Original Research Article

Evaluation of Meibomian Gland Dysfunction Before and After Surgical Correction of Cicatricial Entropion of the Upper Eye Lid

Abstract

Background: The meibomian gland dysfunction (MGD) is one of the most important causes of dry eye. MGD is a term used to describe a group of disorders linked by functional abnormality of Meibomian gland. The aim of this study was to evaluate meibomian gland dysfunction before and after surgical correction of cicatricial entropion of the upper eye lid by two different techniques: tarsal fracture technique and anterior lamellar reposition with grey line split technique.

Methods: This randomized study included thirty consecutive eyes who were randomly divided into two equal groups according to the surgical technique: group (A) that included cases who underwent tarsal fracture technique and group (B) that included cases who underwent anterior lamellar reposition with gray line split technique. Patients were subjected to complete history taking, Ophthalmic examination, Assessment of the visual acuity (VA), Slit lamp bio-microscopy, Measurement of intraocular pressure (IOP), Posterior segment examination, Assessment of dry eye.

Results: The preoperative TBUT was insignificant between group A and group B (p=0.689). The preoperative meibography was insignificant between the group A and group B (p=0.992). The mean postoperative TBUT after 1month in group A was 8 ± 2.38 seconds while in group B was 8.50 ± 2.72 seconds with no statistically significant difference between the two groups (p=0.596). The mean postoperative meibography (meibomain gland dropout percentage) after 1month in group A was 51.27 ± 15.69 while in group B was 49.85 ± 19.19 with no statistically significant difference between the two groups (p=0.825).

Conclusions: meibomain gland dropout by meibography and TBUT increased postoperatively in both group A and group B but more in group A with no statistically significant difference due to small number of cases. Cicatrcial entropion of upper eye lid can be corrected effectively by two different types of surgery: tarsal fracture technique and anterior lameller reposition. Infrared meibography is a good indicator of diagnosis of MGD.

Keywords: Meibomian Gland Dysfunction, Surgical Correction, Cicatricial Entropion, Upper Eye Lid.

Introduction:

Upper eyelid entropion is an eyelid malposition in which the upper eyelid margin is turned inward against the globe. It can cause ocular morbidity. It is an uncommon condition in the western World, in contrast to a number of the developing countries, where trachoma is endemic [1].

Cicatricial entropion is produced when there is a vertical shortening of the tarsus secondary to scarring of ocular tissue brought about by disorders such as trachoma, Steven-Johnson syndrome, ocular cicatricial pemphigoid, herps zoster, trauma, chemical injuries, or thermal burnies [2].

The meibomian gland dysfunction (MGD) is one of the most important causes of dry eye.

MGD is a term used to describe a group of disorders linked by functional abnormality of Meibomian gland. MDG can lead to altered tear film composition, ocular surface disease, ocular and eye discomfort, and evaporative dry eye [3].

Meibomian gland dysfunction is a chronic, diffuse, abnormality of the meibomian gland, commonly characterized by terminal duct obstruction, and or qualitative/quantitative changes of glandular secretions. This may result in alteration of tear film, symptoms of eye irritation, clinically apparent inflammation and ocular surface disease [4].

Patient may have original pathology of MGD before surgery. Preoperative Evaluation of the patient detect degree of MGD. Post operative Evaluation will detect if MGD improved or get worse [5].

Transverse tarsal incision during surgical correction of upper lid entropion by tarsal fracture technique may interrupt the meibomian gland running in tarsal plate and affect the tear film stability [6].

The aim of this study was to evaluate meibomian gland dysfunction before and after surgical correction of cicatricial entropion of the upper eye lid by two different techniques: tarsal fracture technique and anterior lamellar reposition with grey line split technique.

Patients and Methods:

This prospective randomized interventional study included thirty consecutive eyes with upper eye lid moderate cicatricial entropion and was carried out at Ophthalmology Department, Tanta University hospitals, Tanta, Egypt. The study was conducted for duration of 1 year from January 2021 to January 2022. The study was done after being approved from the institutional ethical committee, Tanta University. Written informed consent was obtained from all the participants included.

Inclusion criteria were patient diagnosed with cicatricial entropion. **Exclusion criteria** were any type of entropion other than cicatricial one or lower lid entropion, previous upper eye lid surgery or trauma, previous lacrimal surgery and tarsus abnormality, ptosis, or artificial eye.

