Original Article / Оригинални рад

Tanja Kalezić¹,², Ivana Vuković¹,³, Vedrana Pejin¹, Svetlana Stanojlović¹,², Nemanja Karamarković⁴, Dijana Risimić¹,², Marija Božić¹,², Aleksandra Radosavljević¹,²

Dry eye examination – benefits of Ocular Surface Disease Index (OSDI) questionnaire with clinical testing

Испитивање сувог ока – предности упитника за индекс предње површине ока (OSDI) са клиничким тестовима

¹University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
²University Clinical Centre of Serbia, Clinic for Eye Diseases, Belgrade, Serbia;
³University Clinical Centre of Serbia, Clinic for Gynecology and Obstetrics, Belgrade, Serbia;
⁴University Clinical Centre of Serbia, Clinic for Cardiac Surgery, Belgrade, Serbia

Received: December 4, 2021
Revised: April 26, 2022
Accepted: April 27, 2022
Online First: May 5, 2022
DOI: https://doi.org/10.2298/SARH211204045K

*Accepted papers are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of the Serbian Archives of Medicine. They have not yet been copy-edited and/or formatted in the publication house style, and the text may be changed before the final publication.

Although accepted papers do not yet have all the accompanying bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: the author’s last name and initial of the first name, article title, journal title, online first publication month and year, and the DOI; e.g.: Petrović P, Jovanović J. The title of the article. Srp Arh Celok Lek. Online First, February 2017.

When the final article is assigned to volumes/issues of the journal, the Article in Press version will be removed and the final version will appear in the associated published volumes/issues of the journal. The date the article was made available online first will be carried over.

*Correspondence to:
Tanja KALEZIĆ
Ibarska 9, 11000 Belgrade, Serbia
E mail: tanjakalezic@gmail.com
Dry eye examination – benefits of Ocular Surface Disease Index (OSDI) questionnaire with clinical testing

Испитивање сувог ока – предмети упитника за индекс предње површине ока (OSDI) са клиничким тестовима

**SUMMARY**

**Introduction/Objective** Dry eye is a multifactorial disease with up to 50% in population. It is characterized by a loss of homeostasis of the tear film and accompanied by ocular symptoms. Ocular Surface Disease Index (OSDI) questionnaire is designed to provide a rapid assessment of the symptoms. The aim of this study was to evaluate diagnostic capacity of OSDI.

**Methods** A prospective, randomized and observational study was conducted at the Clinic for Eye Disease, Clinical Center of Serbia, between December 2018 and February 2019. The OSDI questionnaire was used to rate the severity of dry eye disease. Schirmer I test, tear break-up time test (TBUT), Rose Bengal test and lid-parallel conjunctival folds (LIPCOF) test were performed as a clinical proof of the symptoms.

**Results** A total of 27 patients, 15 male (55.4%) and 12 female (44.6%), with mean age of 60 ± 15 years were included in the study. The average value of OSDI score was 26.37 ± 23.98 (0–80). Schirmer I test and Rose Bengal test for right and left eye, as well as BUT test for left eye were positively correlated with OSDI score (Spearman correlation coefficient).

**Conclusion** OSDI questionnaire is fast, reliable, and cheap test. In our study we have found correlation between OSDI score and other clinical tests, except with LIPCOF test. At this moment, the questionnaire that could be the gold standard for dry eye disease diagnosis doesn’t exist, therefore further studies concerning this topic are needed.

**Keywords:** dry eye; OSDI questionnaire; LIPCOF; Schirmer test; TBUT test; Rose Bengal test

**САЖЕТАК**

**Увод/Циљ.** Суво око је болест са инциденцом и до 50% у популацији. То је мултифакторијална болест површине ока где губитак хомеостазе сузног филма прати очне симптоме. Occular Surface Disease Index (OSDI) је упитник који омогућава брзо постављање дијагнозе. Циљ овог рада је прогнали дијагностичке вредности теста OSDI у болести сувог ока и градацији тежине у односу на налаз релевантних клиничких тестова.

