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ARAŞTIRMA/RESEARCH

Comparison of life quality scores of ranibizumab-treated patients with age-related macular degeneration

Ranibizumab uygulanan yaşa bağlı makula dejenerasyonlu hastalarda yaşam kalitesi skorlarının karşılaştırılması

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Abstract

Purpose: To evaluate the visual acuity, fluorescein angiography, optic coherence tomography and life quality of patients diagnosed with exudative age-related macular degeneration and administered with intravitreal Ranibizumab injection.

Material and Methods: This study included of 48 different patients who were diagnosed as exudative age-related macular degeneration and administered with ranibizumab injection. In this study, demographic characteristics, pre- and post-injection corrected visual acuity, angiography, optic coherence tomography alteration and the scores of quality of life questionnaire were prospectively analyzed.

Results: The patients were followed up for 20±1 months on average. After ranibizumab injection, 12 patients (25%) gained ≥3 lines of visual acuity, 28 patients (58.3%) gained ≤3 lines of visual acuity, 6 patients (12.5%) lost ≤3 lines of visual acuity and 2 patients (4.2%) lost ≥3 lines of visual acuity. The increase in Early Treatment Diabetic Retinopathy Study was lower in patients with Hypertension and positive family history In this study, it was determined that The National Eye Institute Visual Function Questionnaire score increased in patients with improving visual acuity after ranibizumab injection and the difference was statistically significant.

Conclusion: Visual acuity was found to improve in patients with exudative age-related macular degeneration and treated with intravitreal ranibizumab injection. The National Eye Institute Visual Function Questionnaire provided reliable results in patients with age-related macular degeneration and the questionnaire score was determined to increase following the treatment.

Key words: Ranibizumab; macular degeneration

Öz

Amaç: Eksudatif tip yaşa bağlı makula dejenerasyonu saptanan ve intravitreal Ranibizumab enjeksiyonu yapılan hastalarda görme keskinlikleri, floresein anjiyografi, optik koherens tomografi ve yaşam kalitesi değişimini değerlendirmek.

Gereç ve Yöntem: Bu çalışma eksudatif tip yaşa bağlı makula dejenerasyonu olan ve ranibizumab enjeksiyonu yapılan 48 hastayı içermektedir. Bu çalışmada hastaların demografik özellikleri, enjeksiyon öncesi ve sonrası düzeltilmiş görme keskinlikleri, anjiyografi, optik koherens tomografi değişiklikleri ve yaşam kalitesi anketi skorları prospektif olarak değerlendirildi.

Bulgular: Hastalar ortalama 20±1 ay süreyle takip edildi. Ranibizumab enjeksiyonu sonrası görme keskinliğinde, 3 sıra ve üzerinde kazanımı olan 12 hasta (%25), 3 sıradan az kazanımı olan 28 hasta (%58.3), 3 sıradan az kaybı olan 6 hasta (%12.5) ve 3 sıradan fazla kaybı olan 2 hasta (%4.2)'dır. Yüksek tansiyon ve aile hikayesi pozitif olan hastalarda Erken Tedavi Diyabetik Retinopati Çalışmasındaki artış daha düşük oldu. Bu çalışmada, ranibizumab enjeksiyonu sonrası görme keskinliği artan hastalarda Ulusal Göz Enstitüsü Görsel Fonksiyon Anketi yaşam kalitesi değerlerinin arttığı tespit edildi ve bu fark istatistiksel olarak anlamlı bulundu.

Sonuç: İntravitreal ranibizumab enjeksiyonu ile tedavi edilen eksudatif tip yaşa bağlı makula dejenerasyonlu olguların görme keskinliğinde artış saptandı. Yaşa bağlı makula dejenerasyonu olan hastalarda Ulusal Göz Enstitüsü Görsel Fonksiyon Anketi güvenilir sonuçlar verdi ve işlem sonrası ankette puan artışı saptandı.