The cases were randomly divided into two equal groups according to the surgical technique using the closed envelope technique. The numbers from 1 to 30 were written in flat pieces of papers and put in closed envelopes that were randomly distributed to the participants. The cases with the odds number were allocated to group A while the cases with the even numbers were allocated to group B. **Group (A):** Included fifteen eyes with moderate cicatricial entropion who underwent tarsal fracture technique. **Group (B):** Included fifteen eyes with moderate cicatricial entropion who underwent anterior lamellar reposition with gray line split technique.

All patients were subjected to: a) complete history taking including **general history** (Personal demographic data, Complaint and present history and Medical and family history). **Ophthalmic history (**History of ocular trauma and ocular surgery). **History of the current disease (**Patient's first complaint, Onset of the disease and duration and its progression).

Ophthalmic examination: 1) **External examination** [Detailed lid examination]: Extent of involvement (generalized or localized), State of tarsal plate (existence of shrinkage or loosening), Any other lid abnormalities, Detailed examination of lid margin, meibomain gland orifices and detection of type of meibomain gland secretions. 2) **Assessment of the visual acuity (VA)** [Unaided visual acuity and best corrected visual acuity]. Assessment of the VA was done using Landolt's VA chart. 3) **Slit lamp biomicroscopy:** By the slit lamp biomicroscopy (Haag Streit BP 900) (Haag-Streit, Koeniz, Switzerland) to assess: Corneal clarity (opacities, scars and descemetoceles), Lid margin, meibomain gland orifices, AC for depth and regularity, Pupil shape, size, regularity and reactivity. 4) **Measurement of intraocular pressure (IOP):** Intraocular pressure was measured using Goldman applanation tonometer. 5) **Posterior segment examination** using indirect ophthalmoscope and slit lamp biomicroscopy with auxillary contact lens. 6) **Assessment of dry eye: a) Tear film break up time**. In testing for Tear film break up time, sodium fluorescein dye was added to the eye and the tear film is observed under the slit lamp while the patient avoids blinking until tiny dry spots develop. Interpretation of data (>10 seconds is thought to be normal, 5 to 10 seconds, marginal, and < 5 seconds is considered low). B) **Ocular Surface Staining: Type of drops used (**Fluorescein drops 1%). **Conduct of Test:** Dye was instilled, Slit-lamp is set, Cornea: The upper eyelid is lifted slightly to grade the whole corneal surface, Conjunctiva: To grade the temporal zone, the subject looks nasally; to grade the nasal zone the subject looks temporally.

Grading Score: Staining is represented by punctate dots on a series of panels (A-E). Staining ranges from 0-5 for each panel and 0-15 for the total exposed inter-palpebral conjunctiva and cornea. The dots are ordered on a log scale [7].

Investigation

Meibography : Using CSO Sirius® Pentacam device designed by C.S.O Italia, Florence. (Figure 1), with the Phoenix-Meibography Imaging software module.

Patient position: The patient is seated with his or her chin on the chinrest and forehead against the forehead strap and asked to fixate straight ahead on the fixation target (blue circular ring).

Technique: Measurements was performed according to their respective manufacturer's guidelines. A guided tridimensional manual acquisition was used to bring the device into focus along with a central fixation light, and when the instrument showed a green light the acquisition was taken.

Results: The MGs that did not transvere the total tarsal plate were indicated as a "dropout." The Phoenix software gave the measurements of the dropout by percentage, as well as grouped the dropout by a scale within the area, which was highlighted by the users' free-hand tool: grade 0, no loss at all; grade 1, ≤25%; grade 2, 26%–50%; grade 3, 51%–75%; and grade 4, greater than 75% [8].

Meibography by lid transillumination (standard meibography): Meibography was performed, similarly to others, by using a transillumination device for vitrectomy with a fiberoptic light source (Millenium system, Bausch & Lomb®, San Leandro, CA, USA) with a 20-gauge disposable fiber light guide [9].

