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Challenges in the Diagnosis and Management of Anterior Blepharitis

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Introduction

Blepharitis is defined as inflammation of the eyelids, classified according to anatomical location: anterior (eyelid skin, base of the lashes including the eyelash follicle) or posterior (meibomian glands) blepharitis.[1] Although blepharitis is one of the most common ocular disorders, epidemiological data on the condition is lacking, making prevalence difficult to assess. A 2009 survey of eyecare practitioners reported observing blepharitis in 37%–47% of patients in their clinical practice.[2] This observation may vary depending on the age, sex, and types of patients (i.e., dry eye) in the practice. Younger females are found to have more acute short-term presentation of blepharitis, whereas older, more fair-skinned females present with chronic blepharitis often concurrent with rosacea.[3] Large population-based studies, using a standardized definition and diagnostic technique, are needed to properly assess the prevalence and incidence of blepharitis and to allow for study comparisons among various age groups.

The ocular surface, including the lid margin, has a natural flora or microbiome, which is imperative in maintaining the health and defence mechanism of the ocular surface.[4,5] This can be affected by age, gender, inflammation, disease,

medication, cosmetics, and treatment (systemic or topical).[5] An overgrowth of microbes or an imbalance of the natural flora may result in an inflammatory response, leading to blepharitis, conjunctivitis, keratitis, or a combination of these.

Challenges in the diagnosis of anterior blepharitis

Various causative factors of blepharitis include bacterial (often staphylococcal), viral (herpes simplex, molluscum contagiosum), fungal (seborrheic), and parasitic (pediculosis palpebrarum, Demodex). Numerous other conditions may be associated with eyelid inflammation, such as immunological (Steven-Johnson's syndrome, graft versus host disease), dermatoses (i.e., psoriasis), eyelid tumours, trauma (including chemical, thermal, radiation), and toxic (medicamentosa).[1] Symptoms are similar across all types of blepharitis and may include: ocular irritation; conjunctival hyperemia; tearing; burning; itching; blurred or fluctuating vision; loss of lashes; photophobia; contact lens intolerance; and recurrent styes, typically worse in the morning.[1] It is clinically valuable to explore the timing of symptoms as this can differentiate from other causalities such as tear film evaporation, which typically worsens throughout the day. Blepharitis can progress to ocular surface inflammation and tear film disturbances, and can exacerbate ocular allergy and dry eye. The myriad of symptoms and the chronic nature of blepharitis, coupled with the ambiguity of its etiology, renders its diagnosis and management challenging for the clinician.

In addition to a comprehensive case history to assess severity, laterality, timing, and duration of symptoms, an external examination of the eyelids, with particular attention given to the lid margin, eyelashes, tear film, and ocular surface, is essential.[1] The lid margin should be assessed for uniformity, hyperemia, and telangiectasia. The eyelashes should be observed for misdirection (trichiasis), loss (milphosis/ciliary madarosis), and type and location of debris, if present. Diagnostic ophthalmic dyes are used to assess for tear film stability and the integrity of the ocular surface.

A careful examination of eyelash debris can be valuable in directing the clinician toward an etiology of anterior blepharitis. Staphylococcal blepharitis typically presents as matted, yellowish, hard scales or collarettes found anywhere along the eyelash. The collarettes move from the base to the tip of the eyelashes with eyelash growth. Milphosis and trichiasis are common in bacterial blepharitis.[1] Conversely, seborrheic blepharitis presents as oily, greasy debris on the lashes; however, it originates in the eyelid skin and is rarely associated with lash loss or misdirection.[1] This condition is typically co-managed with dermatology due to its dermatological etiology.

Demodex blepharitis[6,7] is caused by a microscopic parasite, which is light sensitive and resides in the human eyelash follicle (*Demodex folliculorum*) during the day. The debris on the eyelashes appears as a gelatinous clear sleeve surrounding the lash at its base, termed cylindrical dandruff (CD). CD is pathognomonic for Demodex and remain at the base of the eyelash despite eyelash growth, which is clinically relevant to assist in the differentiation with other types of anterior blepharitis.[8] Having the patient look down at the slit lamp will reveal the base of the eyelashes more clearly. CD along the upper lid margin may be overlooked if the observation is restricted to primary gaze. In cases of dermatochalasis of the eyelid, pulling the folded eyelid upwards while in downward gaze will also assist the visualization of the base of the eyelashes. The Demodex mite has a life cycle of 14–18 days, therefore frequent mating is crucial for effective propagation. Transmission is by direct contact from one individual to another; consequently, family members sharing a dwelling should be examined.