**Методе** Проспективна, рандомизована и опсервациона студија бавиће се Клиници за очне болести Универзитетског Клиничког центра Србије, у периоду од децембра 2018. до фебруара 2019. године. Упитник OSDI је коришћен ради евалуације симптома и корелације са клиничким тестовима. Клинички тестови примењени у овој студији су Ширмеров тест I, tear break-up time test (TBUT), тест Rose Bengal и lid-parallel conjunctival folds (LIPCOF).

**Резултати** Укупно је било 27 болесника – 15 мушкараца (55.4%) и 12 жена (44.6%), просечне старости од 60 ± 15 година. Просечна вредност OSDI скора у студији је била 26.37 ± 23.98 (0–80). Пронађена је позитивна корелација са OSDI скором између Ширмера I и теста Rose Bengal за десно и лево око, као и TBUT теста за лево око (Спирманов коефицијент корелације).

**Закључак** Упитник OSDI је брз, поуздан и јефтин тест који добро процењује постојање и тежину сувог ока. У нашој студији пронађена је корелација OSDI упитника са свим клиничким тестовима у дијагностици сувог ока, изузев теста LIPCOF. Тренутно не постоји упитник који би представљао златни стандард у дијагностици сувог ока, те су даља истраживања у овом смеру неопходна.

**Кључне речи:** суво око; упитник OSDI; LIPCOF; Ширмеров тест; TBUT; тест Rose Bengal

**INTRODUCTION**

Dry eye is multifactorial eye surface disease, characterized by loss of tear film homeostasis and eye symptoms [1]. It is one of the most frequent reasons for visiting ophthalmologist, so it represents significant outlay for health care system [2]. Most of the patients have mild symptoms, but sometimes very complex interventions are necessary to avoid further progression to corneal ulcer and conjunctival scarring [3]. Contact lens wear and
refractive surgery can cause a dry eye [4]. In etiology of dry eye main factors are tear film instability, hyperosmolarity, inflammation, eye surface damage and neurosensory abnormalities [1]. Sjogren syndrome, transplantation (graft versus host reaction) and aging can also cause dry eye [5].

Following nowadays knowledge, ocular and lacrimal inflammation take main role because they are making defects of corneal and conjunctival cells and causing symptoms [1]. What is happening is proved on molecular and biochemical level, where is also shown that lower levels of androgen and higher levels of pro inflammatory cytokines followed by loss of immunologic homeostasis of lacrimal gland and eye surface lead to pathological changes [6]. Neurogenic mechanisms- loss of innervation and lower sensitivity can also cause a dry eye [4].

Dry eye disease (DED) is one of the most prevalent ophthalmic disorders in general population, and it can go up to 50% in different studies [2].

In classification of dry eye disease, we have two big categories: aqueous tear-deficient dry eye (Sjogren syndrome dry eye) and evaporative dry eye (Non Sjogren syndrome dry eye) [7]. Aqueous tear-deficient dry eye implies that dry eye is due to a failure of lacrimal tear secretion, and it represents about 10% of all cases. Evaporative dry eye is due to deficiency in lipid part of tear film, which is manifested with higher evaporation. The main cause is Meibomian gland dysfunction, and it represents 85% of all cases [8]. Blepharitis, eyelid margin inflammation is a cause, and also a consequence of Meibomian gland dysfunction, but in differential diagnosis we also need to think of rosacea, atopy, seborrheic dermatitis and staphylococcal infection [1].

Etiological important factors in dry eye disease are female gender and ageing (low levels of androgen play main role in Meibomian gland disfunction) [8]. Except those, important factors also are lagophthalmos, decreased blinking, systemic autoimmune diseases, atopy, vitamin A deficiency and external conditions with low air humidity [9]. A number of questionnaires have been developed, and they are in use in combination to help to make a dry eye diagnosis, but none of them, separately, has required sensitivity and specificity to be a gold standard [10]. The clinical presentation of dry eye disease is very variable, what makes a diagnosis even more difficult. Patients frequently have unspecific symptoms such as visual disturbance, ocular discomfort, photophobia, itching, and irritation. Sometimes patients can experience excessive tearing because of discomfort. Symptoms doesn’t have strong correlation.
with clinical findings, especially if there is low pain tolerance [11]. For the purpose of making diagnosis, checking severity of disease, starting the management and follow up, many questionnaires have been made, and one of them is Dry Eye questionnaire (DEQ-5) [12] and OSDI [13].

