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ORIGINAL PAPER

Global improvement in meibomian glands after chalazion surgery demonstrated by meibography

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Abstract

Purpose To evaluate the use of meibography as an objective measure of the effects of incision & curettage (I&C) chalazion surgery on meibomian gland loss and morphology as well as dry eye syndrome.

Methods This prospective, interventional clinical study included adult patients with a primary chalazion which persisted despite conservative treatment. All patients underwent I&C surgery. The following parameters were compared both preoperatively and 21 days postoperatively: meibography, tear breakup time (TBUT), Schirmer test, meibum expression, tear meniscus height, meibomian gland dysfunction (MGD) grading, and the Ocular Surface Disease Index (OSDI).

Results Thirty eyelids were enrolled in the study. The mean age ± SD was 40.56 ± 13.94 years. Meibography demonstrated a significant decrease in meibomian gland loss ($P=0.00$) and improvement in morphology. The most common meibomian gland pathology preoperatively noted was morphological signs of atrophy that included fluffy areas and tortuous glands. Both of these findings improved postoperatively ($P=0.04$ and $P=0.02$, respectively). There were a significant change in MGD grading and a significant decrease in meibum expression score postoperatively ($P=0.00$). TBUT and tear meniscus height also improved significantly ($P=0.00$ and $P=0.003$, respectively). The OSDI score improved significantly as well ($P=0.00$).

Conclusion While incision and drainage surgery is a time-honored, standard treatment for chalazion, meibography now demonstrates a global improvement in the meibomian glands, not just the ones involved with the chalazion. In addition to the improvements in the clinical and dry eye syndrome parameters improvements, meibography findings demonstrate that early I&C surgery restores the meibomian glands architecture significantly.

Keywords Chalazion, meibography · Meibomian gland morphology · Meibomian gland loss · Dry eye · Incision and curettage

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Introduction

Meibography was developed about 30 years ago as an objective method of direct observation of the

meibomian glands in vivo for the diagnosing of meibomian gland dysfunction (MGD). Previous studies have shown significant meibomian gland loss (MGL) in symptomatic MGD patients compared to asymptomatic patients [1]. Early meibography was conducted using a probe that was placed against the everted eyelid, causing significant discomfort. In recent years, new non-contact meibography techniques have been developed, minimizing patient discomfort and thus increasing its popularity [2–4].

A chalazion, a chronic lipogranulomatous inflammation of one or more meibomian glands in the eyelid [5], may lead to or be secondary to MGD, or it may occur incidentally [6]. Patients with a chalazion may suffer from irritation, discomfort, and other dry eye symptoms. Standard treatment can include warm compresses, topical antibiotics, or corticosteroid ointments. If the lesion persists, then treatment options can include incision and curettage (I&C), intralesional corticosteroid injections, or botulinum neurotoxin type A injection [4, 7–12]. Dry eye syndrome secondary to meibomian gland dysfunction often occurs in patients prone to chalazia [13, 14]. I&C surgery is a widely used procedure among ophthalmologists and oculoplastic surgeons to treat chalazia. However, the effect and timing of I&C surgery on meibomian gland morphology are not yet fully understood. The purpose of this prospective study was to evaluate the effect of I&C surgery on meibomian gland morphology via an objective measurement such as meibography. In addition, objective and subjective measurements related to dry eye were recorded. To our knowledge, this is the largest study that has included both pre- and post-op meibography data including meibomian gland loss and morphologic characteristics among chalazion patients.

Methods

Study population

This prospective study included adult patients with a primary chalazion who were seen in the oculoplastic clinic between October 2019 and August 2020. The inclusion criteria were as follows: adult patients 18 years or older, males or females with a primary chalazion which persisted despite conservative treatment (warm compresses, in addition to topical antibiotic, or steroid ointments) for one month. Exclusion criteria included contact lens use, connective tissue disease, thyroid eye disease, glaucoma, previous ocular or orbital surgery, pterygium, previous history of radiation to the face area, skin disorders such as rosacea, seborrhea and atopic dermatitis, and use of systemic drugs that may cause blepharitis, including tricyclic antidepressants, anti-Parkinson's medication, selective serotonin re-uptake inhibitors, retinoid analogue medications, and hormonal replacement therapy.

