

Ocular surface microbiome transplantation in dogs: Treat to target on 'Gut-Eye Axis'

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ABSTRACT

The ocular surface microbiome transplantation (OSUM) is an organized group of microorganisms along with owned genes residing on eye surface. The latter collection is a normal trait for eye health with a participant protection role. In the present original article of prospective case series the presenting author aimed at reporting natural treatment with OSUM, as because of microbiome modulation of 'treat to target' purpose. A healthy donor dog (n=1), confirmed free of infectious and systemic diseases, was selected as the source of ocular microbiota. Sterile swabs were obtained from both eyes of the donor and directly applied to the affected eyes of seven recipient dogs presenting with ocular conditions: canine allergic conjunctivitis (n=3), canine visceral leishmaniasis co-morbidity with infectious ulcerative keratitis (n=1), keratoconjunctivitis sicca (n=1), canine monocytic ehrlichiosis-related infectious ulcerative keratitis (n=1), and vision loss (n=1). Each recipient underwent 1–2 sessions of OSUM, with a minimum interval of 48 hours between applications. No additional ophthalmologic interventions or medications were applied. Complete recovery was observed in 3/7 dogs (42.9%), partial recovery in 1/7 (14.3%), while 3/7 (42.9%) showed no response. Among allergic conjunctivitis cases, resolution times were 4, 7, and 10 days, respectively. Partial recovery was recorded in the keratoconjunctivitis sicca case, whereas no recovery was achieved in cases with vision loss or ehrlichiosis-related keratitis. This natural treatment modality, unless this technique was developed by the presenting author, could substitute drug usage at least for canine allergic conjunctivitis along with microbiome modulation.

Keywords: Conjunctivitis, dog, gut-eye axis, Microbiome transplantation, One Health, ocular microbiome.

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Introduction

Taking into account the terminology for OSUM; it confers all sort of commensal and/or pathogenic microorganisms harboured/existed on eye (McDermott, 2013). The surface of the ocular cavity has been uninterrupted display to environmental factors and exhibits several commensal microorganisms

Methodology comprising microbiota in general was classified as culture-based (Fernández-Rubio et al., 2010; Hori et al., 2008) techniques and non-culture-based (i.e., immunoassays targeting microbe-secreted peptides/microbial antigen and metagenomic

sequencing, purposed at detecting microbial RNA or DNA techniques (Clarridge, 2004; Rausch et al., 2019). 16S ribosomal RNA (rRNA) is frequently established for bacterial species, whereas 18S rRNA and internal transcribed spacer have all been performed for fungi (Clarridge, 2004; Rausch et al., 2019). The ocular surface harbors a fragile microbial niche due to environmental influences and treatment habits; therefore, ocular surface microbiome transplantation (OSUM), with its potential to reduce antibiotic use and rapid clinical response, is a significant biotherapy candidate within the One Health/SDG-3 agenda. Recent

developments regarding the burden of ocular diseases (Sarasaki and Zuhria, 2025), documenting the presence of drug-resistant strains in the veterinary field (Istiana *et al.*, 2025), and resistance studies conducted within the food chain (Sudarmadi *et al.*, 2020) highlight the need for joint management across the animal, human, and environment axis. On the human health front, fungal agents and indicators of antifungal resistance reinforce the criticality of antimicrobial stewardship (Monita *et al.*, 2025). Findings that microbiota-based approaches can offer clinical efficacy comparable to antibiotics in certain indications (Sowmya *et al.*, 2023) and evidence on antibiotic misuse (Mathew *et al.*, 2025) may provide grounds for considering OSUM as an option to reduce antibiotic use. It may also provide support for approaches to improving the incidence of infectious diseases (Maulina *et al.*, 2025).

To the present author's knowledge, natural treatment remedies, if possible, are warranted due to the side effects of drugs used in canine medicine and ophthalmology. As microbiome relative abundances were not investigated in this study, the presenting author decided to target different ophthalmological problems in dogs referred to gastroentero-dermatology referral at Feline Dermatology Group facilities, located at the University of Aydin Adnan Menderes, A faculty of Veterinary and Department of Internal Medicine.