Treatment of cicatrcial entropion:

Surgical techniques: A) Tarsal fractures technique: The operation was under local anesthesia by local infiltration of 2% lidocaine through 1: 100,000 epinephrine. Traction sutures were made by sewing 4/0 silk sutures at the lid margin. skin incision was made 4 mm above the lid margin. Dissection of orbicularis was done to expose the tarsus. Three double armed (Vicryl 6/0) are passed first through the lid margin behind the eyelashes then passed transversely through the distal part of the tarsus, and finally passed again through the lid

margin and tied to evert the eyelid margin, skin is closed with interrupted vicryl 6/0 sutures. Postoperative treatment with topical antibiotics and steroids ointment for 6 weeks, and systemic antibiotics and anti-inflammatory for 1 week. **B) Anterior lamellar reposition technique:** The operation was done under local anesthesia by local infiltration of 2 % lidocaine through 1: 100,000 epinephrine. The eyelid margin incised in grey line posterior to abnormal eyelash from the lateral commissure to just lateral to the lacrimal punctum. Then dissection is done toward the superior tarsal border. The anterior lamella (skin and muscle flap) was then recessed and fixed to tarsus 4 mm above the lid margin with 6-0 Vicryl horizontal mattress sutures. Postoperative treatment with topical antibiotics and steroids ointment for 6 weeks, and systemic anti-inflammatory and anti-biotics for 1 week. Post operative imagining of meibomain gland with meibography done after 1 month postoperatively with the same apparatus and technique.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

Results:

There was no statistically significant difference between the two groups regarding patients' demographics, the associated comorbidities and laterality of eyes affection. Table 1

Table 1: Demographic data and comorbidities in the two study groups

Items	Group A (n= 15)	Group B (n= 15)	p-value
Age (years)	72.80 ± 6.70	71.93 ± 7.06	t = 0.345 P= **0.733**
Sex			
Male	5 (33.3%)	6 (40%)	$\chi 2$= 0.495 P = 0.571
Female	10 (66.7%)	9 (60%)	

Comorbidities			
DM	5 (33.3%)	3 (20%)	MC = 1.127 P = 0.461
HTN	5 (33.3%)	5 (33.3%)	
DM + HTN	2 (13.3%)	3 (20%)	
Laterality of eyes affection			
Unilateral	11 (73.3%)	10 (66.7%)	FET = 0.159 P = 0.690
Bilateral	4 (26.7%)	5 (33.3%)	

t: Independent samples, t-test $\chi 2$: Chi-square test, MC: Monte-Carlo test, FET: Fischer's exact test

In group A, there were 5 eyes (26.3%) with mild entropion, 9 eyes (47.4%) with moderate entropion and 4 eyes (26.3%), while in group B, there were 5 eyes (25%) with mild entropion, 11 eyes (55%) with moderate entropion and 4 eyes (20%) with severe entropion with no statistically significant difference between the two groups (p= 0.384). In group A, there were 5 eyes (26.3%) with mild MGD, 11 eyes (57.6%) with moderate MGD and 3 eyes (15.8%) with severe MGD, while in group B, there were 6 eyes (30%) with mild entropion, 10 eyes (50%) with moderate entropion and 4 eyes (20%) with severe MGD with no statistically significant difference between the two groups (p= 0.258). Table 2

Table 2: Grading of entropion and grading of MGD in the eyes of the two study groups

Grading of entropion	**Group A (n= 19)**	**Group B (n= 20)**	**p-value**
Mild	5 (26.3%)	5 (25%)	MC = 1.706 P = 0.384
Moderate	9 (47.4%)	11 (55%)	
Severe	4 (26.3%)	4 (20%)	
Grading of MGD			
Mild	5 (26.3%)	6 (30%)	MC = 1.528 P = 0.258
Moderate	11 (57.6%)	10 (50%)	
Severe	3 (15.8%)	4 (20%)	

MC: Monte-Carlo test

The mean preoperative TBUT in group A was 9.87 ± 2.45 seconds while in group B was 10.27 ± 2.95 seconds with no statistically significant difference between the two groups (p=0.689). The mean preoperative meibography in group A was 45.10 ± 15.22(percentage of gland loss) while in group B was 45.04 ± 18.73 with no statistically significant difference between the two groups (p=0.992). Table 3 and Figure 1

Table 3: Preoperative tear break up time and meibography in the two study groups

Items	Group A (n= 19)	Group B (n= 20)	p-value
Tear break up time	9.87 ± 2.45	10.27 ± 2.95	t = -0.404 P= **0.689**
Meibography	45.10 ± 15.22	45.04 ± 18.73	z = 0.010 P= 0.992