Patients with Demodex blepharitis may or may not be symptomatic. Of those who are symptomatic, itching, specifically along the lash line, is often reported.[9] This can be an additional element to assist in the differential diagnosis of anterior blepharitis. Comorbidities of Demodex infestation (termed demodicosis) include meibomian gland dysfunction (MGD); blepharitis; keratitis; chalazion; dry eye; acne rosacea; and contact lens intolerance and discontinuation, further rendering the etiology of blepharitis challenging.[10-15] There is a 2.5-fold increased risk of Demodex in blepharitis patients and a 3-fold increase in patients with acne rosacea.[10] Demodex blepharitis is confirmed with eyelash epilation and subsequent microscopic observation for confirmation of mites. In a clinical setting, microscopes are not readily available, hence alternative methods are suggested to observe the presence of mites *in situ*. Slit lamp observation can be achieved by selecting eyelashes with CD and, using a tweezer, can be rotated[16] or pulled

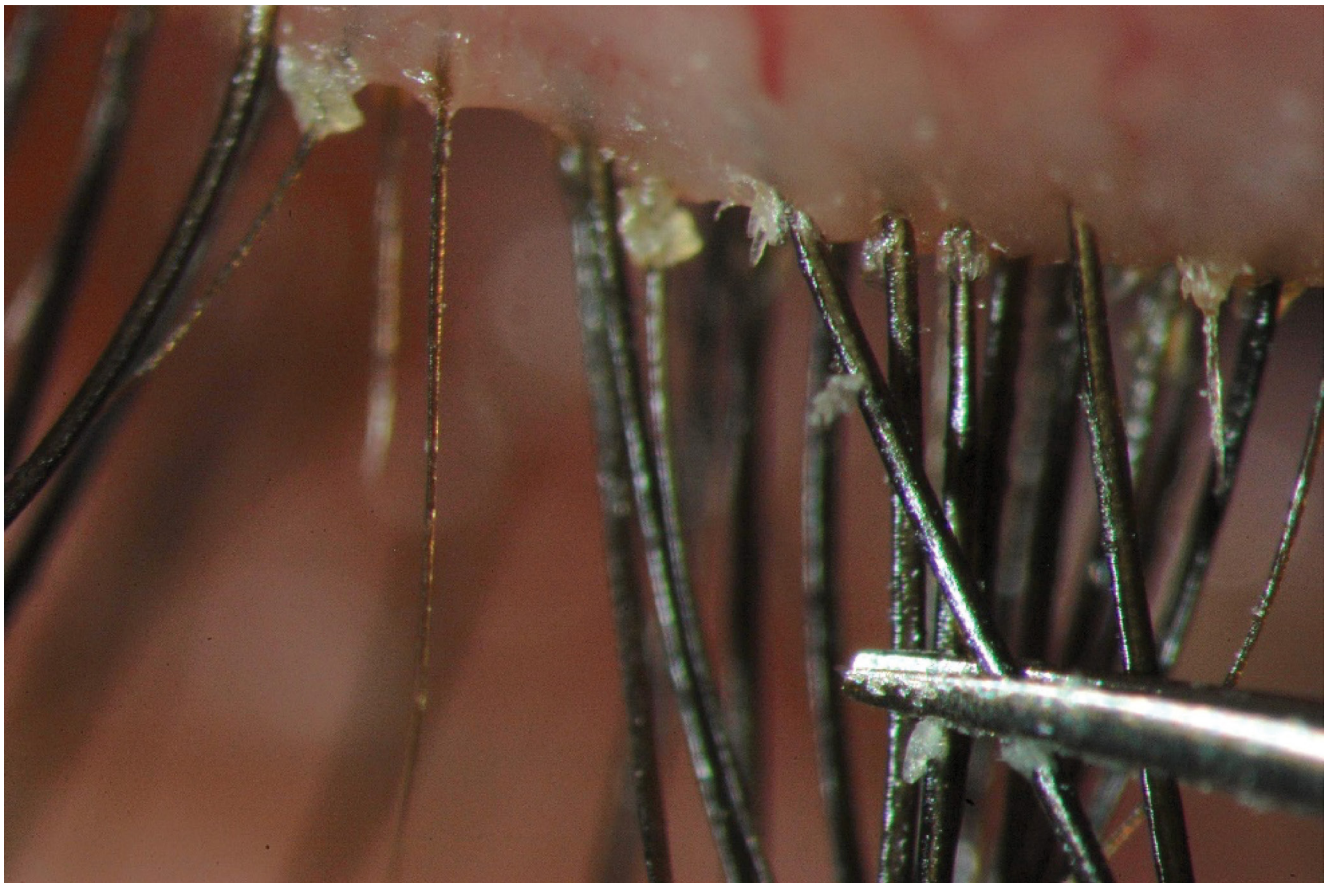

Figure 1. Lateral tension of an eyelash with cylindrical dandruff (CD) revealing the clear tail of a Demodex mite at the base of the lash; *photo courtesy of Etty Bitton.*

laterally[17] (**Figure 1**) to stimulate the mite tail to exit partially from the follicle. Since the mite is clear in colour, it may be necessary to remove the CD or pull it down along the lash shaft, prior to manipulation to facilitate the observation of the mite.[17]

Challenges in the Management of Anterior Blepharitis

Management of anterior blepharitis can be complex due to its multifaceted etiology and comorbidities. Consequently, the therapeutic management of anterior blepharitis should focus on decreasing the overgrowth of microbes (bacteria, virus, fungus, or parasite), to reduce inflammation and improve symptoms, in an attempt to restore the natural ocular flora. Management of anterior blepharitis can include at-home therapies (i.e., lid hygiene, therapeutics) or in-office procedures (i.e., microblephaoexfoliation, intense pulse light). Lid hygiene is a cornerstone treatment for all types of blepharitis.