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COMPARISON OF THE SCHEIN AND OSDI QUESTIONNAIRE AS INDICATOR OF TEAR FILM STABILITY IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY

Background: *The aim of this research was to determine which of two chosen questionnaires for subjective symptoms of dry eye (Ocular Surface Disease Index and Schein questionnaire) is more reliable in the assessment of dry eye in patients with schizophrenia.*

Subjects and methods: *Our research included 80 patients (160 eyes) of both sexes with schizophrenia ranging between the age of 25 and 55 who have been taking one of three antipsychotic drugs namely clozapin, olanzapin, quetiapin for five or more years and were in a stable phase of the disease or remission. All participants were required to satisfy all included and excluded criteria. They all filled out the Schein and OSDI questionnaires for assessment of subjective symptoms. Tear break-up time test (TBUT) for objective evaluation of tear film stability was also performed. In order to determine the correlation between two subjective and objective tests we calculated Spearmans correlation coefficients.*

Results: *Obtained results of the correlation between OSDI questionnaire and TBUT test for the right eye was $r=-0.73$; $p<0.01$ and for the left eye was $r=-0.72$; $p<0.01$. Results of the correlation between Schein questionnaire and TBUT test for the right eye was $r=-0.62$; $p<0.01$ and for the left eye was $r=-0.60$; $p<0.01$. A detailed analysis shows that there are no statistically significant differences between the correlations. Both subjective questionnaires are statistically significantly and negatively related to the TBUT test, showing that an increase in the results on the OSDI and Schein's questionnaires led to the decreases in the results on the TBUT test.*

Conclusion: *In patients with schizophrenia the OSDI and Schein questionnaires are equally reliable in the assessment of subjective symptoms of Dry eye disease. Considering that, OSDI is more common in clinical practice and includes questions regarding quality of life, it would have certain advantages and it is recommended for use in patients with schizophrenia.*

Key words: *Schein questionnaire - OSDI questionnaire - tear film stability - schizophrenia*

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INTRODUCTION

Schizophrenia as an example of true mental illness is still the biggest challenge in psychiatry today. Patients with schizophrenia are mostly young people for whom the disease gradually disrupts most life activities requiring long-term and, in most cases, lifelong treatment and medication (Jakovljević 2011, Begić et al. 2015). Psychiatric patients, and especially patients with schizophrenia have 15 to 30 years shorter life expectancy then the rest of the population (Hannerz et al. 2001, Laursen et al. 2014, Baxter et al. 2016, Tiihonen et al. 2016, Taipale et al. 2018). They suffer from a number of somatic comorbidities, that are somewhat related to long term use of psychopharmacotherapy and partially to the fact that patients with schizophrenia neglect their physical health (Crump et al. 2013, Šimunović Filipčić & Filipčić 2018). When caring for patients with schizophrenia one of the somatic systems that gets neglected is the organ of sight or the eye although studies have shown that visual impairments are one of the most important features of schizophrenia (Jurišić et al 2020). It has been proven that many somatic chronic patients who take permanent chronic therapy for diabetes, glaucoma and hypertension, or use topical ophthalmological medications or wear contact lenses may experience some form of dry eye syndrome (DES) that can severely impair quality of life (QOL). (Jaanus et al. 1992, Wong et al. 2011, Askeroglu et al. 2013, Kaštelan et al. 2013a,b). Due to long-term and often lifelong use of various psychopharmaceuticals and antipsychotics, psychiatric patients may have damage and tear film disfunction with various symptoms from the dry eye syndrome, which further impairs their quality of life (Wen et al. 2012, Labbe et al. 2013). Various questionnaires are available to assess the subjective symptoms of dry eye in order to better detect the deterioration of the tear film stability (Schiffman et al. 2000, Okumura et al. 2020). However, these questionnaires may be misunderstood or inadequately filled and therefore produce unreliable results. The aim of this study was to investigate and prove which of the two selected questionnaires for

examining dry eye symptoms, either Ocular Surface Disease Index questionnaire (OSDI) or Schein's questionnaire, is better in practice for assessing subjective symptoms in patients with schizophrenia. It also aimed to show which questionnaire corresponds more closely to the findings that are obtained by the more objective Tear break-up time test (TBUT).