Anahtar kelimeler: Ranibizumab; makula dejenerasyonu

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INTRODUCTION

Age-related macular degeneration (AMD) is one of the leading reasons for vision loss and blindness in patients over 50 years of age1. Choroidal neovascularization (CNV), exudative or wet, is seen in only 10% of AMD patients and results in serious vision loss and it accounts for 80% of legal blindness2-4. Vascular endothelial growth factor (VEGF) plays a key role in retinal and subretinal fluid accumulation with increasing vascular permeability and neovascularization in pathogenesis of neovascular AMD, which reduces quality of life through affecting vision quality in old population. Ranibizumab, developed for the treatment of all subtypes of AMD, was approved in 2006. It has proved to be a reliable treatment method and quite effective in antiVEGF treatment of CNV5. In AMD, patient's vision acuity can be evaluated by such techniques as FA and optic coherence tomography (OCT), while various other tests are required for the evaluation of sociological and psychological effects. In this regard, it is important to assess the quality of daily life of patients, and therefore, the results of quality of life questionnaire are gradually gaining more importance6.

The aim of our study is to make clinical evaluations of FA and OCT changes in intravitreal ranibizumab-treated patients, compare quality of life results in pre- and post-treatment periods and determine to what extent this treatment increases quality of life.

MATERIALS AND METHODS

The study included a total of 48 patients who applied to Retina Unit of Department of Ophthalmology, Faculty of Medicine diagnosed with exudative AMD in ophthalmological examination and recommended with intravitreal ranibizumab injection. Patients with another evident ophthalmological disorder that could affect visual acuity and CNV development due to other ocular diseases like pathologic myopia and ocular histoplasmosis were not included in the study.

For this study, permission was granted from Ethical Committee of Faculty of Medicine. And all the patients included in the study were given detailed information about the study and their informed consents were obtained. The patients who applied to the Department of Ophthalmology and took intravitreal ranibizumab injection due to exudative age-related macular degeneration were prospectively evaluated. The evaluation criteria included FA and OCT changes in pre- and post-treatment periods, the best visual acuities corrected by sliding scales of snellen and ETDRS (Early Treatment of Diabetic Retinopathy Study), results of quality of life questionnaire and demographic characteristics. In addition, anterior segment examination with biomicroscope and dilated fundus examination with 78 D lens were performed.

The National Eye Institute Visual Function Questionnaire (NEI-VFQ) used in this study is a vision specific measurement method of health-related quality of life. This method gives a numeric outcome related to quality of life and enables comparison among patients. It is a 51-item questionnaire form developed to measure the effects of vision-specific functions and various ocular conditions on quality of life. NEI-VFQ 25 is a short form of NEI-VFQ7-11. The lesion size and type were determined in pre- and post-treatment periods for all patients. The quality of life questionnaire (VFQ-25-TR) was filled by the same researcher before and after ranibizumab injection to patients. Patients were subject to 3 doses of ranibizumab injection at an interval of one month and their controls were made in the 1st week, 1st month, 3rd month of injection and every three months in the subsequent period. For each control, the best corrected vision acuity (BCVA) was measured with Snellen and ETDRS scales, while fundus images were taken by Topcon Image Net and OCT images were obtained by spectral OCT SLO OPKO/OTI. Furthermore, ophthalmologic examination was made by biomicroscope and OCT and CNV were controlled. At the end of three injections, FA was controlled and post-treatment quality of life questionnaire was filled out again.

SPSS 18.0 packet software was used for the statistical analysis of data. Categorical measurements were summarized as numbers and percentages, while continuous measurements were given as mean and standard deviation (median and minimum-maximum, where needed). Chi-square test statistic was used for the intergroup comparison of categorical measurements. For the comparison of dependent measurements (e.g. pre and post), t-test was used if assumptions were met, and otherwise, Wilcoxon Signed Rank test was used. For the

analysis of interactions between continuous measurements, Pearson correlation was used if the assumptions were met, and otherwise, Spearman correlation was used. Statistical significance was set to 0.05 for all analyses.

