

# Lid Wiper Epitheliopathy in Benign Essential Blepharospasm and Hemifacial Spasm: Cross-Sectional Study

## Benign Esansiyel Blefarospazm ve Hemifasiyal Spazmda Kapak Silici Epitelyopati: Kesitsel Çalışma

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**ABSTRACT Objective:** To evaluate lid wiper epitheliopathy (LWE) in benign essential blepharospasm (BEB) and hemifacial spasm (HFS), and to analyze the relationship between dry eye and involuntary contractions of the m.orbicularis oculi by comparing unaffected and affected eyes of HFS patients. **Materials and Methods:** BEB or HFS patients who underwent botulinum toxin injections were included in this comparative two-eye study. Based on the Jankovic rating scale, the frequency and severity of the contractions were recorded. Corneal staining and LWE at the upper eyelids had been detected utilizing the Oxford and Korb grading schemes, respectively. Patients were compared in terms of contractions, corneal staining score, and LWE. The two eyes of patients were also compared within each other. **Results:** Eighty-two eyes were analyzed (43 with BEB, 39 with HFS). There was no significant difference in terms of contractions, corneal staining, and LWE between BEB and HFS ( $p>0.05$ ). Corneal staining and LWE in both eyes of BEB patients were similar ( $p>0.05$ ). However, corneal staining and LWE were significantly lower in unaffected eyes than affected eyes in patients with HFS ( $p=0.001$ ). **Conclusion:** The fact that corneal staining and LWE are higher in both eyes of BEB patients and in the affected eye of HFS patients may be evidence that the pressure of the eyelid on the ocular surface and the frequency and amplitude of blinking have a role in the etiopathogenesis of LWE. In the follow-up of both, LWE is one of the examination findings that should be investigated together with dry eye tests.

**ÖZET Amaç:** Benign esansiyel blefarospazm (BEB) ve hemifasiyal spazmda (HFS) göz kapağı silici epitelyopatisini (KSE) değerlendirmek ve HFS hastalarının etkilenmemiş ve etkilenmiş gözlerini karşılaştırarak kuru göz ile m.orbicularis oculi istemsiz kasılmaları arasındaki ilişkiyi analiz etmek. **Gereç ve Yöntemler:** Bu karşılaştırmalı iki göz çalışmasına botulinum toksini enjeksiyonu yapılan BEB veya HFS hastaları dahil edildi. Jankovic derecelendirme ölçeğine göre kasılmaların sıklığı ve şiddeti kaydedildi. Sırasıyla Oxford ve Korb derecelendirme şemaları kullanılarak üst göz kapaklarında kornea boyanması ve KSE tespit edildi. Hastalar kontraksiyon, kornea boyanma skoru ve KSE açısından karşılaştırıldı. Hastaların iki gözü de kendi içinde karşılaştırıldı. **Bulgular:** Seksen iki göz analiz edildi (43'ü BEB'li, 39'u HFS'li). BEB ve HFS arasında kontraksiyon, kornea boyanması ve KSE açısından anlamlı fark yoktu ( $p>0.05$ ). BEB hastalarının her iki gözünde kornea boyanması ve KSE benzerdi ( $p>0.05$ ). Ancak kornea boyanması ve KSE, etkilenmemiş gözlerde, HFS'li hastaların etkilenen gözlerine göre anlamlı derecede düşüktü ( $p=0.001$ ). **Sonuç:** BEB hastalarının her iki gözünde ve HFS hastalarının etkilenen gözünde kornea boyanması ve KSE'nin daha yüksek olması, göz kapağının oküler yüzeye uyguladığı basıncın ve göz kırpması sıklığı ve amplitüdünün KSE etyopatogenezinde rol oynadığının kanıtı olabilir. Her ikisinin takibinde KSE, kuru göz testleri ile birlikte araştırılması gereken muayene bulgularından biridir.

**Keywords:** Benign essential blepharospasm;  
dry eye syndromes; hemifacial spasm

**Anahtar Kelimeler:** Benign esansiyel blefarospazm;  
kuru göz sendromları; hemifasiyal spazm

**TO CITE THIS ARTICLE:**

Yalçinkaya Çakır G, Şerefoğlu Çabuk K, Çakmak S, Çakır İ, Aşık Nacaroğlu Ş, Öztürk Karabulut G, et al. Lid wiper epitheliopathy in benign essential blepharospasm and hemifacial spasm: Cross-sectional study. Türkiye Klinikleri J Ophthalmol. 2024;33(2):75-80.

