OPEN

Eyelid Exfoliation Treatment Efficacy and Safety in Dry Eye Disease, Blepharitis, and Contact Lens Discomfort Patients: A Systematic Review

Antonio Ballesteros-Sánchez, OD, PhD†, Beatriz Gargallo-Martínez, OD, PhD†‡, Ramón Gutiérrez-Ortega, MD, PhD†‡,* and *José-María Sánchez-González, OD, PhD**

Purpose: To determine the efficacy and safety of eyelid exfoliation treatment in dry eye disease (DED), blepharitis, and contact lens (CL) discomfort patients.

Methods: A systematic review that included only full-length randomized controlled studies, reporting the effects of eyelid exfoliation treatment in 2 databases, PubMed and Web of Science, was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement. The search period was between October 29, 2022 and December 6, 2022. The Cochrane risk of bias tool was used to analyze the quality of the studies selected.

Results: A total of 7 studies were included in this systematic review. Eyelid exfoliation treatment influence on DED, blepharitis, and CL discomfort were analyzed in 6, 4, and 2 studies, respectively. Eyelid exfoliation treatment achieved a better improvement than control group interventions in all reported variables. The mean differences between both groups were as follows: Ocular Surface Disease Index score of –5.0 ± 0.9 points, tear breakup time of 0.43 ± 0.2 seconds, ocular surface staining of –1.4 ± 1.5 points, meibomian glands secretions of 1.2 ± 1.1 points, meibomian glands yielding liquid secretion of 0.6 ± 0.3 points, microorganism load of –3.2 ± 4.7 points, and Contact Lens Dry Eye Questionnaire-8 of –2.15 ± 0.1 points. Minimal discomfort (n = 13) and eyelid irritation (n = 2) were the main complications after an eyelid exfoliation treatment.

Conclusions: Eyelid exfoliation is a safe and effective treatment that should be indicated for DED, blepharitis, and CL discomfort.

Key Words: blepharitis, contact lens discomfort, dry eye disease, eyelid exfoliation treatment, meibomian gland dysfunction

(*Asia Pac J Ophthalmol (Phila)* 2023;12:315–325)

Submitted December 17, 2022; accepted February 6, 2023.

From the *Department of Physics of Condensed Matter, Optics Area, University of Seville, Seville, Spain; †Department of Ophthalmology, Clínica Novovisión, Murcia, Spain; and ‡Department of Ophthalmology, Optometry, Otorhinolaryngology and Anatomic Pathology, University of Murcia, Murcia, Spain.

This study received funding from the VI University of Seville's Own Research Plan (English editing services).

The authors declare no competing financial interests.

Address correspondence and reprint requests to: Antonio Ballesteros-Sánchez, University of Seville, Reina Mercedes Street, 41012, Seville, Spain. E-mail: antbalsan@alum.us.es

ISSN: 2162-0989
DOI: 10.1097/APO.0000000000000607

INTRODUCTION

Eyelid exfoliation is a novel in-office treatment that works by cleaning the eyelashes and exfoliating the eyelid margins to remove the accumulated biofilm debris, epithelial keratinization, and capped meibomian glands, resulting in better meibum outflow.[1] This treatment may be known as microblepharoexfoliation (MBE) or eyelid debridement-scaling (LDS) when it is performed with the BlephEx instrument (BlephEx LLC) or the stainless-steel golf club spud (Hilco Wilson Ophthalmics), respectively. Currently, evidence suggests that all forms of dry eye disease (DED) have an evaporative component because ocular surface hyperosmolarity can only arise in response to evaporation.[2] Meibomian gland dysfunction (MGD) is the most common form of evaporative dry eye, and it is characterized by meibomian gland atrophy and dropout due to terminal duct obstruction and/or changes in meibum quality and quantity.[2,3] MGD causes tear film evaporation, leading to tear hyperosmolarity, which promotes the release of inflammatory mediators and proteases that cause damage to the ocular surface, resulting in the usual symptoms of DED, such as gritty and foreign body sensation.[4] In addition, other conditions may alter the lipid layer tear film and lead to tear film evaporation, such as blepharitis[2,5] and contact lens (CL) wear.[6,7]

Blepharitis is chronic eyelid inflammation based on progressive bacterial biofilm maturation along the eyelid margin.[8] Lipase activity by commensal eyelid bacteria may disrupt meibum from meibomian glands, resulting in a deficient outer protective lipid layer tear film.[9,10] In addition, the presence of Demodex folliculorum mites on the eyelid margin is another known pathogenic risk factor for blepharitis.[11,12] A recent study by Akkucuk et al[13] reported that 75.5% of patients with blepharitis had Demodex folliculorum, which may be identified clinically by the pathognomonic sign of collarettes at the eyelash base.[14,15] As blepharitis progresses, meibomian gland dropout and cicatricial eyelid changes can occur.[16,17]

CL wear has also been associated with reduced lipid layer thickness and tear stability,[18] leading to CL discomfort.[19,20] Some studies have suggested that patients with CL discomfort have a higher prevalence of MGD.[21–23] Moreover, Alghamdi et al[24] reported that CL wearers had poor meibum expressibility compared with non-CL wearers, leading to meibomian gland obstruction. Therefore, healthy meibomian gland morphology and secretion are crucial for successful contact lens fitting.[25]