RESULTS

The study included a total of 48 patients with a mean age of 69.81±9.843 (50-90) and diagnosed with wet AMD. The patient group consisted of 23 (48%) females and 25 males (52%). Of these patients, 14 (29%) had hypertension and 1 (2%) had diabetes. 23 patients (48%) were smoker and 6 patients (13%) had a positive family history. The lesions consisted of 36 (75%) subfoveal and 12 (25%) juxtafoveal lesions. In terms of lesion type, 19 (39.6%) were predominantly classic CNV, 18 (37.5%) occult CNV and 11 (22.9%) minimally classic CNV. The mean follow-up period of patients was 20±1 months.

Patients could read 49.29±5.8 (0-127) letters in ETDRS scale on average prior to treatment, while they were able to read 55.23±6.77 (0-152) letters after the treatment. The difference was statistically significant (p=0.003).

When the changes of visual acuity are categorized by ETDRS scale, it is seen that 12 patients (25%) gained 3 or more lines, 28 patients (58.3%) gained less than 3 lines, 6 patients (12.5%) lost less than 3 lines and 2 patients (4.2%) lost 3 or more lines. In the comparison of ETDRS changes by CNV, the statistical difference was not statistically significant (p=0.465). However, there was a statistically significant difference between CNV location and ETDRS (p=0.010). There was no significant difference between ETDRS changes and such factors as sex, smoking status and DM, while ETDRS increase was found lower in patients with HT (p=0.155) and positive family history (p=0.077) (Table 1).

Table 1. Demographic characteristics of the cases

Age (year)	Mean (±Standard deviation)	69.81±9.84
	Range of values	3 (50-90)
Sexuality (%)	Female	23 (48%)
	Male	25 (52%)
Type of choroidal neovascular membrane (%)	Predominantly classic	19 (39.6%)
	Minimally classic	11 (22.9%)
	Secret	18 (37.5%)
Location of choroidal neovascular membrane (%)	Subfoveal	36 (75%)
	Juxtafoveal	12 (25%)
Smoking status (%)	Smoker	23 (48%)
	Non-smoker	25 (52%)
Family history (%)	Present	6 (13%)
	Non-present	42 (87%)
Hypertension (%)	Present	14 (29%)
	Non-present	34 (71%)
Diabetes mellitus (%)	Present	1 (2%)
	Non-present	47 (98%)

The mean lesion width in FA was 5169.44±210.49 μm (2102-8285) prior to treatment while it was reduced to 4765.83±192.10 μm (1415-7300) after three ranibizumab injections. The difference was statistically significant (p<0.001). In FA, 47 patients (97.9%) had leakage prior to treatment, while leakage was detected in 20 patients (41.7%) after treatment. And, FA leakage was reduced or completely stopped in 28 patients (58.3%) (Figure 1).

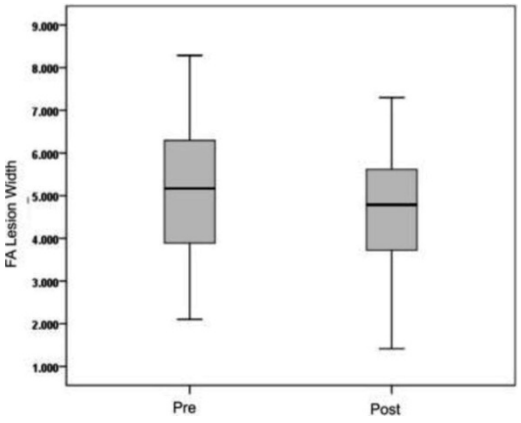

Figure 1. Changes in FA lesion width in pre- and post-treatment periods.

The central macular thickness was measured as 384.08±26.78 μm (140-890 μm) in OCT prior to treatment and it was reduced to 298.40±23.88 μm (140-885 μm) after treatment. Subretinal or intraretinal fluids were evident in 33 patients (68.8%) in OCT prior to treatment, while they persisted in 17 patients (35.4%) after treatment (p<0.001) (Figure 2).

