Case finding of dry eye disease in Norwegian optometric practice: a cross-sectional study

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Abstract
Optometrists are primary eye care providers, and it is essential that they efficiently identify patients who will benefit from dry eye management. The aim of the study was to explore case finding of dry eye disease (DED) in optometric practice.

A cross-sectional study examining dry eye symptoms and signs in 186 patients (18–70 years of age) attending a routine eye examination, with DED defined according to the criteria of the Tear Film and Ocular Surface Society Dry Eye Workshop II. Standard statistical tests were used, and clinical diagnostics were explored using sensitivity, specificity, and receiver-operating curve (ROC) statistics.

Fifty-six patients were contact lens wearers, and they were significantly younger than the non-contact lens wearers (mean age 35 (SD = 1) versus 48 (± 2) years). The mean best corrected visual acuity (BCVA) in the better eye was 1.0 (± 0.1) (decimal acuity). There was no difference in BCVA between contact lens wearers and non-contact lens wearers. The mean Ocular Surface Disease Index (OSDI) score was 22 (± 19), and 138 patients had at least one positive homeostasis marker. Eighty-six had DED, 52 had signs without symptoms, and 23 had symptoms without signs of DED. The sensitivity and specificity of OSDI in detecting any positive homeostasis marker were 62% and 54%, respectively. In all, 106 patients had meibomian gland dysfunction (MGD), of which 49 were asymptomatic. In a ROC analysis, an OSDI ≥ 13 showed a diagnostic ability to differentiate between patients with a fluorescein breakup time (FBUT) < 10 seconds and a fluorescein breakup time ≥ 10 seconds, but not between patients with and without staining or MGD.

The majority of patients had dry eye signs and/or dry eye symptoms. Routine assessment of FBUT and meibomian glands may enable case finding of DED in optometric practice.

Keywords: dry eye disease, Ocular Surface Disease Index, meibomian gland dysfunction, tear breakup time, ocular staining

Introduction
The Tear Film and Ocular Surface Society Dry Eye Workshop II (TFOS DEWS II) defines dry eye disease (DED) as “a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles” (Craig et al., 2017). The prevalence of DED varies from 5% to 50%, depending on the study population and diagnostic criteria, and is higher among females, in older age groups, and among people of Asian ethnicity (Stapleton et al., 2017). DED is associated with ocular pain and irritation, blurred vision, and anxiety and depression, and may limit daily activities and reduce work effectiveness and quality of life. Consequently, DED has significant socioeconomic implications (Li et al., 2012; Stapleton et al., 2017; Uchio et al., 2014; Wan et al., 2016).

According to the TFOS DEWS II report, the diagnosis of dry eye should include assessment of both dry eye symptoms and tear film homeostasis markers (Wolffsohn et al., 2017). When DED is confirmed, further testing for sub-classification of DED and grading of severity is needed as treatment should be tailored to the type and severity of DED. Tests that differentiate evaporative dry eye (EDE) from aqueous deficient dry eye (ADDE) are essential as these conditions are managed differently (Jones et al., 2017).

Visual function is affected in DED, and decreased vision and transient blurring of vision are common complaints in DED patients (Ishida et al., 2005). Meibomian gland dysfunction (MGD) is the leading cause of EDE and associated ADDE. Among people with DED, 13% to 50% have MGD (Arita et al., 2019; Uchio et al., 2006; Viso et al., 2011). In people over 40 years of age, 38% to 68% have MGD, dependent on population and applied diagnostic criteria (Stapleton et al., 2017). Patients may have MGD without symptoms; these patients are often undiagnosed (Blackie et al., 2010). The TFOS International Workshop on Meibomian Gland Dysfunction (MGD report) suggests that meibomian gland expression should be part of routine examination in adults and that dry eye work-up should be undertaken in patients with MGD regardless of symptoms (Tomlinson et al., 2011).

Optometrists are primary eye care providers, and it is essential that they efficiently identify patients who will benefit from dry eye management. Studies report significant differences in examination of dry eye patients and a potential to enhance the identification of patients at risk of DED (Downie et al., 2013; Downie et al., 2016; van Tilborg et al., 2015), consequently indicating a need to improve and standardise the examination and diagnosis of DED in optometric practice. The aim of this study was to explore case finding of DED in general Norwegian optometric practice.

