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USE OF VETSHIELD®/SOFTSHIELD® COLLAGEN CONTACT LENSES IN MELTING CORNEAL ULCERS IN DOGS: 342 CASES (2013-2022)

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Abstract

Melting corneal ulcers in dogs develop secondary to the imbalance between proteinases and proteinase inhibitors in the healing process of corneal wounds. Common complications of melting corneal ulcers in dogs are descemetocele, staphyloma and uveitis, which can lead loss of vision. Medical records of 342 dogs diagnosed with melting corneal ulcers from May 2013 to November 2022 treated surgically using VetShield® and SoftShield® collagen bandage lenses and third eyelid flap. Dogs included in the study had a clinical diagnosis of melting corneal ulcer without evidence of retinal detachment or lens luxation confirmed by ocular ultrasonography. 204/342 cases (59.65%) of treated dogs regained their vision and corneal transparency; 113/342 cases (33.04%) had corneal fibrosis and pigmentation with improved vision; 17/342 cases (4.97%) had lost vision due to corneal scarring and 8/342 (2.34%) underwent intrascleral prosthesis due to secondary glaucoma as a complication. Placement of bandage collagen lenses and third eyelid flap in melting corneal ulcers in dogs is an easy, straightforward surgical procedure which can be performed by any veterinarian practitioner with good results.

Key words*: bandage collagen lens, corneal scar, melting corneal ulcer, third eyelid flap.*

INTRODUCTION

Melting ulcerative keratitis in dogs is a serious condition with a high risk of corneal perforation and blindness (Famose, 2014). Maintenance and repair of corneal stromal extracellular matrix (ECM) requires a tightly coordinated balance of ECM synthesis, degradation and remodeling in which proteolytic enzymes (proteinases) perform important functions (Ollivier et al., 2007; Gellat ,2013). Ulcerative keratitis in dog is associated with initially high levels of tear film proteolytic activity, which decrease as the ulcer heals. The proteinase levels in melting ulcers remain elevated leading to rapid progression of the ulcers (Ollivier et al., 2007). The most common bacterial species associated with canine keratomalacia are *Pseudomonas aeruginosa* and β-hemolytic *Streptococcus* sp. (Tsvetanova et al., 2021).

Melting corneal ulcers usually have an underlying infectious cause, but non-infectious causes are also possible. Risk factors for the development of corneal melting ulcers include ocular trauma and ocular exposure particularly in brachycephalic breeds due to lagophthalmos. Quantitative or qualitative tear film deficiencies are predisposing factors and play an important role in the imbalance between proteolytic enzymes and protease inhibitors.

Depending on the depth of the stromal defect, treatment of melting corneal ulcers can be medical or surgical (Williams et al., 2017).

When the melting process progresses despite the medical management, surgery is indicated to avoid corneal perforation and permanent blindness. Surgical stabilisation in response to progression of stromal loss was required in less than half of the cases in one study (Guyonnet et al., 2022.

Reported surgical techniques in melting corneal ulcers include: corneoconjunctival transposition (CCT), conjunctival grafts, porcine small intestinal submucosal (SIS) graft (Vanore et al., 2007) (ACellVet®) porcine urinary bladder submucosa (Chow et al., 2015), (ACell®) bioscaffolding matrix (Keenan et al., 2020) (Tutopach®) bovine pericardium graft (Dulaurent et al., 2014), amniotic membrane transplantation (Gimenez et al., 2015; Ion et al., 2016; Costa et al., 2019) (BioCorneoVet®) porcine corneal stroma xenograft (Sanitillo et al., 2021) and Vetrix BioSIS plus® (Barachetti et al., 2020). A newer treatment modality used in human and veterinary medicine is the corneal

collagen cross-linking (CXL), which uses riboflavin and UV-A irradiation to increase corneal stability (Williams et al., 2017). The aim of this study is to report the use of VetShield® and Softshield® collagen bandage lenses as a treatment option in the management of melting corneal ulcers in dog. To the authors' knowledge, this is the first report of its use in melting corneal ulcers in dogs evaluating the long-term postoperative outcome in regards to corneal transparency, scarring, integrity, and maintenance of vision.

