

QUALITATIVE INTERPRETATION OF VISUAL ACUITY IN DRY EYE PATIENTS

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Abstract: *The purpose of this prospective observational study is to evaluate contrast sensitivity in dry eye patients using LCD CHART PROJECTOR (CC-100 Series 2015). Contrast sensitivity was determined in 42 eyes of 21 patients with dry eye (the dry eye group) and 22 eyes of 11 healthy volunteers (the control group) with normal (VA=1) corrected or uncorrected visual acuity. We measured the contrast sensitivity at 4 contrast levels using 9 grading frequencies. Analyses with the Mann-Whitney U test showed significant differences (CS lowering) between the study and control group from the spatial frequency of 4.24 cpd ($P=0.042<0.05$) to spatial frequency of 24 cpd ($P=0.000<0.05$).*

Key words: *contrast sensitivity, dry eye, fluctuating vision, spatial frequencies.*

1. Introduction

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface [4]. Tear hyperosmolarity secondary to desiccating stress activates intracellular signaling pathways within corneal and conjunctival epithelial cells, resulting in the release of proinflammatory cytokines, including interleukin 1, tumor necrosis factor, and interleukin 6. These cytokines activate cells of the innate immune system (macrophage and neutrophils) which

release cytokines promoting the activation and maturation of immature antigen-presenting cells. Upon reaching the lymph nodes via the lymphatic vessels, mature antigen-presenting cells induce effector helper T-cell 1 and 17. These T cells, primed against ocular surface antigens, travel to the ocular surface through efferent blood vessels, bind to ocular surface antigens, and become activated. Chemical mediators released by the activated T cells perpetuate the inflammatory pathway and cause tissue destruction [6], [13].

Ocular surface inflammation leading to dry eyes can be caused by altered tear-film composition, reduced tear production, poor lid function, environmental conditions, or diseases such as Sjögren's syndrome.

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Anticholinergic drugs, estrogens, and selective serotonin reuptake inhibitors (SSRIs) can also cause dry eyes. Older age and female sex are risk factors [12]. Are described 2 types of dry eye: Aqueous-Deficient dry eye (Sjögren's syndrome primary/secondary, systemic drugs, lacrimal gland duct obstruction, lacrimal deficiency) and Evaporative dry eye (allergic conjunctivitis, contact lens use, vitamin A deficiency, low blink rate, lipid deficiency, MGD, preservatives in ocular medication) but most DED (dry eye disease) is a combination of subtype due to factors that promote ocular surface inflammation [1], [2].

There is a low correlation between symptoms (ocular discomfort/pain, redness, fluctuating vision, itching, ocular irritation, excess tearing) and signs (redness, low Schirmer I, low BUT, corneal and conjunctival staining, mucous discharge) [8], [10], [14].

The available literature suggests that DED has a substantial economic burden, with indirect costs making up the largest proportion of the overall cost due to a substantial loss of work productivity. In addition, DED has a substantial negative impact on physical, and potentially psychological function and health-related quality of life across the countries examined. A number of studies also indicated that health-related quality of life burden increases with the severity of disease [5], [10].

Visual acuity (VA) has traditionally been the gold standard for assessing the visual capacity of our patients. However, this measure only relates to an ability to resolve details of maximum contrast and fails to provide information on how an object of poor contrast is viewed, even when the object is large [5].

Over the last few years, besides quantifying VA, there has been increased interest in its qualitative interpretation,

largely because of the present surge in refractive surgery. Thus, several methods have been developed to assess a subject's quality of vision, most of which are based on determining contrast sensitivity [5].

Indeed, a large number of eye pathologies, including keratoconjunctivitis Sicca, have been associated with altered contrast sensitivity [5].

The functional impact of DED and the qualitative interpretation of VA can be reflected in contrast sensitivity [9]. Starting from this statement, the aim of the present prospective observational study was to evaluate contrast sensitivity in a group of patients with dry eye and a control group using the LCD CHART PROJECTOR (CC-100 Series 2015).

2. Materials and Methods

The study populations comprised 42 eyes of 21 patients with dry eye (the dry eye group) and 22 eyes of 11 healthy volunteers (the control group) with normal (VA=1) corrected or uncorrected visual acuity. All subjects gave their consent, based on the Declaration of Helsinki, to participate at the study after the type of the study has been explained. The study was carried out with patients who visited the Ophthalmology Clinic of Emergency Hospital of Sibiu, Romania.

Materials:

- for the Visual Acuity measurement the ETDRS Chart was used.
- The Ocular Surface Disease Index (OSDI) was used for the assessment of symptoms related to dry eye disease and their effect on vision.
- dry eye diagnosis was based on the methodologies of 2007 Report of the International Dry Eye Workshop (DEWS).
- the spatial frequency contrast sensitivity was determined with LCD CHART PROJECTOR (CC-100 Series 2015).