Methods
The study had a cross-sectional design. The study population was recruited from people attending for a routine eye examination by one dedicated optometrist in each of three Krogh Optikk practices in Trondheim and Oslo, Norway. To minimize observer bias, the optometrists followed written instructions on how to perform the dry eye examination, and standardised equipment was used for all patients. All patients aged 20 to 70 years attending for an eye examination or a contact lens fitting/follow-up during the period between 15th December 2015 and 1st February 2016 were invited to participate. All patients were given oral and written information and gave informed consent to take part in the study. Patients with other known ocular surface inflammations, previous trauma affecting the tear film examination, or known hypersensitivity to lissamine green and/or fluorescein were excluded from the study.

Data collection
The scheduled routine examination was undertaken, including patient history of contact lens wear, the use of systemic medication and computer screens, as well as decimal visual acuity at six metres equivalent distance. Further, a full dry eye examination was performed. The dry eye examination included the Ocular Surface Disease Index (OSDI) questionnaire, assessment of tear meniscus height (TMH), fluorescein tear breakup time (FBUT),
corneal and conjunctival staining, meibum expressibility, and meibum quality. The sequence of tear film tests was the same for all patients, starting with the least invasive tests first.

The participants started by answering the OSDI questionnaire. The OSDI questionnaire consists of 12 questions about symptoms, visual function, and environmental triggers, based on patients’ experience of symptoms in the previous week. Each question was answered on a scale from 0 (none of the time) to 4 (all of the time). The total composite score (0–100) was calculated according to the formula of Schiffman et al. (2000). A normal ocular surface score is in the range of 0–12; a score of ≥ 13 was set as the criterion for dry eye symptoms. In all, 109 patients (58.6%) had dry eye symptoms; of these, 41 (38.3%) had both MGD and reduced TMH (see Table 1). Among all patients, 34 (37.6%) had both MGD and reduced TMH, 6 (8.3%), 3 (8.8%) and 5 (18.5%), respectively, did not have positive homeostasis markers (dry eye signs). In these 86 had dry eye symptoms (OSDI score ≥ 13) (see Table 1). Reduced FBUT and staining were not associated with sex, age, or contact lens wear.

Statistics

The data were analysed in frequency and summation tables. Group differences and associations were analysed with standard parametric and non-parametric statistical tests: chi-square, Student’s t-test, and Spearman correlation. Clinical diagnostics were explored by the calculation of sensitivity and specificity and receiver operating curve (ROC) statistics. A p-value of < 0.05 was considered statistically significant.

Ethics

The research conformed to the Declaration of Helsinki, and the study was approved by the Regional Committee for Medical and Health Research Ethics (2015/2492).

Results

In all, 186 patients were examined, of which 118 (63%) were female. Their mean age was 44 years (± 15), ranging from 20 to 70 years. The mean age of females was 44 years (± 14), and the mean age of men was 45 years (± 15). Fifty-six patients (30%) were contact lens wearers; the contact lens wearers were significantly younger than non-contact lens wearers (mean age 35 (± 1) versus 48 (± 2) years), Student’s t-test p < 0.001. All patients had normal vision; the mean best corrected decimal visual acuity (BCVA) in the better eye was 1.0 (± 0.1). BCVA was correlated with age (r = 0.294, p < 0.001). There was no difference in BCVA between contact lens wearers and non-lens wearers or between males and females.

The patients’ mean OSDI score was 22 (± 19). The OSDI score was not associated with sex, age, contact lens wear, or BCVA. In all, 109 patients (58.6%) had dry eye symptoms; of these, 41 (37.6%), 26 (23.9%) and 42 (38.5%) had mild, moderate, and severe symptoms, respectively. In all, 138 patients (74.2%) had at least one positive homeostasis marker of DED (FBUT < 10 seconds and/or staining > Oxford grade 1), of these 86 had dry eye symptoms (OSDI score ≥ 13) (see Table 1). Reduced FBUT and staining were not associated with sex, age, or contact lens wear.