Surgical treatment was performed at a minimum of two weeks after failure of conservative treatments and less than three months from the patient's initial complaint and presentation. During those two weeks preoperatively, patients were asked to discontinue all conservative treatment measures in order to eliminate any effect of the previous treatments on the study measurements. Written informed consent was obtained from all the study participants. All I&C procedures were performed via tarsal conjunctival side and without removing the meibomian gland capsule and by the same ophthalmologist (S.H.A.). All patients were treated postoperatively with Tobrex 0.3% (tobramycin) ointment for ten days.

This study was approved by the local institutional review board of Baruch Padeh Medical Center and adhered to the principles of the Declaration of Helsinki.

Clinical assessments

All study participants were evaluated 1–7 days prior to surgery and 20–22 days postoperatively. Each patient underwent ophthalmic examination, including visual acuity, intraocular pressure, and posterior segment examination. In addition, each patient underwent an ocular surface evaluation at both visits, which included the following:

Objective evaluation

1. Meibography was performed by capturing infrared images with the BG-4 M noncontact meibography system (SBM Sistemi, Turin, Italy). Images were digitally analyzed using Integrated Complete Platform software (ICP) [15], which provided analysis of the working and non-working gland areas and compared the glands of the

patient subject with standard diagnostic evaluation scales. Two ophthalmologists (S.H. and S.H.A.) carried out the meibography examination to ensure a good and consistent eversion of the examined eyelid. Meibo-scan results showed the following:

A. Morphologic characteristics of the meibomian glands (based on the DREAM study research group protocol) included the following [16]:

- *Distorted glands:* Parallel course of normal glands is not followed.
- *Distorted glands:* Parallel course of normal glands is not followed.
- *Tortuous glands*: A minimum of one prominent tortuous configuration in the gland should be seen. Tortuous configuration is considered worse than distorted.
- *Shortened gland:* Gland is shorter than the normal length.
- *Thickened glands*: Width of gland is equal to or more than twice the width of a normal gland.
- *Thinned glands*: Width is less than half the width of a normal gland.
- *An overlapping gland:* Crosses over or under its adjacent glands(s).
- *Ghost glands:* Normal meibomian gland configuration is absent and the glands are pale.
- *Abnormal gaps:* The gap between two adjacent glands is at least twice normal.
- *Fluffy areas:* Amorphous white substance replaces normal gland architecture.

B. Meibomian gland loss was defined as the percentage of gland loss in relation to the total tarsal area of the everted lid. (Range 0–100%).

2. Meibum expression–expressibility of meibomian gland secretions was evaluated by digitally compressing the lid against the globe where the chalazion was located, just below or above the lash line against the globe over an area spanning five visible meibomian gland orifices [17]. The number of meibomian glands from which meibum could be expressed was quantitated on a 4-point scale: 0 = all 5 glands; 1 = 3–4 glands; 2 = 1–2 glands, and 3 = 0 glands.

Dry eye evaluation

1. Tear meniscus height was measured as the distance between the edge of the lower eyelid and the top of the reflex from the tear strip. A value of ≤ 0.1 mm is normal, while ≥ 0.25 mm indicates reflex tearing and/or sub-optimal tear drainage [18].
2. Tear breakup time (TBUT) is a measure of tear film stability and represents the time until the breakup of the precorneal tear film after the initial blink. Three consecutive measurements of the TBUT after the instillation of fluorescein were taken, and the mean value was calculated. A TBUT of 10 s or more is considered normal [19].
3. Schirmer test 1 was performed without anesthesia using Schirmer tear test strips (Med Devices Lifesciences, London, UK). A result of > 10 mm in 5 min is considered normal [20].
4. MGD findings were performed by slit lamp examination and evaluated according to a standard grading scale for MGD [21]:

A. Abnormal lid margin findings:

0 = no or slight redness in the lid margin conjunctiva. No telangiectasia crossing meibomian gland orifices.
1 = lid margin conjunctiva redness. No telangiectasia crossing meibomian gland orifices.
2 = lid margin conjunctiva redness with telangiectasia crossing meibomian gland orifices, distribution of less than half the full lid length.
3 = lid margin conjunctiva redness and telangiectasia crossing meibomian gland orifices, distribution of half or more of the full lid length.

B. Lid margin irregularity:

0 = no lid margin irregularities.
1 = fewer than 3 lid margin irregularities, shallow notching.

2 = 3 or more lid margin irregularities, deep notching.

C. Lid margin thickening:

0 = no lid margin thickening.
1 = lid margin thickening with or without localized rounding.
2 = lid margin thickening with diffuse rounding.