The inclusion criteria in the study are:

Dry eye group: subjects between 18-70 years old, OSDI more than 11 points, corneal and/or conjunctival staining (using OXFORD scheme with special coloration: fluorescein and lissamine green), the values of the Schirmer test I less/equal than 10 mm (without anaesthesia), Tear breakup time (TBUT) less/equal than 5 seconds, Visual Acuity AO= 1 (corrected or uncorrected), spherical equivalent less/equal +/- 4D, no other ocular disease (except dry eye).

Control group: subjects between 18-70 years old, OSDI less or equal than 10 points, without corneal/conjunctival staining, Schirmer test I more than 15 mm (without anaesthesia), Tear breakup time (TBUT) greater than 15 seconds, Visual Acuity AO= 1 (corrected or uncorrected), spherical equivalent less/equal +/- 4D, no ocular disease.

Each patient followed the study protocol: on the same day that a patient completed all the inclusion tests, contrast sensitivity was determined for each eye. The visual acuity(VA) to each eye is tested with ETDRS Chart (LCD CHART PROJECTOR (CC-100 Series 2015) and all study patients (control and dry eye group) had each eye VA=1.00 (corrected or uncorrected) . Every patient has completed the OSDI questionnaire. After the Schirmer test I was performed, the assessment of corneal and conjunctival staining is made with special colorations (fluorescein and lissamine green) using OXFORD Scale for grading the corneal or conjunctival damage and for the determination of tear breakup time.

Measurements were taken using the LCD CHART PROJECTOR (CC-100 Series 2015). The Spatial Frequency Contrast Sensitivity Test of this device can be customized by setting the amount of spatial frequencies and contrast levels. The result gives valuable information on the patients contrast visual acuity. Test results

are displayed in a graph which is printable as well [16]. (Fig. 1)



Fig. 1. Lcd Chart Projector (CC-100 Series 2015)

NAME																							
AGE																							
SEX	FEMININ	MASULIN																					
ENVIRONMENT	URBAN	RURAL																					
PATHOLOGICAL PERSONAL HISTORY																							
OSDI (points)																							
TBUT	OD	OS																					
SCHIRMER I (mm)	OD	OS																					
STAINING SCHEMA OXFORD	<table border="1"> <thead> <tr> <th>PANEL</th> <th>GRADE</th> <th>CRITERIA</th> </tr> </thead> <tbody> <tr> <td>A</td> <td>0</td> <td>Equal to or less than panel A</td> </tr> <tr> <td>B</td> <td>I</td> <td>Equal to or less than panel B, greater than A</td> </tr> <tr> <td>C</td> <td>II</td> <td>Equal to or less than panel C, greater than B</td> </tr> <tr> <td>D</td> <td>III</td> <td>Equal to or less than panel D, greater than C</td> </tr> <tr> <td>E</td> <td>IV</td> <td>Equal to or less than panel E, greater than D</td> </tr> <tr> <td>>E</td> <td>V</td> <td>Greater than panel E</td> </tr> </tbody> </table>	PANEL	GRADE	CRITERIA	A	0	Equal to or less than panel A	B	I	Equal to or less than panel B, greater than A	C	II	Equal to or less than panel C, greater than B	D	III	Equal to or less than panel D, greater than C	E	IV	Equal to or less than panel E, greater than D	>E	V	Greater than panel E	
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>E	V	Greater than panel E																					

Fig. 2. The study protocol

LCD CHART PROJECTOR (CC-100 Series 2015) is able to accurately determine contrast sensitivity in a relative rapid and simple automated manner.

The test is conducted at a distance of 4m from the screen and takes about 4 minutes per eye. We measured the contrast sensitivity at 4 contrast levels, 100%, 30%, 10% and 3% using grading frequencies:1.50cpd, 2.12cpd, 3.00cpd, 4.24cpd, 6.00cpd, 8.49cpd, 12.00cpd,

16.97cpd, 24.00cpd. Background luminance of 200 candelas per square meter (Fig. 3)

It provides data on contrast sensitivity by means of an automated method based on the stimulus that is a sine wave grading. All stimuli were static, generated in gray scale, circularly symmetric [3].

