Electrophysiologic Changes After Panretinal Argon Laser Photocoagulation in Patients with Diabetic Retinopathy

Diyabetik Retinopatili Olgularda Panretinal Argon Lazer Fotokoagülasyon Sonrası Elektrofizyolojik Değişiklikler*

Ayşe ÖNER[1], Cengiz AKARSU[2], Hatice ARDA[3], Koray GÜMÜŞ[4], Sarper KARAKÜÇÜK[1], Ertuğrul MİRZA[1]

ABSTRACT

Purpose: The aim of this study is to evaluate the changes in functions of the retina and electrophysiologic tests after panretinal photocoagulation (PRP) in patients with diabetic retinopathy.

Material and Methods: 21 eyes of 21 diabetic patients with diabetic retinopathy who received laser treatment were included in the study. At each visit a complete ophthalmic examination was performed including electrophysiologic tests (ERG, PERG, PVER and FVER).

Results: When compared with pretreatment values there was not a statistically significant reduction in the amplitudes and latencies of P50 and N95 waves of PERG, P 100 waves of PVER at the first month recordings after PRP. However we found a statistically significant reduction in the b wave amplitude of rod response, maximal combined response and cone response at the first month recordings after PRP.

Conclusion: These findings indicated that both rods and cones could be damaged during the PRP treatment, however the damage might be more significant in the rod photoreceptors.

Key Words: Argon laser, diabetic retinopathy, electrophysiology.

ÖZ

Amaç: Bu çalışmanın amacı diabetik retinopatili olgularda panretinal argon laser fotokoagülasyon (PRF) sonrası retina fonksiyonlarında ve elektrofizyolojik testlerde oluşan değişiklikleri değerlendirmektir.

Gereç ve Yöntem: Lazer tedavisi alan 21 olgunun 21 gözü çalışmaya dahil edildi. Her kontrolde elektrofizyolojik testleri (ERG, PERG, PVER and FVER) de içeren tam oftalmolojik muayene yapıldı.

Bulgular: Tedavi öncesi değerler ile PRF'den bir ay sonraki değerler karşılaştırıldığında PERG'in P50 ve N95 dalgasının, PVER'in P100 dalgasının amplitüd ve latansları arasında istatistiksel olarak anlamlı farklar yoktu. Bununla beraber birinci ayda yapılan kayıtlarda rod yanıtının, maksimal kombine yanıtın ve kon yanıtının b dalga amplitüdünde anlamlı olarak azalma saptandı.

Sonuç: Bu bulgular PRF sırasında her iki tür fotoreseptörün de hasar görebileceğini ancak rodlardaki hasarın daha belirgin olabileceğini gösterir.

Anahtar Kelimeler: Argon lazer, diabetik retinopati, elektrofizyoloji.

Bu çalışma TOD 44. Ulusal Oftalmoloji Kongresi, (Antalya, 2010) sunulmuştur.

1- M.D. Professor, Erciyes University Faculty of Medicine, Department of Ophthalmology, Kayseri/TURKEY
ONER A., aoner@erciyes.edu.tr
KARAKUCUK S., sarperkarakucuk@gmail.com
MIRZA E., gemirza@mynet.com
2- M.D, Erciyes University Faculty of Medicine, Department of Ophthalmology, Kayseri/TURKEY
AKARSU C., cakarsu@hotmail.com
3- M.D. Asistant Professor, Erciyes University Faculty of Medicine, Department of Ophthalmology, Kayseri/TURKEY
ARDA H., harda@erciyes.edu.tr
4- M.D. Associate Professor, Erciyes University Faculty of Medicine, Department of Ophthalmology, Kayseri/TURKEY
GUMUS K., drkorayg@hotmail.com

Geliş Tarihi - Received: 17.03.2014
Kabul Tarihi - Accepted: 27.08.2014
Ret-Vit 2015;23:21-25

Yazışma Adresi / Correspondence Adress: M.D. Professor, Ayse ONER
Erciyes University Faculty of Medicine, Department of Ophthalmology, Kayseri/TURKEY

Phone: +90 530 283 16 11
E-mail: aoner@erciyes.edu.tr

INTRODUCTION

Diabetes mellitus is a chronic disorder characterized by the impaired metabolism of glucose due to insulin deficiency or its resistance, leading to hyperglycemia and late development of vascular and neuropathic complications. Diabetic retinopathy is a potentially blinding complication of diabetes mellitus.[1-3]