MATERIALS AND METHODS

Medical records of 342 dogs diagnosed with melting corneal ulceration from May 2013 to November 2022, that underwent VetShield® or Softshield® collagen bandage lens placement, followed by a third eyelid flap, were reviewed.
All dogs underwent complete ophthalmic and physical examination. Signs of blepharospasm, mucopurulent discharge, corneal edema, stromal dissolution (Figure 1), corneal vascularization (Figure 2), conjunctivitis and uveitis (Figure 3) were recorded.

Figure 1. OD Melting corneal ulcer with corneal edema and dissolution in a 7 year- old Crossbred

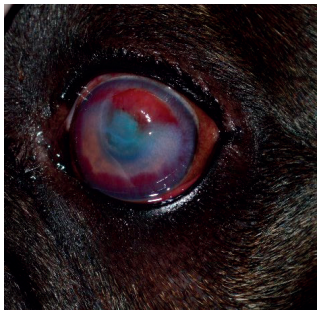


Figure 2. OS Melting corneal ulcer with corneal vascularization in a 3 year-old French Bulldog

Figure 3. OS Melting corneal ulcer, secondary uveitis in a 4 year-old French Bulldog

Dogs were included in the study only if there was no retinal detachment or lens luxation as confirmed by ocular ultrasound (Codreanu et al., 2022). Prior to surgery, additional diagnostic tests, such as complete blood count and serum biochemistry were performed in every case.
Dogs were placed under general anesthesia after pre-medication with dexmedetomidine (Dexdomitor 0.1 mg/ml, Orion Pharma) 15 mcg/kg, ketamine (Ketamidor 100 mg/ml, Richter Pharma, Austria) 5 mg/kg and butorphanol (Butomidor 10 mg/ml, Richter Pharma, Austria) 0.2 mg/kg IM. Anaesthesia was induced with propofol (Propofol Lipuro 10 mg/ml, Braun Germany) 2-4 mg/kg IV. The patients were intubated, maintained on oxygen and isoflurane 1.5-2% (Anesteran, Rompharm S.A., Romania).
The cornea was flushed using saline solution and a drop of tropicamide (Tropicamida®, S.C. Rompharm Company SRL, Ilfov, Romania) was applied for pharmacologic mydriasis.
After placement of the eyelid speculum, antibiotic eye drops were instilled (ofloxacin, Floxal®, Bausch & Lomb Rochester, NY, SUA or tobramycin, Tobrom® S.C. Rompharm Company SRL, Ilfov, Romania).

Figure 4. Softshield® collagen bandage lenses, original packaging

For tectonic support of the cornea, VetShield® bandage collagen lenses (Vetshield Collagen Corneal Shield 72 hr, Oasis Medical Inc, USA) or Softshield® (Figure 4) bandage collagen lenses (Softshield Collagen Corneal Shield 72 hr, Oasis Medical Inc, USA) were used.
Preparation of the cornea was carried out by removing the corneal epithelium using a sterile cotton swab. The collagen bandage lens was hydrated with saline (Figure 5) and inverted.

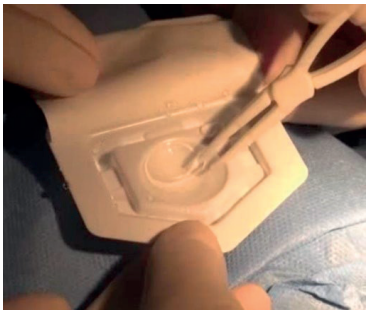


Figure 5. The collagen lens is hydrated using saline

The antibiotic eyedrops were instilled in the concave surface of the collagen lens (Figure 6) and placed on the corneal surface (Figure 7).