[18] Any mechanical cleaning of the lid margin and lashes will initially remove some of the debris and may even improve symptoms short term; however, unless antimicrobials are used, mechanical cleaning will not address the etiology of the blepharitis. The challenge for clinicians is to better understand the ingredients in lid hygiene formulations in order to identify which of these have antimicrobial properties. This will enable improved targeting of the specific type of anterior blepharitis.

Tea tree oil (TTO)[19] based lid cleansers possess antibacterial, antifungal, and antiparasitic properties and should be considered when a mixed presentation of anterior blepharitis is suspected or when the etiology is unknown. The most abundant ingredient in TTO is terpinen-4-ol (T4O),[20] which possesses a strong demodectic affinity; therefore, it is best suited for the management of Demodex blepharitis. Lid hygiene products with TTO and T4O are often in diluted concentrations as, in higher concentrations, they can cause significant

irritation to the skin and eyes.[21,22] A trial with TTO/T4O lid cleanser can be performed in-office, to educate patients, set patient expectations, and enhance compliance.[21,22] A recent *in vitro* study found T4O to be toxic to meibomian gland epithelial cells, even at very low concentrations.[23] Although further investigation in a clinical setting is warranted, clinicians should consider this finding when recommending T4O-containing lid hygiene products due to the proximity of the meibomian gland orifice along the lid margin.

Lid cleansers with caprylol glycine, hypochlorous acid (HOCl) and okra-based polysaccharide (Abelmoschus esculentus) can be useful in managing blepharitis as they, too, possess antimicrobial properties.[24-27] The added advantage of HOCl is its selective bactericidal activity, affecting the bacterial load while preserving the normal biofilm structure.[26] HOCl is available in spray form and can be used directly on closed lids or applied to a cotton pad for mechanical use along the lid margin. Using a full-spectrum antibiotic ointment on the lids will alleviate bacterial overgrowth unselectively, which may affect the homeostasis of the natural ocular microbiota.