Table 1: Signs of dry eye disease, MGD and reduced tear meniscus height in participants with and without dry eye symptoms, n (%).

|                     | All      | Asymptomatic | Symptomatic |
|---------------------|----------|--------------|-------------|
| n                   | 186      | 77           | 109         |
| FBUT < 10 seconds   | 78 (41.9)| 26 (33.7)    | 52 (47.7)   |
| FBUT < 10 seconds and staining > Oxford grade 1 | 52 (28.0) | 21 (27.3) | 31 (28.4) |
| Staining > Oxford grade 1 | 8 (4.3)  | 5 (6.5)      | 3 (2.8)     |
| MGD                 | 72 (38.7)| 30 (38.9)    | 42 (38.5)   |
| MGD and TMH < 0.2 mm | 34 (18.3)| 19 (24.7)    | 15 (13.7)   |
| TMH < 0.2 mm        | 27 (14.5)| 11 (14.3)    | 16 (14.7)   |

Note: FBUT = Fluorescein breakup time; MGD = Meibomian gland dysfunction; TMH = Tear meniscus height. Decimals rounded to nearest tenth.

In all, 106 (57.0%) patients had MGD, 49 (46.2%) of these were asymptomatic. Reduced TMH was found in 61 (32.8%) patients, of these 30 (49.2%) were asymptomatic. Among all patients, 34 (18.3%) had both MGD and reduced TMH (see Table 1). Among the symptomatic patients with MGD, MGD and reduced TMH, and reduced TMH, 6 (8.3%), 3 (8.8%) and 5 (18.5%), respectively, did not have positive homeostasis markers (dry eye signs). In all, 86 patients (46.2%) had DED (see Table 2). DED was not associated with sex, age, contact lens wear or BCVA. MGD and reduced TMH were not correlated with DED, sex or contact lens
wear. MGD, but not reduced TMH, was correlated with age ($r_s = 0.255$, $p < 0.001$) (see Table 3). DED could be classified in 99 (68.6%) of the patients with DED (see Table 2). There was no statistically significant difference in the type of DED between males and females or between contact lens wearers and non-contact lens wearers.

Table 2: Prevalence and sub-classification of dry eye disease by sex, n (%).

|                      | All  n=186 | Male n=68 | Female n=118 |
|----------------------|-----------|----------|-------------|
| Dry eye disease      | 86 (46.2) | 26 (38.2)| 60 (50.8)   |
| EDE                  | 36 (19.4) | 9 (13.2) | 27 (22.8)   |
| Unclassifiable       | 27 (14.5) | 9 (13.2) | 18 (15.3)   |
| Mix of EDE and ADDE  | 12 (6.5)  | 2 (2.9)  | 10 (8.5)    |
| ADDE                 | 11 (5.9)  | 6 (8.8)  | 5 (4.2)     |

Note: ADDE = Aqueous deficiency dry eye, EDE = Evaporative dry eye. Decimals rounded to nearest tenth.

Twenty-three patients (12.4%) had dry eye symptoms without dry eye signs, and 52 (28.0%) had dry eye signs without symptoms (see Figure 1). The sensitivity and specificity of OSDI in detecting any positive homeostasis marker were 62% and 54%, respectively. Table 4 shows the diagnostic accuracy of OSDI $\geq 13$ in identifying people with positive homeostasis markers for DED and MGD. In a ROC analysis, OSDI $\geq 13$ showed a diagnostic ability to discriminate between patients with fluorescein breakup time $< 10$ seconds and fluorescein breakup time $\geq 10$ seconds, but not between patients with and without staining or MGD. The optimal cut-off value for the OSDI score was 10.41.

Table 3: Correlation between MGD and reduced TMH and age, gender, contact lens wear and DED.

|                | Age | Gender | Contact lens wear | DED          |
|----------------|-----|--------|-------------------|--------------|
| MGD            | 0.255* | 0.062 | 0.005 | −0.022 |
| TMH            | 0.045 | −0.040 | −0.062 | −0.120 |

Note: DED = Dry eye disease; MGD = Meibomian gland dysfunction; TMH = Tear meniscus height. *Statistically significant Spearman correlation $p < 0.001$.