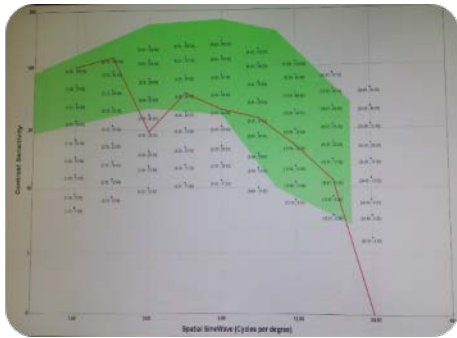


Fig. 3. Contrast Sensitivity Curve

Data analysis was performed using SPSS software (version 20) [11]. For continuous variables the normality criteria were checked using Kolmogorov-Smirnov test. Mann-Whitney U test was used for comparison between study and control groups, in case of continuous variables (presented as mean \pm standard deviation). A p-value less than 0.05 was considered statistically significant [8]. For graphical representation we used simple error bar (representing 95% confidence interval for mean).

3. Results and Discussions

The mean age of the study subjects was M=53.57 (SD=12.13) in the dry eye group and M=51.45(SD=8.21) in the control group (p=0.609).

The figure below shows the mean \pm SD values of contrast sensitivities for the nine spatial frequencies tested with vertical sine-wave gradings for both groups (Fig. 4).

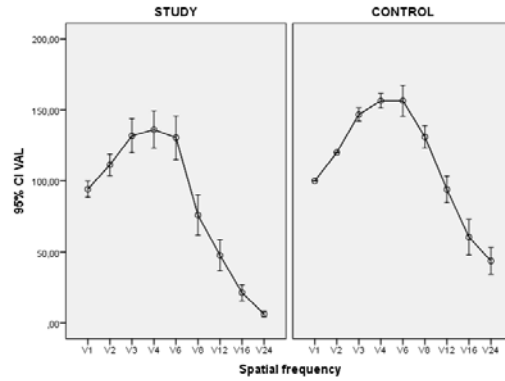


Fig. 4. The mean \pm SD values of contrast sensitivity

With the use of vertical sinusoidal frequency, we obtain increased sensitivity in the midrange frequencies and decreased sensitivity at low and high frequencies.

Table 1
Study vs control group spatial frequency means

Spatial frequency	Group	Mean	SD	P
1.50	Stdy	94.2	18.07	0.138
	Control	100.00	,00	
2.12	Study	111.36	24.07	0.095
	Control	120.00	,00	
3.00	Study	131,79	38,35	0.169
	Control	146,73	10,59	
4.24	Study	136,18	42,46	0.042
	Control	156,45	11,48	
6.00	Study	130,45	49,41	0.022
	Control	156,50	24,44	
8.49	Study	75,95	45,17	0,000
	Control	130,98	18,03	
12.00	Study	47,64	35,20	0,000
	Control	94,09	21,19	
16,97	Study	21,33	18,12	0,000
	Control	60,48	28,17	
24,00	Study	6,29	6,40	0,000
	Control	43,68	21,20	

Analyses with the Mann-Whitney U test showed significant differences (CS lowering) between the study and control

group from the spatial frequency of 4.24 cpd ($P=0.042<0.05$) to spatial frequency of 24 cpd ($P=0.000<0.05$) (Table 1).

The mean \pm SD values of contrast sensitivities for the nine spatial frequencies tested with vertical sine-wave gradings for each eye in case of both groups show as follows:

- decreased sensitivity between *right eye* of the dry eye group and right eye of the control group from the spatial frequency 8.49 cpd ($p=0.004<0.05$) to spatial frequency 24.00 cpd ($p=0.000<0.05$)
- decreased contrast sensitivity between *left eye* of the DED patients and left eye of the control patients starting from the spatial frequency 6.00cpd ($p=0.026<0.05$) to the 24.00 cpd ($p=0.000<0.05$). (Fig. 5)

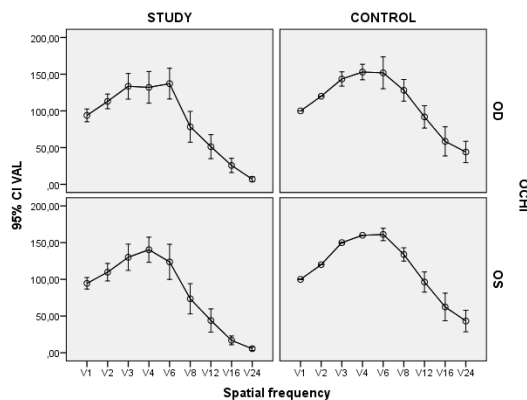


Fig. 5. OD and OS contrast sensitivities

This findings indicate that contrast sensitivity was lower in the dry eye group than in the control group, in particular between spatial frequencies 4.24 cpd and 24.00 cpd.

Altered contrast sensitivity in patients with dry eye has been previously reported and noted that contrast sensitivity was worse in a group of patients with keratoconjunctivitis Sicca compared with a group of subjects matched according to age) [9].

