Correlation Between the Findings of Optical Coherent Retinal Tomography (OCT), Stereo Biomicroscopic Images from Fundus of an Eye and Values from Visual Acuity of Diabetic Macular Edema

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ABSTRACT

Introduction: Diabetic maculopathy is the major cause of reduced visual acuity in patients with non-proliferative diabetic retinopathy and occurs on average in 29% of patients who have diabetes for 20 or more years. Aim: The aim of this study is to re-examine the correlation between the findings of optical coherence retinal tomography, stereo bio-microscopic images from fundus of an eye and values from visual acuity of diabetic macular edema. In addition, the aim is to show the importance of various ophthalmic tests for establishing diagnosis in time. Material and methods: The research sample consisted of 90 subjects-patients from Cabinet for photographic documentation, fluorescein angiography and laser photocoagulation in Department of Ophthalmology at the University Clinical Centre in Sarajevo. The study was a one-year long, prospective, clinical study. Results: Research has shown a positive correlation between the various tests that are applied for the diagnosis of diabetic macular edema. Accurate and early diagnosis is of great importance for the treatment in time of this disease by applying laser photocoagulation, intravitreal injections of Anti-VEGF drugs or surgical treatment by Pars Plana Vitrectomy. Key words: diabetic macular edema, visual acuity, optical coherence tomography, fundus stereo biomicroscopy

1. INTRODUCTION

Diabetic maculopathy is the major cause of reduced visual acuity in patients with non-proliferative diabetic retinopathy and occurs on average in 29% of patients who have diabetes for 20 or more years (1). Previous research discovered that the prevalence of diabetic maculopathy is proportional to duration of diabetes (2). The most important change that occurs in diabetic maculopathy is diabetic macular edema. Maculopathy usually defines the presence of retinal edema in the area of the posterior part of the eye that structurally and functionally damages the macular region (3). Macular edema is defined as the accumulation of liquids and other substances (lipids, proteins), which leads to a thickening of retinal tissue and its functional decrease. The cause of macular edema emergence, pathophysiology explains by the disturbed functioning of hemato-retinal barrier (4). Inflammatory factors and increased levels of vascular endothelial growth factors involved in establishing macular edema (5). In addition to medical history, diagnosis can be established on the basis of ophthalmic findings: of visual acuity, stereo bio-microscopic fundus examination, recording and analyzing computerized retinal tomography (OCT) (6, 7), fundus imaging (FF), fluorescein angiography (FA) (8, 9, 10).

2. AIM OF RESEARCH

The aim of this study is to re-examine the correlation between the findings of optical coherence retinal tomography, stereo bio-microscopic images from fundus of an eye and values from visual acuity of diabetic macular edema. In addition, the aim is to show the importance of various ophthalmic tests for establishing diagnosis in time.

3. MATERIALS AND METHODS

Approach to the study was based on set objectives by choosing the most homogenic sample to minimize the poly-causality of observed parameters. The patients have all fulfilled the inclusion criteria: Patients older than 50 years, both sexes, where the diagnosis of diabetes is discovered at least 12 months prior to inclusion in the study.
Patients who are not suffering from other chronic diseases such as hypertension, end stage renal disease, anaemia, infectious diseases and other systemic diseases.

Following subjects are excluded from the research:
- Patients who have other eye diseases: monocular, eye injuries, earlier eye surgery, glaucoma, uveitis, cataracts, degenerative disease, retinal and choroidal detachment.
- Patients who underwent panretinal laser photocoagulation as well as patients who received intravitreal therapy.
- In patients with diabetic maculopathy who have “high risk” proliferative retinopathy, which can lead to severe vision loss, panretinal laser photocoagulation is urgently indicated.

The study sample consisted of 90 subjects-patients from Cabinet for photographic documentation, fluorescein angiography and laser photocoagulation in Department of Ophthalmology at the University Clinical Centre in Sarajevo. All patients were diagnosed with clinically significant diabetic macular edema in at least one eye. 90 selected participants were formed into three groups based on the level of the best corrected central visual distance acuity. The study was a one-year long, prospective study. All patients completed the following ophthalmological tests: determination of best corrected visual acuity at distance of 6m using a Snellen’s optotype, Goldmann’s Applanation tonometry, biomicroscopic examination of anterior and posterior eye segment and computerized tomography of the retina.