SUBJECTS AND METHODS

The study included 80 patients with schizophrenia (160 eyes) of both sexes, ranging between the age 25 to 55. All participants were on the continuous therapy for over five years with one of the three named antipsychotics (clozapine, olanzapine and quetiapine) and are in a stable phase or remission of the primary disease. The diagnosis of schizophrenia (F 20) was made by psychiatric specialists who treat particular patients and in accordance with the criteria of the International Classification of Diseases (ICD-10). As these patients have been treated for schizophrenia for five or more years, the diagnosis in all patients was verified by two or even more psychiatric specialists and according to the available medical documentation. Patients were taking medium prescribed therapeutic doses of the selected antipsychotic, as following: olanzapine 10-20 mg daily, clozapine 100 to 400 mg daily and quetiapine 400 to 800 mg daily. The use of other antipsychotics or antidepressants was not allowed. As anxiolytics and hypnotics are frequently used by psychiatric patients, their use was allowed but all efforts were done to minimise the doses. Study excluded all the patients taking medication for diabetes, hypertension, thyroid disease, glaucoma or various allergies as it is known that medication can cause the dysfunction of the tear film. Therefore, no participants were on antidiabetics, antihypertensives, antidepressants, thyroid drugs, antihistamines, antiepileptics or any kind of oral contraceptives. Regular smokers were not included in the study and no alcohol was allowed prior to the test date, with exclusion of participants with a history of any alcohol abuse. Menopausal female patients were also excluded.

For ethical reasons, study excluded all severe mental patients with appointed legal guardian or representative. Additional excluding criteria were eye trauma, acute infection, glaucoma, any eye surgery within the last year and contact lens wearers. All patients in the study group were solely on the oral therapy with one of the three selected antipsychotics. Study also excluded patients on the long-acting form of olanzapine (ZypAdhera) that is administered intramusularly every 2-4 weeks, but only included those on oral therapy with the other two antipsyhotics (clozapine and quetiapine). These three antipsychotics (clozapine, olanzapine and quetiapine), were chosen for this study as they are the most simmilar in their chemical structure, action mechanism and receptor profile. These three drugs form a homogeneous group with a simmilar antipsyhotic effect within a wide range of modern antipsyhotics available. Every effort was done that there are equal number of participants on each antipsyhotic. However, subgroups were not formed.

The method of obtaining and protecting collated data respects all current International and Croatian data protection acts and conventions. The research was conducted on the voluntary basis and according to all ethical standards. The purpose and procedure of the study was thoroughly explained to all participants before signing the informed consent to participate in the research. There is a file with a signed consent to participate in the survey for each partaker. Furthermore, each participant had the opportunity and the right to withdraw their consent or withdraw from participation in the study at any point and without giving reasons.

Applied methods of survey were completely harmless and painless for all participants. The identity of the participants was protected, by creation of the personal code for each one, consisting of their initials and birth dated. All data was kept confidential with access allowed to the researches only. To assess the subjective symptoms of dry eyes all participants completed following two questionnaires: OSDI (Ocular Surface Disease Index) and Schein’s questionnaire. In addition, all of them underwent an objective tear film stability test, known as Tear break-up time test (TBUT), for which standard opthamology equipment was used.

OSDI questionnaire consists of 12 questions that are trying to assess the frequency of subjective problems occuring as part of the dry eye surface disease.

The patient answers each question by rounding off the number on the scale from 0 to 4, each representing the frequency of each symptom in the past week. Number 4 indicates that the particular symptom has been constantly present, while 0 indicates complete absence of the symptom in the past week. The final result of the questionnaire is obtained according to the following formula: Nx5/12, where N denotes the sum of the frequency of the occurrence for each individual symptom. Results in range from 0 to 12.00 are considered normal. The values from 13.00 to 22.00 are considered the mild form of dry eye, while range of 23.00 to 32.00 indicates moderate to medium form of the disease. Cases with results over 33.00 for the OSDI questionnaire are considered a severe form of dry eye.

In addition to the above, OSDI questionnaire is divided in three parts; first five questions are relating to the subjective symptoms of dry eye (A), second part are four questions in relation to visual function (B) with the third part of three questions relating to the environmental factors (C).

Schein's questionnaire for assessing the subjective symptoms of dry eye is simpler and consists of six questions only. Answers are rated from 0 indicating never to

4, meaning continuous presence of the symptom. Total score is a maximum of 24, with optimum cut-point at 7.5 (Jerry et al. 2019).

