Dry Eye and Dry Skin - Is There a Connection?

Igor Petriček
KBC Zagreb: Klinicki Bolnicki Centar Zagreb
Sania Vidas Pauk
KBC Zagreb: Klinicki Bolnicki Centar Zagreb
Martina Tomić
KB Merkur: Klinicka Bolnica Merkur
Bulum Tomislav (tomobulum@gmal.com)
Merkur Clinical Hospital: Klinicka Bolnica Merkur

Research Article

Keywords: Dry eye syndrome, Quality of Life, Ocular surface, Skincare, Tears

Posted Date: April 26th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-326914/v1

Version of Record: A version of this preprint was published at Ophthalmic Epidemiology on December 29th, 2021. See the published version at https://doi.org/10.1080/09286586.2021.2021539.

Abstract

Aim: To enquire whether patients with dry eye symptoms also report dry skin, whether their perception could be corroborated with objective measurement, and whether dry eye disease might be suspected based on patients' anamnesis.

Methods: This cross-sectional study included 50 subjects (25 with and 25 without dry eye symptoms). Schein questionnaire was used to determine the severity of dry eye symptoms. Ocular signs were assessed by conjunctival hyperemia, ocular surface staining, Meibomian gland expression, tear film lipid layer thickness, tear break-up time, lid parallel conjunctival folds, Schirmer test, and meibometry. Skin dryness was assessed by patients' perception of their facial skin dryness and measured by sebumeter.

Results: Subjects without dry eye symptoms had self-reported oilier facial skin than those with dry eye symptoms ($p<0.001$). Sebumetry scores measured on the forehead and cheek were significantly higher in subjects without dry eye symptoms than dry eye subjects ($p=0.003$). After adjustment for age and gender in a logistic regression analysis, dry eye was independently and significantly associated with dry skin (AOR 0.69, $p=0.040$), higher LIPCOF score of both eyes (AOR 2.28, $p=0.028$), lower sebumetry score of the forehead (AOR 0.98, $p=0.041$) and cheek (AOR 0.98, $p=0.041$), and shorter TBUT score after gland expression (AOR 0.90, $p=0.018$).

Conclusion: This study showed that ocular dryness was subjectively and objectively positively correlated to facial skin dryness - patients reliably described their skin condition: people with dry facial skin also had drier eyes.

Introduction

The eye's primary function is to see, and in that role, all its parts form a single organ. However, it is frequently ignored that the ocular surface is also part of the overall body surface, which predominantly consists of skin. The eye with tear film protects itself from drying, and so does the skin for the rest of the body, which enables the body to retain its hydration. In that sense, both parts of the body surface perform the same task.

Dry eye is a medical problem of epidemic proportions. In the last three decades, awareness of dry eye disease (DED) has risen considerably worldwide. It is a growing public health concern causing ocular discomfort, fatigue, and visual disturbance that interferes with quality of life (QoL), including aspects of physical, social, psychological functioning, daily activities, and workplace productivity. According to the literature, the prevalence of dry eye ranges from 5 to 30 % in individuals over the age of 50, with women consistently having a 1,3 – 1,5 times higher prevalence rate than men in all studies that measured both signs and symptoms [1]. On the other hand, dry skin (xerosis cutis) is the most common skin disorder, more frequently among women and older people, with prevalence ranging from 5.4 % to 85.5 % [2]. DED is

defined by Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) and amended by the TFOS DEWS II [3, 4].

At the same time, millions of people, especially women, complain of dry skin and use cosmetics to alleviate this discomfort. However, dry skin is not labeled as a disease, nor people who have it experience it as a disease but as a condition. It is characterized by a lack of the appropriate amount of water in the most superficial layer of the skin, the epidermis [5]. It is not inflamed or diseased, just dry. Overall, there is a lack of reports describing it at all.

When eye care practitioners examine the dry eye patients and ask them about their skin type, very frequently, such patients also complain of having dry skin, especially women.