Discussion

In this study, most participants had symptoms or signs of dry eye disease, and almost half had dry eye disease. The prevalence of DED is at the high end of the previously reported prevalence range (Stapleton et al., 2017). This may reflect the diagnostic criteria in our study. We defined DED based on symptoms and signs according to the guidelines of the TFOES DEWS II report (Wolffsohn et al., 2017). The definition of dry eye disease in previous studies varies in terms of cut-off values for symptoms and signs, as well as in study populations (Stapleton et al., 2017). Studies using both OSDI and signs report a prevalence of 8.7–10.7%; however, these studies applied a higher cut-off criterion for OSDI ($\geq 23$ and $\geq 22$), and one also applied a lower cut-off criterion for TBUT (Hashemi et al., 2014; Malet et al., 2014). This may explain the higher prevalence found in our study as the TFOES DEWS II also included patients with mild symptoms (OSDI score 13–22) in the diagnosis. Furthermore, the present study included patients attending for a routine eye examination, and they may therefore be more likely to have visual and ocular problems since they are seeking eye care. Nevertheless, our study illustrates the importance of dry eye assessment in optometric practice.

DEd was not found to be associated with sex, age, or contact lens wear. These findings contradict other studies, which have shown increased prevalence of DED with increasing age (Farrand et al., 2017; Stapleton et al., 2017), a higher prevalence of DED in females than in males (Hashemi et al., 2014; Stapleton et al., 2017), and that DED is associated with contact lens wear (“The Epidemiology of Dry Eye Disease: Report of the Epidemiology Subcommittee of the International Dry Eye Workshop”, 2007). The lack of association between DED and sex, age, and contact lens wear in our study may reflect the inclusion of all stages of DED and the relatively young age of our participants. Moreover, age-related DED as well as contact lens complications in the younger contact lens wearers could mask differences between contact lens wearers and non-contact lens wearers. Previous studies have shown that differences between males and females become significant only in older age (Paulsen et al., 2014; Stapleton et al., 2017), and comparable studies have examined patients of higher age than in our study. Also, the lack of difference in DED between male and female could be due to the low sample size, and few men included in the study. Our findings may imply that case finding of dry eye disease in optometric practice is equally important in men and women, as well as in both contact lens wearers and non-contact lens wearers.

One in five participants with dry eye symptoms did not have findings of dry eye disease, and seven out of ten asymptomatic participants had findings of dry eye disease. This finding is supported by previous studies that have reported a lack of consis-
tendency and low association between signs and symptoms in DED (Bartlett et al., 2013; Stapleton et al., 2017). This reflects the need for evidence-based guidelines in optometric practice including both symptoms and signs of DED to detect affected patients. By only using history and symptoms, including a questionnaire, some patients who might benefit from management of DED will likely continue to be undetected.

The OSDI score significantly differed between participants with and without reduced TBUT. This may reflect an unstable or irregular tear film, affecting optical quality and causing visual disturbance (Herbaut et al., 2019; Koh, 2018). However, there was no significant difference in BCVA between participants with and without DED. Nevertheless, vision may be affected even though visual acuity is normal, as an unstable tear film may cause higher order aberrations (Koh, 2018). Measurement of higher order aberrations was outside the scope of this study. Moreover, the association between TBUT and dry eye symptoms may also relate to dryness of the ocular surface caused by evaporation.

Reduced TBUT differentiated between participants with and without MGD, and MGD may cause both ocular discomfort and visual disturbance through a reduced function of the lipid layer, increasing tear evaporation and impeding the spread of the tear film over the ocular surface (Green-Church et al., 2011; Millar & Schuett, 2015). MGD may reduce lipid layer thickness and alter the lipid composition of the tear film, and previous studies report reduced TBUT in all subtypes of MGD (Xiao et al., 2020), as well as improved TBUT and reduced symptoms when MGD is treated (Kim et al., 2017; Lee et al., 2017). The unstable tear film caused by MGD may cause corneal exposure and staining, and in turn further destabilise the tear film (McMonnies, 2018), increasing tear evaporation and worsening the condition. Half of participants with MGD in our study had no symptoms. The MGD report suggests that dry eye work-up should be undertaken in patients with MGD regardless of symptoms (Tomlinson et al., 2011). This highlights the value of including TBUT as well as the measurement of meibomian gland function in routine eye examinations to detect DED. Almost half of the patients in the study had DED and required treatment to restore homeostasis. In addition, nearly one third were predisposed to DED, and one in ten had pre-clinical dry eye, which should also be considered for the preventive treatment of DED (Craig et al., 2017). This underlines the potential role of the optometrist in case finding, prevention, diagnosis, and management of DED.