t: independent samples t-tests z: Mann-Whitney test

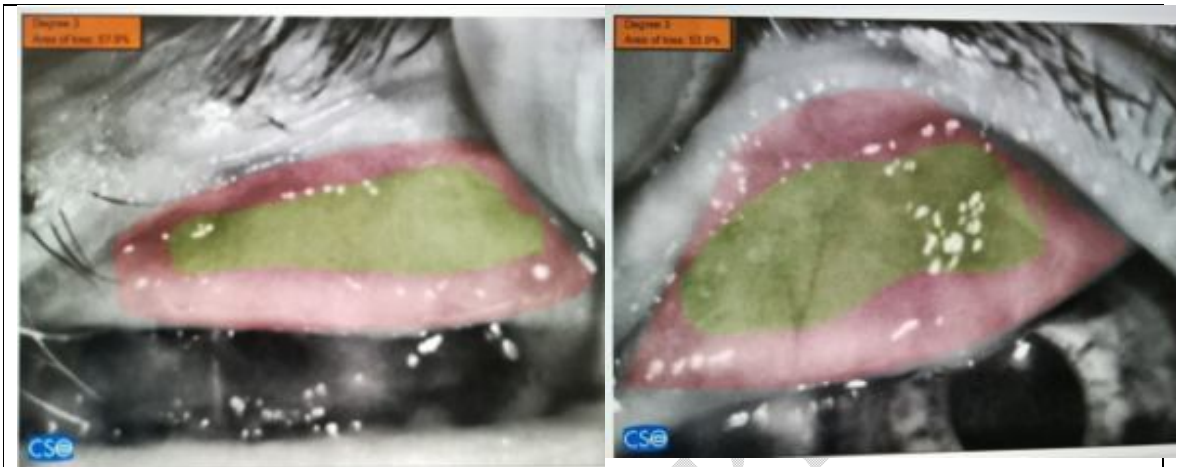

Figure 1: Preoperative and Postoperative meibography

The mean postoperative TBUT after 1month in group A was 8 ± 2.38 seconds while in group B was 8.50 ± 2.72 seconds with no statistically significant difference between the two groups (p=0.596). The mean postoperative meibography after 1month in group A was 51.27 ± 15.69 while in group B was 49.85 ± 19.19 with no statistically significant difference between the two groups (p=0.825). Table 4

Table 4: 1-month post-operative tear break up time and meibography in the two study groups

Items	Group A (n= 19)	Group B (n= 20)	p-value
Tear break up time	8 ± 2.38	8.50 ± 2.72	t = -0.536 P= **0.596**
Meibography	51.27 ± 15.69	49.85 ± 19.19	z = 0.223 P= 0.825

t: independent samples t-tests, z: Mann-Whitney test

The mean preoperative TBUT in group A was 9.87 ± 2.45 seconds while the mean postoperative TBUT was 8 ± 2.38 seconds. There is high statistically significant decrease in the TBUT postoperative as compared with preoperative value. The mean preoperative meibography in group A was 45.10 ± 14.22 while the mean postoperative meibography was

51.27 ± 15.69. There is high statistically significant increase in the meibography postoperative as compared with preoperative value. Table 5

Table 5: Comparing between preoperative and postoperative tear break up time and meibography in group A

Items	Preoperative (n= 19)	Postoperative (n= 19)	p-value
Tear break up time	9.87 ± 2.45	8 ± 2.38	t = 24.357 P < 0.001*
Meibography	45.10 ± 14.22	51.27 ± 15.69	t = -18.303 P < 0.001*

t: Paired samples t-tests, z: Wilcoxon Signed rank test, *: Statistically significant (p<0.05)

The mean preoperative TBUT in group B was 10.27 ± 2.95 seconds while the mean postoperative TBUT was 8.50 ± 2.72 seconds. There is high statistically significant decrease in the TBUT postoperative as compared with preoperative value. The mean preoperative meibography in group B was 45.04 ± 18.73 while the mean postoperative meibography was 49.85 ± 19.19. There is high statistically significant increase in the meibography postoperative as compared with preoperative value. Table 6

Table 6: Comparing between preoperative and postoperative tear break up time and meibography in group B

Items	**Preoperative (n= 20)**	**Postoperative (n= 20)**	**p-value**
Tear break up time	10.27 ± 2.95	8.50 ± 2.72	t = 18.412 P < 0.001*
Meibography	45.04 ± 18.73	49.85 ± 19.19	z = -13.002 P < 0.001*

t: Paired samples t-tests, z: Wilcoxon Signed rank test, *: Statistically significant (p<0.05)

The percent of change in the TBUT in group A showed a decrease by 19.81± 5.21 that was higher as compared with group B, but it didn't achieve a statistically significant difference 17.72 ± 3.50 (p=0.208). The percent of change in the meibography in group A showed an increase by 14.85 ± 4.62 that was higher as compared with group B, but it didn't achieve a statistically significant difference 12.23 ± 5.04 (p=0.149). Table 7