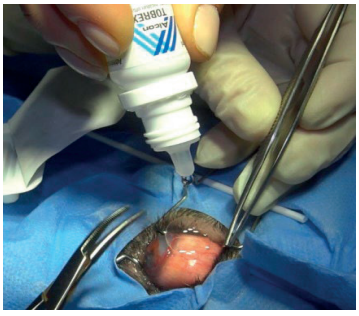


Figure 6. The antibiotic eyedrop sollution is instilled in the concave surface of the collagen lens

Figure 7. Placement of the collagen lens on the corneal surface

The air bubbles were removed from under the bandage collagen lens by applying gentle pressure using sterile cotton tipped applicators. Subsequently, the collagen lens remains well-adhered to the corneal surface.
A complete third eyelid flap was placed using a simple interrupted suture (Vicryl 3/0, Ethicon, Johnson & Johnson, Germany) in order to mantain the collagen lens on the corneal surface (Figure 8).

Figure 8. Clinical appearance of the third eyelid flap

In brachycephalic dogs, the third eyelid flap was placed between the third eyelid margins and the superior conjunctival fornix owing to a short nictitating membrane and shallow orbit. The short third eyelid appears to be a characteristic in these breeds (Figure 9).

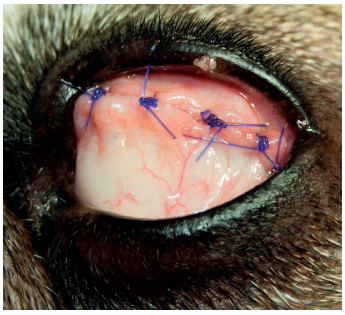


Figure 9. Sutures placed between the third eyelid leading edge and the superior conjunctival fornix

Postoperatively, the use of Elizabethan collar was mandatory (Figure 10). The sutures were removed after 21 days.
Postoperative medications included doxicycline (Ronaxan® 20 mg, Boehringer Ingelheim, Germany) 10 mg/kg SID for 14 days; probiotics (Synbiotic D-C®, ADM Protexin Limited, GB) for 14 days; local antibiotics (ofloxacin, Floxal®, Bausch & Lomb Rochester, NY, SUA)

for 21 days and kanamycin ointment applied BID on the third eyelid sutures (Kanamicina®, SC Antibiotice SA, Iasi, Romania) for 21 days.

Figure 10. The use of Elizabethan collar is mandatory after the surgery

Postoperatively, dogs were re-evaluated weekly and the ocular ultrasound was performed to evaluate the diameter of the eye globe, the corneal healing process and to detect possible complications that can occur such as anterior and posterior synechiae, pupillary seclusion, descemetocele or retinal detachment. After sutures' removal at 21 days, dogs were re-evaluated at 2 and 6 months.

The melting corneal ulcers were considered healed when the fluorescein test was negative, cornea was transparent, with minimal scarring and dogs regained vision.

RESULTS AND DISCUSSIONS

The melting corneal ulcers had been treated by referring veterinarians for a median of 5 days (range: 1–10 days) prior to enrolment in this study. The patients received medical treatment consisted of topical and systemic antibiotics and artificial tears with hyaluronic acid.

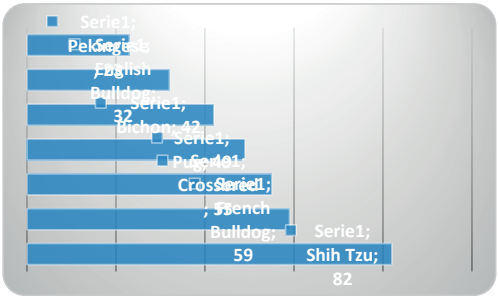
All the surgeries were performed by the same clinician (Iuliana Ionascu) at the Ophthalmology Department of the Faculty of Veterinary Medicine, Bucharest.

The dog breeds included in the study (table 1) were Shih Tzu (n=82), French Bulldog (n=59), Crossbred (n=55), Pug (n=49), Bichon (n=42), English Bulldog (n=32) and Pekingese (n=23).

The median age was 7 years, with a range between 7 months and 13 years.