Laser photocoagulation is accomplished by directing a focused laser beam of a discrete wavelength onto specified parts of the retina. Its absorption in a variety of intra-ocular pigmented retinal layers, causes a local rise in temperature which in turn causes denaturation of tissue proteins and coagulative necrosis. Laser treatment is used to treat diabetic macular edema either in the form of focal or grid using small spot size, short duration and low power enough to produce whitening of the retina. Panretinal photocoagulation (PRP) is indicated for the treatment of high-risk proliferative diabetic retinopathy and eyes with severe non-proliferative diabetic retinopathy (NPDR) and early proliferative diabetic retinopathy (PDR) that are at high risk for progression or for poor outcome. The aim of PRP is to prevent the onset or induce the regression of neovascularization without vitreous hemorrhage or fibrovascular proliferation. This is performed by destroying the ischemic peripheral retina with '1500-3000' burns that spare the disk, the macula and maculopapillary nerve bundle. It is done using enough power to produce a mild-to-moderate white burn, using shorter burn duration for patients' comfort. This will result in concentrating the remaining retinal blood flow onto the macula and adjacent important areas. Laser photocoagulation is not without adverse effect.[4,5]

The evaluation of the functional properties of the diabetic retina with objective methods, such as electroretinography (ERG), pattern ERG (PERG), and visual evoked response (VER), is an important aspect of the diagnostic and therapeutic approach to diabetic retinopathy.[6,7] The focus of this paper will be to evaluate the changes in functions of the retina and electrophysiologic tests after PRP in patients with diabetic retinopathy.

MATERIAL AND METHOD

This prospective, non-comparative case series included 21 eyes of 21 diabetic patients (13 women, 8 men) with diabetic retinopathy who received laser treatment according to Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol.[4]

Exclusion criteria were as follows: (I) subjects who had previous therapies for diabetic retinopathy (laser therapies, including grid-laser treatment and/or PRP, intravitreal injection of any drugs, vitreous surgery), (II) Type I DM (since the progression of the retinopathy is different from type II), (III) any media opacities (cataract, vitreous opacities, corneal opacities etc.), any ocular disease apart from diabetic retinopathy (optic nerve, retina etc.) that may affect electroretinographic evaluation, (IV) A best corrected visual acuity less than 0.1 (since PERG results are likely to be affected by low vision), (V) subjects receiving systemic treatment that may affect electroretinographic evaluation.

The study protocol was approved by the Local Ethical Committee. The research followed the tenets of the Helsinki Declaration. After explaining to the patients the purpose of the study and the possible outcomes, informed consent was obtained from all patients prior to the interventions.

At each visit (before and after the laser treatment), a complete ophthalmic examination was performed which included, best corrected visual acuity testing, applanation tonometry, slit-lamp examination, dilated fundus biomicroscopy, and fundoscopy, color fundus photography, fluorescein angiography and electrophysiological testing including ERG, PERG, patern VER (PVER) and flash VER (FVER).

Laser Procedure: PRP is indicated for the treatment of eyes with severe NPDR and early PDR that are at high risk for progression or for poor outcome according to the results of ETDRS.[4] Our standard technique for full PRP included '1600-2000' laser burns using '300- 500' micron spots, separated from each other by one half burn width at 0.2 s duration which was performed in four or five sessions separated by 1-2 weeks. Focal or grid laser was done before PRP treatment with 100 micron spots, 0.1 s duration and 100 mv laser power.

Electrophysiological Tests: All of the electrophysiologic tests were recorded with Tomey Primus 2.5 (Tomey GmbH, Erlangen, Germany) in accordance with the guidelines of the International Society for Clinical Electrophysiology of Vision (ISCEV).[8-10] FVER, PVER and PERG procedures were done first with an undilated pupil followed by ERG test which was performed with a dilated pupil.

Statistical Analysis: All statistical analysis were performed using the software SPSS 10.0 for Windows (SPSS Inc., Chicago, IL, USA). A p value of 0.05 or less was considered as statistically significant; student t- test was used to analyze the electrophysiologic parameters. The results were expressed as mean values with their standard deviation (SD).