Materials and methods

Brief explanation of OSUM as a novel and natural manipulation of the ocular surface microbiome

As a brief description, the same donor was used with frequent vaccination, low glycemic index nutrition, and well-monitored health conditions. This 3-year-old dog served as a donor for all the recipient dogs (n=7), with demographic data given in Table 1. Two sterile swabs were used for microbiota transplantation (Figure 1). Sampling was performed from the donor dog, with one swap from each eye, and transplantation was performed to the recipient dogs' same side of the eye. As soon as the sampling was taken, the swap was transferred to the recipient dog while the donor and recipient

dogs were side by side. No medium or sterile saline was applied during the transplantation procedure. This encouraged us to use entirely natural language.

The donor dog was evaluated for infectious diseases with the Snap 4Dx® test (*Anaplasma* spp., *Ehrlichia canis*, *Borrelia burgdorferi*, *Dirofilaria immitis*) and the Snap Leishmania rapid test, and all results were found negative. The dog selected as a donor underwent the aforementioned analyses, as well as hematological and routine biochemical tests. It was also ensured that the dog had a full vaccination history and had no history of life-threatening illnesses. Descriptive demographic information of the recipient dogs is presented in Table 1. Briefly, the cases included a 4-year-old Terrier, a 5-year-old mixed breed dog, a 7-year-old female German Shepherd with Canine Visceral Leishmaniasis, a 7-year-old Doberman, a dog diagnosed with keratoconjunctivitis sicca, and a Great Dane with a corneal lesion associated with Canine Monocytic Ehrlichiosis (a 4-year-old mixed breed male). No additional ophthalmologic examinations (slit-lamp microscopy, fluorescein staining, etc.) were performed. OSUM applications were performed in 1–2 sessions, depending on the clinical response, with a minimum interval of 48 hours between sessions. All applications were performed with the informed consent of the owners.

Treatment outcomes were assessed based on objective clinical criteria, including resolution or persistence of conjunctival hyperemia, ocular discharge, corneal opacity, vascularization, and vision status. In cases with allergic conjunctivitis, the clinical scoring system (grading of mild, moderate, or severe signs, data not shown) was applied at baseline and after treatment. Recovery was categorized as complete (total resolution of clinical signs), partial (improvement in inflammation and discomfort with persistence of certain signs such as tear deficiency or corneal opacity), or no recovery (no clinical improvement). All dogs were followed up for a minimum of 10 days.

In the present study, no comprehensive statistical analyses were performed. Instead, recovery times of the cases were descriptively

presented in tabular form. Accordingly, the evaluation at this stage was limited to basic descriptive data based on the recovery periods.

Table 1. Clinical outcome data related to microbial transplantation to the ocular surface

Case details with demographic data		No of OSUM and its origin and resource [heterologue or autologue in origin]	Treatment outcome
I	Terrier, 4 years old, with vision loss	2/heterologue	No recovery
II	Crossbred, 5 years old, with canine allergic conjunctivitis/grading moderate with a final scoring of 6	1/heterologue	Complete recovery in 4 days
III	German Shepherd Dog with Canine Visceral Leishmaniasis co-morbidity, infectious ulcerative keratitis	2/heterologue	Partial recovery/blurred vision was nearly lost
IV	Doberman, 7 years old, with canine allergic conjunctivitis/ grading mild with a final scoring of 3	1/heterologue	Complete recovery in 7 days
V	Crossbred with canine allergic conjunctivitis/grading moderate with a final score of 6	2/heterologue	Complete recovery in 10 days
VI	keratoconjunctivitis sicca		Partial recovery
VII	Danaua with Canine Monocytic Ehrlichiosis-related infectious ulcerative keratitis	1/heterologue	No recovery