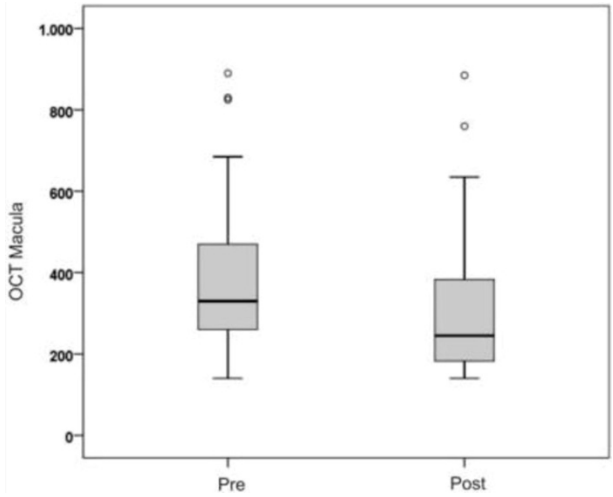

Figure 2. Changes in OCT macula in pre- and post-treatment periods

The mean score of NEI-VFQ 25 Quality of Life Questionnaire was 50.40±3.02 (6.21-93.07) prior to ranibizumab injection and it was determined as 59.26±3.03 (12.14-95) after three injections. The difference was statistically significant (p<0.001). The pre- and post-treatment changes in quality of life scale are given below (Figure 3).

Test results were lower in patients who filled out NEI-VFQ 25 Quality of Life Questionnaire and had low visual acuity in both eyes (6.21). The results were relatively higher in patients with low visual acuity in one eye, while patients with high socioeconomic level had lower scores even if they had low visual acuity in one eye. There was no statistically significant gain between CNV type and change in quality of life (p=0.363). However, the p level between CNV location and change in quality of life was 0.155. The increase in quality of life was higher in patients with juxtafoveal CNV than those

with subfoveal CNV. Furthermore, visual acuity increased more in patients with juxtafoveal CNV. Age and having disorder in one or both eyes were determined to have a significant effect on quality of life ($p<0.05$).

There was a significant relation between the increases in visual acuity and quality of life ($R2=0.683$; $p<0.001$). However, there was no statistically significant relation between CNV type and regression of lesion after ranibizumab injection ($X2=1.847$; S.D.=2; $P=0.397$). In the study, lesion resulted in disciform scar or neovascular scar in 41 patients (85.4%), while further intravitreal injections were recommended for 7 patients (14.6%) due to persisting CNV. FA and OCT images of the patients are given below (Figures 4-9).

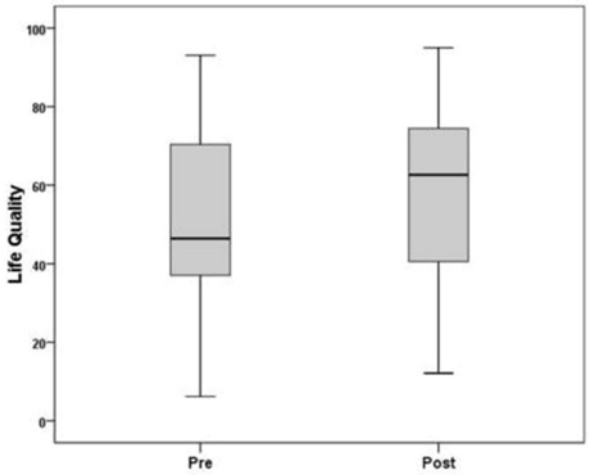

Figure 3. Changes in quality of life questionnaire in pre- and post-treatment periods