Three out of ten cases of DED had normal TMH and normal meibomian gland function. This was not associated with contact lens wear, and the data were collected in winter, ruling out seasonal allergy and contact lens wear as likely explanations. Therefore, this may reflect other causes of staining and reduced TBUT, such as mucin deficiency and reduced blink rate and blink completeness (McMonnies, 2018) that also affect tear film stability. Mucin deficiency may contribute to increased tear evaporation (Willcox et al., 2017). Evaluation of blink rate, blink completeness, and evaluation of the mucin layer of the tear film may provide further explanation of the underlying cause of DED.

The strength of this study is that it represents a true, real-life clinical setting. All the dry eye tests used are well-known, standardised tests available to optometrists without the need for additional expensive instrumentation. However, the lack of tear osmolarity in our test battery may have underestimated the prevalence of DED. The use of FBUT instead of NIBUT may have affected tear film stability and underestimated the frequency of reduced breakup time and consequently DED. Moreover, it would also be useful to include meibography to support the diagnosis of MGD.

In opposition to the discussed possible underestimation of DED, there could also be a selection bias in our study, overestimating the prevalence of DED, as people having symptoms may be more eager to participate in the study than participants without symptoms. Our study was undertaken in 2015–2016, prior to the publication of the DEWS II report, hence this study did not include triaging questions that can differentiate DED from signs and symptoms of other causes (Wolfsohn et al., 2017). However, our analysis did not find any correlation between DED and risk factors like contact lens wear and medication use. Hence the prevalence of DED in our study likely represents true DED. The inclusion of three optometric practices and three different optometrists could also have introduced observer bias into the findings. However, written instructions for the dry eye assessment were given to the optometrists to ensure standardised examination and reduce bias.

Conclusion

In our study, the majority of patients had dry eye signs and/or dry eye symptoms. More than four out of five benefitted from management of dry eye and pre-clinical findings of dry eye, or advice on pre-disposition to dry eye. Screening with the OSDI questionnaire showed a low sensitivity and specificity in identifying patients with and without positive homeostasis markers. Including assessment of FBUT and meibomian glands in the routine eye examination may enhance case finding of patients with dry eye or those at risk of developing dry eye. The additional use of the OSDI questionnaire in patients with positive homeostasis markers will identify patients with DED or patients at risk of developing DED.

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Conflicts of Interest

The authors declare no conflict of interest.

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Avdekking av tørre øyne i norsk optometrisk praksis: en tverrsnittstudie

Sammendrag
Optikere er en del av primærhelstjenesten, og det er viktig at de hensiktsmessig diagnostiserer pasienter som kan nytte av behandling av tørre øyne. Målet med studien var å utforske hvordan tørre øyne kan avdekkas i optometrisk praksis.

En tverrsnittstudie, som undersøkte symptomer og tegn på tørre øyne blant 186 pasienter (18-70 år) ved rutinemessigsynundersøkelse. Tørre øye ble definert i henhold til kriteriene i «Tear Film and Ocular Surface Society Dry Eye Workshop II». Standard statistiske tester ble benyttet, og diagnosisk kvalitet ble vurdert ved analyse av sensitivitet, spesifisitet og ROC-kurveanalyse.