Tear film stability test or TBUT examines the quality of the precorneal tear film. The test is performed by installing a single drop of 1% fluorescein standard solution into the lower fornix or conjuctival sac of each eye. Any excess fluid is removed. The patient is instructed to make at least 3-5 full blinks. When the cobalt blue light on the biomicroscope turns on (next to the yellow filter) the observed patient is instructed to blink once more and then to keep the eyes open. From that moment the time is measured in seconds, until the point that dark spots appear in the fluorescein-stained tear film. The above measurement is performed three times for each eye. If the measurements differ, they should be repeated until three of the similar value measurements are obtained. If the measured values differ significantly, TBUT test is described as unreliable. Therefore, the cobalt light is used to measure the time that elapses from blinking to the appearance of dark spots indicating the cracking of the precoroneal tear film while the participant's eye is open. The test uses seconds as unit of measurement. It is expected that breaking of the normal tear film should occur after 10 seconds. Shorter time than 10 seconds indicates that the tear film is instable; a condition that is often caused by a disorder of the lipid or mucinous component of the tear film.

In order to determine the relation between two subjective questionnaires (OSDI and Schein questionnaire) with an objective TBUT test, Spearman correlation coefficients were calculated on the basis of the above study of 80 patients with schizophrenia or 160 eyes.

RESULTS

In our pattern was 80 patients with schizophrenia, 40 (50%) male and 40 (50%) female age between 25 and 53 years with arithmetic mean of M=40.3. They take antipsyhotic therapy from 60 to 120 and more months with arithmetic mean of M=83.6 months. All demografic characteristics of paticipants are shown in Table 1.

The results shown in the Table 2. seem to indicate that OSDI (total score) is better associated with TBUT test than the Schein questionnaire. However, more detailed analyses of the significance of the difference in correlations show that statistically there is no significant difference between the correlations shown in the table. Obtained results of the correlation between OSDI questionnaire and TBUT test for the right eye was r=-0.73; p<0.01 and for the left eye was r=-0.72; p<0.01. Results of the correlation between Schein questionnaire and TBUT test for the right eye was r=-0.62; p<0.01and for the left eye was r=-0.60; p<0.01. A detailed analysis shows that there are no statistically significant differences between the correlations. Both subjective questionnaires are statistically significantly and negatively related to the TBUT test, showing that an increase in the results on the OSDI and Schein's questionnaires led to the decreases in the results on the TBUT test. All correlations are significant with 1% risk, and are of medium size (Figure 1, 2, 3, 4).

Table 1. Demografic characteristic of patients with schizophrenia

	N	%
Sex		
male	40	50.0
female	40	50.0
Education		
elementary school	3	3.8
high school	53	66.3
higher school	22	27.5
university	2	2.5
Working		
unemployed	40	50.0
employed	27	33.8
retaired	3	3.8
unable for work	10	12.5
Antipsyhotic		
olanzapin	26	32.5
clozapin	25	31.3
quetiapin	29	36.3

N - number of patients with schizophrenia

Table 2. Sperman's correlation coefficients

	TBUT right eye	TBUT left eye
OSDI - total score	-0.73*	-0.72*
OSDI - symptoms	-0.67*	-0.68*
OSDI - visual function	-0.57*	-0.54*
OSDI - environmental impacts	-0.59*	-0.59*
Schein questionnaire	-0.62*	-0.60*

OSDI - Ocular Surface Disease Indeks; TBUT - Tear break-up time test; * - statistically significant with risk 1%

DISCUSSION

Due to long term use of antipsychotics and often unhealthy lifestyle, patients with schizophrenia have a number of somatic comorbidities that greatly impair their quality of life. One of the coexisting conditions that is not given enough attention in patients with schizophrenia is certainly dry eye syndrome. According to the current knowledge DED can be defined as a multifactorial disease of the tears and eye surface that results in symptoms of discomfort, visual disturbances and tear film instability with possible damage to the eye surface (Guyton et al. 2009, Kaštelan et al. 2013, Messmer et al. 2015). The condition is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface. It is proven that excessive smoking