Having this in mind, is there a connection? Do people with dry skin also have dry eyes, and if they do, what may be the cause - the same for both parts of the body surface?

As Meibomian glands produce meibum, the skin's sebaceous glands produce an oily substance called sebum to protect the outer layer of skin from losing water. If the skin does not have enough sebum, it loses water and feels dry, like DED. The new definition recognizes dry eye as a multifactorial disease resulting from numerous interacting causes that influence tear film homeostasis, e.g., age, sex, gender, hormone imbalance, environmental causes, inflammation, neurogenic, iatrogenic, low blink rate, lid disorders, vitamin A deficiency, allergies and psychological causes [4, 6]. Many of them also result in dry skin. Aging decreases sebum production. Excessive bathing, showering, or scrubbing of the skin also excessively removes sebum. Dry indoor air, exposure to wind and sun, diabetes or skin allergies, thyroid gland disorders, Sjogren's syndrome, and various medications also cause the same condition [7]. So, both conditions have much in common.

One of the most prominent DED and dry skin features is that both conditions occur more frequently in women than in men and older people. Moreover, the female gender by itself is a significant risk factor for the development of DED.

Sex hormones, especially androgens, are essential in regulating lacrimal, Meibomian, and sebaceous glands function, imbalance of which is associated with both aqueous-deficient, evaporative DED [8–11], and dry skin [12]. Many other hormones, sex-related differences in brain organization, cognitive ability, and pain perception are responsible for dry eye sex-related prevalence differences and may play an important role in dry skin prevalence differences [13, 14].

Keeping in mind all the above mentioned, authors were surprised in not enabling to find any study comparing ocular and skin dryness.

The purpose of this study was to enquire whether patients with dry eye symptoms also report having dry skin and whether their perception could be corroborated with objective measurement. These answers could help DED diagnosing and treatment, and prevent disease complications that impact patients' vision, daily activities, QoL, and working abilities.

Subjects And Methods

This cross-sectional study included 50 subjects examined by the first author during his routine clinical work in his adult general ophthalmology outpatient practice. Twenty-five subjects were with and twenty-five without dry eye symptoms. The study protocol was approved by the Institutional Ethics Committee and was performed according to the guidelines of the Declaration of Helsinki.

The subjects received both written and oral information about the study and signed written informed consent.

Inclusion criteria required subjects to be 18 or older, have normal other anterior ocular surface findings, not be contact lens wearers, not use any topical ophthalmic medication, and have no severe dermatological diseases. Excluded were all subjects with previous ocular trauma, acute infection, glaucoma, ocular surgery in the past years, any other ocular surface diseases and irregularities, systemic diseases, or medications that would alter the ocular surface or skin, and subjects who cooperated poorly.

Clinical parameters screened were severity of dry eye symptoms using Schein questionnaire [15].

Ocular signs were measured by conjunctival hyperemia, fluorescein surface staining, Meibomian gland expression (EGM), tear film lipid layer thickness (LLT) using a handheld tool, tear break-up time (TBUT) before and after Meibomian gland expression, lid parallel conjunctival folds (LIPCOF), and Schirmer test (double void).

Conjunctival hyperemia was assessed using Cornea and Contact Lens Research Unit (CCLRU) grading scale [16].

LLT was measured before any eye manipulation and after Meibomian gland expression using a slit lamp and a handheld lipid layer examination instrument [17, 18].

TBUT was measured using standardized fluorescein strips (Biotech, Fluorescein Sodium Ophthalmic Strip USP). The upper lid of the eye was slightly lifted, and the fluorescein strip was moistened with saline. The excess fluid was shaken off from the strip, and it was then used to stain the ocular surface. The procedure was repeated after Meibomian gland expression [19].

LIPCOF was observed, without fluorescein, on the bulbar conjunctiva in the area perpendicular to the temporal and nasal limbus, above the lower lid with a slit lamp microscope using ~ 25 magnification and scored counting the number of folds (0–4) [20].