RESULTS

Demographic characteristics of the patients are shown in table 1. Twenty one eyes of 21 patients (13 females, 8 males) were included in this study. All of the patients had diabetic retinopathy due to type II diabetes mellitus. Mean age of the patients was 63.8±7.2 years. The visual acuity of all eyes were better than 1/10 Snellen lines and the mean value of the visual acuity before the treatment was 0.46±0.14 Snellen lines. One eye had mild vitreus hemorrhage, however it was possible to see the details of the fundus and to perform the PRP. Anterior segment evaluations were normal and the intraocular pressure measurements were in normal limits in all patients before and after treatment. One month after PRP the visual acuity improved in 4 eyes (19%), remained unchanged in 9 eyes (42.8%) and deteriorated only one Snellen line in 8 eyes (38.2%). None of the patients showed a decrease in visual acuity more than 2 lines after the treatment. The mean value of the visual acuity after the treatment was 0.45±0.15 Snellen lines and the difference was not statistically significant (p>0.05). No ocular and systemic adverse event occured during or after the treatment period.

When compared with pretreatment values there was not a statistically significant reduction in the amplitudes of P50 and N95 waves at the first month recordings after PRP (p>0.05), (Table 2).

The results of the F-VER and P-VER values are shown in Table 3. When compared with pretreatment values there was not a statistically significant change in the amplitudes and latencies of P 100 waves at the first month recordings after PRP (p>0.05). The results of the ERG responses are shown in table 4.

Table 1: *Demographic characteristics of the patients.*

Gender (Female/Male)	13/8
Age (Year)	63.8±7.2
Duration of diabetes (Year)	17.2±2.7
Glucose level (mg/dl)	189.9±53.3
HbA1c level (%)	8.5±1.1

Table 2: *The results of PERG tests.*

	Before treatment	After treatment	p value
P50 amplitude (μv)	1.66±0.89	1.84±0.98	0.333
P50 wave latency (ms)	56.35±5.74	54.44±7.35	0.297
N95 wave amplitude (μv)	3.01±1.37	2.88±1.61	0.790
N95 wave latency (ms)	93.17±17.73	96.27±6.24	0.473

Table 3: *The results of FVER and PVER before and after the treatment of PRP.*

VER Tests	Before treatment	After treatment	p value
Flash VER P100 amplitude (μv)	11.23±5.95	11.89±5.97	0.653
FlashVER P100 latency (ms)	102.42±23.57	107.85±20.83	0.180
Patern VER P100 amplitude (μv)	6.27±2.46	5.89±2.22	0.495
Patern VER P100 latency (ms)	104.01±15.67	108.23±16.88	0.366

Table 4: *The results of electrophysiological tests before and after treatment (amp: μV lat: ms).*

ERG Tests	Before treatment	After treatment	p value
Rod response b wave amplitude	113.00±38.76	70.50±37.01	**0.000**
Rod response b wave latency	81.49±13.44	87.26±8.17	0.088
Maximal combined response a wave amplitude	81.99±27.60	68.99±31.77	0.206
Maximal combined response a wave latency	32.76±39.04	28.91±21.68	0.680
Maximal combined response b wave amplitude	188.76±56.50	140.67±73.98	**0.036**
Maximal combined response b wave latency	71.88±103.40	74.29±13.28	0.393
Cone response a wave amplitude	19.56±4.03	17.96±3.83	0.162
Cone response a wave latency	17.02±2.81	18.71±3.01	0.348
Cone response b wave amplitude	56.51±18.15	40.16±33.18	0.047
Cone response b wave latency	31.86±3.03	49.49±71.87	0.278

When compared with pretreatment values we found a statistically significant difference in the b wave amplitude of rod response, maximal combined response and cone response at the first month recordings after PRP ($p<0.05$). Although there was a decrease in the amplitudes of other ERG responses and there was a delay in the latencies of all ERG responses, the differences were not statistically significant.

DISCUSSION

Results of the ETDRS[4] and Diabetic Retinopathy study (DRS)[5] have provided the strongest evidence to establish the place of panretinal photocoagulation as a standard technique for treating severe non-proliferative and proliferative diabetic retinopathy. Full PRP as used by ETDRS and DRS included 1200 or more burns separated from each other by one half burn width. It also had shown that panretinal photocoagulation reduces the risk of moderate and severe visual loss by 50% in patients with severe NPDR and PDR.