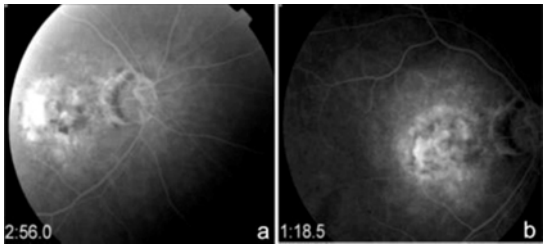

Figure 4. Pre-(a) and post-treatment (b) of subfoveal classic CNVM

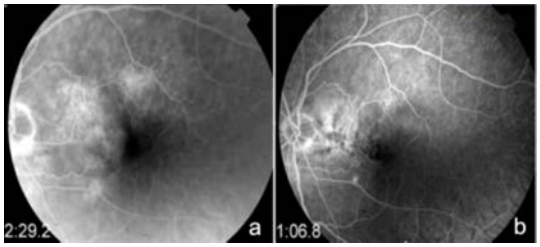

Figure 5. Pre- (a) and post-treatment (b) of juxtafoveal hidden CNVM

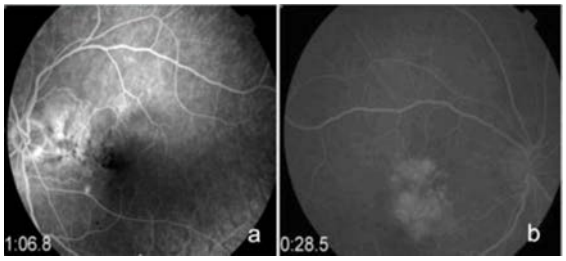

Figure 6. Pre- (a) and post-treatment (b) of subfoveal hidden CNVM

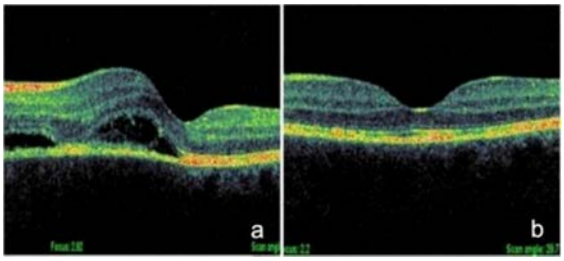

Figure 7. Pre- (a) and post-treatment (b) of serous PED

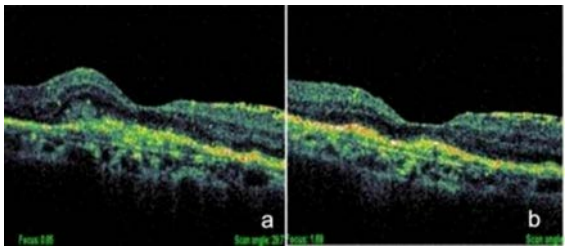

Figure 8. Pre- (a) and post-treatment (b) of subfoveal classic CNVM

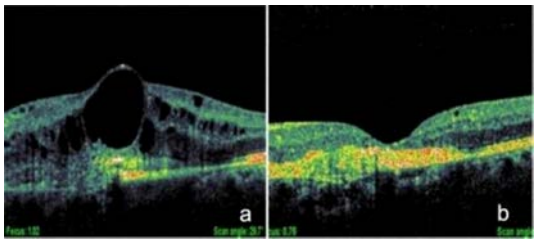

Figure 9. Pre- (a) and post-treatment (b) of patients with intraretinal fluid.

DISCUSSION

AMD is one of the most important reasons for advanced age-related central vision loss in the developed countries. In today's world, this disorder has become an even more important public health problem with the increasing life expectancy. In our study, age, sex, smoking status and family history of the cases were questioned as social risk factors and systemic diseases were also researched.

The previous studies have reported various results for AMD frequency in males and females. Although no significant gender difference was detected considering AMD prevalence in BMES study groups, early and late AMD prevalence and incidence were found higher in males in studies conducted in Japan. These rates were higher in females in NHANES III and BDES study groups[12-14]. The sample group of the current study consisted of 25 male patients (52%) and 23 female patients (48%), and there was no significant gender difference.