The Schirmer test (double void) was assessed by folding the Schirmer paper strip (5 x 35 mm) at the notch, hooking the folded end over the temporal one-third of the lower lid margin measuring the length of wetting from the notch after 5 min. The procedure was performed with topical anesthetic and eyes closed [21].

Meibometry was performed using a commercially available meibometer (Courage + Khazaka Electronic GmbH, Germany). In assessing the skin dryness, subjects were asked how they felt their facial skin, dry or oily, on a scale from − 5 (very dry) to + 5 (very oily). Facial skin oiliness was measured using a commercially available sebumeter (Courage + Khazaka electronic GmbH, Germany). Both instruments use the photometric method: when oiled, the matte-surfaced synthetic tape becomes transparent and thus lets more light through it. The more light is transmitted through the strip - the higher lipid content is [22–24]. Both measurements were performed as recommended by the manufacturer: sebumetry from the clean, untreated, and unwashed forehead and cheek skin, and meibometry from lower left eyelid margin, first unmanipulated and then after Meibomian gland expression.

Statistical analysis was performed by Statistica software package version 13.3 (TIBCO Inc., USA). The normality of data distribution was tested by the Shapiro-Wilks test and homogeneity of variance by Leven test. Results of descriptive analyses were expressed as median (minimum-maximum) for continuous and ordinal data and numbers for categorical data. Differences in distributions of continuous data were evaluated by t-test for independent variables and Mann-Whitney test. The nonparametric test was used to analyze the differences between ordinal and continuous data when the assumption of homogeneity of variance for tested variables was not met. Differences in distributions of categorical data were assessed by the Chi-square test. The Spearman rank correlation test was used. Binary univariate and multiple logistic regression analyses were used to assess the strength and independence of associations. p value of less than 0.05 was considered statistically significant.

Results

This study included 50 subjects (9 males, 41 females) with a median age of 49.5 (min 20 - max 78) years. According to the dry eye symptoms evaluated by the Schein questionnaire, subjects were divided into two groups: group 1 - subjects without dry eye symptoms (Schein questionnaire score 0) and group 2 - subjects with dry eye symptoms (Schein questionnaire score 1 or > 1).

Descriptive statistics of basic characteristics, skin type, and dry eye signs of subjects included in the study are presented in Table 1. Subjects in group 2 were older than those in group 1 (62 years *vs.* 34 years, $p < 0.001$). In group 2, there were more women than in group 1 (24 *vs.* 8, $p = 0.010$). Subjects without dry eye symptoms had self-reported oilier facial skin than those with dry eye symptoms ($p < 0.001$). The two groups did not significantly differ in conjunctival hyperemia (CCRLU) of the right and left eye ($p = 0.473$). Dry eye subjects had higher LIPCOF scores of the right and left eye than subjects without dry eye symptoms ($p = 0.003$). No differences in CCRLU and LIPCOF scores between the right and left eye within the examined groups were found (Wilcoxon test, $Z = 0.000$, $p = 1.000$; table not shown). There were no differences in meibometry scores before and after expression between groups. Sebumetry scores measured on the forehead and cheek were significantly higher in subjects without dry eye symptoms than dry eye subjects ($p = 0.003$). In both groups sebumetry score of the forehead was higher than sebumetry score of the cheek (Wilcoxon test, group 1: $Z = 4{,}372$, $p < 0.001$, group 2: $Z = 4{,}060$, $p < 0.001$; table not shown). There were no differences in LLT scores before and after expression between the groups ($p =$

0.930; p = 0.899). TBUT scores both before and after Meibomian gland expression were significantly longer in subjects without dry eye symptoms than those with dry eye symptoms (10 seconds *vs.* 3 seconds, p = 0.001; 18 seconds *vs.* 4 seconds, p < 0.001).