The Schirmer Tear Test had low values in all cases (0 mm/min to 10 mm/min). The intraocular pressures were within the normal range in the early stage of the melting corneal ulceration and were lower in dogs with secondary uveitis.

Table 1. Dog breeds included in the study



Of all dogs (n=342), included in this study (Table 2), 160 dogs (46.78%) presented with 25% of the cornea affected (Figure 11, Figure 12); 131 dogs (38.31%) had 50% of the cornea affected (Figure 13, Figure 14) and 51 dogs (14.91%) had 100% of the cornea affected by ulceration (Figure 15, Figure 16).

Visual acuity was decreased in patients from groups A and B and absent in patients from group C.

Table 2. The size (%) of the corneal surface affected, highlighted by the fluorescein test

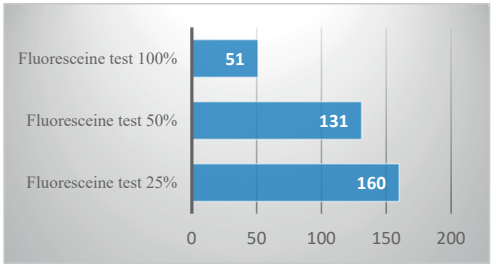


Figure 11. OD Melting corneal ulcer. The fluorescein test is positive on less than 25% of the corneal surface. (7 year-old Crossbred)

Figure 12. OS Melting corneal ulcer. The fluorescein test is positive over25% of the corneal surface. (4 year-oldEnglish Bulldog)

Figure 13. OS Melting corneal ulcer. The fluorescein test is positive over 50% of the corneal surface. (11 year-old Caniche)

Figure 14. OD Melting corneal ulcer. Note the malacic appearance of 50% of the corneal surface. (2 year-old Pug)

Figure 15. OD Melting corneal ulcer. Corneal vascularization is bordering the ulcer and the fluorescein test is positive over 100% of the corneal surface. (3 year-old French Bulldog)

Figure 16. OD Melting corneal ulcer. Note the malacic appearance and the positive fluorescein test over 100% of the corneal surface. (10 year-old Bichon)

Microbiology analysis was not performed, however according to the studies on bacterial flora (McKeever et al., 2021) in dogs with melting corneal ulcers (*S. pseudintermedius, ß-hemolytic Streptoccocus spp., and P. aeruginosa*) ceftriaxone (Cefort®, S.C. Antibiotice, S.A., Iasi, Romania) was administered intraoperatively 20 mg/kg IV.

Moreover, the pharmacokinetics study (Bowden et al., 2022) of extended release parenteral ceftiofur (Excede®) in canine tear film compared with minimal inhibitory concentrations (MICs) of ceftiofur against common ocular pathogens in dog is extremely low compare to concentration after a single injection (up to 10 days in tear compartment), we used in our study one single dose of ceftriaxone intraoperatively.

Collagen bandage lenses should be placed on the corneal surface immediately after hydration.

Between two types of bandage collagen lenses used in this study, there are differences related to the texture after their hydration using saline.

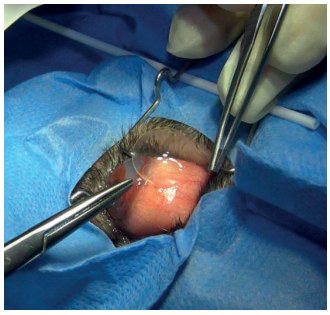


Figure 17. The stable shape of the VetShield® collagen lens after hydration

VetShield® bandage collagen lenses remain in a stable shape after hydration and are easy to

mobilize and place on the corneal surface (Figure 17).
The SoftShield® bandage collagen lens tends to fold over itself after hydration (Figure 18) and is more difficult to place on the corneal surface. After application and fixation, both types of collagen lenses remain firmly attached to the corneal surface.