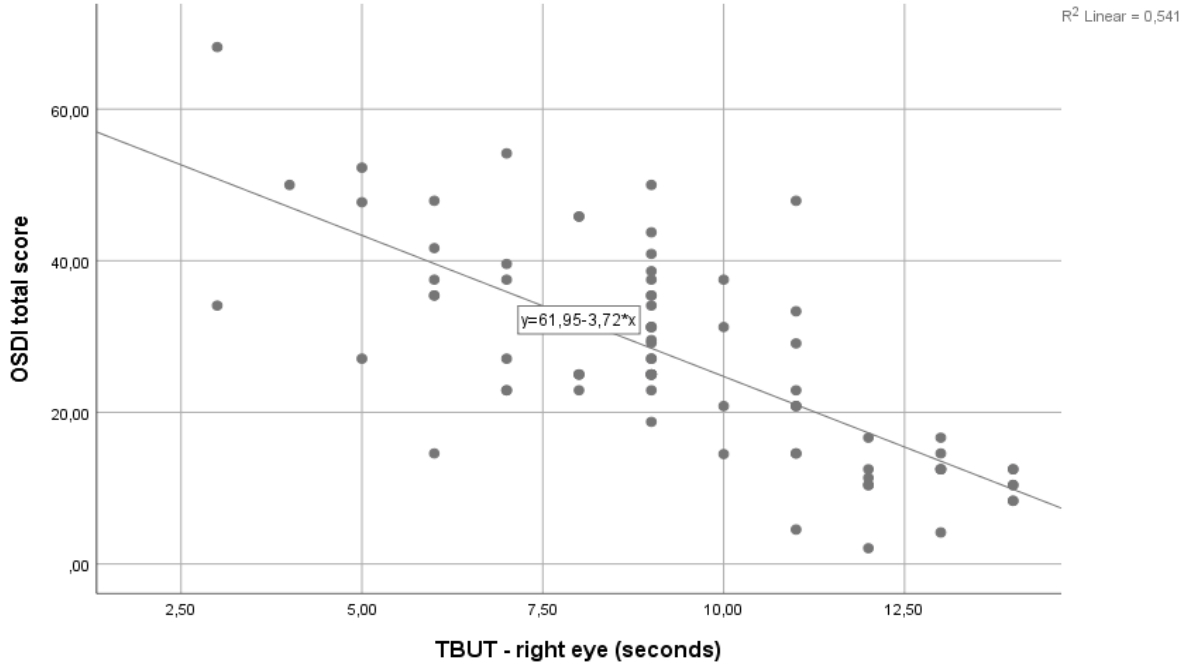

Figure 1. Scattering diagram of the OSDI (total score) and TBUT (right eye) results