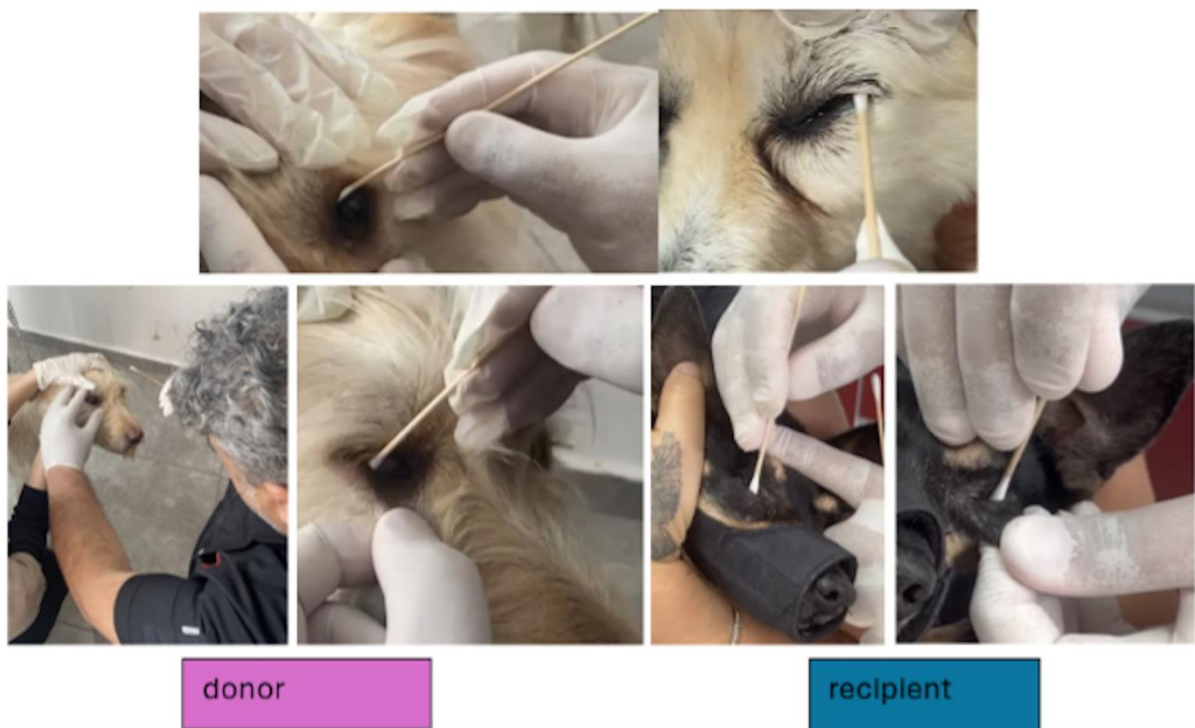


Figure 1. During stages of OSUM, a) a sterile swab sample was prepared and on the hand of the present author ready for collection, b) OSUM manipulation and collection of ocular surface microbiome, which was then transferred to the recipient

Result

The outcomes related to the microbiome transplants and treatment outcomes of the 7 evaluated cases are presented in Table 1. Figures 2 and 3 show the pre-transplant and post-transplant recovery statuses.

Complete recovery occurred in 3/7 dogs (42.9%), partial recovery in 1/7 (14.3%), while 3/7 (42.9%) were non-responders. Partial recovery was defined as an evident reduction of

ocular surface inflammation and clinical discomfort without full restoration of ocular function. In the keratoconjunctivitis sicca case, improvement in ocular redness and discharge was noted, although tear deficiency and residual keratitis persisted. Similarly, in the ehrlichiosis-related ulcerative keratitis case, corneal opacity and vascularization regressed partially, but visual impairment remained.



Figure 2. Dog with canine allergic conjunctivitis/grading moderate with a final scoring of 6. a) Day 0 prior to OSUM and b) thereafter, day 4 on OSUM treatment. Clinical recovery was satisfactory. Furthermore, c) 1 month later showing no recurrence following OSUM