Therapeutics for anterior blepharitis can include antibiotics, antivirals, and antifungals, depending on the clinical presentation and to assist in restoring the ocular flora. For Demodex blepharitis, therapeutics can include topical and systemic ivermectin and metronidazole.[28] Clinical trials with a recently developed antiparasitic agent, lotilaner ophthalmic solution, used twice a day for 28 days, has shown promise in reducing mite counts even after cessation, although this agent is not currently approved for use in Canada.[29]

In addition to at-home therapies, in-office procedures can be performed for anterior blepharitis. Microblepharoexfoliation (MBE) can be used for any type of anterior blepharitis to physically remove debris and biofilm along the lashes and lid margin. This involves use of a manual sponge with an antimicrobial lid cleanser, or mechanically, using a hand-held instrument with a rotating, disposable micro-sponge.[28] The procedure to clean all four lids can take between 5 and 10 minutes and a topical anaesthetic can be used to render the patient more comfortable. Treatment can be repeated in 4 to 6 months. Taking pre- and post-treatment photos (**Figure 2**) is useful in demonstrating to patients the benefits of the deep cleaning provided by MBE.

Intense pulse light (IPL) is well known in dermatology in the management of inflammatory diseases such as acne rosacea.[30] IPL has also been shown to improve meibomian gland expression and enhance the tear film in evaporative dry eye.[31] In addition, IPL has been shown to be effective against demodicosis, even for younger patients (5–16 years old).[32,33]

Conclusion

The diagnosis and management of anterior blepharitis can be challenging for the clinician and a source of frustration for the patient. A comprehensive history coupled with a detailed observation of the lid margin and eyelashes can assist the clinician in gaining an improved understanding of the source of the blepharitis, and guide the patient toward more appropriate management options. There are a multitude of lid hygiene products, pharmaceutical treatments, and in-office procedures available for the management of anterior blepharitis, to alleviate symptoms, improve ocular esthetics, and maintain the integrity of the ocular surface. Keeping abreast of these product innovations and technologies will be rewarding for your practice and your patients will be most appreciative.