OSDI questionnaire has been made by Outcomes Research Group at Allergan Inc, in order to provide fast evaluation of ocular irritation symptoms in connection with dry eye disease and their impact on vision [13]. Therefore, the aim of this study was to evaluate diagnostic capacity OSDI questionnaire in assessment of the dry eye disease and the severity of disease relative to clinical diagnostic procedures.

**METHODS**

This study was a prospective, randomized and observational study, conducted at the Clinic for Eye Disease, University Clinical Center of Serbia at the Department of Cornea and External Eye Disease, between December 2018 and February 2019. Patients were randomized upon the arrival for a clinical examination such as cataract or blepharitis, and had no previous history of dry eye treatment. Anamnestic characteristics were collected at the beginning of the study. Participation was voluntary and informed consent was obtained from each participant. Ethical approval was obtained from the Institutional Review Board (IRB).

The 12-item Ocular Surface Disease Index (OSDI) questionnaire is a self-administered questionnaire used to rate the severity of dry eye disease. Responses to each item were scored on a 5-point Likert scale, where 0 indicates "none of the time"; 1 indicates "some of the time"; 2 indicates "half of the time"; 3 indicates "most of the time" and 4 indicates "all of the time". The OSDI score calculates on the basis of the given formula: \( \text{OSDI} = \frac{(\text{sum of scores for all questions answered}) \times 100}{(\text{total number of questions answered}) \times 4} \). The OSDI is assessed on a scale of 0 to 100, with higher scores representing greater disability [14].

For the purpose of this study, additional clinical measures were performed.
Schirmer I test

The Schirmer I test was used to determine flow of the tears produced by the tear glands and measures the basal and reflex secretions of the main and accessory glands. It is performed using calibrated, bended strips of a non-toxic filter paper. On the lateral and middle-third of the lower eyelid, a shorter folded end is attached, in order to avoid irritation of the cornea. This test is performed without previously applied anesthesia, and on both eyes at the same time. The test length is 5 minutes, and after removing strips from lower eyelids, we measure the amount of wetting of the paper strips. The limit values of Schirmer I tests for dry eye disease are ≤10mm/5min [15].

Tear break-up time test (TBUT)

Tear breakup time (TBUT) is a clinical test used to assess the stability of tear film. It is performed by instilling a small amount of fluorescein on the ocular surface of the lower eyelid, after which the respondent was asked to blink, in order to spread fluorescein evenly across the surface of the eye. Then, patient is instructed to keep their eyes opened, without blinking. Using cobalt blue illumination, the TBUT is recorded as the number of seconds elapsed between the patients last blink of an eye and presence of the first defect in the tear film. The normal values of the TBUT test are over 10 seconds, and the results below this value indicate that there is a disruption in the quality of the tear film [15].

Rose Bengal test

The Rose Bengal test is used to indirectly measure the presence of reduced tear volume, detecting damaged and devitalized epithelial cells that have lost the role of creating tears. The results of this test can be read immediately. On the surface of the eye, we observe three zones: cornea, nasal and temporal part of conjunctival staining. Points from 0 to 3 are assigned to each of these zones, depending on whether there is no coloring, if there are few colored dots, lots of colored dots or if confused zones are present. The positive result of this test are four or more points for all three zones combined, with a maximum of nine points [16].
LIPCOF test

A small folds, parallel to the lower lid margin, in infero-nasal and infero-temporal quadrants of the bulbar conjunctiva are defined as Lid-parallel conjunctival folds (LIPCOF), and they were first described by Höh et al. [17]. LIPCOF correlates with reduced mucin production and with epitheliopathy of the eyelid edge. Using the method described by Höh et al., the LIPCOF test graded from 0 to 3, by the slit lamp examination [17]. According to the comparison of the number of conjunctival folds with the height of the normal tear meniscus height there is a scale of grading. In grade 0, no fold appears; in 1, a single small fold appears smaller than the normal tear film meniscus; in grade 2, multiple folds up to the height of normal tear meniscus appear; and in grade 3, multiple folds higher than the normal tear meniscus appear.