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Peer review under responsibility of Türkiye Klinikleri Journal of Ophthalmology.

Received: 23 Jun 2023

Received in revised form: 24 Feb 2024

Accepted: 26 Feb 2024

Available online: 29 Mar 2024

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One of the most important physiological roles of the eyelids resides in safeguarding the cornea through the judicious dissemination of tear film across the ocular surface. Any aberrations in tear film composition or its even distribution over the ocular surface precipitate dry eye disease, thereby leading to visual impairment and discomfort.<sup>1</sup> Benign essential blepharospasm (BEB) is defined as bilateral orbicularis oculi dystonia characterized by uncontrollable contractions and blinking.<sup>2</sup> Hemifacial spasm (HFS) is a unilateral disease characterized by involuntary contraction of muscles innervated by the facial nerve, including the orbicularis oculi.<sup>3</sup> Notably, a discernible portion of patients afflicted with periocular focal dystonia has been shown to concurrently experience dry eye disease.<sup>4,5</sup>

The area of the eyelid interfacing with the ocular surface is designated as the lid wiper, presumed to play a pivotal role in the uniform distribution of tear film during the act of blinking.<sup>6</sup> This region of the eyelid extends from the nasal to the temporal canthus and from the mucocutaneous junction to the subtarsal fold.<sup>6</sup> Lid wiper epitheliopathy (LWE) is an epithelial disorder characterized by staining of the conjunctival epithelium at the margin of the upper lid with dyes such as fluorescein, rose bengal, and lissamine green, first described by Korb et al. in contact lens wearers.<sup>7</sup> The main contributing factor to LWE is believed to be increased friction between the lid wiper and ocular surface as a result of insufficient lubrication.<sup>8</sup> Factors contributing to this phenomenon include dry eye conditions and exacerbations induced by aberrant blinking patterns, deficient surface lubricity of contact lenses, and unfavorable environmental conditions.<sup>8</sup>

Although there are studies on LWE with dry eye patients, to our knowledge, there is only one study addressing LWE in individuals with periocular dystonia.<sup>6,9-14</sup> The purpose of this study was to assess LWE in the context of both BEB and HFS, two conditions characterized by periocular dystonia. Furthermore, the study aims to scrutinize the correlation between dry eye and involuntary contractions of the orbicularis oculi by juxtaposing unaffected and affected eyes of HFS patients.

## MATERIAL AND METHODS

In the current study, we included consecutive patients with BEB or HFS who applied for botulinum toxin injection between December 2019-May 2020 in the University of Health Sciences Türkiye, Beyoğlu Eye Training and Research Hospital, İstanbul, Türkiye.

Patients between the ages of 18-60, who have never used contact lenses before, who had no corneal or conjunctival pathology such as nophthalmos, scar, or atopic conjunctivitis, who did not have entropion-ectropion or eyelid deformity, who had not undergone eyelid surgery, who have not used topical drops, and who have not had botulinum toxin injection before was included. Patients who had a history of ocular surgery, ocular surface disease (such as ocular rosacea, ocular pemphigoid), and took medicine that could cause dry eye were excluded from the study.

Demographic data of patients, frequency, and severity of contractions according to the Jankovic rating scale were noted.<sup>15</sup> Grading for the frequency was as follows: 0 points, never; 1 point, slightly increased frequency of blinking; 2 points, eyelid fluttering lasting less than 1 second in duration; 3 points, eyelid spasm lasting more than 1 second, but eyes open more than 50% of the waking time; 4 points, functionally blind due to persistent eye closure more than 50% of the waking time. Grading for the severity was as follows: 0 points, no contraction; 1 point, minimal increased blinking present only with external stimuli; 2 points, mild, but spontaneous eyelid fluttering; 3 points, moderate, very noticeable spasm of eyelids only, mildly incapacitating; 4 points, severe, incapacitating spasms of eyelids and possibly other facial muscles. Each patient was administered the McMonnies questionnaire (MQ), which is routinely performed in our clinic before botulinum toxin injection, to interactively evaluate the presence of dry eye.<sup>16</sup> Then observer who was blind to the status of patients and results of questionnaire graded corneal staining and LWE at the upper eyelids of patients' eyes according to the Oxford and Korb grading schemes, respectively.<sup>17,18</sup> Grading of the sagittal width of fluorescein and staining of the lid wiper was as follows: grade 0,  $\leq 25\%$  of the width of wiper; Grade 1, 25-50% of the width of wiper; Grade 2, 50-75% of

the width of wiper; Grade 3,  $\geq 75\%$  of the width of the wiper.