Table (7): Percent of change in TBUT and Meibography in the two study groups

Items	**Group A (n= 19)**	**Group B (n= 20)**	**p-value**
Percent of change of tear break up time (%)	19.81± 5.21	17.72 ± 3.50	t = 1.290 P = 0.208

Percent of change of Meibography (%)	14.85 ± 4.62	12.23 ± 5.04	z = -1.484 P = 0.149

t: independent samples t-tests z: Mann-Whitney test

Discussion

Cicatricial entropion of the upper lid is caused by vertical tarsoconjunctival contracture that leads to inward rotation of the lid margin resulting in ocular irritation by the inward turning of the eyelashes or keratinized lid margin causing corneal ulcerations and opacifications [10].

In the current study, the mean age of the cases in group A is 72.80 ± 6.70 years and the mean age of the cases in group B is 71.93 ± 7.06 years with no statistically significant difference between the two groups (p=0.733). There are 5 males (33.3%) and 10 females (66.7%) in group A while there are 6 males (40%) and 9 females (60%) in group B, with no statistically significant difference between the two groups (p=0.571).

There is higher female predominance in the current study. This came in agreement with [11] who included 20 upper eyelids of 20 patients with recurrent upper lid entropion. These patients were randomly divided into two groups with follow up period for at least 6 months post-operative. Group A: 10 upper eyelids underwent anterior lamellar recession. Group B: 10 upper eyelids underwent tarsal fracture and marginal rotation. These patients were 8 males (40%) and 12 females (60%). Age ranged from 45 to 80 years with an overall mean age of 62.5 years. There was no statistically significant difference between the two groups as regarding the age and sex like our current study.

This also came in accordance with [12] who showed that among the cases with cicatricial entropion included in their study, there are 73.3% females and 26.7% males.

In the current study, there is no statistically significant difference in the type of entropion between the cases in the two study groups. The highest percentage of the cases had moderate entropion that represented 47.4% and 55% in group A and group B respectively.

This was in the same line with El Samkary et al. [13] who included 20 cases with upper eyelid entropion. Among them, there are 6 cases (30%) with mild entropion and 14 cases (70%) with moderate entropion.

Anterior lamellar reposition with lid margin splitting keeps the integrity of the meibomian gland and avoids following iatrogenic dry eye, this seems especially important in trachoma trichiasis cases [14].

In the current study, there is no statistically significant difference in the mean TBUT and meibography both preoperative and postoperative between two groups of two types of surgery.

On the same way, there is high statistically significant decrease in the TBUT postoperative as compared with preoperative value and there is high statistically significant increase in the meibography postoperative as compared with preoperative value in both groups.

The percent of change in both parameters was higher in group A, yet it didn't reach a statistically significant value.

Pervious study of Aric vaidya at al. [15] show that meibomain gland dysfunction does not resolve after surgical correction of involutional entropion, possibly due to irreversible changes in eye lid margin and loss of meibomain glands. This may match with our study.

On the other hand, there is a study published in British Journal of ophthalmology show that after surgical management of upper eye lid entropion most tear films clinically improved, but 60% of patients require no addition tear product they use. This may mismatch with our study which shows that meibomain gland dysfunction become more worse postoperatively.

According to the study of Samia-Aly et al. simple anterior lameller repositioning,used to management of cicatrcial entropion, can be effective in managing patients with meibomain gland inversions secondary to meibomain gland dysfunction giving them symptomatic relieve when all medical treatments fail. This is the first case series describes this simple surgical

technique in managing of this subgroup of patients. This is opposite of what we found in our study.

There were several limitations to this study. First, the sample size was small. Larger numbers of subjects will give much better result. However, as there was little variation of the results among the eyelids, our results can considered clinically valid.

Secondary, follow up period of the patients was comparatively shorter, as long follow up time could have given much clearer ideas about the surgery effect.

Conclusions:

Cicatrcial entropion of upper eye lid can be corrected effectively by two different types of surgery: tarsal fracture technique and anterior lameller reposition. Infrared meibography is a good indicator of diagnosis of MGD. Preoperative and postoperative meibography of meibomain gland and break up time test show that there is slightly increase in meibomain gland dysfunction postoperatively due to breakdown of some meibomain glands. Meibomain gland dysfunction was more in group A with tarsal fracture technique than in group B.

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