Statistical analysis

Numerical data were presented as arithmetic mean and median with corresponding measures of variability (standard deviation, minimal and maximal value, range). Categorical data were presented as absolute numbers with frequencies. Differences of OSDI questionnaire results according to gender were analyzed by Mann Whitney U test. Spearman correlation coefficients were calculated to explore the relationship between LIPCOF test grade and patient’s age. P < 0.05 was considered statistically significant. Statistical analysis was done using IPSS 1.3 program.

RESULTS

A total of 27 patients, 15 male (55.4%) and 12 female (44.6%), with mean age of 60 ± 15 years (ranging from 22 to 82 years) were included in the study (Table 1).

The average value of OSDI score in our study population was 26.37 ± 23.98, ranging from 0 to 80. The median value of Schirmer I test was 6 for right eye (ranging from 0 to 12),
and 3 for left eye (ranging from 0 to 10). Median values of LIPCOF test, Rose Bengal test and BUT test are presented in Table 2.

The correlations between OSDI score and age, as well as Schirmer I, LIPCOF, Rose Bengal and BUT test results are presented in Table 3. As is shown in the table 3, Schirmer I test for right and left eye were positively correlated with OSDI score: rho = 0.639; p < 0.001 and rho = 0.540, p = 0.004, respectively. Rose Bengal test (OD rho = 0.458, p = 0.016; OS rho = 0.193, p = 0.334), and BUT test for left eye (rho = 0.439, p = 0.022) were also positively correlated with OSDI score (Table 3).

No statistically significant difference was found between OSDI score and gender (p = 0.136) (Figure 1). Also, no correlation between age of the respondents and OSDI score was found (rho = 0.099, p = 0.623).

**DISCUSSION**

The results of this study showed that OSDI score was positively correlated with age, as well as Schirmer I, Rose Bengal and BUT test results. Also, no statistically significant difference was found between OSDI score and gender and no correlation between age of the respondents and OSDI score. This study is limited by small group of patients but some further testing within bigger groups would be suggested for better validation of the findings.

The core pathophysiological mechanisms of dry eye are lower tear production, higher evaporation, or their combination, with tear film hyperosmolarity and eye surface inflammation [1]. In clinical observation it was found patients usually do not meet the criteria of making the diagnosis of disease by all tests, so more classifications were made, of which is most popular one from Copenhagen. This phenomenon is probably consequence of multifactorial ethiology of dry eye. Copenhagen criteria are including three main factors-changes in aqueous layer (Schirmer), higher level of evaporation (TBUT) and eye surface defects (Rose Bengal Staining) [3]. By using more tests, the chance of making correct diagnosis is rising, but the consensus which combination, besides best specificity and sensitivity, would cover other aspects such as severity, quality of life, and follow up, doesn’t exist [3]. To overcome this problem,
questionnaires like DEQ-5, McMonnies and OSDI are added to battery of clinical examinations [10].

In this study in which 27 patients took part the values of OSDI score matches with OSDI scores in other studies in this field. Mean age of patients in our study is slightly higher than in other studies [18]. In literature overview, we found that the significant correlations between OSDI questionnaire and clinical examinations are common [19]. In general, positive correlation is most common between OSDI score and BUT test [19, 20, 21]. The potential explanation for this correlation can be complex etiologic mechanisms in dry eye disease, which implicit on symptoms, and individuality of clinical status which OSDI evaluates in regard to other aspects that every other test is evaluating.

When we analyzed LIPCOF clinical test results, we have found that almost 50% of patients have negative results, and just 20% of patients were positive to this test and similar findings are found by other studies. It is not in correlation to positive findings between OSDI score and LIPCOF grade in our study [21]. Further study of etiopathogenic mechanisms, symptoms and different aspects that every single test evaluates, as well as more patients included would help in clarification of these differences.