Patients were grouped according to their diagnosis: BEB as Group 1, HFS as Group 2. The parameters of the two groups and two eyes of patients in each group were compared. The right eyes of patients in Group 1 and the affected eyes of Group 2 were used in the comparison of the two groups.

According to the Jankovic rating scale, each group was divided into subgroups according to contraction severity and frequency. Those with severity/frequency of contractions' scores of 0, 1, and 2 and those with scores of 3, 4 were compared in terms of corneal staining and LWE.

Statistical analysis was performed with the SPSS (SPSS, v.20, Chicago, IL, USA). All data were normally distributed according to the Kolmogorov-Smirnov test and results were expressed as mean $\pm$ standard deviation. Independent-sample t-test was used for comparison. A p-value of  $<0.05$  was considered significant.

#### RESEARCH ETHICS STANDARDS COMPLIANCE

All procedures were performed in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The written informed consent was obtained from all patients. The study was approved by the University of Health Sciences Türkiye Ethics Committee with decision number 25/21 on November 27, 2020.

## RESULTS

Forty-three patients with BEB (23 females, 20 males) and 39 patients with HFS (14 females, 25 males) were included in the study. All HFS patients had primary HFS, and none had a family history, trauma, or facial nerve palsy. The mean age was  $62.56\pm 13.12$  (range: 36-79) and  $58.13\pm 8.83$  (range: 41-69) years in groups 1 and 2, respectively. There was no difference between groups in terms of age ( $p=0.08$ ). Disease duration was similar in both groups ( $p=0.07$ ),  $3.44\pm 1.08$  months in the Group 1 and  $3.05\pm 0.79$  months in the Group 2.

In Group 1, the number of eyes with contraction severity scores of 1, 2, 3, and 4 was 5, 10, 28, and 0, while the number of eyes with contraction frequency scores of 1, 2, 3, and 4 was 4, 13, 18, and 4, respectively. In Group 2, these numbers were 8, 10, 21, and 4 for contraction severity, and 3, 18, 18, and 0 for contraction frequency, respectively.

The mean score of the Jankovic rating scale, MQ, the mean corneal staining according to the Oxford scheme, and the mean LWE (Korb grade) of the two groups are shown in Table 1. The severity and frequency of contractions, Oxford score, and Korb grade were similar in the two groups ( $p>0.05$ ). MQ scores were also similar in the two groups ( $p>0.05$ ).

The mean Oxford score and the mean Korb grade of both eyes of patients in Group 1 and Group 2 are demonstrated in Table 2. There was no significant difference in Oxford score and Korb grade be-

**TABLE 1:** The mean score of the Jankovic rating scale, the McMonnies questionnaire, the mean corneal staining score, and the mean lid wiper epitheliopathy of the two groups.

	Group 1	Group 2	p value*
Jankovic rating scale			
Severity of contractions	2.53 $\pm$ 0.91	2.55 $\pm$ 0.82	0.95
Frequency of contractions	2.53 $\pm$ 0.91	2.36 $\pm$ 0.67	0.61
McMonnies questionnaire score			
Mean	15.37 $\pm$ 7.77	12.00 $\pm$ 4.82	0.21
Range	2-30	5-22	
Corneal staining score	0.95 $\pm$ 0.62	1.15 $\pm$ 0.69	0.72
Lid wiper epitheliopathy	1.47 $\pm$ 0.61	1.73 $\pm$ 0.65	0.29

Group 1: Benign essential blepharospasm; Group 2: Hemifacial spasm; \*Independent sample t-test was used for comparison of two groups. The right eyes of patients in Group 1 and the affected eyes of Group 2 were used in the comparison.