Based on best corrected central visual distance acuity, three groups were formed:
- Group I: 30 patients whose best corrected visual acuity was 0.7 or better.
- Group II: 30 patients whose best corrected visual acuity was before 0.2 to 0.6.
- Group III: 30 patients whose best corrected visual acuity was 0.1 or less.

Determination of visual acuity (VA): Best corrected visual acuity (BCVA) was measured at 6m distance without correction or with the appropriate corrections using the Snellen optotype. For examining the anterior and posterior eye segment was used biomicroscope with Slit light (SLIT LAMP: LSL 532S MOD. 1449-675. Carl Zeiss Meditec, AG, JENA, Germany). Establishment of CSME diagnosis based on stereo bio-microscopic fundus examination was done based on the ETDRS criteria for defining the CSME. Only for the purpose of this research was formed gradation scale, so that this finding could be included in the statistical analysis. All diagnosed diabetic maculopathies were classified into four gradation scale groups and marked with levels.

Coherent tomography of the retina (OCT) was performed on all patients at beginning of the research on the device (STRATUS OCT. MODEL 3000th Carl Zeiss Meditec, JENA GERMANY).

Statistical data analysis: nominal and ordinal vari-ables in the study were analyzed by $\chi^2$ test, and on the lack of expected frequencies Fisher’s exact test was used. For continuous variables in the study, the symmetry of their distribution was firstly analyzed using the Kolmogorov-Smirnov test. When the distribution of continuous variables was symmetrical, the arithmetic mean and the standard deviation were used to show the average value and measures of dispersion.

For comparison of variables were used parametric tests (student’s-test and ANOVA test, paired t test).

| Control Variables | Subject age | Duration of DM | HbA1c | Visual acuity before LFK |
|-------------------|-------------|----------------|-------|-------------------------|
| Group 1           | Correlation | 1.000          | 0.303 | 0.129                   | -0.106                   |
|                   | Significance (2-tailed) | .       | 0.004 | 0.227                   | 0.322                   |
|                   | df          | 0              | 87    | 87                      | 87                      |
| Group 2           | Correlation | .303           | 1.000 | 0.253                   | -0.261                   |
|                   | Significance (2-tailed) | .       | .     | 0.017                   | 0.013                   |
|                   | df          | 87             | 0     | 87                      | 87                      |
| Group 3           | Correlation | 0.129          | 0.253 | 1.000                   | -0.235                   |
|                   | Significance (2-tailed) | .       | .     | 0.017                   | 0.027                   |
|                   | df          | 87             | 87    | 0                       | 87                      |

| Group Total | Correlation | -0.106         | -0.261 | -0.235                 | 1.000                   |
|            | Significance (2-tailed) | .       | .     | .                      | .                      |
|            | df          | 87             | 87    | 87                     | 0                       |

Table 1. Correlation of independent variables (group) in relation to the dependent variable age of the patients, duration of DM, HbA1c values and visual acuity before LFK
The differences in average values FT before LFK, inside Table 4.

4. DISCUSSION

When the distribution of continuous variables was unsymmetrical, for showing average value and a

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test showed a statistically significant difference in the leveling group during bio-microscopic fundus examination before LFK had level 1, 2, 19 (63.3%), and then grade 3, 11 (36.7%). No subjects had level 4 before LFK. Most subjects from the group 2 during bio-microscopic fundus examination, before LFK, had level 3, 19 (63.3%), and level 2, 10 (33.3%). Whereas, only one subject had a level 4 before LFK. Most subjects from the group 3 during bio-microscopic fundus examination, before LFK, had level 3, 17 (56.7%), and level 4, 10 (33.3%). Only 3 (9.4%) patients had level 2 before LFK. Chi square test showed a statistically significant difference in the leveling group during bio-microscopic fundus examination before LFK. The best results on level 1 had the group 1. \( \chi^2 = 30.82, p < 0.005 \).