Table 1
Basic characteristic, skin type and dry eye signs in subjects divided into two groups according to dry eye symptoms evaluated by Schein questionnaire.

	Group 1 (n = 25)	Group 2 (n = 25)	Z[a] Chi[b] t[c]	p
Age (years)*	34 (20–64)	62 (20–78)	3.59[a]	**< 0.001**[a]
Gender (m/f)**	8/17	1/24	6.64[b]	**0.010**[b]
Self-reported drier or oilier facial skin (1–10)*	5 (3–8)	2 (1–9)	-4.12[a]	**< 0.001**[a]
CCLRU right eye (0–4)*	0 (0–0)	0 (0–2)	0.72[a]	0.473[a]
CCLRU left eye (0–4)*	0 (0–0)	0 (0–2)	0.72[a]	0.473[a]
LIPCOF right eye (0–3)*	1 (0–2)	2 (0–3)	2.96[a]	**0.003**[a]
LIPCOF left eye (0–3)*	1 (0–2)	2 (0–3)	2.96[a]	**0.003**[a]
Meibometry prior to gland expression Max***	354.64 ± 143.94	396.08 ± 132.09	1.06[c]	0.294[c]
Meibometry prior to gland expression Area*	1920 (976–4880)	2164 (965–5291)	0.52[a]	0.600[a]
Meibometry after gland expression Max***	477.52 ± 189.97	474.28 ± 184.09	-0.06[c]	0.951[c]
Meibometry after gland expression Area*	2654 (482–9230)	3220 (903–9252)	-0.12[a]	0.907[a]
Sebumetry forehead*	208 (97–240)	160 (29–265)	-2.95[a]	**0.003**[a]
Sebumetry cheek***	152.72 ± 53.32	101.84 ± 54.78	-3.13[c]	**0.003**[c]
LLT before gland expression*	3 (2–5)	3 (2–5)	-0.09[a]	0.930[a]
LLT after gland expression*	5 (3–5)	5 (3–5)	-0.13[a]	0.899[a]
TBUT before gland expression*	10 (2–35)	3 (0–25)	-3.26[a]	**0.001**[a]

* median (min-max) ** numbers *** mean ± SD [a] Mann-Whitney test [b] Chi-square test df = 1 [c] t-test df = 48

Abbreviations: Group 1 - without dry eye symptoms (Schein questionnaire score 0) and Group 2 - with dry eye symptoms (Schein questionnaire score 1 or > 1); CCLRU - Cornea and Contact Lens Research Unit; LIPCOF - Lid Parallel Conjunctival folds; LLT - Lipid Layer Thickness; TBUT - Tear Film Break-up Time.

	Group 1 (n = 25)	Group 2 (n = 25)	Z[a] Chi[b] t[c]	p
TBUT after gland expression*	18 (2–40)	4 (0–25)	-3.29[a]	< 0.001[a]

* median (min-max) ** numbers *** mean ± SD [a] Mann-Whitney test [b] Chi-square test df = 1 [c] t-test df = 48

Abbreviations: Group 1 - without dry eye symptoms (Schein questionnaire score 0) and Group 2 - with dry eye symptoms (Schein questionnaire score 1 or > 1); CCLRU - Cornea and Contact Lens Research Unit; LIPCOF - Lid Parallel Conjunctival folds; LLT - Lipid Layer Thickness; TBUT - Tear Film Break-up Time.

Self-reported skin type (1 dry – 10 oily) was significantly negatively correlated with LIPCOF score of both eyes (p = 0.039), significantly positively with sebumetry score of the forehead (p = 0.037) and marginally positively with sebumetry score of the cheek (p = 0.058). No significant correlation was observed between the skin type and the presence of conjunctival hyperemia, meibometry score, LLT score, and TBUT score before and after gland expression (Table 2).

Table 2
Correlation between self-reported skin type and dry eye signs.