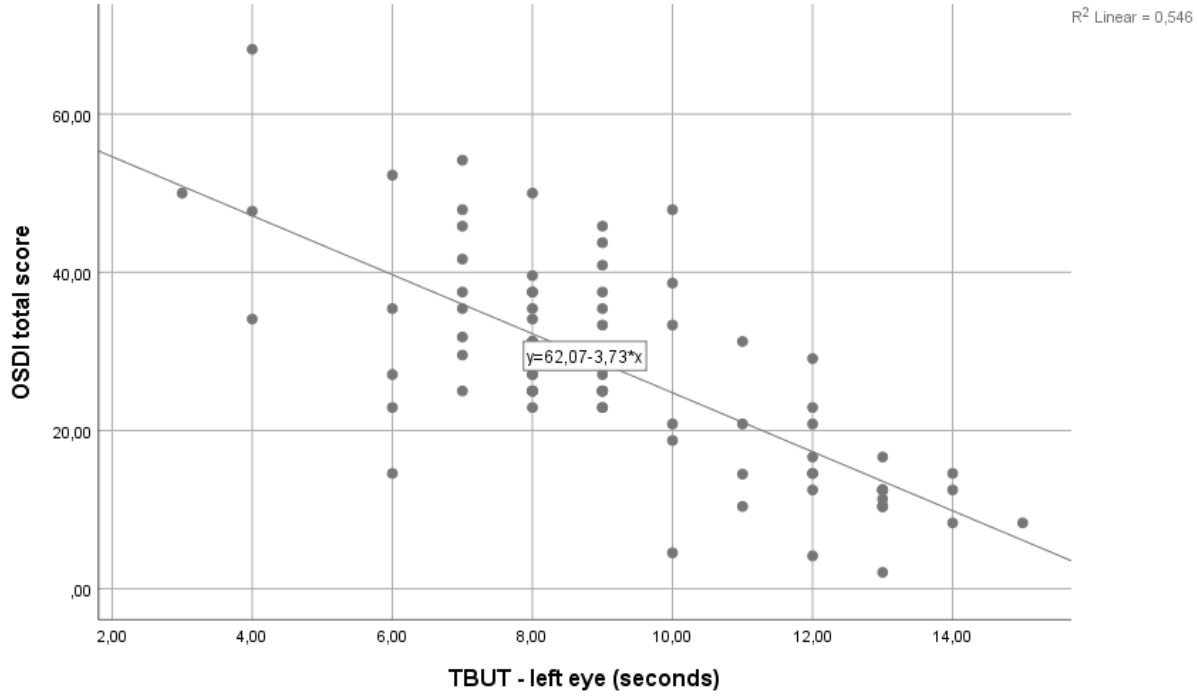

Figure 2. Scattering diagram of the OSDI (total score) and TBUT (left eye) results

can influence normal tear production (Altinors et al. 2006, Thomas et al. 2012) so regular smokers were not included in the study. For consumption of alcohol is also proven to adversly affect the tear film (Kim et al. 2012), so no alcohol was allowed prior to the test date, with exclusion of participants with a history of any alcohol abuse. Hormonal imbalance can also influence the quality of the tear film (Ruprecht et al. 1976), so menopausal patients were excluded, too. In people with dry eye syndrome, not enough tears are produced or the tears are of poorer quality. They may experience persistent symptoms similar to irritation, scratching or burning in the eyes, a feeling of a foreign body and may also notice changes in visual acuity. Advanced dry eye syndrome can eventually result in permanent damage to the surface of the eye and therefore lead to serious changes in visual acuity (O'Brien et al. 2004, Messmer et al. 2015, Gulati et al. 2017). The diagnosis of the ocular surface disease is based on the patient's symptoms and medical history. It should include questions

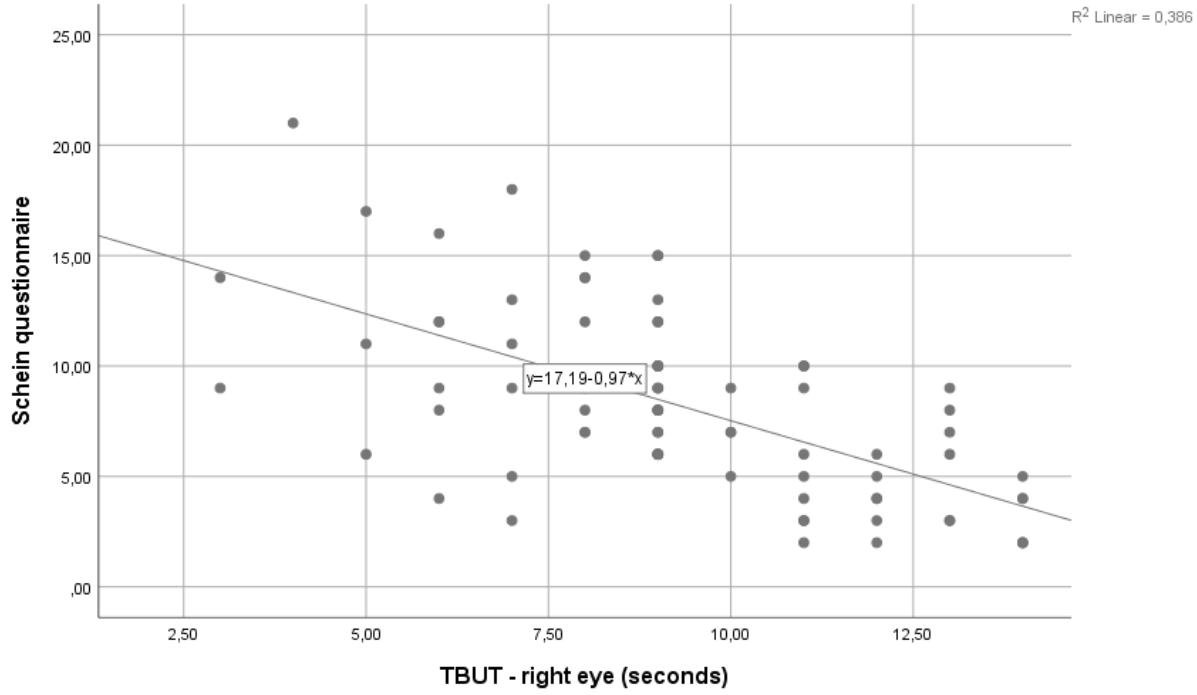

Figure 3. Scattering diagram of the Schein questionnaire and TBUT (right eye) results

