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Randomized Prospective Evaluation of Microblepharoexfoliation BlephEx as Adjunctive Therapy in the Treatment of Chalazia

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Purpose: Chalazia are benign eyelid lesions caused by the obstruction and inflammatory reaction of the meibomian glands. *Demodex* mites are one potential cause of chalazia leading to mechanical obstruction of the meibomian gland. In this prospective randomized study, we examine a novel approach to treating chalazia with the use of microblepharoexfoliation (MBE), an in-office lid hygiene technique that exfoliates the eyelid margins.

Methods: Fifty patients with clinical evidence of acute chalazion were enrolled in this study. Subjects were randomly assigned to a MBE plus lid hygiene group (23 patients, mean age 66.6 ± 16.6 years) or a lid hygiene alone group (27 patients, mean age 62.1 ± 14.4). The MBE plus lid hygiene group received MBE treatment and were evaluated 1 month after the baseline visit. The main outcome measured was the resolution of the chalazion at the 1-month follow-up visit.

Results: The lid hygiene plus MBE treatment group demonstrated a statistically significant resolution of the chalazion compared with the lid hygiene group alone ($P = 0.007$; chi-square test). Among the MBE plus hygiene group, 87% of the patients had resolution of their chalazion as opposed to the lid hygiene alone group, which had 44% resolution.

Conclusions: This is the first prospective, randomized clinical trial that demonstrated efficacy of MBE as a noninvasive adjunctive treatment method for chalazion resolution.

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Chalazia are common lipogranulomatous lesions resulting from the blockage and subsequent inflammation of the meibomian glands.[1] It is one of the most common benign eyelid lesions, with a reported prevalence of 0.57% in a large observational study.[2] Although most chalazia are typically asymptomatic, larger ones can cause visual dysfunction as a consequence of mechanical ptosis or induced astigmatism.[3] The treatment of chalazia initially begins with conservative treatment (lid hygiene) including warm saline compresses; surgery is considered second line for chalazia refractory to conservative management.[2,4] Other treatments for chalazia include oral doxycycline, antibiotic–steroid ointments, and meibomian gland expression.[5,6]

One suspected cause of chalazia is the *Demodex* mite, the most common human skin ectoparasite.[7] Although chalazia are most often due to ocular rosacea or generalized lid inflammation, *Demodex* has been characterized as a possible risk factor for recurrent chalazia in adults.[1,8] The 2 species known to infest the skin of humans are *Demodex folliculorum (D. folliculorum)* and *Demodex brevis (D. brevis)*.[9,10] Although the exact mechanism of how *Demodex* mite infestation results in chalazia formation remains undetermined, suggested theories include the mite causing mechanical obstruction leading to meibomian gland dysfunction and that the exoskeleton of the mite could induce a granulomatous reaction.[7] A histopathologic study examining full-thickness eyelid wedge resections reported that mean numbers of *D. folliculorum* were significantly higher in biopsies with chalazia when compared with biopsies without chalazia, and that *D. brevis* was only found in meibomian glands that had chalazia.[11]

A novel approach to the treatment of *Demodex* infestation of the eyelid is the use of microblepharoexfoliation (MBE).[12–14] MBE is a novel method of in-office lid hygiene that works by exfoliating the eyelid margins to remove accumulated biofilm debris along with any *Demodex* mites to clean the lid margin, reduce lid inflammation, and improve meibomian gland function. Although studies have investigated MBE use in the context of blepharitis, no study to the best of our knowledge has examined the use of MBE for the

treatment of chalazia. In this prospective randomized study, we aim to evaluate the utility of MBE for resolving chalazia in conjunction with traditional lid hygiene. Second, we attempt to correlate *Demodex* infestation with the incidence and severity of chalazia.

METHODS

The purpose of the study was to evaluate microblepharoexfoliation (MBE) treatment using the BlephEx rotating brush (2500 rpm) as adjunctive therapy for chalazia. This investigation was a prospective, randomized, institutional review board (IRB)-approved study of 50 consecutive patients with chalazia and was conducted at 2 sites, Ophthalmic Consultants of Long Island (OCLI) in Rockville Centre, NY, and Nassau University Medical Center (NUMC) in East Meadow, NY. The duration of the study was 1 month.