Smoking is a serious risk factor for wet and dry AMD. It has been observed in the BMES; BDES and RES study groups that smoking is an independent and controllable risk factor in the development of AMD[15,16]. In this regard, 23 (48%) out of 48 patients included in the present study were smoker. Smoking status was positive in approximately 1 of each 2 patients. In the study, no statistically significant difference was detected between treatment and ETDRS change (gain or loss) in smoking patients.

Considering systemic diseases, 14 (29%) out of 48 patients were determined to have hypertension and 1 patient (2%) had diabetes mellitus. The relation between AMD and diabetes mellitus could not be established in epidemiological studies, which was supported by the results of the current study. In the studies of Hyman et al.[17] and BMES[18], a statistically significant relation was detected between neovascular AMD and diastolic blood pressure. In our study, HT prevalence was determined as 29% among the patients, and ETDRS increase was lower in patients who were treated and had HT compared to those without HT. The difference was statistically significant. It is considered that HT takes part in pathogenesis of AMD and negatively affects the response to the treatment. Establishing cardiovascular stability in AMD patients applying to polyclinic positively affected the prognosis, as well.

In addition, ETDRS increase was found lower in patients with 13% of positive family history in the current study. This indicates that prognosis was more negative in patients with HT and positive family history. Assink et al.[19] reported that patients with positive family history are under higher risk of developing late AMD, which supports our findings.

The results of two-year MARINA study have demonstrated that the most important indicators of visual prognosis are visual acuity, KNVM size and KNVM type. In the current study, ETDRS increase was higher in patients with higher initial visual acuity and the difference was statistically significant[20,21]. Furthermore, there was no significant relation between KNVM type and visual prognosis in the study. However, visual prognosis was better in juxtafoveal lesions.

It is concluded that ranibizumab has more positive effects on BCVA, prevents vascular leakage, increases retinal thickness, and consequently, strengthens visual acuity and visual functions. It has also fewer side-effects compared to other treatment methods[22]. In our study, visual acuity increased both in snellen and ETDRS scales following ranibizumab injection and the difference was statistically significant. At present, there is a growing need for subjective and patient-based evaluations of visual

function in order to determine treatment methods. Questionnaires assessing the effects of therapeutic interventions on life quality of patients provide more subjective and comprehensive information. National Eye Institute Visual Function Questionnaire (NEI-VFQ), the most widely used questionnaire of health-related quality of life, is the first quality of life questionnaire translated into Turkish by Toprak et al.[6]. Besides decreasing visual acuity, some other complaints like low contrast detection, photopsia, low color vision and light-induced glare could also be present in AMD. Quality of life questionnaire becomes more important as it simultaneously evaluates all these symptoms. General health problems and all other problems about near acuity, peripheral vision, color vision, dark vision, mental health and social functions are simultaneously taken into consideration in NEI-VFQ questionnaire used in the current study. The numerical outcome of all these functions provides a unique guidance.

In this study, such factors as age and having disorder in one or both eyes were determined to have significant effects on quality of life. There was a significant relation between the increases in visual acuity and quality of life. Test results were lower in patients filling in NEI-VFQ 25 quality of life questionnaire and having low visual acuity in both eyes (6.21%). Patients with low acuity in one eye had relatively higher results, while some patients with low acuity in one eye had interestingly lower results in quality of life. This can be attributed to the fear of losing the present vision.

Iyigun and Bayer[23] carried out a study on 210 individuals and investigated the reliability and validity of NEI-VFQ in patients with cataract, glaucoma, diabetic retinopathy and AMD. Consequently, a strong relation was detected among global and subgroups of NEI-VFQ test in all disease groups ($r>0.80$). There was also a statistically significant difference between control and patient groups.

In conclusion, this test was accepted as a valid and reliable method for determining the quality of life in patients with chronic ophthalmological disorder. Similarly, in the current study, NEI-VFQ 25 Quality of Life results were determined to increase in patients whose visual acuity increased after intravitreal ranibizumab injection and the difference was statistically significant[24,25].

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