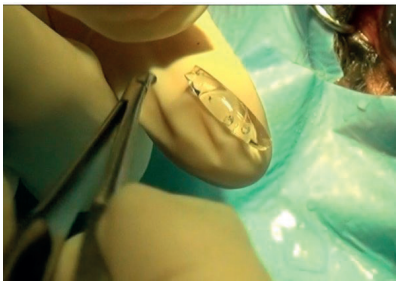


Figure 18. The SoftShield® collagen lens folded over itself after hidration

In 96 brachycephalic patients (28%), the third eyelid flap was placed between the leading edge of the nictitating membrane and the conjunctiva of the superior conjunctival fornix. In this breed, limited third eyelid excursion is a common characteristic.
204/342 dogs (59.65%) in group A and B, had minimal corneal scarring or transparent cornea at 21 days after the surgery, when the sutures were removed and had a negative fluorescein test. Furthermore they were visual and continued long term treatment with 1.2% hyaluronic acid and aminoacids (an-Hypro®, An-Vision, Germany). Re-evaluations at 2 and 6 months after the surgery revealed normal Schirmer Tear Test readings and transparent cornea (Figure 19, Figure 20 and Figure 21) or with minimal scarring.

Figure 19. Case from Figure 2, clinical appearance 2 months after surgery. Transparent cornea and negative fluorescein test.
(3 year-old French Bulldog)

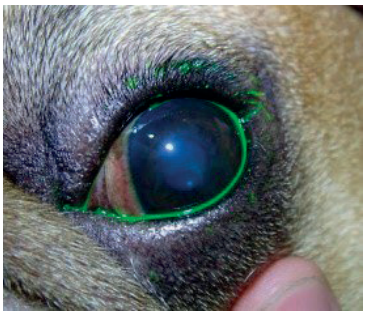


Figure 20. Case from Figure 3, clinical appearance 2 months after surgery revealing cornealtransparency and negative fluorescein test
(4 year-old French Bulldog)

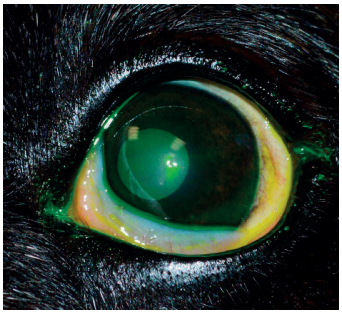


Figure 21. Case from Figure 3, clinical appearance 2 months after surgery. The dog regained vision, the cornea maintained itss transparency and was fluorescein negative (4 year-old English Bulldog)

In 87/342 of dogs in group A and B (25.44%), corneal vascularisation was reported, 21 days later, when the sutures were removed. The blood vessels were reaching the periphery of the bandage collagen lens with negative fluorescein test (Figure 22).

Figure 22. Case from Figure 13, clinical appearance 21 days postoperatively (2 year-old Pug)

These cases were prescribed long-term 1.2% hyaluronic acid and amino acid drops (an-Hypro®, An-Vision, Germany) and healing eye

drops (ii-2018) containing sodium hyaluronat, acetylcysteine and insulin (Ionascu et al., 2020) twice a day. A follow-up performed 2 months later revealed minimal corneal scarring (Figure 24) or corneal vascularisarion reaching the centre of the opaque cornea but the dogs were visual (Figure 23).

Figure 23. Case from Figure 12, clinical appearance 2 months after surgery.Corneal scarring and vascularization are noted (11 year-old Caniche)

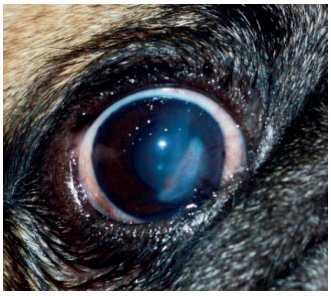


Figure 24. Case from Figure 21, clinical appearance 2 months after surgery. Corneal scarring is noted (2 year-old Pug)

The dogs included in group C (51 cases) were presented with the entire cornea affected and for which postoperative outcome showed the greatest variability.

Figure 25. Case from Figure 15, clinical appearance 2 months after surgery. Note the central corneal vascularization (3 year-old French Bulldog)

19/51 dogs from group C (5.55%) had corneal ulcers that were considered healed within 2 months with corneal opacity and persistent focal central vascularization (Figure 25) or with corneal opacity and diffuse persistent vascularization (Figure 26).