The lowest average value of TMV before LFK had subjects from the group 1. Subjects from group 1 had statistically significant low value FT before LFK (\( p < 0.05 \)). Chi square test showed a statistically significant difference in leveling by qualitative OCT (\( p = 0.013 \)). Average values of HbA1c are correlated with the duration of diabetes mellitus and negatively correlated with visual acuity before LFK (\( p = 0.013 \)). Average values of HbA1c are correlated with the duration of diabetes mellitus and negatively correlated with visual acuity before LFK (\( p = 0.027 \)). Visual acuity before LFK is negatively correlated with the duration of diabetes mellitus and average values of HbA1c. Visual acuity is decreased when values of HbA1c are increased and when the subject is longer a diabetic.

According our results : Age of the patients is correlated with the duration of diabetes mellitus; older respondents have a longer duration of diabetes mellitus \( df = 87, p = 0.004 \). With other variables, age is not correlated. Duration of diabetes is correlated with age (\( p = 0.004 \)), with average values of HbA1c (\( p = 0.017 \)), and negatively correlated with visual acuity before LFK (\( p = 0.013 \)). Average values of HbA1c are correlated with the duration of diabetes mellitus and negatively correlated with visual acuity before LFK (\( p = 0.027 \)). Visual acuity before LFK is negatively correlated with the duration of diabetes mellitus and average values of HbA1c. Visual acuity is decreased when values of HbA1c are increased and when the subject is longer a diabetic.

Most of the subjects from group 1 during bio-microscopic fundus examination before LFK had level 2, 19 (63.3%), and then grade 3, 11 (36.7%). No subjects had level 4 before LFK. Most subjects from the group 2 during bio-microscopic fundus examination, before LFK, had level 3, 19 (63.3%), and level 2, 10 (33.3%). Whereas, only one subject had a level 4 before LFK. Most subjects from the group 3 during bio-microscopic fundus examination, before LFK, had level 3, 17 (56.7%), and level 4, 10 (33.3%). Only 3 (9.4%) patients had level 2 before LFK. Chi square test showed a statistically significant difference in the leveling group during bio-microscopic fundus examination before LFK. The best results on level 1 had the group 1. \( \chi^2 = 30.82, p < 0.005 \).

The lowest average value of TMV before LFK had subjects from the group 1. Subjects from group 1 had statistically significant low value FT before LFK (\( p < 0.05 \)). Chi square test showed a statistically significant difference in leveling by qualitative OCT findings within a group, \( \chi^2 = 65.706, p = 0.001 \). The largest number of subjects from group 1 has a level 1, and most of the subjects from group 3 has a level 4.