Subjective evaluation

Ocular Surface Disease Index (OSDI) is a 12-item questionnaire that is designed to provide a rapid assessment of the subjective symptoms of ocular irritation that are consistent with dry eye disease and their impact on vision-related functioning. The OSDI is scored on a scale of 0–100, with higher scores representing greater disability [22].

Statistical Analysis

Categorical variables were presented as absolute numbers and percentages, and continuous variables were presented as means and standard deviations. The Wilcoxon signed rank test was used to compare continuous or ordinal scores, and Mcnemar's exact test was used to compare categorical scores of different evaluations of the patients pre- and post-chalazion surgery. Values with $P < 0.05$ were considered significant.

For categorial variables, we used the Fischer exact test, and values of $P < 0.05$ were considered significant. The difference between upper and lower lids with respect to change in MGL percent was tested using a mixed ANOVA. All statistical analyses were performed using R Statistical software (version 4.1.0; R Foundation for Statistical Computing, Vienna, Austria).

Results

Thirty eyelids of 24 patients were enrolled in the study. Six patients had chalazia in both eyes, and each eye was considered separately. All eyelids underwent I&C procedure. The mean age ± SD was 40.56 ± 13.94 years (range 20–69 years). The male-to-female ratio was 14:10, and the upper/lower eyelid ratio was 16:14. All patients had a total resolution of their chalazia in their postoperative ophthalmic examination. The results of the dry eye assessments are summarized in Table 1.

Objective parameters of dry eye

Postoperatively, there was improvement in the two parameters measured by meibography. First, there was significant decrease in MGL following the I&C procedure (Fig. 1). Secondly, there was improvement in the meibomian gland morphology. The most common meibomian gland morphology preoperatively included fluffy areas and tortuous glands, indicating an atrophic configuration (12/30 and 9/30 eyelids, respectively), and both of these improved postoperatively ($P = 0.04$ and $P = 0.02$, respectively). The most common postoperative meibomian gland morphology

Table 1 Summary of dry eye assessment pre- and postoperatively

	Preoperative average value	Postoperative average value	*P* value*
Visual acuity	0.96	0.96	1
OSDI**	18.96	5.23	0.00
TBUT***	3.7	6.1	0.00
Schirmer test	15.33	17.27	0.066
Vascular changes of lid margin	1.07	0.53	0.00
Irregularities of eyelid margin	1	0	0.034
Thickening of eyelid margin	0.53	0	0.001
Percentage of meibomian gland loss	53.16	27.5	0.00
Meibum expression	1.7	0.7	0.00
Tear meniscus height	0.24	0.166	0.003

*P value according to Wilcoxon signed rank test

**OSDI—Ocular Surface Disease Index

***TBUT—Tear Break-Up Time

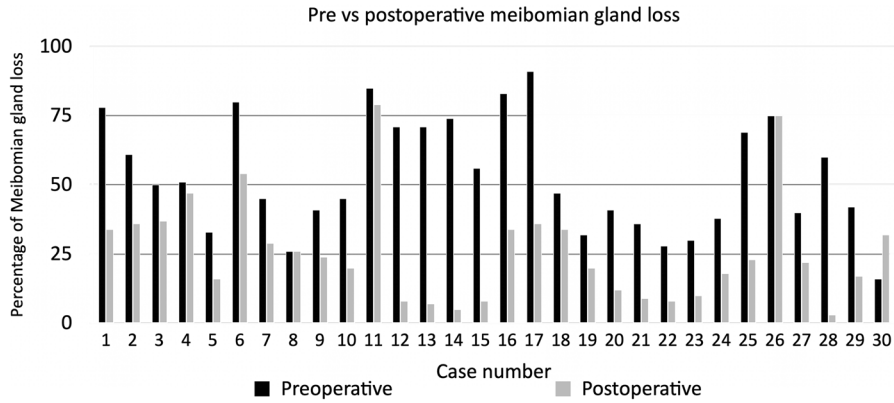

Fig. 1 Pre- versus postoperative percentage of meibomian gland loss among the included eyelids. A significant decrease in meibomian gland loss was observed postoperatively (Wilcoxon signed rank test, $P=0.00$)

included distorted and shortened glands (15/30 and 12/30 eyelids, respectively) which are considered closer to the normal configurations (Figs. 2 and 3). In addition, there was a significant improvement in the three parameters of MGD grading postoperatively ($P=0.00$) compared to pre-op levels.