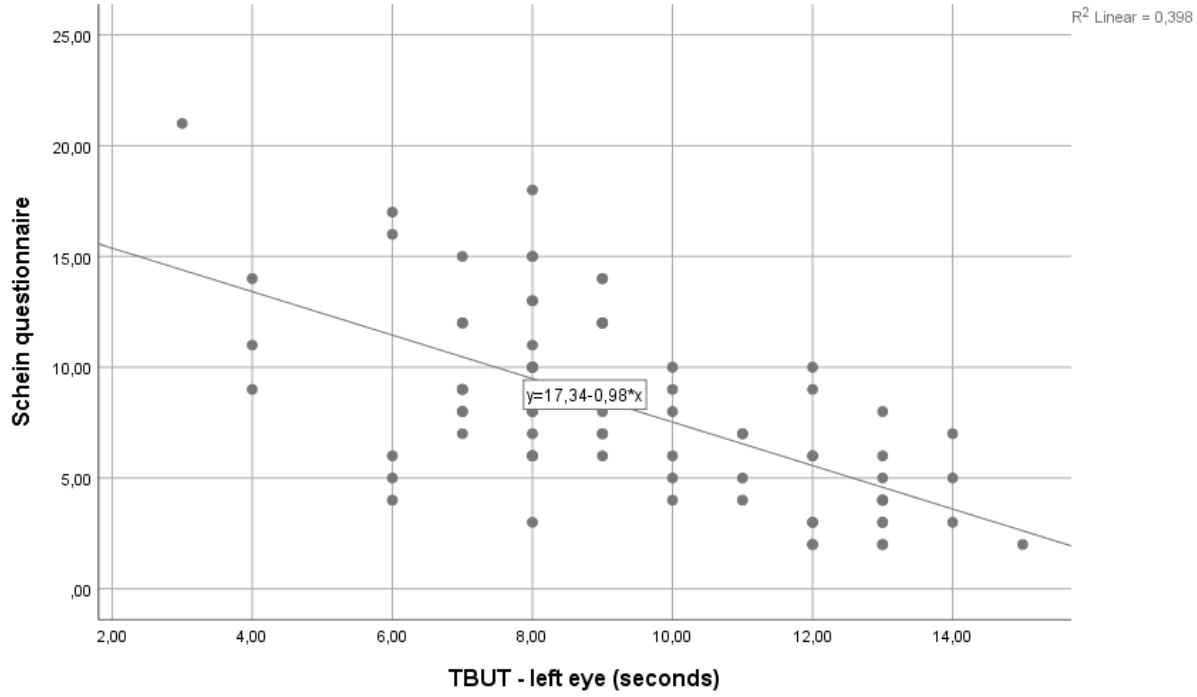

Figure 4. Scattering diagram of the Schein questionnaire and TBUT (left eye) results

about regular medication and all the possible exposure to the disease contributing factors. In order to be able to decide on the most appropriate treatment, doctors should be aware of all currently available external and diagnostic tests (Bahren et al. 2006, Kaštelan et al. 2013). Questionnaires allow for the rapid and efficient collection of relevant data and can greatly facilitate the diagnosis of ocular surface disorders. Dry eye index questionnaires and results may be useful for detecting the presence of dry eye and assessing the effect of therapeutic treatment. At present there are several questionnaires available, the most common being the Ocular Surface Disease Index (OSDI) (Schiffman et al. 2000). However, there is still no standardized questionnaire on dry eye disease that would be universally accepted. Following analysis of the patient's anamnesis and conducting a questionnaire it is necessary to perform a clinical examination of the anterior segment

and objective tests in order to confirm the diagnosis of dry eye (O'Brien et al. 2004, Tavares et al. 2010). Patients with schizophrenia may not report much of that disorder, but it greatly impairs the quality of life especially in younger patients, who are in the process of education or full employment.