	Self-reported skin type (1 dry – 10 oily)		
	Spearman R	t(N-2)	p
CCLRU right eye (0–4)	-0.056	-0.389	0.699
CCLRU left eye (0–4)	-0.056	-0.389	0.699
LIPCOF right eye (0–3)	-0.293	-2.121	**0.039**
LIPCOF right eye (0–3)	-0.293	-2.121	**0.039**
Meibometry before gland expression Max	-0.193	-1.362	0.180
Meibometry before gland expression Area	-0.153	-1.073	0.289
Meibometry after gland expression Max	-0.049	-0.337	0.737
Meibometry after gland expression Area	-0.160	-1.122	0.267
Sebumetry forehead	0.296	2.149	**0.037**
Sebumetry cheek	0.270	1.941	**0.058**
LLT before gland expression	0.161	1.127	0.265
LLT after gland expression	-0.001	-0.006	0.995
TBUT before gland expression	0.194	1.369	0.177
TBUT after gland expression	0.129	0.902	0.372

Abbreviations: CCLRU - Cornea and Contact Lens Research Unit; LIPCOF - Lid Parallel Conjunctival folds; LLT - Lipid Layer Thickness; TBUT - Tear Film Break-up Time.

Self-reported skin type (1 dry – 10 oily) was significantly negatively correlated with all investigated dry eye symptoms except for no significant correlation between the type of the skin and the presence of dry eye symptoms during winter (Table 3).

Table 3
Correlation between self-reported skin type and dry eye symptoms.

	Self-reported skin type (1 dry – 10 oily)		
	Spearman R	t(N-2)	p
Dryness (0–4)	-0.425	-3.249	**0.002**
Grittiness (0–4)	-0.365	-2.717	**0.009**
Burning (0–4)	-0.422	-3.228	**0.002**
Redness (0–4)	-0.463	-3.621	**< 0.001**
Crusts (0–4)	-0.427	-3.270	**0.002**
Difficult opening eyes (0–4)	-0.474	-3.729	**< 0.001**
More symptoms in winter (yes/no)	0.240	1.713	0.093
More symptoms in wind (0–4)	-0.428	-3.279	**0.002**
More symptoms at computer (0–4)	-0.395	-2.982	**0.004**
More symptoms at TV (0–4)	-0.395	-2.982	**0.004**
More symptoms during driving (0–4)	-0.349	-2.582	**0.013**
Visual acuity fluctuations (0–4)	-0.433	-3.329	**0.002**

Table 4 presents basic characteristics, skin type, and dry eye signs associated with dry eye by means of binary logistic regression analyses. The strongest associations were found for older age (OR 1.07, p = 0.001) and female gender (OR 11.29, p = 0.001), while significant relations were found for dry skin (OR 0.57, p = 0.002), higher LIPCOF score of both eyes (OR 2.73, p = 0.002), lower sebumetry score of the forehead (OR 0.98, p = 0.007) and cheek (OR 0.98, 0.005), and shorter TBUT score before (OR 0.88, p = 0.008) and after gland expression (OR 0.87, p = 0.002). After adjustment for age and gender, most of the associations also remained independently and significantly associated with dry eye, except TBUT score before gland expression (AOR 0.92, p = 0.096).

Table 4
Basic characteristics, skin type, and dry eye signs associated with dry eye by means of logistic regression analysis.