Clinical retinal photocoagulation is predominantly a thermal photocoagulation of the melanin-containing retinal epithelial cells. This results in thermal destruction of the retinal pigment epithelium cells, the adjacent photoreceptors, and to some degree the choriocapillaris.[11]

Laser photocoagulation is not without adverse effect. The major adverse effects of PRP include visual field constriction, night blindness, color vision changes, accidental laser burn to macula.[12,13] Increased diabetic macular edema (DME) following argon laser PRP has been observed for decades.[13,14] Eyes with macular edema undergoing PRP for severe NPDR or PDR are twice as likely to lose 2 or more lines of visual acuity at 6 weeks post treatment as are eyes without macular edema (18% vs 9%), presumably because of worsened macular edema.[15]

In a recent study, Shimura and associates[14] report the effects of PRP on 64 consecutive patients with severe NPDR or early PDR, no visual symptoms, and 20/20 or better visual acuity. The study reported that four session PRP separated by 2 weeks with simple focal laser treatment for the macular edema would avoid parafoveal thickening. In our study we performed focal or grid laser before PRP treatment and PRP was done in 4 sessions seperated by 1-2 weeks period. The PERG results after PRP showed no amplitude reduction and none of the patients showed a decrease in visual acuity more than 2 lines after the treatment. Our findings suggest that performing PRP in seperated sessions with preceding macular laser would avoid worsening of macular edema and preserve the central macular function.

There are severeal studies including electrophysiological results after PRP in the literature. In a study by Ogden et al. the ERGs from 14 patients with proliferative diabetic retinopathy were recorded before and after peripheral retinal ablation by photocoagulation and they reported a decrease of ERG amplitude that varied from 10 to 95% among the patients, an increase in ERG latency and implicit time in several patients. This suggests a wide variability in the area of retina affected by the treatment, and the possibility of an effect of the procedure on adjacent untreated retina in some diabetic patients.[16] In an other study,[17] ERG responses were measured in diabetic patients before, during, and after panretinal photocoagulation treatment with argon laser. The laser applications reduced considerably the amplitudes of the a and b waves of the ERG. These findings indicated that the photocoagulation treatment not only destroyed the retinal areas directly illuminated by the laser beam, but also affected the functional integrity of adjacent areas. These additional effects resulted in subnormal signal transmission from the photoreceptors to the proximal retina. In an other electroretinographic study it was found that amplitude reductions were higher for scotopic b-waves and implicit times did not change significantly.[18] In our study, amplitude reductions were found in b waves of the rod, maximal combined and cone responses and reduction was higher for the rod b wave. These changes in the ERG amplitudes are consistent with defects in the midretinal layer and may reflect sensitivity losses at the level of the receptors. There may be a number of reasons for these electroretinographic changes, among them reduction in number of photoreceptor or change in channel density within the photoreceptor outer segments could be mentioned. As a result, we found photoreceptor function to be altered after PRP and both of the photoreceptors could be damaged during the PRP treatment, however the damage might be more significant in the rod photoreceptors.

In a study including color vision, PVER and PERG tests after argon laser treatment, it was found that PERG amplitudes were significantly reduced one day after the laser treatment, while 5 weeks after the laser coagulation, visual acuity and PERG amplitudes recovered to pretreatment values. Since fluorescein angiography revealed no macular changes after laser treatment, the possibility of a reversible functional light damage after blue-green argon laser coagulation is discussed.[19] In our study, there was no significant reduction in the amplitudes of PERG and PVER test in the first month recordings. We did not perform the tests during the first month after PRP, so we did not have the results of electrophysiological tests during the recovery period. This unaffected results of PVER and PERG might be due to the timing of the tests or as discussed before this might be due to the technique of the PRP application which might minimize the damage to the retina.

Another study,[20] investigated retinal function in relation to spot size and scatter density after panretinal laser coagulation which compared 400 comparatively large laser spots with 1500 small spots and subjective parameters (visual acuity, perimetry, dark adaptation, photostress), as well as objective functions (ERG, electro-oculogram) were studied preoperatively and then postoperatively over a time span of 6 months. When the pairs of eyes were compared, persistent visual field scotomas as detected by computerized static perimetry, occurred less frequently in eyes subjected to small coagulation spots, although this tendency was not statistically significant. In our study, we used small spot size (300 µm) to reduce the damaging effect of PRP to the retina.

There are some limitations of this prospective study. The follow-up period might be longer than 6 months to investigate the persistance of the electrophysiological effects. This study is going on and 6 months and one-year follow-up results will be published in the future. Multifocal ERG test may be added to the electrophysiological tests to strenghten the scientific value of the study.

Future prospective, randomized, controlled studies are needed including long term follow-up periods and new electrophysiological techniques which compare different kind of laser devices.

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