At the baseline visit, subjects were randomized to receive an in-office MBE treatment (BlephEx LLC; Franklin, TN) or not. All subjects were instructed about the probable etiology of their chalazia being blocked ducts through a patient/physician conference aided by a diagram of the lid margin and meibomian glands (Fig. 1) and instructed to perform lid hygiene with warm saltwater soaks twice daily until the next study visit (lid hygiene instruction sheet, adapted from Perry and Serniuk[1] (Table 1). Subjects were re-evaluated at the second visit approximately 1 month later.

The IRB (Biomedical Research Alliance of NY) and IRB of NuHealth (NUMC) approved this study, and the study was performed in accordance with the tenants of the Declaration of Helsinki. Although subjects did not receive direct compensation for their participation, all fees related to ophthalmic examination including slit-lamp examination, testing, and treatments for all study visits were waived.

Patients were expected to be recruited from 2 cohorts of patients from OCLI and NUMC. Because of delays of the NUMC IRB, all 50 patients were recruited from OCLI. Study subjects were required to be 18 years or older with the ability to consent for eye examination, diagnostic testing, and noninvasive ophthalmic office procedures (epilation). All patients were examined by an experienced clinician and had to have clinical evidence of chalazion in the acute, inflammatory phase on slit-lamp examination and symptoms from their chalazion for 7 days or less. All lesions that were not clearly chalazia were not included in this study. Potential subjects also had 1 eyelash epilated and examined under the microscope to assess for *Demodex* positivity with the total number of *Demodex* mites on the lash counted and recorded. Subjects were excluded if they were pregnant, younger than 18 years, lacked the ability to consent for diagnostic procedures, illiterate, or had BlephEx (MBE) treatment within 1 month of study enrollment.

After the discussion and the procurement of informed consent for participation in this study, subjects were enrolled and given an identification (ID) number ranging from 1 to 50, which were preassigned to either A (MBE plus lid hygiene) or B (lid hygiene alone) using a randomization table based on block randomization.[15] For the 50 total subjects, there were no 2 ID numbers with the same enrollment number and if a patient exited the study secondary to any reason, their study ID number was vacated and was not reused. Subjects randomized to group A received MBE treatment performed in the office by a certified technician, and all subjects (groups A and B) were given verbal and written instructions to perform lid hygiene with twice daily warm saltwater-soaked cotton balls for 1 month.[16]

A window of up to 7 days before or 14 days after the exact date and 1 month after the baseline visit were considered to be acceptable to assess subjects at the 1-month follow-up interval. An eyelash was epilated at the 1-month visit to check for *Demodex* positivity on light microscopy, with the total number of Demodex mites on the field counted and recorded. A complete evaluation was performed, which consisted of a comprehensive slit-lamp examination, assessment of chalazion presence and size, administration of the Ocular Surface Disease Index (OSDI) questionnaire, tear osmolarity testing, Lissamine green staining of the ocular surface, matrix metalloproteinase-9 (MMP-9) tear level testing, and Schirmer 1 testing. Subjects in the lid hygiene group who did not receive MBE were given an opportunity to have the MBE procedure performed at the 1-month visit. Meibomian gland expression was not conducted during this study because of the level of pain associated with this procedure.[6]

The OSDI questionnaire, which consists of 12 questions assessing eye comfort, was performed at each visit and was used to qualify and quantify the degree of eye irritation and symptoms of dry eye in a standardized fashion.[17] The TearLab Osmolarity System (TearLab Corporation, San Diego, CA) was used for tear osmolarity testing that was performed by wetting a filter paper with a sample of the