	OR (95%CI)	p	AOR (95%CI)*	p*
Age (years)	1.07 (1,03-1.11)	**0.001**	/	/
Gender (female)	11.29 (1.29–98.89)	**0.001**	/	/
Self-reported drier or oilier facial skin (1–10)	0.57 (0.39–0.81)	**0.002**	0.69 (0.48–0.98)	**0.040**
LIPCOF right eye (0–3)	2.73 (1.43–5.19)	**0.002**	2.28 (1.09–4.77)	**0.028**
LIPCOF left eye (0–3)	2.73 (1.43–5.19)	**0.002**	2.28 (1.09–4.77)	**0.028**
Meibometry before gland expression Max	1.00 (0.99-1.00)	0.290	1.00 (0.99-1.00)	0.452
Meibometry before gland expression Area	1.00 (1.00–1.00)	0.518	1.00 (0.99-1.00)	0.546
Meibometry after gland expression Max	1.00 (0.99-1.00)	0.950	1.00 (0.99-1.00)	0.574
Meibometry after gland expression Area	1.00 (1.00–1.00)	0.878	1.00 (0.99-1.00)	0.777
Sebumetry forehead	0.98 (0.96–0.99)	**0.007**	0.98 (0.96–0.99)	**0.041**
Sebumetry cheek	0.98 (0.97–0.99)	**0.005**	0.98 (0.97-1.00)	**0.044**
LLT before gland expression	0.96 (0.57–1.64)	0.892	1.08 (0.57–2.07)	0.797
LLT after gland expression	1.00 (0.40–2.50)	1.000	1.61 (0.51–5.04)	0.414
TBUT before gland expression	0.88 (0.79–0.97)	**0.008**	0.92 (0.83–1.02)	0.096
TBUT after gland expression	0.87 (0.80–0.95)	**0.002**	0.90 (0.82–0.98)	**0.018**
* OR adjusted for age and gender				
Abbreviations: LIPCOF - Lid Parallel Conjunctival folds; LLT - Lipid Layer Thickness; TBUT - Tear Film Break-up Time.				

Discussion

Is there a correlation between gender, age, DED, and facial skin oiliness? In this study, subjects without dry eye symptoms reported oilier facial skin than those with dry eyes. Women, especially older ones, more frequently had dry eye symptoms and complained of dry skin.

Zlatogorski and Dikstein have shown in their study performed on 270 male and 382 female subjects aged 20–95 that sebum quantity, measured by sebumeter on the forehead and face, does not change in male subjects but decreased in female subjects, especially in age groups older than 40. The postulated reason for that was a decrease in circulating androgens [25].

Another issue is how accurate patients are in their assessment of their facial skin type. Laufer and Dikstein performed research in 1996 on 103 female subjects aged 19–82 [26]. After being asked to self-assess their skin type, sebumetry was performed on their foreheads, cheeks, and necks. There was a statistically relevant correlation between self-reported skin type and sebumetry measurement: 95% of women who reported dry skin had low sebumetry values on their forehead, 100% on the cheek, and 87% neck. Also, a significantly larger number of women reported drier skin after menopause, and sebumetry measurements corroborated their self-assessment.

The present study similarly showed that skin dryness self-assessment reliably describes its actual condition, especially in older women who predominantly have dry eyes.

In his study conducted on 200 subjects, 100 with dry eye symptoms and 100 without, the first author found similar results among his female subjects: women with dry eye symptoms more frequently reported skin dryness, and this correlation neatly corresponded with age - older women had drier eyes and drier skin. No such correlation was found among men [19].

This finding corroborates data from the research done in 2013 by Luebberding, Krueger, and Kerscher [27]. A total of 300 healthy male and female subjects (20–74 years) were selected following strict criteria, including age, sun behavior, or smoking habits. Hydration level, sebum production, and pH values were measured at the forehead, cheek, neck, volar forearm, and dorsum of the hand. Sebum production in male skin was always higher and stayed stable with increasing age, whereas sebum production in women progressively decreased over a lifetime. Authors concluded that skin physiological distinctions between the sexes exist and are particularly remarkable concerning sebum production and pH value.

This skin data remarkably mirrors dry eye epidemiology - it is more frequent among women, significantly older ones. However, this similarity is usually ignored, and dry eye is usually being regarded and treated as an exclusively ocular disorder.