There was no significant difference in Schirmer test score pre- and postoperatively; however, TBUT and tear meniscus height also improved significantly ($P=0.00$ and $P=0.003$, respectively). When comparing upper lid vs lower lid meibography parameters: The most common meibomian gland morphology preoperatively was tortuous and fluffy glands in upper and lower lids, respectively (9/16 and 10/14, respectively), and both of these improved postoperatively ($P=0.04$ for both). In addition, there was no significant difference in the changes of MGL between upper and lower lids results ($P=0.469$). When evaluating the aging effect on the study acquisition, the age was not associated with any of the parameters including meibography data.

Subjective parameter of dry eye

The OSDI score improved significantly postoperatively (18.96 vs. 5.23, respectively, $P=0.00$).

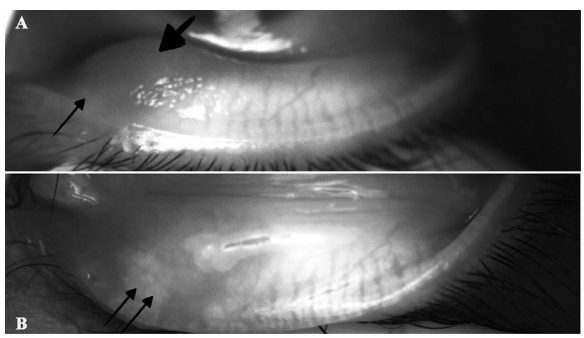

Fig. 2 Meibomian gland morphology for the lower lid with chalazion (wide arrow): Preoperatively, amorphous white substance seen medially represents fluffy area, corresponding to where normal glands should have been (narrow arrow) (**A**). Postoperatively, morphology improved (**B**) and became shortened glands as the glands do not extend to its full normal length (narrow arrows)

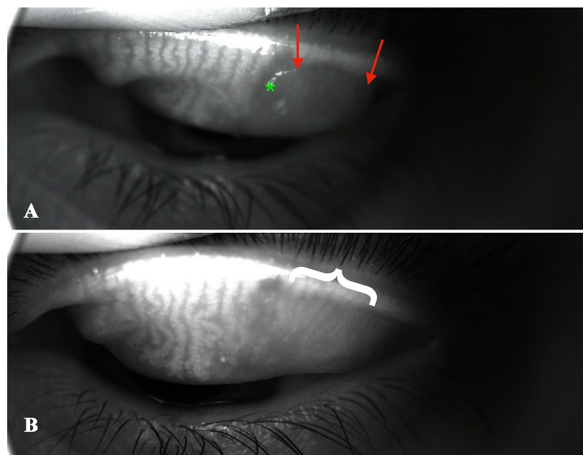

Fig. 3 Meibomian gland morphology for upper lid with chalazion (asterisk): **A** the chalazion affected the meibomian glands morphology beyond its region (between the arrows); **B** the lateral glands morphology (brackets) was improved postoperatively

Discussion

From the results of meibography in our series, we have found that the chalazion affected an extensive area of meibomian glands beyond its immediate focal location. Meibography also demonstrated that meibomian gland morphology and gland loss improved significantly postoperatively across the eyelid compared to preop levels.

The morphological changes noted preoperatively can be explained by the pressure induced by a single chalazion on adjacent glands. This may cause inflammation of the neighboring glands which resolves postoperatively. In our study, the diameter of each chalazion was not evaluated. However, the results of our meibography studies demonstrated that the preoperative meibomian glands morphologic characteristics improved postoperatively across the entire affected eyelid in all of our cases. This is a new and unique finding as I&C surgery for a single chalazion appears to affect nearly the entire meibomian gland morphology in the affected eyelid.

This far-reaching effect may be explained by acini regeneration after chalazion resolution. Normally, there are proliferating progenitor cells in the periphery of the meibocytes that constantly produce new meibocytes constantly [23]. During chalazion formation, new meibocytes are not produced secondary to inflammation. Therefore, the acini structure cannot be visualized or thereby distorted in meibography. A previous study demonstrated that it takes approximately 13 days for newly produced meibocytes to shed in the meibomian gland [24]. The improvement we observed after I&C surgery may be a result of reduced inflammation leading to faster meibocytes regeneration. This finding also correlated with the significant improvement in meibomian gland loss noted in meibography and with an improvement in MGD grading.

There are few studies in the literature describing chalazia and meibography. Moreover, none of these studies have examined meibography and the dry eye parameters that were examined in our prospective study. Fukuoka and associates examined changes in the meibomian gland morphology in the eyes after chalazion excision [25]. They compared seven eyelids with a previous history of chalazion excision vs. seven healthy eyelids. The chalazion excision group was associated with greater dropout and a shortened meibomian glands morphology, which they deduced via meibography images. The study was retrospective, and the mechanism for this finding was unclear.