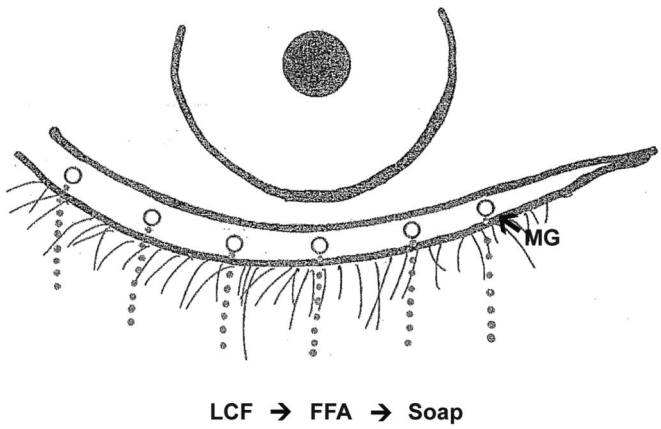

FIGURE 1. Diagram of the lid margin and meibomian glands. LCA is long-chain fatty acids, FFA is free fatty acids. With time, MGD (meibomian gland dysfunction) leads to this biochemical change in the meibum leading to saponification (soap formation) in the tear film. This message was given to the patient and told the blockage of the outlet ducts of the MGs (meibomian glands) leads to chalazia formation. The goal of lid hygiene is to alleviate this blockage and conservatively treat the inflammation.

TABLE 1. Instructions for Lid Hygiene

Reasoning for lid hygiene	This is a simple way to alleviate the problems with seborrheic blepharitis, chronic conjunctivitis, and chalazion. It represents an attack on the accumulated oil secretions of the lid gland. The normal secretions are released through small pores in the front of the lashes of the eyelid. In some people, these secretions accumulate and lead to many different problems. The key to treating all these problems is to clear the lid margins of these built-up secretions. Lid hygiene is the means to achieve this end.
Warm saline soaks	One-half teaspoon of table salt with 1 quart of warm water will give a saline solution (saltwater) that is equal to that in the normal body fluids. This saltwater should be warm to hot, but be careful not to make it too hot because the skin of the eyelids is the thinnest in the body and is very easily burned. Use sterile cotton balls soaked in the saltwater solution that have been slightly wrung. Place 1 on the eye with the lids closed, and let it remain until it cools. Replace with fresh, warm cotton balls and continue this for 10 minutes. This will dissolve the secretions, help soothe burning eyes, and decrease the redness of the lids.
Cleaning the lashes	Using a cotton-tipped applicator moistened with warm to hot saltwater, the lashes are gently brushed from the base toward the ends of the lashes. For the upper lid, this is easy because the eye can remain closed. For the lower lid, this is more difficult and requires extra care. Pull down the lower lid so as to avoid brushing the cotton-tipped applicator against the cornea. The lashes should be cleansed twice a day for the first week.

patients' tears. This is then analyzed by the TearLab system for osmolarity with >308 mOsm/L considered abnormal.[18,19]

The InflammaDry immunoassay (RPS Diagnostics, Sarasota, FL) was used to detect elevated levels of inflammatory marker MMP-9 in tears.[20] A designated filter paper was touched to the patient's tear meniscus and then exposed to the buffer solution. After 10 minutes, results will appear as either a solitary blue line (negative test) or blue and red lines (positive test).

Lissamine green staining of the ocular surface, which stains degenerated and dead cells, as well as mucous fibrils, was performed and graded according to the Oxford Score of 0 to 5 (https://www.aao.org/image/oxford-grading-system). The Schirmer 1 test was performed by placing a standard Schirmer filter paper strip in the inferior fornix without anesthetic and having the eyes closed for 5 minutes. The paper is then removed, and the distance of moisture migration along the paper is measured to quantify both basal and reflex aqueous tear production.[21]

The primary outcome measured in this study was the resolution of chalazion defined as cessation of symptoms and a residual chalazion of 2 millimeters or less. The secondary outcome correlating *Demodex* infestation with chalazion incidence and finally evaluating clinical examination, tear osmolarity testing, Schirmer 1 level, MMP-9 level, Lissamine green staining, and OSDI score for any correlations.

Statistical Package for the Social Sciences version 26 (SPSS Inc., Chicago, IL) was used for data collection and descriptive statistical analyses. When appropriate, chi-square and t-tests were performed to compare groups with $P < 0.05$ for significance.

RESULTS

There was a total of 50 patients with confirmed chalazion who were enrolled in this study: 23 randomized to the MBE plus lid hygiene treatment group and 27 were randomized to the lid hygiene alone group. There were 2 patients who were lost to follow-up in the lid hygiene group. Of the 50 patients, 32 patients (64%) experienced resolution of their chalazion and 16 patients (32%) did not have resolution; the MBE plus lid hygiene group demonstrated a statistically significant resolution of chalazion compared with the lid hygiene alone group ($P = 0.007$; χ^2 test). In the lid hygiene alone group, 44% (12) of patients' chalazion resolved and 48% (13) of patients' chalazion did not. In the MBE plus lid hygiene group, 87% (20) of patients had their chalazion resolve, whereas 13% (3) did not have their chalazion resolve. The demographic characteristics and baseline test results of both treatment arms were relatively evenly matched with no significant differences, as given in Table 2. No patient in either group developed new chalazia during this month-long observation period.