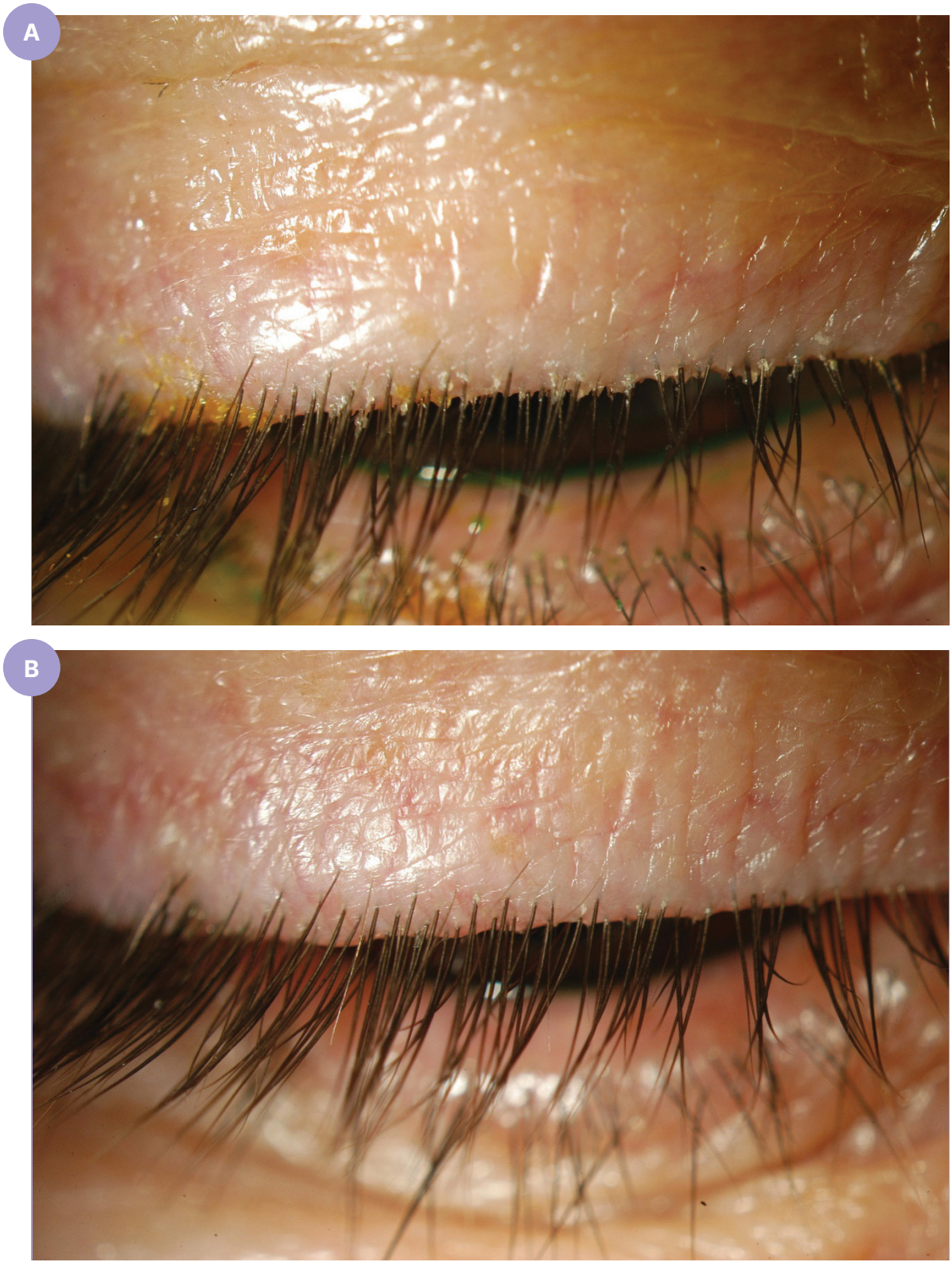

Figure 2. A) Pre-microblepharoexfoliation (MBE) appearance revealing cylindrical dandruff (CD) debris along the base of the upper lid; **B)** Post-microblepharoexfoliation immediately following treatment of the upper lid; *photo courtesy of Etty Bitton.*

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References

1. Amescua G, Akpek EK, Farid M, et al. Blepharitis preferred practice pattern(p). Ophthalmology 2019;126(1):56-93.
2. Lemp MA, Nichols KK. Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. Ocul Surf 2009;7(2 Suppl):S1-S14.
3. Putnam CM. Diagnosis and management of blepharitis: an optometrist's perspective. Clin Optom (Auckl) 2016;8:71-78.
4. Fredricks DN. Microbial ecology of human skin in health and disease. J Investig Dermatol Symp Proc 2001;6(3):167-169.
5. Aragona P, Baudouin C, Benitez Del Castillo JM, et al. The ocular microbiome and microbiota and their effects on ocular surface pathophysiology and disorders. Surv Ophthalmol 2021;66(6):907-925.
6. Kemal M, Sumer Z, Toker MI, et al. The prevalence of Demodex folliculorum in blepharitis patients and the normal population. Ophthalmic Epidemiol 2005;12(4):287-290.
7. Fromstein SR, Harthan JS, Patel J, et al. Demodex blepharitis: clinical perspectives. Clin Optom (Auckl) 2018;10:57-63.
8. Gao YY, Di Pascuale MA, Li W, et al. High prevalence of Demodex in eyelashes with cylindrical dandruff. Invest Ophthalmol Vis Sci 2005;46(9):3089-3094.
9. Sedzikowska A, Oseka M, Grytner-Ziecina B. Ocular symptoms reported by patients infested with Demodex mites. Acta Parasitol 2016;61(4):808-814.
10. Sedzikowska A, Oseka M, Skopinski P. The impact of age, sex, blepharitis, rosacea and rheumatoid arthritis on Demodex mite infection. Arch Med Sci 2018;14(2):353-56.
11. Luo X, Li J, Chen C, et al. Ocular demodicosis as a Potential Cause of Ocular Surface Inflammation. Cornea 2017;36 Suppl 1(Suppl 1):S9-S14.
12. Ayyildiz T, Sezgin FM. The Effect of ocular Demodex colonization on Schirmer test and OSDI scores in newly diagnosed dry eye patients. Eye & contact lens 2020;46 Suppl 1:S39-S41.