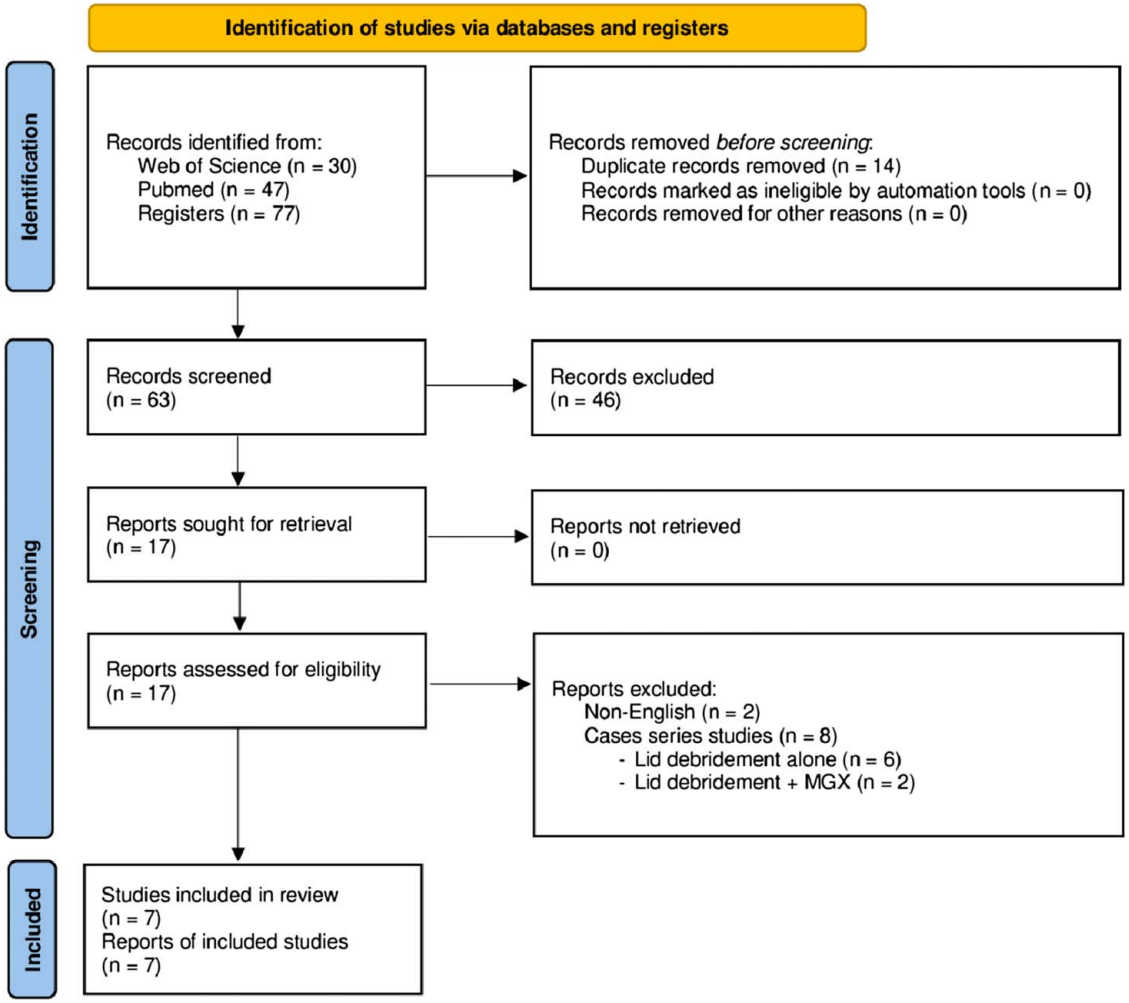

FIGURE 1. Flowchart study selection process according to the PRISMA statement. MGX indicates meibomian glands expression; PRSIMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

To date, some published studies have evaluated the efficacy of eyelid exfoliation treatment in DED,[26–31] blepharitis,[10,28,30,31] and CL discomfort.[10,29] However, to our knowledge, no systematic reviews have explored the available literature regarding clinical applications of eyelid exfoliation treatment. Therefore, the purpose of this systematic review was to evaluate whether MBE and LDS are safe and effective treatment options for DED, blepharitis, and CL discomfort in the available scientific literature.

METHODS

Data Sources and Search Strategy

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses.[32,33] We identified 77 articles published before December 6, 2022, through the following databases: PubMed and Web of Science. The data search strategy with Boolean operators was as follows: (lid debridement OR lid debridement-scaling OR LDS OR blepharon exfoliation OR blephEx OR blepharoexfoliation OR microblepharoexfoliation OR MBE) AND (dry eye OR meibomian gland dysfunction OR MGD OR blepharitis OR demodex blepharitis). The references of the retrieved articles were reviewed to identify other related studies if they met the inclusion criteria.

Study Selection

All those 77 articles identified through the search strategy were considered and analyzed. Duplicate studies were removed by DistillerSR software (DistillerSR Inc.). The remaining studies underwent additional screening stages, which included title screening, abstract screening, and full-text screening. Studies unrelated to the topic were excluded from the review during the title and abstract screening. Full-text screening studies that did not include eyelid exfoliation treatment were also excluded from the review. These studies were reviewed by 2 investigators who selected them according to the inclusion and exclusion criteria.

The inclusion criteria were as follows: human studies, full-length original articles, and prospective randomized controlled studies. The exclusion criteria included non-English publications and unindexed journals. There were no restrictions placed on the country, in which the study was performed, the follow-up period, the sample size, or the results of the studies.

Quality Assessment and Data Extraction

The data from each study were collected and summarized independently in tables designed by 2 researchers. The following information was obtained from each article: (1) author and date of publication (year), (2) study design, (3)

TABLE 1. Summary of Included Randomized Controlled Trials

Author (Date)	Design	Follow-Up (months)	Patients (TG/CG)	Age* (TG/CG)	Sex (F/M)	Eyes	Eyelid Exfoliation Device	Clinical Application	Intervention	Control	Complications	CoI
Korb et al[1] 2013	MC, RD, CT, DM	1	28 (16/12)	54.8 ± 15 (55.9 ± 15/ 53.7 ± 15.0)	20/8	56	Golf club spud	DED	MBE + AT and warm compresses	AT and warm compresses	No discomfort (n = 28)	Yes
Ngo et al[2] 2015	MC, RD, CT, UM	1	13 (7/6)	60.2 ± 9.5 (58. ± 8.1/ 62.3 ± 11.6)	13/0	26	Golf club spud	DED	MBE alone	No intervention	Minimal discomfort (n = 13)	NR
Murphy et al[3] 2017	MC, RD, CT, MK	1	86 (28/58)	41.8 ± 16.2 (44.3 ± 18.6/ 40.6 ± 15.0)	NR	172	BlephEx	Blepharitis	MBE and 1,2-Octanediol	Terpinen-4-ol Or 1,2-Octanediol	NR	No
Siddireddy et al[4] 2019	MC, RD, CT, UM	0.25	30 (NR)	23 (18-41) (NR)	24/6	60	BlephEx	CL discomfort	MBE alone	Hypoallergenic foam cleanser	NR	No
Epstein et al[5] 2020	MC, RD, CT, DM	2	46 (23/23)	73.3 ± 5.4 (71.0 ± 5.8/ 75.6 ± 5.0)	38/8	92	BlephEx	Blepharitis	MBE and Terpinen-4-ol	MBE and Sham scrubs	NR	NR
Siddireddy et al[6] 2020	MC, RD, CT, UM	0.25	30 (NR)	23 (18-41) (NR)	24/6	60	BlephEx	Blepharitis CL discomfort	MBE alone	Hypoallergenic foam cleanser	NR	No
Amir Arabi et al[7] 2023	MC, RD, CT, UM	2	81 (42/39)	53.5 ± 8.1 (53.0 ± 7.7/ 54.1 ± 8.5)	46/35	162	BlephEx	Blepharitis	MBE and Terpinen-4-ol	Sham MBE and Terpinen-4-ol	Eyelid Irritation (n = 2)	No

AT indicates artificial tear; CG, control group; CL, contact lens; CoI, conflict of interest; CT, controlled; DED, dry eye disease; DM, double-masked; MBE, microblepharoexfoliation; MC, monocentric; MK, masked; NR, not reported; RD, randomized; TG, treatment group; UM, unmasked.

*Expressed as mean ± SD or median (interquartile range).