With this research, we wanted to compare two subjective questionnaires and their application in order to successfully detect eye disorders commonly affecting patients with schizophrenia. We also wanted to find out how much the results of the subjective questionnaires matched the findings of the objective test showing the instability of the tear film. The simpler Schein questionnaire, with only 6 questions is proven to be equally valid compared to the OSDI questionnaire and it is more suitable in case for the need of a quick assessment of subjective symptoms. But at present, the OSDI questionnaire is the most commonly used in practice and we would like to avoid stigmatization of patients with schizophrenia and wrong perception that they are not able to understand more complicated questions. While examining subjective symptoms, it is possible to have different understanding of the questions asked in the questionnaires as well as their interpretation. In case of patients with schizophrenia successful completion of the questionnaire may be affected further by their lack of motivation or concentration, which will influence the reliability of the data.

Therefore, in order to avoid possible dispersion and inadequacy of the obtained answers in our study, questionnaire was conducted by the same examiner, offering all the necessary additional information. Care was taken that all participants had ample time to give answers. We believe this gave us uniformity and better validity of the collated results, providing reliable answers that can be interpreted with greater certainty. It is important to mention that all the participants were in the state of very good and stable remission and were cooperative throughout. We consider that to be very important considering the examined group of patients with schizophrenia whose understanding and feelings relating to subjective disorders can be influenced by their mental state.

There are several different questionnaires to examine the subjective symptoms of tear film dysfunction, such as OSDI, the Schein questionnaire, the IDEEL questionnaire (Impact of Dry Eye Living questionnaire), DEQ 5 (Dry Eye Questionnaire 5), adapted for various studies. However, the OSDI questionnaire is most frequently used both in the research and in clinical practice (Schiffman et al. 2000, Dougherty et al. 2011). We found it interesting to compare various subjective questionnaires or their match with the results of the objective measurements. That especially applies for use with psychiatrics patients, where questionnaires should be as adequate and simple as possible to provide a reliable and valid data.

This would provide the most optimal questionnaire or test on subjective symptoms of dry eye to be used for schiziophrenic and other psychiatric patients. It would be important for the most optimal questionnaire to be simple and understandable, which would facilitate its application and raise motivation. When measuring and comparing the results of mentally healthy population, there are large discrepancies between subjective and objective results. Therefore, various questionnaires about subjective symptoms have been in use, all in order to find the most optimal one. Subjective tests must always be clinically confirmed by objective measurements.

In patients with schizophrenia, the psychological factor influencing subjective measurements may be even more pronounced than in patients with depression and anxiety. Patients with schizophrenia often have difficulty concentrating or making judgment, suffer with low motivation and may also have depressive symptoms or anxiety, all of which may affect the outcome. All of this depends on the stage of the disease. The greater influence of the psychological factor on the results of the subjective test, which are then unreliable. That would be expected in the stages of worsening mental state. Therefore, in our study, an important criterion was that patients with schizophrenia were in the state of good and stable remission of mental illness in order to obtain as reliable data for analysis as possible and to avoid the influence of psychological factors to such an extent as to affect results.

CONCLUSION

To assess the subjective symptoms of dry eye, there are several questionnaires, none of which are generally accepted. In patients with schizophrenia OSDI and Schein questionnaire are equally reliable in the assessment of subjective symptoms of dry eye as it is shown by a comparison of their results with an objective tear film stability test (TBUT). For the purpose of quick assessment of the subjective symptoms of dry eye in patients with schizophrenia, the shorter and simpler Schein questionnaire may be used. However, considering that OSDI is more common in clinical practice, it is also recommended for use in patients with schizophrenia. Researches like this encourage an integrative and holistic approach in treatment of patients with schizophrenia, highlighting the importance of their overall health. This is important not just because of the possible impact of somatic problems on the primary disease, but also as it greatly impacts their daily functioning and quality of life.

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Conflict of interest: None to declare.

Contribution of individual authors:

Ivana Bakija: conception and design of this manuscript, the literature research, the data collection, revision of the results and making conclusions.

Igor Filipčić & Ivona Šimunović Flipčić: revising the article critically for important intellectual content.

Marija Bogadi & Marta Gotovac: colection data and literature research.

Snježana Kaštelan: design of this manuscript and with ophtalmological exams performing TBUT test, revising the article critically and making conclusions.

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