13. Liang L, Ding X, Tseng SC. High prevalence of demodex brevis infestation in chalazia. Am J Ophthalmol 2014;157(2):342-348 e1.
14. Jalbert I, Rejab S. Increased numbers of Demodex in contact lens wearers. Optom Vis Sci 2015;92(6):671-678.
15. Tarkowski W, Moneta-Wielgos J, Mlocicki D. Demodex sp. as a potential cause of the abandonment of soft contact lenses by their existing users. Biomed Res Int 2015;2015:259109. doi: 10.1155/2015/259109 [published Online First: 20150721]
16. Mastrota KM. Method to identify Demodex in the eyelash follicle without epilation. Optom Vis Sci 2013;90(6):e172-174.
17. Muntz A, Purslow C, Wolffsohn JS, et al. Improved Demodex diagnosis in the clinical setting using a novel in situ technique. Contact Lens & Anterior Eye: The Journal of the British Contact Lens Association 2020;43(4):345-349.
18. Lindsley K, Matsumura S, Hatef E, et al. Interventions for chronic blepharitis. Cochrane Database Syst Rev 2012(5):CD005556. doi: 10.1002/14651858.CD005556.pub2 [published Online First: 20120516]
19. Carson CF, Hammer KA, Riley TV. Melaleuca alternifolia (tea tree) oil: a review of antimicrobial and other medicinal properties. Clin Microbiol Rev 2006;19(1):50-62.
20. Cheung IMY, Xue AL, Kim A, et al. In vitro anti-demodectic effects and terpinen-4-ol content of commercial eyelid cleansers. Contact Lens & Anterior Eye: The Journal of the British Contact Lens Association 2018;41(6):513-517.
21. Ngo W, Jones L, Bitton E. Short-term comfort responses associated with the use of eyelid cleansing products to manage Demodex folliculorum. Eye & Contact Lens 2018;44 Suppl 2:S87-S92.
22. Craig JP, Bitton E, Dantam J, et al. Short-term tolerability of commercial eyelid cleansers: a randomised crossover study. Contact lens & anterior eye: The Journal of the British Contact Lens Association 2022;45(6):101733. doi: 10.1016/j.clae.2022.101733 [published Online First: 20220713]
23. Chen D, Wang J, Sullivan DA, et al. Effects of terpinen-4-ol on meibomian gland epithelial cells in vitro. Cornea 2020;39(12):1541-1546.
24. Guillon M, Maissa C, Wong S. Symptomatic relief associated with eyelid hygiene in anterior blepharitis and MGD. Eye & Contact Lens 2012;38(5):306-312.
25. Petropoulos S, Fernandes A, Barros L, et al. The chemical composition, nutritional value and antimicrobial properties of Abelmoschus esculentus seeds. Food Funct 2017;8(12):4733-4743.
26. Romanowski EG, Stella NA, Yates KA, et al. In vitro evaluation of a hypochlorous acid hygiene solution on established biofilms. Eye & Contact Lens 2018;44 Suppl 2(Suppl 2):S187-S191.
27. Kabat AG. In vitro demodicidal activity of commercial lid hygiene products. Clin Ophthalmol 2019;13:1493-1497.
28. Shah PP, Stein RL, Perry HD. Update on the management of Demodex blepharitis. Cornea 2022;41(8):934-939.
29. Gonzalez-Salinas R, Karpecki P, Yeu E, et al. Safety and efficacy of lotilaner ophthalmic solution, 0.25% for the treatment of blepharitis due to demodex infestation: A randomized, controlled, double-masked clinical trial. Contact lens & Anterior Eye: The Journal of the British Contact Lens Association 2022;45(4):101492. doi: 10.1016/j.clae.2021.101492 [published Online First: 20210728]
30. Cai Y, Zhu Y, Wang Y, et al. Intense pulsed light treatment for inflammatory skin diseases: a review. Lasers Med Sci 2022;37(8):3085-105.
31. Tashbayev B, Yazdani M, Arita R, et al. Intense pulsed light treatment in meibomian gland dysfunction: A concise review. Ocul Surf 2020;18(4):583-594.
32. Zhang X, Song N, Gong L. Therapeutic effect of intense pulsed light on ocular demodicosis. Curr Eye Res 2019;44(3):250-256.
33. Zhai Z, Jiang H, Wu Y, et al. Safety and Feasibility of Low Fluence Intense Pulsed Light for Treating Pediatric Patients with Moderate-to-Severe Blepharitis. J Clin Med 2022;11(11) doi: 10.3390/jcm11113080 [published Online First: 20220530