CONCLUSION

OSDI questionnaire is fast, reliable and cheap test and it is great tool in evaluation of first symptoms of dry eye disease. In our study we have found the correlation between OSDI score and most common clinical diagnostic tests, whereas only LIPCOF test had not been with statistical significance. The gold standard questionnaire that could be for dry eye disease does not still be found therefore further studies with greater number of participants concerning this topic are needed.

Conflict of interest: None declared.
REFERENCES


17. Pult H, Bandlitz S. Lid-parallel conjunctival folds and their ability to predict dry eye. Eye & contact lens 2018 (44): S113-S119. PMID: 29023310 DOI: 10.1097/ICL.0000000000000435


Table 1. Demographic characteristics of the patients

<table>
<thead>
<tr>
<th>Sex, n (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>15 (55.4)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>12 (44.6)</td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>60 ± 15</td>
<td></td>
</tr>
</tbody>
</table>
**Table 2.** Median test values for Schirmer I, lid-parallel conjunctival folds (LIPCOF), Rose Bengal, and tear break-up time (TBUT) tests

<table>
<thead>
<tr>
<th>Test</th>
<th>n</th>
<th>mean</th>
<th>SD</th>
<th>median</th>
<th>minimum</th>
<th>maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schirmer OD</td>
<td>27</td>
<td>5.57</td>
<td>3.03</td>
<td>6.0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Schirmer OS</td>
<td>27</td>
<td>4.09</td>
<td>2.95</td>
<td>3.00</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>LIPCOF OD</td>
<td>27</td>
<td>0.7</td>
<td>0.77</td>
<td>1.00</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>LIPCOF OS</td>
<td>27</td>
<td>0.59</td>
<td>0.64</td>
<td>1.00</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Rose Bengal OD</td>
<td>27</td>
<td>1.89</td>
<td>2.21</td>
<td>1.00</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Rose Bengal OS</td>
<td>27</td>
<td>1.30</td>
<td>1.2</td>
<td>1.00</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>BUT OD</td>
<td>27</td>
<td>4.81</td>
<td>3.17</td>
<td>5.00</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>BUT OS</td>
<td>27</td>
<td>4.7</td>
<td>3.66</td>
<td>3.00</td>
<td>1</td>
<td>14</td>
</tr>
</tbody>
</table>

OD – right eye; OS – left eye
Table 3. Correlation between Ocular Surface Disease Index (OSDI) score and age, Schirmer I, lid-parallel conjunctival folds (LIPCOF), Rose Bengal, and tear break-up time (TBUT) tests

<table>
<thead>
<tr>
<th>Variable</th>
<th>OSDI score</th>
<th>p</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.099</td>
<td>0.623</td>
<td></td>
</tr>
<tr>
<td>Schirmer OD</td>
<td>0.639</td>
<td><strong>0.001</strong></td>
<td></td>
</tr>
<tr>
<td>Schirmer OS</td>
<td>0.540</td>
<td><strong>0.004</strong></td>
<td></td>
</tr>
<tr>
<td>LIPCOF OD</td>
<td>0.114</td>
<td>0.572</td>
<td></td>
</tr>
<tr>
<td>LIPCOF OS</td>
<td>-0.130</td>
<td>0.517</td>
<td></td>
</tr>
<tr>
<td>Rose Bengal OD</td>
<td>0.458</td>
<td><strong>0.016</strong></td>
<td></td>
</tr>
<tr>
<td>Rose Bengal OS</td>
<td>0.193</td>
<td>0.334</td>
<td></td>
</tr>
<tr>
<td>BUT OD</td>
<td>-0.064</td>
<td>0.749</td>
<td></td>
</tr>
<tr>
<td>BUT OS</td>
<td>0.439</td>
<td><strong>0.022</strong></td>
<td></td>
</tr>
</tbody>
</table>

OD – right eye; OS – left eye
Figure 1. Ocular Surface Disease Index (OSDI) score according to sex

![Box plot showing OSDI score by sex](image-url)