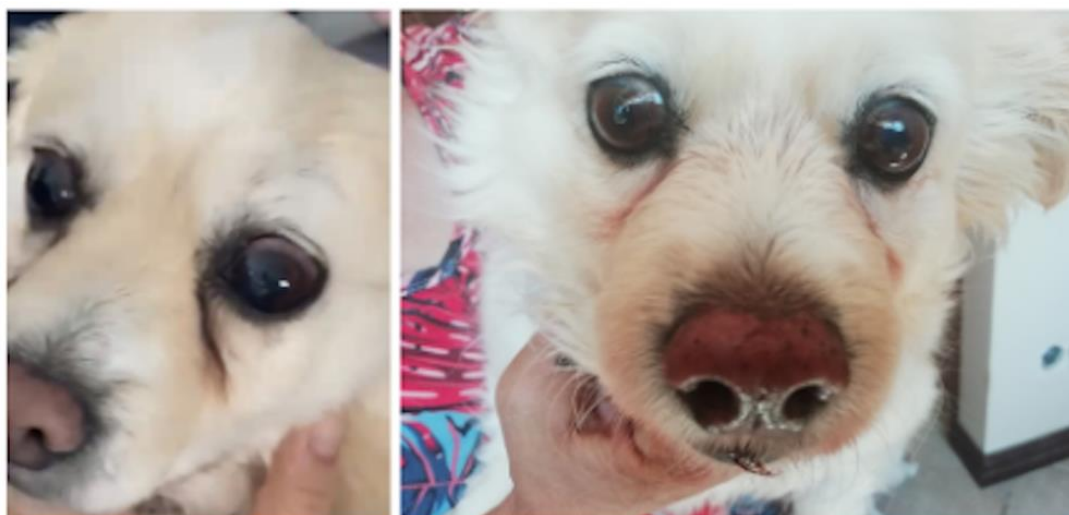


Figure 3. A dog with keratoconjunctivitis sicca. a) Day 0 prior to OSUM and b) thereafter, on day 10 of OSUM treatment. Clinical recovery was evident. Blurred vision was lost following OSUM

Discussion

Denominating terminology such as microbiota describes entire types of microorganisms present in or on the human (McDermott, 2013; Li *et al.*, 2020) and dogs (Leis and Costa, 2020; Rogers *et al.*, 2020) body, total terminology comprising ocular microbiota refers to all ecological niches exhibited in or on the eye. In the present study although 3/7 cases showed complete cure and 1 case showed partial resolution, 3 other cases were not responders. It seemed that a low population of dogs were enrolled, the authors would like to share their preliminary findings in an attempt to exhibit obtained findings which could have helped OSUM disorders on field conditions. Especially the first author's interest to this subject was aroused because of growing number of dogs with gastroentero-dermatological conditions (Gurvits and Robilotti, 2009; Ural *et al.*, 2021; Ural *et al.*, 2023). From this point of view the next paragraph below would in-dept discuss 'gut-eye axis' briefly. There has been novel articles investigating the relationship between ocular surface microbiota and ocular/intestinal microbiome (Potenza *et al.*, 2025; Ebrahimi *et al.*, 2024; Berzack and Galor 2025; Labetoulle *et al.*, 2024). Although we planned to discuss the existing literature regarding our subject, we were unable to find any supporting data. This is because, to the present author's knowledge, OSUM has not been validated or reported. On the other hand, it has been reported that intestinal microbiota alterations have been proposed as the possible route cause of ocular surface diseases (Labetoulle *et al.*, 2024). At the same time, balanced gut microbiota or gut microbiota exhibiting dysbiosis could influence immune response, or proinflammatory conditions could develop, also involving the ocular surface microbiome. For instance, IgA residing on the ocular surface has been significantly elevated when germ-free rodents were housed conventionally or even if they were recolonized with *Bacteroides*, a well-known microbiota member with diminished inflammatory conditions (Kugadas *et al.*, 2017). Interestingly, a relatively fresh review pointed out that fecal microbiota transplantation has been considered as a novel therapeutic approach against glaucoma (Ebrahimi *et al.*, 2024). In the present study, compared with

a special focus on the gut eye axis, we switched the ocular surface microbiome to that of the dogs enrolled herein.

The gut-eye axis, as a proposed postulation, involves gut microbiota dysbiosis along with a disrupted intestinal barrier, which could thus eventually cause the translocation of gut pathogens and, moreover, affect the eye, which is far-flung located from the gut (Moon *et al.*, 2020; Deng *et al.*, 2021). Mechanism of action for pathogenesis exhibited at gut-eye axis included i) systemic inflammation cascade, ii) microbiota-derived metabolites, iii) endotoxemia, iv) immune system modulation, v) gut-associated Lymphoid Tissue, vi) cytokine expression, vii) blood-retina barrier integrity, viii) microbial metabolites and barrier functioning, ix) microbiota and oxidative stress, x) genetic and epigenetic interactions, and xi) host-microbiota interactions (Kammoun *et al.*, 2024). All aforementioned mechanisms might be linked to the gut-eye axis and the probable treatment efficacy obtained in this study.