Femtiseks pasienter brukte kontaktlinser. De var signifikant yngre enn de som ikke brukte kontaktlinser (gjennomsnittsalder 35 (SD = 1) mot 48 (± 2) år). Gjennomsnittlig beste korrigerte visus (BCVA) på det beste øyet var 1.0 (± 0.1) (desimalvisus). Det var ingen forskjell i BCVA mellom kontaktlinsebrukere og ikke-kontaktlinsebrukere. Gjennomsnittlig Ocular Surface Disease Index (OSDI) score var 22 (± 19) og 138 pasienter hadde minst en positiv homeostasemarkør for tørt øye. Åttiseks pasienter havde tørre øyne, 52 hadde tegn uten symptomer, og 23 hadde symptomer uten tegn på tørre øyne. OSDI hadde en sensitivitet og spesifisitet på henholdsvis 62% og 54% på å avdekkje homeostasemarker for tørre øye. I alt hadde 106 pasienter meibomsk kjerteldysfunksjon (MGD), hvorav 49 var asintomatiske. ROC-kurveanalyse viste at en OSDI-score ≥ 13 kan skille mellom pasienter med fluorescein “break-up-time” (FBUT) < 10 sekunder og en FBUT ≥ 10 sekunder, men ikke mellom pasienter med og uten staining eller MGD.

Flerntallet av pasientene som kom til rutinemessig synundersøkelse hadde tegn og/eller symptomer på tørre øyne. Rutinemessig undersøkelse av FBUT og meibomske kjertler kan gjøre det mulig å avdekkje tørre øyne i optometrisk praksis.

Nøkkelord: tørre øyne, Ocular Surface Disease Index, meibomsk kjerteldysfunksjon, fluorescein break-up time, punktat fargeopptak, staining

Ricerca sui casi di occhio secco in una clinica optometrica norvegese: uno studio trasversale

Riassunto
Gli optometristi sono i primi a fornire trattamento per la salute oculare ed e’ essenziale che identifichino efficientemente i pazienti che possono beneficiare dal trattamento di occhio secco. Lo scopo di questo studio e’ di esplorare i risultati di una ricerca sulla malattia dell’occhio secco in una clinica optometrica.

Uno studio trasversale ha esaminato sintomi e segni di 180 pazienti (18 a 70 anni) i quali sono stati sottoposti a una visita dell’occhio di routine con l’occhio secco definito secondo i criteri del Tear Film and Ocular Surface Society Dry Eye Workshop II. Test statistici standard sono stati utilizzati e test clinici diagnosticci considerando sensibilita’, specificita’ e la curva statistica ROC.

Cinquantasei pazienti erano portatori di lenti a contatto e significativamente piu’ giovani che i non-portatori con un’eta’ di 35 (SD = 1) contro 48 (± 2) anni. La media della miglior acuita’ visiva corretta (BCVA) nell’occhio migliore era 1.0 (± 0.1) (acuita' decimale). Non e’ stato differenza statisticamente significativa in BCVA tra portatori e non portatori di lenti a contatto. La media (SD) del punteggio dell’Ocular Surface Disease Index (OSDI) e’ stato 22 (± 19), e 138 pazienti hanno avuto almeno un marcato dell’omeostasi positivo. A 86 pazienti e’ stato diagnosticato l’occhio secco, 52 hanno avuto segni senza sintomi e 23 hanno avuto sintomi senza segni di occhio secco. La sensibilita’ e specificita’ dell’OSDI in differenziare qualsiasi marcato di omeostasi furono 62% e 54% rispettivamente. 106 pazienti sono stati diagnosticati con disfunzione delle ghiandole di meibomio (MGD), di cui 49 furono asintomatici. Nell’analisi ROC, l’OSDI ≥ 13 ha dimostrato un’elevatissima specificita diagnostic per differenziare tra soggetti con tempo di rottura lacrimale effettuato con fluoresceina (FBUT) < 10 secondi e FBUT ≥ 10 secondi, ma non tra pazienti con e senza colorazione con fluoresceina o MGD.

La maggior parte dei pazienti considerati ha avuto segni o sintomi da occhio secco. La valutazione di routine di FBUT e delle ghiandole di meibomio possono aiutare a scoprire casi di occhio secco nella clinica optometrica.

Parole chiave: malattia dell’occhio secco, Ocular Surface Disease Index, disfunzione delle ghiandole di meibomio, tempo di rottura lacrimale, colorazioni oculari