TABLE 2. Baseline, End Follow-Up and Differences (End Follow-Up − Baseline) Outcomes in the Treatment Group

	DED						Blepharitis		CL Discomfort
Author (Date)	**OSDI (0–100)**	**SPEED (0–28)**	**TBUT**	**OSS**	**MGS (0–4)**	**MGYLS (0–15)**	**Microorganism Load**	**Lipase Activity**	**CLDEQ-8 (0–37)**
Korb et al[26] (2013)									
Baseline	NR	13.4 ± 4.6	NR	NR	2.6 ± 1.3	NR	NR	NR	NR
End follow-up	NR	10.5 ± 3.8	NR	NR	3.8 ± 1.4	NR	NR	NR	NR
Difference $_{E-B}$	—	**−2.9***	—	—	**1.2***	—	—	—	—
Ngo et al[27] (2015)									
Baseline	63.2 ± 13.3	NR	3.1 ± 0.8	6.6 ± 2.9	1.0 ± 1.2	0.0 ± 0.0	NR	NR	NR
End follow-up	46.9 ± 19.4	NR	3.4 ± 1.0	5.0 ± 3.9	3.1 ± 1.7	0.6 ± 1.0	NR	NR	NR
Difference $_{E-B}$	**−16.3***	—	**0.3**	**−1.6***	**2.1***	**0.6**	—	—	—
Murphy et al[28] (2018)									
Baseline	30.1 ± 19.8	NR	NR	NR	NR	NR	6.5 (1–25)	NR	NR
End follow-up	12.8 ± 12.8	NR	NR	NR	NR	NR	2.7 (0–9)	NR	NR
Difference $_{E-B}$	**−17.3***	—	—	—	—	—	**−3.8***	—	—
Siddireddy et al[29] (2019)									
Baseline	NR	NR	9.5 ± 1.0	NR	NR	NR	NR	NR	12.3
End follow-up	NR	NR	9.9 ± 1.0	NR	NR	NR	NR	NR	9.7
Difference $_{E-B}$	—	—	**0.4***	—	—	—	—	—	**−2.6***
Epstein et al[30] (2020)									
Baseline	19.1 ± 8.5	NR	NR	0.9 ± 0.3	1.5 ± 0.2	1.9 ± 0.3	4.7 ± 1.5	NR	NR
End follow-up	15.1 ± 8.9	NR	NR	0.7 ± 0.3	1.6 ± 0.2	2.2 ± 0.3	2.6 ± 1.2	NR	NR
Difference $_{E-B}$	**−4.0**	—	—	**−0.2**	**0.1**	**0.3**	**−2.1***	—	—
Siddireddy et al[10] (2020)									
Baseline	NR	NR	NR	NR	NR	NR	129.2 ± 16.5	50.5 ± 4.7	12.3
End follow-up	NR	NR	NR	NR	NR	NR	87.5 ± 13.7	26.5 ± 8.7	9.6
Difference $_{E-B}$	—	—	—	—	—	—	**−41,7***	**−24.0***	**−2.7***
Amir Arabi et al[31] (2023)									
Baseline	33.7 ± 12.9	NR	7.4 ± 2.4	NR	NR	NR	4.8 ± 1.3	NR	NR
End follow-up	22.6 ± 8.2	NR	8.9 ± 2.3	NR	NR	NR	2.6 ± 1.1	NR	NR
Difference $_{E-B}$	**−11.1***	—	**0.4***	—	—	—	**−2.2***	—	—
Mean ± SD $_{E-B}$†	**−12.1 ± 5.3**	—	**0.7 ± 0.5**	**−0.9 ± 0.7**	**1.1 ± 0.8**	**0.5 ± 0.2**	**−12.5 ± 16.9**	—	**−2.6 ± 0.1**

The significance of bold values* is $P < 0.05$.

CL indicates contact lens; CLDEQ-8, Contact Lens Dry Eye Questionnaire-8; DED, dry eye disease; MGS, meibomian gland secretion; MGYLS, meibomian gland yielding liquid secretion; NR, not reported; OSDI, Ocular Surface Disease Index; OSS, ocular staining score; SPEED, standard patient evaluation of eye dryness; TBUT, tear breakup time.

*Statistical significance level $P < 0.05$.

†Mean ± SD $_{E-B}$ values of the Difference $_{E-B}$ for each variable.

mean follow-up of all patients in the whole procedure (expressed in months), (4) number of patients, (5) mean age of the patients (expressed in years), (6) patient sex (male/female), (7) number of eyes involved, (8) eyelid exfoliation device, (9) clinical application of eyelid exfoliation, (10) study group intervention, (11) control group intervention, (12) patient experience, and (13) conflicts of interest.

Regarding the results of the studies, the following data were collected: (1) Ocular Surface Disease Index (OSDI, values from 0 to 100)[34]; (2) Standard Patient Evaluation of Eye Dryness Questionnaire (SPEED, values from 0 to 28)[35]; (3) tear breakup time [TBUT, expressed in seconds]; (4) ocular surface staining (OSS, assessed with Oxford grading score or Sjogren's International Collaborative Clinical Alliance Ocular Staining Score)[36,37]; (5) meibomian gland secretions (MGS, grading from 0 to 4, where grade 0 is no expression, grade 1 is "ropy" meibum, grade 2 is turbid and viscous oil appearance, grade 3 is turbid oil, and grade 4 is normal meibum)[38]; (6) meibomian glands yielding liquid secretions (MGYLS; defined as the number of MGYLS, values ranging from 0 to 15)[38]; (7) microorganism load (reported as Demodex folliculorum count or gram-positive cocci and rods recorded as colony-forming units per swab)[10,39]; (8) lipase activity [defined as the clearance zones in the tributyrin agar after overnight incubation, expressed in millimeters][10]; (9) Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8, values ranging from 0 to 37)[40]; and finally (10) author's opinion expressed by commenting in favor or against of eyelid exfoliation treatment. Baseline and end-of–follow-up values for all these variables were collected in the treatment (T) and control (C) groups. Intragroup clinical outcomes were defined as "end follow-up (E)—baseline (B) differences". Intergroup clinical outcomes were defined as "T group $_{(E-B)}$—C group $_{(E-B)}$ differences". Mean ± SD (range) for each variable was calculated to report intragroup and intergroup clinical outcomes.

The literature that remained after the full-text screening was examined to assess the quality of the studies. To avoid the risk of bias, 2 dependable authors created a synopsis based on the Cochrane risk of bias tool,[41] which includes the following items: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other sources of bias. A third

TABLE 3. Baseline, End Follow-Up and Differences (End Follow-Up – Baseline) Outcomes in the Control Group