The OSUM harbour microecological niche is resident on the corneoconjunctival surface and within the tear film. Regarding dogs, ocular anatomical surface area is vulnerable to keratoconjunctivitis sicca and infectious ulcerative keratitis, frequently treated with topical antibacterials (Gerding *et al.*, 1988; Lin and Petersen-Jones, 2007; Murphy *et al.*, 1978; Prado *et al.*, 2005; Tolar *et al.*, 2006; Wang *et al.*, 2008; Whitley, 2000). Regarding altered OSUM abundances in relationship with ocular surface disorders, evidence from data shows that the latter resident commensal niche prevents the eye from opportunistic/pathogenic species growth (Gilger, 2008; Kugadas and Gadjeva, 2016). Moreover, antibiotic prescription could influence the composition and firmness of microbial groups (Langdon *et al.*, 2016; Sandmeyer *et al.*, 2017; Suchodolski *et al.*, 2009; Varges *et al.*, 2010). In the present case report series herein, nearly all dogs received unnecessary antibiotic applications, which could have hastened relevant clinical findings.

Taking into account previous research investigating ocular surface bacterial load for apparently healthy individuals, by use of traditional culture-based methods (Furiani *et al.*,

2011; Gerding and Kakoma, 1990; McDonald and Watson, 1976; Prado *et al.*, 2005; Tolar *et al.*, 2006; Whitley, 2000). Regarding percentages of entire culture positivity among healthy canine eyes, altered from 29 to 45%, frequently observed Gram-positive bacteria [i.e., *Staphylococcus*, *Streptococcus*, *Bacillus*, and *Micrococcus* spp.]. On the other side, Gram-negative bacteria [i.e., *Moraxella*, *E. coli*, *Pseudomonas*, *Acinetobacter*, *Neisseria*, *Klebsiella*, and *Enterococcus* spp.] presented less than 4% relative abundance (Furiani *et al.*, 2011; Gerding and Kakoma, 1990; McDonald and Watson, 1976; Prado *et al.*, 2005; Tolar *et al.*, 2006; Whitley, 2000). In an interesting study performed in 2020, investigators sought to detect bacterial composition of OSUM both in clinically healthy dogs and in those subjected to topical antibiotic therapy. Frequently determined families were *Pseudomonadaceae*, *Micrococcaceae*, *Pasteurellaceae*, and other relevant ones in which major bacterial taxa belonging to OSUM remained consistent during and after topical antibiotic treatment (Rogers *et al.*, 2020). In this study, as 7 dogs were enrolled, the present authors did not have time, nor did we have any financial budget for investigating OSUM. If it were the case, the OSUM application would thus be based on high evidence of proof, and no one could thus criticize the absence of treatment success monitoring by relative abundances of microbiota. However, all 7 dogs were referred for the final decision of the presenting author, as they all visited several clinics with unsuccessful treatment attempts with traditional eye prescriptions/medications. The present authors were not specifically ophthalmologists; however, their background in microbiota-targeted treatment experience for 25 years aroused their interest in manipulating the ocular surface microbiome. To the authors' knowledge, this case series is the first reported application in both veterinary and human medicine based on the principle of transferring the ocular surface microbiome from a healthy donor directly to sick dogs. Existing literature has largely focused on defining the composition of the ocular microbiome or evaluating the effects of topical antibiotic and probiotic applications; however, the direct microbiome transfer approach used in this study has not been previously

reported. In this respect, the study is clinically important, particularly due to its potential to reduce antibiotic use and its ability to achieve complete resolution in allergic conjunctivitis cases within a short period (4–10 days).

One of the limitations of the present study might be that we do not have the possibility to investigate microbiota alterations before and after treatment. At the time of writing, we still do not know the dynamics of microbiome (this was a self-budget project without any support of economics in which, however, this treatment modality is unable to enable us to receive clinical recovery. We as clinicians are in a hurry, even if cases with ocular diseases and comorbidity, to those of cases with emergency triage, do not allow us to wait for laboratory analytes. However, the low sample size and the lack of microbiome composition analysis are major factors limiting the generalizability of the findings. In conclusion, we could claim that OSUM might be beneficial for a possible and practical approach to treat several different diseases regarding the 'gut-eye axis'.

Conclusion

This natural treatment modality, unless this technique was developed by the presenting author, could substitute drug usage at least for canine allergic conjunctivitis, along with microbiome modulation.

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