Figure 26. Case from Figure 16, clinical appearance 2 months after surgery. Note the opaque cornea and diffuse corneal vascularization (10 year-old Bichon)

Six months after surgery, the corneal scarring reduced in size and 19/51 patients regained their vision (Figure 27).

Figure 27. Case from figure 25, clinical aspect 6 months after the surgery. Minimal corneal scarring (3 years old French Bulldog)

17/55 dogs from group C (4.97%) healed with a significant corneal scarring (Figure 28, Figure 29) or pigmentation (Figure 30) and visual loss.

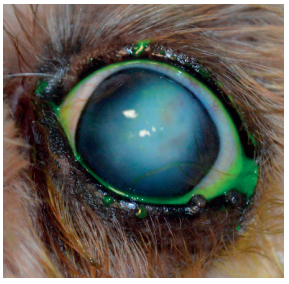


Figure 28. OS Corneal scarring, clinical appearance 6 months after surgery. Visual reflexes were absent. (9 year-old Crossbred)

Figure 29. OS Corneal scarring, clinical appearance 6 months after surgery. Visual reflexes were absent (1 year-old Shih Tzu)

Figure 30. OD Corneal scarring and pigmentation, clinical appearance 6 months after surgery. Visual reflexes were absent (7 year-old Shih Tzu)

7/51 dogs in group C (2.05%) underwent a second surgery (placement of SoftShield® collagen lens and third eyelid flap) owing to third eyelid flap sutures breakdown at seven days postoperatively (Figure 31, Figure 32).
Studies in animals with corneal epithelial defects and keratectomy wounds have shown that SoftShield® collagen lenses have a significant role in re-epithelialisation and reduction of stromal inflammation and edema (Eshar et al., 2011; Ion et al., 2016; Willoughby et al., 2002).
Softshield® lenses have a dissolution time of 72 hours, however the sutures were only removed at 21 days to allow a complete corneal healing. According to the author's experience (Unpublished data), when the sutures were prematurely removed before the 21 days cut-off, for example at 7 days after the surgery, the cornea is most often not healed, has stromal edema, and moderate vascularization (Figure 32).
Therefore, in those cases, dogs underwent a second procedure to have the contact lens and third eyelid flap replaced.

Figure 31. Clinical appearance 7 days after the first surgery. Note the corneal vascularization and opacity (7 year-old English Bulldog)

Figure 32. Clinical appearance 7 days after the first surgery. Note the moderate corneal vascularization (1 year-old Pug)

Clinical appearance 6 months after the second surgery in 7/51 dogs shown improved corneal vascularization (Figure 33) and central corneal opacity at the site where the collagen bandage lens is embedded into the corneal structure (Figure 34).

Figure 33. Case from Figure 28, clinical appearance 2 months after the second surgery. Note minimal corneal vascularization and opacity (7 year-old English Bulldog)

Figure 34. Case from Figure 29, clinical appearance 2 months after the second surgery. Note the central corneal scar (1 year-old Pug)

8/51 dogs in group C (2.34%) developed secondary glaucoma after the surgery likely owing to to pupillary seclusion. These cases subsequently underwent evisceration and intrascleral prosthesis (Figure 35).

Figure 35. OD Intrascleral prosthesis (6 year-old English Bulldog)

At the six months follow-up 204/342 (59.65%) dogs had a transparent cornea and intact visual reflexes. Topical 1.2% hyaluronic acid and amino acid eye drops gel (an-Hypro®, An-Vision, Germany) was prescribed to all dogs diagnosed with keratoconjunctivitis *sicca* (Gronkiewicz et al., 2017).

113/342 (33.04%) dogs had intact visual reflexes, but with corneal scarring and pigmentation. 17/342 (4.97%) dogs lost their visual reflexes due to corneal scarring and 8/342 (2.34%) dogs underwent intrascleral prosthesis surgery.