We have to ask ourselves one intriguing question: *If dry skin and dry eye accompany each other, do they have at least partially the same cause?*

There were no differences in meibometry scores before and after expression between the groups. Meibometry is a method described in several published papers [22–23, 28]. However, when performed as instructed by the manufacturer, it produced low repeatability values, which eventually failed to detect dry eye patients or correlate with other measured parameters.

Conclusion

This study showed that ocular dryness is correlated to facial skin dryness. People with dry skin also have drier eyes. Both being parts of the body surface, it is clear that the ocular dryness could not be observed as the solely ocular condition but as the general body surface problem. As both body surface parts play the same role in dehydration prevention, there has to be the same regulator of this function.

As this study showed that patients reliably assessed their facial skin condition, this information may be important to practitioners lacking necessary equipment to objectively examine the ocular surface, like in family medicine, to help their patients: patients with chronic ocular symptoms who also report dry skin may have them due to dry eye. It also may be necessary for eye care professionals. The presence of dry eye and dry skin symptoms simultaneously is highly suspected of DED, and therefore, it might be considered even based on patients' history. Early diagnosis and treatment of DED could relieve dry eye symptoms, alleviate the disease severity and, consequently, improve life quality, including physical, social, psychological, and workplace productivity.

Declarations

ACKNOWLEDGEMENT:

Conflict of Interest: None.

Funding: “This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.”

Authorship: “All authors mentioned fulfil the criteria for authorship as per ICMJE guidelines. Anyone who does not meet the criteria has not been included.”

Financial Disclosure: “No author has a financial or proprietary interest in any material or method mentioned.”

Informed consent: “Informed consent was obtained from all individual participants included in the study.”

References

1. Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F et al TFOS DEWS II Epidemiology Report (2017) Ocul Surf 15(3):334–365. doi:10.1016/j.jtos.2017.05.003
2. Hahnel E, Lichterfeld A, Blume-Peytavi U, Kottner J (2017) The epidemiology of skin conditions in the aged: A systematic review. J Tissue Viability 26(1):20–28. doi:10.1016/j.jtv.2016.04.001
3. International dry eye workshop (2007) The definition and classification of dry eye disease: report of definition and classification subcommittee of international dry eye workshop. Ocul Surf 5:75–92
4. Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK et al (2017) TFOS DEWS II Definition and Classification Report. Ocul Surf 15(3):276–283. doi:10.1016/j.jtos.2017.05.008