**TABLE 2:** The mean corneal staining score and the mean lid wiper epitheliopathy of both eyes of patients.

		Corneal staining score	Lid wiper epitheliopathy
Group 1	Right eye	0.95±0.62	1.47±0.61
	Left eye	0.95±0.62	1.47±0.61
	p value*	1.00	1.00
Group 2	Affected eye	1.55±0.69	1.73±0.65
	Unaffected eye	0.73±0.47	1.09±0.30
	p value*	<b>0.004</b>	<b>0.01</b>

\*Independent sample t-test was used for comparison of two eyes within the groups; Group 1: Benign essential blepharospasm; Group 2: Hemifacial spasm.

tween the two eyes of patients with BEB ( $p>0.05$ ). However, the mean Oxford score and the mean Korb grade were significantly lower in unaffected eyes compared to affected eyes in patients with HFS ( $p=0.001$  for both of them).

Table 3 demonstrates the comparison of subgroups determined according to the Jankovic rating scale in terms of Oxford score and Korb grade. Oxford score and Korb grade were found to be similar between the subgroups divided according to the frequency of contractions in both groups ( $p>0.05$ ). However, in both groups, Oxford score and Korb grade were significantly increased in those with a contraction severity score of 3-4 compared to those with a contraction severity score of 0-1-2 ( $p$  values of 0.04 and 0.001 for Group 1, 0.01 and 0.003 for Group 2, respectively).

## DISCUSSION

In our study, we compared corneal fluorescein staining and LWE of BEB and HFS patients with dry eye symptoms who were similar in terms of contraction frequency and severity. These two groups did not differ significantly in terms of LWE and corneal fluorescein staining. However, LWE and corneal staining were similar in both eyes in BEB patients, while LWE and corneal staining were significantly higher in the affected eye in HFS patients. This differentiation underscores the heterogeneity in ocular surface pathology between these two neurological disorders with ostensibly similar dry eye symptomatology, accentuating the necessity for nuanced clinical considerations in the management of ocular surface health in BEB and HFS patients.

BEB and HFS are diseases characterized by forceful blinking as a result of involuntary spasmodic contractions.<sup>19</sup> In both diseases, dry eye symptoms and signs of varying degrees can be observed.<sup>4,5,20,21</sup> Lu et al. found that the symptoms of BEB and dry eye disease patients were more severe than only dry eye disease patients.<sup>20</sup> Pellegrini et al. emphasized that dry eye symptoms may increase in the course of HFS, and attention should be paid to ocular surface findings during the follow-up of the patients.<sup>21</sup>

**TABLE 3:** The comparison of subgroups determined according Jankovic rating scale in terms of corneal staining (Oxford score) and lid wiper epitheliopathy (Korb grade).

			Oxford score	Korb grade
Group 1	Severity of contractions	Grade 0, 1 and 2	1.17±0.80	1.13±0.35
		Grade 3 and 4	1.58±0.63	1.71±0.66
		p value*	<b>0.04</b>	<b>0.001</b>
	Frequency of contractions	Grade 0, 1 and 2	1.33±0.77	1.39±0.50
		Grade 3 and 4	1.40±0.65	1.60±0.71
		p value*	0.76	0.29
Group 2	Severity of contractions	Grade 0, 1 and 2	1.32±0.78	1.45±0.51
		Grade 3 and 4	1.82±0.39	2.06±0.66
		p value*	<b>0.01</b>	<b>0.003</b>
	Frequency of contractions	Grade 0, 1 and 2	1.39±0.85	1.56±0.51
		Grade 3 and 4	1.67±0.48	1.86±0.73
		p value*	0.23	0.15

\*Independent sample t-test was used for comparison of two eyes within the groups; Group 1: Benign essential blepharospasm; Group 2: Hemifacial spasm.