In regards to surgical treatment of melting ulcers there are several options to re-establish tectonic support and stabilize the cornea with good visual outcome.

A multicentric retrospective study (2010-2017) on cryopreseved amniotic membrane transplantation for the treatment of complicated corneal ulcers in dogs was published by Costa et al., in 2019. Cryopreserved amniotic membrane transplantation (AMT), unilayer, bilayer and multilayer technique was used in 51/114 melting ulcers in dogs with a mean defect size of 6.2 mm (2-18 mm) with high satisfactory visual and cosmetic outcomes.

Santillo et al., in 2021 used porcine corneal stromal xenograft (BioCorneaVet®) in 40 cases (25 perforations, 8 descemetoceles and 9 deep stromal defect) with a diameter ranging from 3 to 10 mm and reported postoperative complications such as mild to severe corneal vascularization, melting and glaucoma.

Use of BioCorneaVet® is also a surgical option for deep stromal defects providing good tectonic support and preserving anatomical integrity and vision (Sanitillo et al., 2021).

Autologous buccal mucous membrane grafts (Mezzadri et. Al., 2021) and corneoconjunctival transposition (CCT) surgery with and without bioscaffolding matrix (ACell®) can be utilized with good results for corneal ulcer repair in dogs (Keenan et al., 2020).

Four-layer porcine small intestinal submucosa (Vetrix BioSIS plus®) used alone as a scaffold for surgical treatment of deep corneal defects had good results in terms of mechanic support and corneal transparency (Barachetti et al., 2020).

Previously reported surgical treatments for deep melting ulcers include porcine small intestinal submucosa (SIS) and third eyelid flap may be an effective alternative to the traditional conjunctival grafts. The advantage of using a SIS graft include good corneal transparency, preservation of corneal integrity and maintenance of vision (Vanore et al., 2017).

For these techniques special equipment is required (surgical microscope, microsurgical kit), but also good knowledge of the technique of corneal suturing.

The surgical protocol for melting corneal ulcers described in the present study can be performed by any veterinarian as it does not require special techniques. Other benefits of this approach include decreased anaesthesia time and lower procedure costs for the owner.

This study included a large number of cases with large corneal defects treated treated by placement of VetShield® and Softshield®

collagen bandage lenses that act as tectonic support, providing tissue to fill the loss of the corneal structure and promoting healing via vascularization from the limbus (Eshar et al., 2011; Ion et al., 2016; Ionascu, 2017; Willoughby et al., 2002). Collagen shields are manufactured from porcine or bovine collagen and three different collagen shields are currently available on the market with dissolution times of 12, 24, and 72 hours (Guber et al., 2019; Willoughby et al., 2002).

At the same time, the third eyelid behaves like an anatomical bandage (Ionascu, 2017; Vanore et al., 2007; Gellat, 2022) and by applying constant pressure for 21 days it maintains the collagen lens on the corneal surface and helps with the healing of the corneal defect. For the surgical success (regaining vision, mechanical support and corneal transparency) a strict protocol was followed. A complete ophthalmic examination and an ocular ultrasound were performed is mandatory before and after the surgery (and every week until the sutures' removal) to evaluate the diameter of the eyeglobe, the corneal healing process and to detect possible complications that might have developed (Codreanu et al., 2022).

In our study, corneal scarring and pigmentation were reported in 113/342 (33.04%), however these dogs regained their vision 2 months postoperatively. Only 5% of dogs lost their vision due to corneal scarring and 2% dogs underwent intrascleral prosthesis surgery due to secondary glaucoma. The complications reported after this type of surgery are similar to other studies (Osinchuk et al., 2022).

CONCLUSIONS

Surgical treatment of melting corneal ulcers in dogs using VetShield® or Softshield® bandage collagen lenses and third eyelid flap may be an effective alternative with good outcome in terms of corneal transparency and vision improvement. Early diagnosis and surgery increase the chances of success in regain patient's vision.

This novel technique can be performed by any veterinarian as it does not require special equipment or knowledge of microsurgical techniques.

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