007) [2] reported healing of corneal ulcerrs occurs with collagenase remodelling, loss of cellularity in the cells and formation of scar or haze. The good therapeutic results achieved during the present study supported the observations of the above authors.

The addition of nutrient supplements in diet was found useful as an adjuvant in the treatment of corneal ulcers in dogs as they were found to induce the anti- inflammatory and immune- modulating effects in eyes and thus contributed to the restoration of the tear production and healing of ulcers (Nagaraj, 2011 and Destefanis *et al.*, 2016) [4, 3].

## Conclusion

The present study detected corneal ulcers in dogs on ophthalmoscopy and fluorescein stain test (FST) and indicated inflammation (blepheritis, conjunctivitis, keratitis) on clinicoophthalmic signs, infectious disease (bacteria) on NPMCE and Pre-corneal Tear Film (PTF) abnormalities *viz*. aqueous deficiency on STT-I, lipid/mucin deficiency on OFT and TFBT, which were contributing to the progressive dysfunction or destruction of lacrimal and Meibomian acinar tissue, conjunctiva and cornea in corneal ulcers in dogs. Administration of ocular Tacrolimus, Cyclosporine (CsA), antibiotic *viz*. Moxifloxacin, oral Protease inhibitors *viz*., Doxycycline and dietary nutrients supplementation were found effective in treatment of the Deep corneal ulcers in dogs.

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