5. Nordstrom KM, McGinley KJ, Kligman AM, Leyden JJ (1989) Sebaceous lipids in xerosis of the skin. J Cutan Aging Cosmet Dermatol 1:29–33
6. Bron AJ, de Paiva CS, Chauhan SK, Bonini S, Gabison EE, Jain S et al (2017) TFOS DEWS II pathophysiology report. Ocul Surf 15(3):438–510. doi:10.1016/j.jtos.2017.05.011
7. Andriessen A (2013) Prevention, recognition and treatment of dry skin conditions. Br J Nurs 22(1):26–30. doi:10.12968/bjon.2013.22.1.26
8. Knop E, Knop N, Millar T, Obata H, Sullivan DA. 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;52:1938–1978. doi: 10.1167/iovs.10-6997c
9. Azcarate PM, Venincasa VD, Feuer W, Stanczyk F, Schally AV, Galor A (2014) Androgen deficiency and dry eye syndrome in the aging male. Invest Ophthalmol Vis Sci 55:5046–5053. doi:10.1167/iovs.14-14689
10. Truong S, Cole N, Stapleton F, Golebiowski B (2014) Sex hormones and the dry eye. Clin Exp Optom 97:324–336. doi:10.1111/cxo.12147
11. Gagliano C, Caruso S, Napolitano G, Malaguarnera G, Cicinelli MV, Amatoet R et al (2014) Low levels of 17-β-oestradiol, oestrone and testosterone correlate with severe evaporative dysfunctional tear syndrome in postmenopausal women: a case–control study. Br J Ophthalmol 98:371–376. doi:10.1136/bjophthalmol-2012-302705
12. Takayasu S, Wakimoto H, Itami S, Sano S (1980) Activity of testosterone 5 alpha-reductase in various tissues of human skin. J Invest Dermatol 74(4):187–191
13. Sullivan DA1, Rocha EM, Aragona P, Clayton JA, Ding J, Golebiowski B et al (2017) TFOS DEWS II Sex, Gender, and Hormones Report. Ocul Surf 15(3):284–333. doi:10.1016/j.jtos.2017.04.001
14. Delattre C, Winstall E, Lessard C, Donovan M, Simonetti L, Minondoet AM (2012) al. Proteomic analysis identifies new biomarkers for postmenopausal and dry skin. Exp Dermatol 21(3):205–210. doi:10.1111/j.1600-0625.2011.01434.x
15. Schein OD, Tielsch JM, Munõz B, Bandeen-Roche K, West S (1997) Relation between signs and symptoms of dry eye in the elderly. A population-based perspective. Ophthalmology 104:1395–1401. doi:10.1016/s0161-6420(97)30125-0
16. Terry RL, Schnider CM, Holden BA, Cornish R, Grant T, Sweeneyet D (1993) al. CCLRU standards for success of daily and extended wear contact lenses. Optom Vis Sci 70(3):234–243. doi:10.1097/00006324-199303000-00011
17. Petricek I (2017) Handheld Tear Film Lipid Layer Thickness and Non Invasive Tear Break up Time Assessment Tool. J Clin Ophthalmol Eye Disord 1(2):1009
18. Pauk SV, Petriček I, Tomić M, Bulum T, Jandroković S, Kalauz M et al (2021) Manual interferometric device for routine non-invasive tear film break-up time assessment. Semin Ophthalmol. doi:10.1080/08820538.2021.1884272
19. Petriček I. The influence of tear film on visual function. PhD thesis: Zagreb, University of Zagreb School of Medicine; 2011

20. Höh H, Schirra F, Kienecker C, Ruprecht KW (1995) Lid-parallel conjunctival folds are a sure diagnostic sign of dry eye. Ophthalmologe 92(6):802–808
21. Abelson MB, Lamberts DW. Dry Eye Update, Excerpta Medica (Amsterdam) 1983; 1–17
22. Chew CK, Jansweijer C, Tiffany JM, Dikstein S, Bron AJ (1993) An instrument for quantifying meibomian lipid on the lid margin: the meibometer. Curr Eye Res 12(3):247–254. doi:10.3109/02713689308999470
23. Chew CK, Hykin PG, Jansweijer C, Dikstein S, Tiffany JM, Bron AJ (1993) The casual level of meibomian lipids in humans. Curr Eye Res 12(3):255–259. doi:10.3109/02713689308999471
24. Crowther JM (2016) Method for quantification of oils and sebum levels on skin using the Sebumeter®. Int J Cosmet Sci 38:210–216. doi:10.1111/ics.12258
25. Zlatogorski A, Dikstein S (2000) Skin surface sebum on the forehead and cheek of adults. 13th International Congress of the International Society of Bioengineering and Skin. International Society of Bioengineering and Skin, Jerusalem, p 46
26. Laufer A, Dikstein S (1996) Objective Measurement and Self-Assessment of Skin-Care Treatments. Cosmetics Toiletries 111:91
27. Luebberding S, Krueger N, Kerscher M (2013) Skin physiology in men and women: in vivo evaluation of 300 people including TEWL, SC hydration, sebumcontent and skin surface pH. Int J Cosmet Sci 35(5):477–483. doi:10.1111/ics.12068
28. Yokoi N, Mossa F, Tiffany JM, Bron AJ (1999) Assessment of meibomian gland function in dry eye using meibometry. Arch Ophthalmol 117:723–930. doi:10.1001/archopht.117.6.723