Analyzing the age structure of subjects in the group, we see that diabetic retinopathy with clinically significant maculopathy usually occurs in the age group 50-70 years of age. Here we must bear in mind that this study was limited to subjects older than 50 years of age. Looking at groups, average age of the group 1 was 62.46 years, the average age of...
the group 2 was 63.42 years, while the average age of the subjects from group 3 was 66.76 years. Moss and Klein (1994) obtained similar results in their study (16). Alice M, Lesley H, G Bradley, Jonathan W, Arliene R, Paul P and associates (2008) in their study concluded that the average age of patients with diabetic maculopathy was 76 years (17). Since their subjects’ average age was higher by about 10 years we must seek an explanation in the fact that their subjects had previously been treated for diabetic maculopathy. Krushkal-Wallis nonparametric test showed that there was no statistically significant difference in the average number of subjects’ years within the group, and that the respondents in terms of age were nearly equalized. This study demonstrated no statistically significant difference between the sexes when it comes to diagnosis of diabetic maculopathy. The results show that among the total subjects were 46 male and 44 female patients. Paerson’s chi square test showed that there was no statistically significant difference in prevalence between men and women among the studied groups. Also, no significant correlation between gender and the analyzed parameters VO, the fundus findings, OCT’s done before LFC. These results correspond to the results of other researchers. Similar results were published in 1991, a research group ETDRS Report Number 9 (18). Alice M, Lesley H, G Bradley, Jonathan W, Arliene R, Paul P and associates (2008) in their study concluded that from the total number of subjects 40% were females (17). The study found that the average duration of diabetes mellitus in group 1 was 10.63 years, average duration of diabetes mellitus in group 2 was 14.46 years and the average duration of diabetes mellitus in group 3 was 18.66 years (Table 4). Krushkal-Wallis nonparametric test showed a statistically significant difference in the average duration of diabetes mellitus between the groups, and that the questioned groups compared to the duration of diabetes mellitus in patients differ substantially. Subjects from third groups have diabetes mellitus the longest, while the ones from first group, the shortest. The explanation of this statistical difference between the groups in duration of diabetes till the point of starting treatment, we need to search on the cultural, socio-economic and war grounds. Davis and associates (1992) have explored both types of diabetes, and concluded that diabetic retinopathy (DR), as a complication after 10 years of diabetes, occurs in approximately 50% of patients, 75% after 20 years of age and 90% of patients after 30 years of age (19). Kohner (1999) in his study states that patients with type II diabetes, i.e. 5% of them, have distinct elements of the DR during establishing diagnosis of diabetes, and approximately 20% of patients have symptoms of DR after two years of diagnosis. Statistics after 10 or more years is the same like the one for patients of type I (20). Different from the research of Kohner and associates, this research was limited by the inclusion criteria on subjects of particular age, whose diabetes was previously diagnosed while newly detected diabetes was not in the study. Tushar and Stuart (2009) in their research discovered that the prevalence of diabetic maculopathy is proportional to duration of diabetes (2). In that study, all patients were analyzed for HbA1c- an indicator of sugar levels in blood during three months. Earlier in the discussion it was stated that the regulation of sugar in blood, blood pressure and lipid regulation was the first step in the treatment of diabetic maculopathy. This is why (inclusion criteria) in the study did not participate subjects with elevated blood pressure. HbA1c, on average, was increased in all groups. ANNOVA test showed that there was no statistically significant difference in average values of HbA1c between the groups (Table 1).

The arisen conclusion is that increased HbA1c call for better glycemic control in patients with diabetic maculopathy. Kollias and Ulbig (2010) in their study reported that the incidence of diabetic retinopathy is decreasing by 76% in patients whose HbA1c is 7.2% compared to 47% of patients whose HbA1c is 9.1% (21). Tushar R, Stuart F. (2009) in their research discovered that the prevalence of diabetic maculopathy is proportional to lesser control of diabetes (20). Yang X, Liu K, Xun X. (2009) in their studies came to similar conclusions (22). Schmid, Neumaier, Stolba and Binder in their research (2006) discovered that there was no statistically significant difference between HbA1c and the effect of laser photoocoagulation in DME (23). Sim and his associates established a statistically significant correlation between OCT and values of visual acuity in patients with diabetes mellitus (24).

5. CONCLUSION

Research has shown a positive correlation between the various tests that are applied for the diagnosis of diabetic macular edema. Accurate and early diagnosis is of great importance for the treatment in time of this disease by applying laser photocoagulation, intravitreal injections of Anti-VEGF drugs or surgical treatment by Pars Plana Vitrectomy. For the accurate and in time diagnosis of CSME it is necessary to apply multiple methods and tests within the ophthalmological examination. The importance is reflected by the fact that the applied therapeutic methods lead to operational invasive methods that irreversibly alter retina. As soon as clinically significant macular edema (CSME) is diagnosed, treatment should be started. Therapy in due course improves the quality of patients’ life and delays serious complications of diabetic retinopathy in the eye. Each applied diagnostic method has its own importance in monitoring any anatomical or functional changes in the eye. By using multiple methods, the disease and the changes it’s causing are understandable. In addition, information provided by the diagnostic methods not only directing therapy but also have a great significance for the prognosis and treatment. Applied diagnostic methods i.e. severity of findings, accompanied by numerical values, are positively correlated.
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