	DED						Blepharitis		CL Discomfort
Author (Date)	**OSDI (0–100)**	**SPEED (0–28)**	**TBUT**	**OSS**	**MGS (0–4)**	**MGYLS (0–15)**	**Microorganism Load**	**Lipase Activity**	**CLDEQ-8 (0–37)**
Korb et al[26] (2013)									
Baseline	NR	13.9 ± 5.5	NR	NR	2.7 ± 1.5	NR	NR	NR	NR
End Follow-up	NR	14.5 ± 7.5	NR	NR	2.4 ± 1.1	NR	NR	NR	NR
Difference $_{E-B}$	—	**0.6**	—	—	**−0.3**	—	—	—	—
Ngo et al[27] (2015)									
Baseline	58.3 ± 22.1	NR	2.9 ± 1.5	7.0 ± 4.5	1.3 ± 1.5	0.3 ± 0.5	NR	NR	NR
End follow-up	48.3 ± 29.0	NR	2.8 ± 1.7	8.2 ± 3.5	1.0 ± 0.9	0.0 ± 0.0	NR	NR	NR
Difference $_{E-B}$	**−10.0**	—	**−0.1**	**1.2**	**−0.3**	**−0.3**	—	—	—
Murphy et al[28] (2018)									
Baseline	28.0 ± 20.2	NR	NR	NR	NR	NR	4.3 [0-21]	NR	NR
End follow-up	14.9 ± 16.2	NR	NR	NR	NR	NR	1.9 [0-8]	NR	NR
Difference $_{E-B}$	**−13.1***	—	—	—	—	—	**−2.4***	—	—
Siddireddy et al[29] (2019)									
Baseline	NR	NR	9.5 ± 1.0	NR	NR	NR	NR	NR	12.3
End follow-up	NR	NR	9.7 ± 0.2	NR	NR	NR	NR	NR	11.8
Difference $_{E-B}$	—	—	**0.2***	—	—	—	—	—	**−0.5**
Epstein et al[30] (2020)									
Baseline	16.9 ± 7.9	NR	NR	0.6 ± 0.2	1.6 ± 0.2	2.1 ± 0.3	5.1 ± 1.4	NR	NR
End follow-up	17.2 ± 8.5	NR	NR	0.3 ± 0.3	2.0 ± 0.2	2.1 ± 0.2	2.5 ± 0.9	NR	NR
Difference $_{E-B}$	**0.3**	—	—	**−0.3**	**0.4***	**0.0**	**−2.6***	—	—
Siddireddy et al[10] (2020)									
Baseline	NR	NR	NR	NR	NR	NR	129.3 ± 16.5	50.5 ± 4.7	12.3
End follow-up	NR	NR	NR	NR	NR	NR	99.0 ± 5.5	43.2 ± 10.3	11.8
Difference $_{E-B}$	—	—	—	—	—	—	**−30.3**	**−7.3**	**−0.5**
Amir Arabi et al[31] (2023)									
Baseline	32.9 ± 10.6	NR	8.3 ± 2.9	NR	NR	NR	4.8 ± 1.6	NR	NR
End follow-up	27.1 ± 9.1	NR	9.1 ± 2.7	NR	NR	NR	3.0 ± 1.2	NR	NR
Difference $_{E-B}$	**−5.8***	—	**0.8***	—	—	—	**−1.8***	—	—
Mean ± SD $_{E-B}$†	**−7.2 ± 5.0**	—	**0.3 ± 0.4**	**0.5 ± 0.8**	**−0.1 ± 0.3**	**−0.2 ± 0.2**	**−9.4 ± 12.5**	—	**−0.5 ± 0.0**

The significance of bold values* is $P < 0.05$.

CL indicates contact lens; CLDEQ-8, Contact Lens Dry Eye Questionnaire-8; DED, dry eye disease; MGS, meibomian gland secretion; MGYLS, meibomian gland yielding liquid secretion; NR, not reported; OSDI, Ocular Surface Disease Index; OSS, ocular staining score; SPEED, standard patient evaluation of eye dryness; TBUT, tear breakup time.

*Statistical significance level $P < 0.05$.

†Mean ± SD $_{E-B}$ values of the Difference $_{E-B}$ for each variable.

nonblinded assessor decided the quality of the studies when disagreements occurred between the 2 assessors. This assessment did not determine the exclusion of any study.

RESULTS

Study Characteristics

The study selection process of this systematic review is presented with a flowchart diagram in Figure 1. The design of the included studies was prospective randomized controlled trials published between 2013 and 2023. This systematic review included 628 eyes from 314 patients with a mean age of 47.1 ± 16.1 years. The sex distribution was 165 females (72.3%) and 63 males (27.7%). One study did not report sex distribution.[28] Patient follow-up, expressed in months, ranged from 0.25 months[10,29] to 2 months,[30,31] with a mean follow-up of 1.1 ± 0.6 months. Regarding the eyelid exfoliation device, 2 studies used the stainless-steel golf club spud[26,27] and 5 studies utilized the BlephEx instrument.[10,28–31] Concerning clinical applications of eyelid exfoliation treatment, 2 studies used this treatment for DED,[26,27] 4 studies for blepharitis,[10,28,30,31] and 2 studies for CL discomfort.[10,29] Regarding study group intervention, 2 studies performed eyelid exfoliation treatment alone,[27,29] whereas 5 studies performed eyelid exfoliation treatment combined with antimicrobial lid scrubs composed of terpinen-4-ol[30,31] and 1,2-octanediol[28] or warm compresses.[26] Different interventions were used in the control group, such as warm compresses,[26] terpinen-4-ol,[28] 1,2-octanediol,[28] LidHygenix (Optimed Ltd.),[10,29] eyelid exfoliation treatment combined with sham lid scrubs,[30] sham eyelid exfoliation treatment combined with terpinen-4-ol,[31] and no intervention.[27] One study had conflicts of interest among the authors.[26] More detailed study characteristics are presented in Table 1.

Outcomes

Regarding eyelid exfoliation treatment in DED, 5 studies reported symptom outcomes,[26–28,30,31] of which 4 studies used the OSDI questionnaire[27,28,30,31] and 1 study used the SPEED questionnaire.[26] Five studies also reported sign

TABLE 4. Intergroup Differences [(Treatment Group $_{E-B}$) − (Control Group $_{E-B}$)] Outcomes

	DED						Blepharitis		CL Discomfort	
Author (Date)	**OSDI (0–100)**	**SPEED (0–28)**	**TBUT (s)**	**OSS**	**MGS (0–4)**	**MGYLS (0–15)**	**Microorganism Load**	**Lipase Activity**	**CLDEQ-8 (0–37)**	***F/A***
Korb et al[26] (2013)										
T difference $_{E-B}$	NR	−2.9*	NR	NR	1.2*	NR	NR	NR	NR	*F*
C difference $_{E-B}$	NR	0.6	NR	NR	−0.3	NR	NR	NR	NR	—
Difference $_{T-C}$	—	**−3.5**	—	—	**1.5**	—	—	—	—	—
Ngo et al[27] (2015)										
T difference $_{E-B}$	−16.3*	NR	0.3	−1.6*	2.1*	0.6	NR	NR	NR	*F*
C difference $_{E-B}$	−10.0	NR	−0.1	1.2	−0.3	−0.3	NR	NR	NR	—
Difference $_{T-C}$	**−6.3**	—	**0.4**	**−2.8**	**2.4**	**0.9**	—	—	—	—
Murphy et al[28] (2018)										
T difference $_{E-B}$	−17.3*	NR	NR	NR	NR	NR	−3.8*	NR	NR	*F*
C difference $_{E-B}$	−13.1*	NR	NR	NR	NR	NR	−2.4*	NR	NR	—
Difference $_{T-C}$	**−4.2**	—	—	—	—	—	**−1.4**	—	—	—
Siddireddy et al[29] (2019)										
T difference $_{E-B}$	NR	NR	0.4*	NR	NR	NR	NR	NR	−2.6*	*F*
C difference $_{E-B}$	NR	NR	0.2*	NR	NR	NR	NR	NR	−0.5	—
Difference $_{T-C}$	—	—	**0.2**	—	—	—	—	—	**−2.1**	—
Epstein et al[30] (2020)										
T difference $_{E-B}$	−4.0	NR	NR	−0.2	0.1	0.3	−2.1*	NR	NR	*F*
C difference $_{E-B}$	0.3	NR	NR	−0.3	0.4	0.0	−2.6*	NR	NR	—
Difference $_{T-C}$	**−4.3**	—	—	**0.1**	**−0.3**	**0.3**	**0.4**	—	—	—
Siddireddy et al[10] (2020)										
T difference $_{E-B}$	NR	NR	NR	NR	NR	NR	−41,7*	−24.0*	−2.7*	*F*
C difference $_{E-B}$	NR	NR	NR	NR	NR	NR	−30.3	−7.3	−0.5	—
Difference $_{T-C}$	—	—	—	—	—	—	**−11.4**	**−16.7**	**−2.2**	—
Amir Arabi et al[31] (2023)										
T difference $_{E-B}$	−11.1*	NR	1.5*	NR	NR	NR	−2.2*	NR	NR	*F*
C difference $_{E-B}$	−5.8*	NR	0.8*	NR	NR	NR	−1.8*	NR	NR	—
Difference $_{T-C}$	**-5.3**	—	**0.7**	—	—	—	**-0.4**	—	—	—

The significance of bold values* is $P < 0.05$.