DISCUSSION

Classically, lid hygiene with warm compresses and lid massages can lead to complete resolution of a majority of chalazia within 4 to 6 weeks.[1] If refractory to lid hygiene and other conservative measures, second-line remedies include corticosteroid injections or incision and curettage (I&C).[22,23] These procedural solutions, however, are not without risks such as atrophic skin changes and accidental injection into the ophthalmic artery with the steroid injection or the potential for delayed bleeding and pain with I&C. In procedural

TABLE 2. Summary of the Baseline Characteristics of the Study Treatment Arms

	BlephEx + LH	LH Alone	*P*
Age	66.6 ± 16.6	62.1481 ± 14.4	0.32
Sex	26.1% male 73.9% female	51.8% male 48.1% female	0.06
Race	78.2% White 8.7% Hispanic 13.1% Black	74.1% White 14.8% Hispanic 11.1% Black	0.80
Tear osmolarity	300.7 ± 17.3	292.5 ± 12.1	0.80
Elevated MMP	82.6%	70.3%	0.16
Schirmer 1 test (mm)	16.0 ± 9.5	12.7 ± 8.8	0.22
Conjunctival LG staining (0–4)	1.8 ± 1.3	1.4 ± 0.9	0.22
Corneal LG staining (0–4)	0.9 ± 1.3	0.8 ± 1.1	0.70
Meibography (0–4)	2.0 ± 1.0	2.1 ± 1.2	0.77
OSDI score (0–100)	11.6 ± 11.3	9.9 ± 8.9	0.63
Demodex positivity	17.4%	25.9%	0.60

LH, lid hygiene; LG, Lissamine green; OSDI, Ocular Surface Disease Index.

studies, most patients who underwent these more invasive treatment methods experienced complete resolution of their chalazia (75% to 81%), whereas around one fifth of patients did not have their lesions cured.[23,24] However, in this current study, 87% of patients treated through MBE using BlephEx experienced resolution of their chalazion. MBE, a completely noninvasive treatment modality, achieved resolution rates comparable or even slightly higher than those of the historically more invasive injections and I&C procedures. When compared with the lid hygiene treatment alone group, which had a resolution rate of 44%, significantly higher percentage of patients experienced resolution of their symptoms through MBE ($P = 0.007$). However, no patient in either group developed any new chalazia, supporting the positive effect of lid hygiene. To the best of our knowledge, this is the first study to demonstrate the efficacy of adjunctive MBE for achieving complete resolution of chalazia.

In this study, 22% of patients with chalazia were positive for *Demodex* in their lashes, lower than a previously published prevalence of 69.2%.[9] A possible explanation for the lower prevalence of *Demodex* in this study is that only 1 eyelash was epilated from each eyelid, whereas in the previous study, 2 eyelashes were removed. In addition, the percentage of *Demodex* positivity was similar in both treatment arms of this study, suggesting that the significantly higher rate of chalazion resolution in the MBE group was not due to a difference in the prevalence of *Demodex* infestation but rather was due to the efficacy of the treatment alone. This notion is further supported by the fact that there were no significant differences in the demographics or baseline characteristics of the MBE and lid hygiene alone treatment cohorts. In addition, this indicates that the efficacy of MBE is less likely to be related to the presence of *Demodex* in the patients' lashes.

Although this study was prospective in nature, there were still some limitations. We had a relatively small sample size of 50 patients with abbreviated follow-up. Larger studies with a true control group should be conducted with a longer follow-up. In addition, we only had 1 center included in our trial, limiting the diversity of our patients. Although previous studies using MBE with various scrubs for the treatment of *Demodex* blepharitis showed no significant difference in efficacy between the scrubs, further research should look into the use of different scrubs with MBE to determine whether they can lead to further improvement of chalazia treatment.[12–14] Despite the limitations of this study, it is the first prospective, randomized clinical trial to the best of our knowledge that has demonstrated efficacy of a noninvasive treatment modality, MBE, for chalazia resolution.

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