The dynamics of eyelid motion exert a significant impact on both the ocular surface and the conjunctiva of the eyelid during blinking.<sup>19</sup> As demonstrated through the application of a specular microscope by Mathers and Lemp, blinking leads to the removal of corneal epithelial cells, influencing the corneal epithelium by enhancing the process of exfoliation.<sup>22</sup> Cher used the concept of blink-related microtrauma for epithelial changes associated with mechanical friction.<sup>23</sup> LWE, the term first used by Korb et al., occurs as a result of excessive friction between the ocular surface and the lid wiper.<sup>7</sup> LWE has been proposed to be a result of poor lubrication at the lid wiper-ocular surface interface, which results in mechanical stress to the marginal conjunctiva of the upper eyelid while blinking.<sup>24</sup> It has been reported that the prevalence of LWE is 6 to 16 times higher in dry eye patients compared to the control group.<sup>10</sup>

Yamamoto et al. evaluated the effect of eyelid pressure on LWE in normal eyes using a blepharotensiometer and stated that high pressure is one of the causes of LWE.<sup>25</sup> Yamaguchi and Shiraishi declared that the eyelid pressure is higher in dry eyes than in normal eyes.<sup>26</sup> Although the effect of eyelid pressure on the ocular surface and LWE has been demonstrated by these studies, according to our knowledge, there is only one study in the literature on LWE in patients with BEB and HFS, which are characterized by severe contractions in the periocular muscles.<sup>14</sup> Romero-Caballero et al. reported that all patients with both BEB and HFS had LWE.<sup>14</sup> Unlike their study, our investigation involved a comparative analysis of both eyes in both HFS and BEB patients. Our study constitutes a pioneering effort in the literature, being the first to systematically compare LWE between the eyes of these two distinct patient groups. The high LWE observed in both eyes of BEB patients and the affected eyes of HFS patients prompts consideration of potential etiological factors. Our interpretation posits that the elevated LWE may stem from the concomitant presence of dry eye in these disorders, possibly compounded by the mechanical impact of increased eyelid pressure on the lid wiper region. The corroboration of this hypothesis is further strengthened by the observed pattern of higher corneal staining in eyes exhibiting elevated LWE and the higher

Oxford score and higher Korb grade in eyes with higher contraction severity. Furthermore, our findings align with prior research by Yoshioka et al., establishing a significant correlation between eyelid pressure and ocular surface staining.<sup>19</sup> This correlation, as detected in both BEB and HFS patients in our study, reinforces the notion that increased corneal staining in the affected eyes may indeed be attributed to elevated eyelid pressure. In essence, our comprehensive analysis not only sheds light on the nuanced differences in ocular surface pathology between HFS and BEB patients but also introduces novel insights into the potential interplay of dry eye, mechanical factors, and ocular surface health in these neurological disorders. The identification of such associations may pave the way for more tailored and effective interventions in the management of ocular manifestations in BEB and HFS populations.

Our study has several limitations. One of them was the evaluation of LWE only for the upper lid. However, the lower eyelid was not evaluated because LWE in the lower eyelid is more affected by tear osmolarity than eyelid movements.<sup>11</sup> Since lissamine green and rose bengal was not available in our clinic, LWE and corneal staining could only be evaluated with fluorescein instead of the combination of dyes. Another limitation was that the increased eyelid pressure in BEB and HFS could not be analyzed quantitatively as we did not have a blepharotensiometer in our clinic.

## CONCLUSION

In conclusion, our findings suggest a potential nexus between the etiopathogenesis of LWE and the mechanisms underpinning dry eye conditions. Factors such as the mechanical pressure exerted by the eyelid on the ocular surface, as well as parameters integral to the blink dynamics, including frequency and amplitude, were implicated in both direct and indirect roles in the development of LWE. Consequently, a comprehensive examination approach is necessary during the follow-up of BEB and HFS, wherein LWE should be scrutinized alongside conventional dry eye assessments to gain nuanced insights into their pathophysiological interplay.

### Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** Gülây Yalçinkaya Çakır; Kübra Şerefoğlu Çabuk; **Design:** Kübra Şerefoğlu Çabuk, Semih Çakmak, Gülây Yalçinkaya Çakır; **Control/Supervision:** Şenay Aşık Nacaroğlu, Gamze Öztürk, Korhan Fazıl; **Data Collection and/or Processing:** Gülây Yalçinkaya Çakır; İhsan Çakır, Semih Çakmak; **Analysis and/or Interpretation:** Gülây Yalçinkaya Çakır; İhsan Çakır, Kübra Şerefoğlu Çabuk; **Literature Review:** Gülây Yalçinkaya Çakır; İhsan Çakır; **Writing the Article:** Gülây Yalçinkaya Çakır; **Critical Review:** Kübra Şerefoğlu Çabuk, Semih Çakmak.

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