CL indicates contact lens; CLDEQ-8, Contact Lens Dry Eye Questionnaire-8; DED, dry eye disease; MGS, meibomian gland secretion; MGYLS, meibomian gland yielding liquid secretion; NR, not reported; OSDI, Ocular Surface Disease Index; OSS, ocular staining score; SPEED, standard patient evaluation of eye dryness; TBUT, tear breakup time.

F/A = authors opinion expressed by commenting in favor or against of eyelid exfoliation treatment.

*Statistical significance level $P < 0.05$.

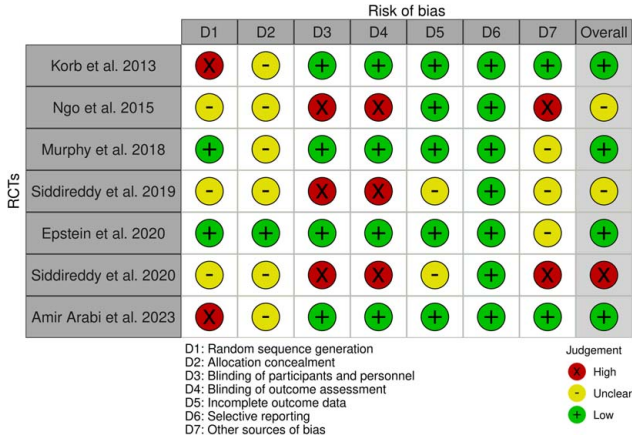

FIGURE 2. Risk of bias summary of the included studies with traffic light plot. The traffic lights represent the author's risk of bias judgment in each domain used to assess the quality of the studies. D indicates domain; RCTs, randomized controlled trials.

outcomes,[26,27,29–31] of which 3 studies evaluated TBUT[27,29,31] and MGS[26,27,30] and 2 studies assessed OSS and MGYLS.[27,30] Concerning eyelid exfoliation treatment in blepharitis, 4 studies evaluated microorganism load[10,28,30,31] and 1 study assessed lipase activity.[10] Regarding eyelid exfoliation treatment in CL discomfort, 2 studies evaluated CL wearer's discomfort with the CLDEQ-8.[10,29]

Intergroup clinical outcomes are presented in Tables 2 and 3. Regarding the treatment group, most of the outcomes achieved an improvement, with a mean OSDI questionnaire score of –12.1 ± 5.3 (–17.3 to –4.0) points, mean TBUT of 0.7 ± 0.5 (0.3 to 0.4) seconds, mean OSS of –0.9 ± 0.7 (–1.6 to –0.2) points, mean MGS of 1.1 ± 0.8 (0.1 to 2.1) points, mean microorganism load of –12.5 ± 16.9 (–41.7 to –2.1) points, and mean CLDEQ-8 of –2.6 ± 0.1 (–2.7 to –2.6) points. The SPEED questionnaire and lipase activity also achieved an improvement of –2.9 points and –24.0 mm, respectively. MGYLS remained almost unchanged with a mean value of 0.5 ± 0.2 (0.3 to 0.6) points. Regarding the control group, most of the outcomes also achieved an improvement, with a mean OSDI questionnaire value of –7.2 ± 5.0 (–13.1 to 0.3) points, mean TBUT value of 0.3 ± 0.4 (–0.1 to 0.8) seconds, mean OSS 0.5 ± 0.8 (–0.3 to 1.2) points, microorganism load of –9.4 ± 12.5 (–30.3 to –1.8) points, and CLDEQ-8 –0.5 ± 0.0 (–0.5 to –0.5) points. The lipase activity also showed an improvement of –7.3 mm, whereas the SPEED questionnaire remained almost unchanged with a value of 0.6 points. MGS and MGYLS also remained almost unchanged with a mean value of –0.1 ± 0.3 (–0.3 to 0.4) points and –0.2 ± 0.2 (–0.3 to 0.0) points, respectively.

Intergroup clinical outcomes are presented in Table 4. Regarding eyelid exfoliation treatment in DED, blepharitis, and CL discomfort, all outcomes were in favor of the treatment group, with a mean OSDI questionnaire score of –5.0 ± 0.9 (–6.3 to –4.2) points, mean TBUT of 0.43 ± 0.2 (0.2 to 0.7) seconds, mean OSS of –1.4 ± 1.5 (–2.8 to 0.1) points, mean MGS of 1.2 ± 1.1 (–0.3 to 2.4) points, mean MGYLS of 0.6 ± 0.3 (0.3 to 0.9) points, mean microorganism load of –3.2 ± 4.7 (–11.4 to 0.4) points, and mean CLDEQ-8 of –2.15 ± 0.1 (–2.2 to –2.1) points. The SPEED questionnaire and lipase activity achieved a treatment group improvement of –3.5 points and –16.7 mm compared with the control group, respectively. Regarding complications, 1 study reported no complications after an eyelid exfliation treatment.[26] However, 2 studies reported nonsevere complications after an eyelid exfoliation treatment, which include minimal discomfort (n = 13)[27] and eyelid irritation (n = 2).[31]

Risk of Bias

The risk of bias summary of the included studies is presented in Figure 2. Risk of bias assessment was classified into 3 evidence level groups: (1) studies with a low risk of bias (Korb and Blackie,[26] Murphy et al.,[28] Epstein et al,[30] and Amir et al[31]), (2) studies with an unclear risk of bias (Ngo et al[27] and Siddireddy et al[29]) and (3) studies with a high risk of bias (Siddireddy et al[10]). The overall risk of bias summary of the domains used in each study is presented in Figure 3. The items used to assess the risk of bias showed an overall low risk of bias, which was > 50%. The Robvis tool (NIHR) was used to create the risk of bias assessment figures.[42]

DISCUSSION

Tear film evaporation is considered the trigger for the ocular surface inflammatory mechanisms that lead to the signs and symptoms of dry eye.[2] For this reason, new treatment options have been designed to improve the lipid layer tear film, thus reducing the tear evaporation ratio.[43,44] Eyelid exfoliation treatments are designed to improve eyelash health