Srinivasan et al. described a case of an eyelid with recurrent chalazia analyzed using the meibography method [26]. The area of a recurrent chalazion showed partial and/or complete meibomian gland loss, and the active chalazion area showed meibomian gland drop out at the affected eyelid. They concluded that meibography allows the clinician to monitor the progression of chalazia via meibomian gland loss in the affected area. However, in their case report, the disappearance of the meibomian gland was specific to the region of the chalazion and not beyond it as it was in our case series. In our study, meibography showed an improvement in MGL and meibomian gland morphology across the entire eyelid following I&C surgery. These findings differ from previous studies.

Our study was prospective case series, and the significant improvement in meibography characteristics was reflected and correlated as well with dry eye parameters objectively and subjectively.

It is not fully understood yet how I&C surgery directly affects dry eye disease. Therefore, we evaluated objective and subjective dry eye parameters, including meibomian gland morphological characteristics and the percentage of meibomian gland loss both before and after I&C surgery. We found a significant improvement in the objective and subjective dry eye parameters postoperatively.

We also utilized a new validated grading scale for lid margin signs in order to ensure consistency and the appropriate reliabilities for MGD grading [21]. The results demonstrated that following I&C surgery, lid margin irregularities, vascularity, and thickening were significantly improved. Moreover, the significant improvement in meibography parameters was correlated with the improvement in the objective and subjective dry eye syndrome parameters after I&C surgery.

We postulate that the lid margin irregularity which is secondary to a chalazion may be the reason for the instability of the precorneal tear film distribution and TBUT reduction, and that these parameters improve after surgical incision and curettage. In addition, the mechanical effect on the eyelid secondary to a chalazion may play a role in the development of dry eye; irregularity and engorgement of vessels in the affected lid margin likely contribute to dry eye, and

this subsequently improves postoperatively. Postoperatively there was a significant improvement in patients' sensation of dry eye as which was reflected in the OSDI questionnaire.

Advantages of meibography include that meibomian gland changes can be easily and quickly assessed in both eyelids [3]. Meibography findings have been reported in normal eyelids, where interestingly, the meibomian glands of the upper eyelids were found to be thinner and longer compared to the lower eyelids. Meibography also demonstrated an increase in the gland drop out in aging, MGD, trachomatous scarring, and orbital radiation [27–29]. However, meibomian gland changes including morphology due to I&C surgery have not been previously reported. A recent prospective observational study regarding the effect of chalazion treatments on meibomian gland included a group of 35 patients with chalazion who were treated with surgery [30]. Unlike in our study, there was no significant difference between meibomian gland loss pre- and postoperatively in meibography. This may be explained by a longer period of chalazion existence prior to surgery in their study, which can lead to fibrosis and less acini regeneration in the eyelid. In addition, meibomian gland morphology and dry eye parameters were not evaluated.

A further analysis was performed in our study to evaluate whether the location of the chalazion (upper versus lower lid) affected the meibography results. We found that there was no significant difference in the changes of MGL between upper and lower lids. Previous published studies have shown that MGL at the lower lid is significantly larger than that of the upper lid [31, 32]. This finding differs from ours. In previous studies, lids with chalazion were not included nor did they undergo I&C surgery, which may help explain the discrepancy. It would be of interest in future studies to compare meibography data between the two lids.

Our study is the largest of its kind in the literature to date which included meibography and evaluation of dry eye parameters. A limitation of our study is that it was not a double-blinded. However, the presurgical ophthalmic examination results were not known by the clinicians during the post-surgical examination, which should have reduced any potential researcher bias.

The mechanism of improvement noted in the meibomian glands and in the dry eye parameters following I&C surgery is still not fully understood. However, our study has further elucidated changes in the meibomian glands which accompany chalazion development and dry eye. Future studies could further investigate how surgery on one gland has apparent wide-reaching effects on other non-involved glands. In addition, a future study could compare meibography after I&C surgery versus other modalities of chalazion treatment such as steroid injection.

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Authors contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Dr. SH, Dr. SHA, and Dr. GH. The first draft of the manuscript was written by Dr. SHA, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Consent to participate and publish Informed consent was obtained from all individual participants included in the study.

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Baruch Padeh medical center (Date 9/10/2019/No. 0078–19-POR).

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