A similar study showed a significant decrease of spatial-contrast sensitivity

from 35 to 70% present in keratoconjunctivitis sicca eyes compared with a group of age-matched normal eyes used as control, what means that tear film disease can affect the transfer function of modulation of the ocular surface [15].

Measuring contrast sensitivity in patients with dry eye brings additional information (compared to visual acuity measurement) and correlated with signs and symptoms (often unsystematized) can guide the diagnosis and treatment of these patients.

The available literature suggests that DED has a substantial economic burden, with indirect costs making up the largest proportion of the overall cost due to a substantial loss of work productivity [10].

4. Conclusions

Starting from the definition of dry eye we know that this ocular surface disease can lead to visual disturbance [4]; in patients with good visual acuity this visual disturbance can be highlighted using contrast sensitivity. Contrast sensitivity values in human eyes have a peak between the 3 cpd and 6 cpd spatial frequencies, so contrast sensitivity peak changes can have a significant effect on visual quality.

DED patients can accuse blurred vision in spite of the normal visual acuity, because of the disruption of the anterior refractive surface of the eye (the tear film). Contrast sensitivity brings additional information for these patients:

QUALITATIVE INTERPRETATION: measured by contrast sensitivity tests.
 QUANTITATIVE INTERPRETATION: measured by visual acuity tests.

References

1. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern® Guidelines. Dry Eye Syndrome. San

- Francisco, CA: American Academy of Ophthalmology; 2013. www.aaopt.org/ppp. Accessed April 14, 2017.
2. Barabino, S., Labetoulle, M., et al.: *Understanding symptoms and quality of life in patients with dry eye syndrome*. In: *Ocul Surf.* (2016); 14, p. 365-376.
 3. Cavalcanti-Galdino, M.K. da Silva, J.A. et al.: *Acute effect of alcohol intake on sine-wave Cartesian and polar contrast sensitivity functions*. In: *Braz J Med Biol Res*, (2014); vol.47 no.4 Ribeirão Preto Apr. Epub Mar 21.
 4. *Definition and Classification Subcommittee of the International Dry Eye Workshop. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye WorkShop (2007)*. 2007;5(2), p. 75-92.
 5. Koc, H., Kocak, I. et al: *The Effects of Superior Temporal Small Corneal Incisions on Tear Level*. In: *American Journal of Ophthalmology & Visual Science* (2016); 1(2), p. 26-30 <http://www.aascit.org/journal/ajovs>, Accessed April 14, 2017.
 6. Leonardi, A., Francisco, C. et al.: *Advances in the science and management of dry eye disease*. In: *EuroTimes ESCRS* (2016); 1, p. 4-5.
 7. Maniu, I.: *Tehnici de analiză a datelor: statistica (Techniques of data analysis: statistics)*. Sibiu. Ed. Univ. „Lucian Blaga”, 2014.
 8. Marshall, L.L., Roach, J.M.: *Treatment of Dry Eye Disease*. In: *Consult Pharm.* (2016); 31, p. 96-106.
 9. Mathews, P.M., Ramulu, P.Y. et al.: *Functional impairment of reading in patients with dry eye*. In: *Br J Ophthalmol.* (2017) Apr; 101(4), p.481-486.
 10. McDonald, M., Patel, D.A. et al: *S.J. Economic and humanistic burden of dry eye disease in Europe, North America, and Asia: a systematic literature review*. In: *Ocul Surf.* (2016); 14, p.144–167.
 11. Mocan, I.: *SPSS Introducere în analiza datelor (Introduction to data analysis)*. Sibiu. Ed. Univ. „Lucian Blaga” Sibiu, 2005.
 12. Perez, V.L., Pflugfelder, S.C., et al.: *Lifitegrast, a novel integrin antagonist for treatment of dry eye disease*. In: *Ocul Surf.* (2016); 14, p. 07-215.
 13. Pflugfelder SC, Stern M, Zhang S, Shojaei A. :*LFA-1/ICAM-1 interaction as a therapeutic target in dry eye disease*. In: *J Ocul Pharmacol Ther.* (2017); 33, p.5-12.
 14. Puell, M.C., Beni'tez-del-Castillo, J.M., et al.: *Contrast sensitivity and disability glare in patients with dry eye*. In: *Acta Ophthalmol. Scand.* (2006); 84, p.527–531.
 15. Rolando, M., Iester, M. et al.: *Low spatial- contrast sensitivity in dry eyes*. In: *Cornea.* 17(4): 376-9, Jul 1998.
 16. CC-100 LCD Chart system , <http://www.topcon-medical.eu/eu/products/87-cc-100-lcd-chart.html#downloads>. Accessed April 19, 2017.