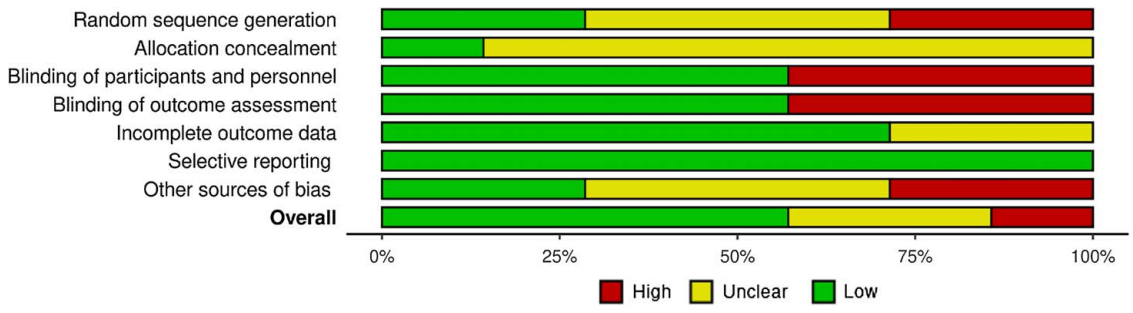

FIGURE 3. Overall risk of bias summary of the domains with bar plot. Bars represent the overall author's risk of bias judgment in each domain presented as percentages.

and meibomian gland expressibility, which is responsible for a healthy lipid layer tear film. This systematic review aimed to report the effects of eyelid exfoliation treatment in conditions that cause tear film evaporation, such as DED, blepharitis, and CL discomfort.

Eyelid Exfoliation Treatment in Dry Eye Disease

Although there are different questionnaires to assess dry eye symptoms, the OSDI questionnaire is the most widely used for DED studies.[45] Ngo et al,[27] Murphy et al,[28] and Amir et al[31] reported a treatment group OSDI questionnaire improvement of –6.3, –4.2, and –5.3 points compared with the control group, respectively. Murphy et al[28] and Amir et al[31] also reported a significant OSDI questionnaire improvement in the control group, which may be because both control groups were treated with eyelid hygiene. Some studies have reported the benefits of eyelid hygiene in dry eye symptoms.[46,47] Murphy et al[46] reported a nonsignificant OSDI questionnaire improvement of –5.5 and –6.5 points after eyelid hygiene treatment with 1,2-octanediol and terpinen-4-ol lid scrubs, respectively. Moreover, Arici et al[47] obtained a significant symptom improvement of 10.1 points with terpinen-4-ol lid scrubs. Score differences between both studies may have been because they used different questionnaires to assess dry eye symptoms. Arici et al[47] used the blepharitis symptoms (BLISS) questionnaire, whereas Murphy et al[46] used the OSDI questionnaire. In addition, Arici et al[47] included 24 patients in the terpinen-4-ol group, whereas Murphy et al[46] included 12 and 13 patients in the 1,2-octanediol and terpinen-4-ol groups, respectively. Sample size differences may explain the statistical results obtained in both studies. Epstein et al[30] also reported a treatment group OSDI questionnaire improvement of –4.3 points compared with the control group. However, they obtained a nonsignificant OSDI questionnaire improvement in the treatment group, which may also be explained by the smaller sample size reported. In addition, it is important to consider that Ngo et al[27] reported a significant treatment group OSDI questionnaire improvement with a smaller sample size than Epstein et al[30] However, these studies are not comparable since both treatment groups received eyelid exfoliation treatment with different devices. Korb and Blackie[26] is the only study that assessed DED symptoms with the SPEED questionnaire, and they reported a treatment group SPEED questionnaire improvement of –3.5 points compared with the control group.

Tear film stability and damage to the ocular surface are recommended by the Tear Film and Ocular Surface Society Dry Eye Workshop II for DED diagnosis.[45] Tear film stability was evaluated by TBUT. Ngo et al,[27] Siddireddy et al,[29] and Amir et al[31] reported a treatment group TBUT improvement of 0.4, 0.2, and 0.7 seconds compared with the control group, respectively. Siddireddy et al[29] and Amir et al[31] also reported significant TBUT improvements in the control groups. This may be because both control groups received eyelid hygiene as an intervention. Moreover, Arici et al[47] reported significant TBUT improvement with terpinen-4-ol lid scrubs after 8 weeks of treatment. Ngo et al[27] reported the lowest noninvasive break-up time (NIBUT) improvement in the treatment group. This may be because they included patients with Sjogren syndrome, who have higher DED and MGD severity.[2] Damage to the ocular surface was assessed by the OSS. Ngo et al[27] reported that eyelid exfoliation treatment alone achieved a treatment group OSS improvement of 2.8 points compared with the control group. However, Epstein et al[30] reported a similar OSS improvement in both groups. This result may have been due to the treatment and control groups receiving eyelid exfoliation treatment, obtaining nonsignificant OSS improvements of 0.2 and 0.3 points, respectively. In addition, score differences between both studies may be explained because Ngo et al[27] assessed OSS with Sjogren's International Collaborative Clinical Alliance Ocular Staining Score, whereas Epstein et al[30] used the Oxford grading score. Therefore, the OSS results are not comparable.

Meibum quantity and quality are recommended by the international workshop on MGD.[38] Meibum quantity was evaluated with MGS. Korb and Blackie[26] and Ngo et al[27] reported that the eyelid exfoliation treatment group obtained an MGS improvement of 1.5 and 2.4 points compared with the control group, respectively. However, Epstein et al[30] reported an MGS improvement of 0.1 and 0.4 in the treatment and control groups, respectively. This result may be because both groups received eyelid exfoliation treatment. Score differences between the aforementioned studies may be because Korb and Blackie[26] and Ngo et al[27] performed LDS, whereas Epstein et al[30] performed MBE. Meibum quality was assessed with MGYLS. Ngo et al[27] and Epstein et al[30] reported that MGYLS remained unchanged in both groups, which suggests that eyelid exfoliation treatment increases the quantity of meibum expressed without improving the quality of meibum. This is in accordance with the mechanism behind eyelid exfoliation treatment, which allows the removal of the epithelial keratinization and debris accumulated in the eyelid margin that prevents the delivery of meibum onto the ocular surface.[26] An increased quantity of meibum expression improves the lipid layer tear film, resulting in a better TBUT and, therefore, lower DED symptoms.

Eyelid Exfoliation Treatment in Blepharitis

Approximately 42% of patients attending eye care practitioners have been diagnosed with blepharitis;[48] therefore, it is a common eye condition.[49] However, blepharitis is often insufficiently treated,[29] leading to a high risk of anxiety and depression due to the eyelid appearance and ocular symptoms, which may affect the patient's social life.[50] Some studies have reported that eyelid hygiene is an effective treatment for blepharitis,[51,52] but this treatment is only limited to eyelash cleaning. Murphy et al[28] and Amir et al[31] reported that eyelid exfoliation treatment combined with eyelid hygiene achieved reductions in Demodex folliculorum of –1.4 and –0.4 points compared with eyelid hygiene alone, respectively. However, Epstein et al[30] reported a similar Demodex folliculorum count improvement in both groups. This result may be due to the treatment and control groups receiving eyelid exfoliation treatment and eyelid hygiene as interventions, obtaining similarly significant reductions in Demodex folliculorum counts of –2.1 and –2.6 points, respectively. Siddireddy et al[10] reported a treatment group microorganism load improvement of –11.4 points compared with the control group. Score differences between the aforementioned studies are due to the type of microorganism load analyzed. Siddireddy et al[10] an-

alyzed gram-positive cocci and bacilli recorded as colony-forming units per swab, whereas Murphy et al,[28] Epstein et al,[30] and Amir et al[31] analyzed the count of Demodex folliculorum present on patient eyelashes as examined by microscopy. Siddireddy et al[10] also reported lipase activity, obtaining a treatment group lipase activity improvement of –16.7 mm compared with the control group. In addition, Wong et al[53] reported that lipase activity remained unchanged after terpinen-4-ol lid scrub treatment for blepharitis. All these results suggest that eyelid exfoliation treatment combined with eyelid hygiene is more effective than eyelid hygiene alone. Eyelid exfoliation treatment also cleans the eyelashes but more efficiently than the lid scrubs used for eyelid hygiene.[31] In addition, eyelid exfoliation treatment is able to remove the microorganism load present on the eyelid margin, reducing the lipase activity that saponifies the meibum and inflames the meibomian glands.[31]

Eyelid Exfoliation Treatment in Contact Lens Discomfort

CL discomfort is one of the main reasons for CL wear discontinuation.[54] There are different risk factors for CL discomfort, of which DED is the most common cause.[55] In addition, some studies have reported that CL wear is associated with higher MGD prevalence,[21–23] resulting in reduced lipid layer thickness and tear stability,[7] increasing the probability of experiencing CL discomfort.[19,20] Siddireddy et al 2019[29] and 2020[10] reported that eyelid exfoliation alone obtained CLDEQ-8 improvements of –2.1 and –2.2 points, respectively, compared with hypoallergenic eyelid cleansing foam. Some studies have suggested that eyelid hygiene reduces CL discomfort in MGD patients.[56] However, this treatment is only effective in certain grades of MGD.[29] These results suggest that eyelid exfoliation treatment is more effective than eyelid hygiene for CL discomfort management. This may be due to the fact that eyelid exfoliation treatment cleans the eyelid margin, removing the meibomian gland capping, which improves their expressibility. Increasing meibum secretion volume leads to a better lipid layer tear film, which reduces the tear evaporation ratio and therefore discomfort symptoms in CL wearers.

Complications

Murphy et al,[28] Siddireddy et al,[10,29] and Epstein et al[30] did not report whether the patients experienced any complications after an eyelid exfoliation treatment. Korb and Blackie[26] and Ngo et al[27] reported that 28 patients experienced no discomfort and 13 patients had minimal discomfort after LDS treatment, respectively. However, Amir et al[31] reported 2 cases of eyelid margin irritation after eyelid exfoliation treatment with the BlephEx instrument. This device performed eyelid exfoliation with a medical-grade microsponge; thus it is common for patients to not experience significant complications after this treatment. In addition, nonsevere complications were reported in the articles included in this systematic review.

Strengths and Limitations

All studies included in this systematic review are randomized controlled studies with an overall low risk of bias. The main limitation of our review is the heterogeneity of the treatment and control group interventions, which complicates comparisons between the included studies. In addition, Korb and Blackie[26] and Ngo et al[27] performed eyelid exfoliation treatment with a stainless-steel golf club spud, whereas Murphy et al,[28] Siddireddy et al,[10,29] Epstein et al,[30] and Amir et al[31] used the BlephEx instrument; thus the methodologies of all studies were not remarkably similar. The short follow-up period is also a limitation that may have influenced the results reported by the included studies. Another limitation is that Ngo et al[27] and Siddireddy et al[10,29] were the only studies that analyzed the efficacy and safety of eyelid exfoliation treatment alone. Therefore, larger, well-designed, strictly blinded, multicenter randomized controlled studies with extensive follow-up are needed to determine the safety and efficacy of eyelid exfoliation treatment alone versus eyelid exfoliation treatment combined with other treatments, such as intense pulse light or meibomian gland expression, and their duration over time.

CONCLUSIONS

This systematic review demonstrated that eyelid exfoliation treatment achieves better results than eyelid hygiene, reporting minimal complications. Concretely, LDS and MBE are effective and safe treatments that should be recommended as a treatment option for DED, whereas MBE should be recommended for blepharitis and CL discomfort. LDS and MBE decrease DED symptoms and increase TBUT. However, there is insufficient evidence to suggest that LDS and MBE improve OSS. In addition, LDS seems to achieve better meibomian gland expressibility than MBE, and a decrease in microorganism load, lipase activity, and CL discomfort has been reported after MBE. Therefore, combining both eyelid exfoliation treatments should be considered when blepharitis and MGD coexist.

REFERENCES

1. Zhu D, Gupta RR, Stein RL, et al. Randomized prospective evaluation of microblepharoexfoliation BlephEx as adjunctive therapy in the treatment of chalazia. *Cornea*. 2023;42:172–175.
2. Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II pathophysiology report. *Ocul Surf*. 2017;15:438–510.
3. Knop E, Knop N, Millar T, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. *Invest Ophthalmol Vis Sci*. 2011;52:1938.
4. Craig JP, Nelson JD, Azar DT, et al. TFOS DEWS II report executive summary. *Ocul Surf*. 2017;15:802–812.
5. Rynerson JM, Perry HD. DEBS—a unification theory for dry eye and blepharitis. *Clin Ophthalmol*. 2016;10:2455–2467.
6. Kojima T, Ibrahim OMA, Wakamatsu T, et al. The impact of contact lens wear and visual display terminal work on ocular surface and tear functions in office workers. *Am J Ophthalmol*. 2011;152:930–940. doi:10.1016/J.AJO.2011.05.025
7. Gomes JAP, Azar DT, Baudouin C, et al. TFOS DEWS II iatrogenic report. *Ocul Surf*. 2017;15:511–538.
8. Amescua G, Akpek EK, Farid M, et al. Blepharitis preferred practice pattern. *Ophthalmology*. 2019;126:56–93.

9. McCulley JP, Shine WE. Meibomian gland function and the tear lipid layer. *Ocul Surf*. 2003;1:97–106.
10. Siddireddy JS, Vijay AK, Tan J, et al. Effect of eyelid treatments on bacterial load and lipase activity in relation to contact lens discomfort. *Eye Contact Lens*. 2020;46:245–253.
11. Liu J, Sheha H, Tseng SCG. Pathogenic role of Demodex mites in blepharitis. *Curr Opin Allergy Clin Immunol*. 2010;10:505–510.
12. Kabataş N, Dogan AŞ, Kabataş EU, et al. The effect of Demodex infestation on blepharitis and the ocular symptoms. *Eye Contact Lens*. 2017;43:64–67.
13. Akkucuk S, Kaya OM, Aslan L, et al. Prevalence of Demodex folliculorum and Demodex brevis in patients with blepharitis and chalazion. *Int Ophthalmol*. 2022. Online ahead of print. doi:10.1007/S10792-022-02523-Y
14. Fromstein SR, Harthan JS, Patel J, et al. Demodex blepharitis: clinical perspectives. *Clin Optom (Auckl)*. 2018;10:57–63.
15. Shah PP, Stein RL, Perry HD. Update on the management of Demodex blepharitis. *Cornea*. 2022;41:934–939.
16. Dougherty JM, McCulley JP. Analysis of the free fatty acid component of meibomian secretions in chronic blepharitis. *Invest Ophthalmol Vis Sci*. 1986;27:52–56.
17. Guillon M, Maissa C, Wong S. Eyelid margin modification associated with eyelid hygiene in anterior blepharitis and meibomian gland dysfunction. *Eye Contact Lens*. 2012;38:319–325.
18. Rohit A, Willcox MDP, Brown SHJ, et al. Clinical and biochemical tear lipid parameters in contact lens wearers. *Optom Vis Sci*. 2014;91:1384–1390.
19. Siddireddy JS, Vijay AK, Tan J, et al. The eyelids and tear film in contact lens discomfort. *Cont Lens Anterior Eye*. 2018;41:144–153.
20. Blanco-Vázquez M, Arroyo-Del-Arroyo C, Novo-Diez A, et al. Is contact lens discomfort related to meibomian gland morphology. *Cont Lens Anterior Eye*. 2022;45:101743.
21. Ong BL, Larke JR. Meibomian gland dysfunction: some clinical, biochemical and physical observations. *Ophthalmic Physiol Opt*. 1990;10:144–148.
22. Ong BL. Relation between contact lens wear and Meibomian gland dysfunction. *Optom Vis Sci*. 1996;73:208–210.
23. Arita R, Fukuoka S, Morishige N. Meibomian gland dysfunction and contact lens discomfort. *Eye Contact Lens*. 2017;43:17–22.
24. Alghamdi WM, Markoulli M, Holden BA, et al. Impact of duration of contact lens wear on the structure and function of the meibomian glands. *Ophthalmic Physiol Opt*. 2016;36:120–131.
25. Sindt CW, Longmuir RA. Contact lens strategies for the patient with dry eye. *Ocul Surf*. 2007;5:294–307.
26. Korb DR, Blackie CA. Debridement-scaling: a new procedure that increases meibomian gland function and reduces dry eye symptoms. *Cornea*. 2013;32:1554–1557.
27. Ngo W, Caffery B, Srinivasan S, et al. Effect of lid debridement-scaling in Sjögren syndrome dry eye. *Optom Vis Sci*. 2015;92:316–320.
28. Murphy O, O'Dwyer V, Lloyd-McKernan A. The efficacy of tea tree face wash, 1, 2-Octanediol and microblepharoexfoliation in tre ating Demodex folliculorum blepharitis. *Cont Lens Anterior Eye*. 2018;41:77–82.
29. Siddireddy JS, Tan J, Vijay AK, et al. The effect of microblepharon exfoliation on clinical correlates of contact lens discomfort. *Optom Vis Sci*. 2019;96:187–199.
30. Epstein IJ, Rosenberg E, Stuber R, et al. Double-masked and unmasked prospective study of terpinen-4-ol lid scrubs with microblepharoexfoliation for the treatment of Demodex blepharitis. *Cornea*. 2020;39:408–416.
31. Mohammad-Rabei H, Arabi A, Shahraki T, et al. Role of blepharoexfoliation in Demodex blepharitis: a randomized comparative study. *Cornea*. 2023;42:44–51.
32. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
33. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ*. 2021;372:160.
34. Dougherty BE, Nichols JJ, Nichols KK. Rasch analysis of the Ocular Surface Disease Index (OSDI). *Invest Ophthalmol Vis Sci*. 2011;52:8630–8635.
35. Ngo W, Situ P, Keir N, et al. Psychometric properties and validation of the Standard Patient Evaluation of Eye Dryness questionnaire. *Cornea*. 2013;32:1204–1210.
36. Bron AJ, Evans VE, Smith JA. Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea*. 2003;22:640–650.
37. Rose-Nussbaumer J, Lietman TM, Shiboski CH, et al. Inter-grader agreement of the Ocular Staining Score in the Sjögren's International Clinical Collaborative Alliance (SICCA) Registry. *Am J Ophthalmol*. 2015;160:1150–1153.
38. Tomlinson A, Bron AJ, Korb DR, et al. The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. *Invest Ophthalmol Vis Sci*. 2011;52:2006–2049.
39. Kheirkhah A, Blanco G, Casas V, et al. Fluorescein dye improves microscopic evaluation and counting of demodex in blepharitis with cylindrical dandruff. *Cornea*. 2007;26:697–700.
40. Chalmers RL, Begley CG, Moody K, et al. Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) and opinion of contact lens performance. *Optom Vis Sci*. 2012;89:1435–1442.
41. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
42. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): an R package and Shiny web app for visualizing risk-of-bias assessments. *Res Synth Methods*. 2021;12:55–61.
43. Tashbayev B, Yazdani M, Arita R, et al. Intense pulsed light treatment in meibomian gland dysfunction: a concise review. *Ocul Surf*. 2020;18:583–594.
44. Markoulli M, Chandramohan N, Papas EB. Photobiomodulation (low-level light therapy) and dry eye disease. *Clin Exp Optom*. 2021;104:561–566.
45. Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II Diagnostic Methodology report. *Ocul Surf*. 2017;15:539–574.
46. Murphy O, O' Dwyer V, Lloyd-McKernan A. The effect of lid hygiene on the tear film and ocular surface, and the prevalence of Demodex blepharitis in university students. *Cont Lens Anterior Eye*. 2020;43:159–168.
47. Arici C, Mergen B, Yildiz-Tas A, et al. Randomized double-blind trial of wipes containing terpinen-4-ol and hyaluronate versus baby shampoo in seborrheic blepharitis patients. *Eye (Lond)*. 2022;36:869–876.
48. Lemp MA, Nichols KK. Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. *Ocul Surf*. 2009;7:S1.

49. Lindsley K, Matsumura S, Hatef E, et al. Interventions for chronic blepharitis. *Cochrane Database Syst Rev*. 2012;2012:CD005556.
50. Chiang CC, Lin CL, Tsai YY, et al. Patients with blepharitis are at elevated risk of anxiety and depression. *PLoS One*. 2013;8:e83335.
51. Koo H, Kim TH, Kim KW, et al. Ocular surface discomfort and Demodex: effect of tea tree oil eyelid scrub in Demodex blepharitis. *J Korean Med Sci*. 2012;27:1574–1579.
52. Ergun SB, Saribas GS, Yarayici S, et al. Comparison of efficacy and safety of two tea tree oil-based formulations in patients with chronic blepharitis: a double-blinded randomized clinical trial. *Ocul Immunol Inflamm*. 2020;28:888–897.
53. Wong K, Flanagan J, Jalbert I, et al. The effect of Blephadex Eyelid Wipes on Demodex mites, ocular microbiota, bacterial lipase and comfort: a pilot study. *Cont Lens Anterior Eye*. 2019;42:652–657.
54. Stapleton F, Bakkar M, Carnt N, et al. CLEAR—contact lens complications. *Cont Lens Anterior Eye*. 2021;44:330–367.
55. Koh S. Contact lens wear and dry eye: beyond the known. *Asia Pac J Ophthalmol*. 2020;9:498–504.
56. Arroyo-Del Arroyo C, Fernández I, Novo-Diez A, et al. Contact lens discomfort management: outcomes of common interventions. *Eye Contact Lens*. 2021;47:256–264.