LASER PHOTOCOAGULATION IN DIABETIC MACULAR EDEMA: EFFECTS ON VISUAL ACUITY AND MACULAR EDEMA

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Abstract - Due to the importance of clinically significant macular edema in diabetic patients, this study is aimed to determine if laser photocoagulation is effective in the treatment of clinically significant diabetic macular edema. In addition, the effects of risk factors are surveyed. This is an existing data study considering patients with clinically significant diabetic macular edema, treated with argon-green laser photocoagulation in Labbafinejad hospital, department of lasertherapy, from 1995 to 1997. In 60 (42.6%) eyes the treatment method was focal, in 22 (15.6%) eyes grid, and in 59 (41.84) modified grid laser photocoagulation was performed. The results are based upon deterioration of visual acuity, occurance of moderate visual loss and improvement or persistence of CSME. We studied 114 eyes from 87 patients. Two years after initial treatment, visual acuity improved in 19.1% of eyes, unchanged in 9.5% and worsened in 71.4% of eyes. After this period the rate of moderate visual loss was 28.6% and CSME was improved in 23.8% of eyes. According to our study, baseline visual acuity and retinopathy severity were two important intervening factors in response to lasertherapy. Comparing our results with natural course of diabetic macular edema, indicates that in assessing visual outcome laser photocoagulation is an effective modality in treatment of CSME, but it is not effective in maintaining or improving visual acuity, which is due to patients delay in visiting ophthalmologists and paying not enough attention to follow-up visits.

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INTRODUCTION

Macular edema is the accumulation of excess fluid in the extracellular space within the retina in the macular area (1). Clinical signs of this fluid accumulation might include retinal thickening and hard exudate, with leakage in fluorescein angiography (2). Macular edema is the leading cause of vision loss in patients with diabetes mellitus and occurs in approximately 10% of the diabetic population (3). Considering diabetes as the most common endocrine disorder involving up to two percent of general population adds more to the importance of surveying retinal complications of this disorder in society (4). The prevalence and incidence of macular edema increases with both longer duration and overall level of concurrent retinopathy. For those patients with twenty or more years duration of disease the prevalence increases to approximately 25%. According to long term epidemiologic studies macular edema occurs in 20.1% of patients with type 1 and 18.6% of patients with type 2 diabetes. Medical attempts to improve diabetic maculopathy have no effect on the macular edema that is the cause for the functional impairment (5, 6), and the principal treatment currently available for macular edema is photocoagulation (7-12). Patz and Schatz were among the first scientists to show that photocoagulation, reduces the risk of moderate visual loss in diabetic macular edema. Reports from the Early Treatment Diabetic Retinopathy Study (ETDRS) demonstrated that focal treatment of clinically significant macular edema was effective in reducing the risk of visual loss by about 50% (13-15). According to some clinical studies paracentral scotomata, subretinal fibrosis (16-17), subfoveal neovascularization, iris burn (18-22), choroidal neovascularization (23) and progressive enlargement of laser scars (24) were complications of laser photocoagulation for diabetic macular edema. In this study we present the results of laser photocoagulation in 114 eyes from 87 patients with diabetic CSME in Labbafinejad Hospital, Department of

Lasertherapy to see if laser photocoagulation is effective in the treatment of diabetic macular edema. Our results are based upon deterioration of visual acuity, occurance of moderate visual loss and improvement or persistence of CSME.

MATERIALS AND METHODS

This study is based on existing data of 114 eyes from 87 patients, with clinically significant diabetic macular edema, treated with argon-green laser photocoagulation in our Department from 1995 to 1997. Ophthalmologic exclusion criteria included all of the following: previous laser photocoagulation within two disc diameters of the center of the macula; preretinal or vitreous hemorrhage at the time of evaluation for entry; proliferative diabetic retinopathy; history of retinal detatchment or retinoschisis; significant media opacity; iris neovascularization; previous retinal or other intraocular surgery that could interfere with adequate treatment or follow-up; history of glaucoma or any other ocular disease, that could affect the assessment of treatment results; myopia of more than 3 dpt; age-related macular degeneration; congenital ocular anomalies; amblyopia and cataract. Those who had cataract extraction before enrollment into the study were not excluded.

Paraclinical data consisted of measaring fasting blood sugar, blood urea nitrogen, serum creatinine, triglyceride and cholesterol levels and urine analysis. In follow-up visits, all of the baseline clinical examinations were recorded again and compared. Outcome assessments were based upon deterioration of visual acuity, occurence of moderate visual loss and improvement or persistence of CSME.

For computerized statistical analysis, the data were gathered as a database, using EPI-6 software. For evaluating the effects of background or confounding factors in outcome assessments, Yat's corrected chi square, was used and when one of the frequencies was less than 5, Fisher's exact test was used. For comparing our results with the results of other studies, we used Z test for comparison of proportions. The method we used for comparing visual acuity results was one-tailed paired t-student test.

It should be noticed that our treatment techniques - focal, grid and modified grid laser photocoagulation - are just the same as ETDRS and Olk's methods (13, 14).

RESULTS

The characteristic features of our patients are as following:

Thirty - four patients were male (43.6%) aged equal or more than 60 years (range= 14-85 years., mode= 60 years). Seventy - six patients had NIDDM (67.4%) and 2 (2.6%) had IDDM. Fifty-seven patients (73.1%) had controlled hyperglycemia with oral hypoglycemic agent (OHA) and 21 (26.9%) used OHA. At the beginning of the study, in 20 patients (25.6%), the duration of diabetes was under 10 years and in 68 patients (74.4%), equal to, or more than 10 years. (range= 3-34 years, mean= 13.25 years, mediam= 13 years, SD= 6.13 years and mode= 10 years). Among our patients, 5 (6.4%) had neuropathy, 5 (6.4%) nephropathy, 32 (41%) hypertension, 12 (15.4%) hyperlipidemia and 13 patients (16.7%) had cardiovascular disorders. Three patients (3.8%) used aspirin, 2 (2.6%) diuretics, 24 (30.8%) antihypertensive agents and 4 (5.1%) used cardiac glycosides. Twelve (10.5%) eyes had mild NPDR, 56 (49.1%) moderate and 46 (40.4%) had severe NPDR. Twenty-two (28.2%) patients had only right eye involvement, 20 (25.6%) had only left eye involvement and in 36 (46.2%) patients both eyes were involved. Among the involved eyes, 58 (50.8%) were on the right and 56 (49.2%) left. In 10.5% (12) of the eyes, there was a positive history of cataract surgery before beginning the study, but considering ocular medial opacity, they were elligible for the study. At the beginning of the study, baseline visual

Table 1. Frequency distribution of baseline visual acuity state in 114 eyes from 87 patients with diabetic CSME, treated in Labbafinejad hospital, department of Lasertherapy, from 1995 to 1997

Baseline Visual Acuity	n	%
20/200-20/40	61	53.5
20/40-20/25	27	23.7
20/25-20/15	26	22.8
Total	114	100%

(range=20/200-20/15, mean= 0.48, mode= 20/40, SD= 0.33)

acuity was determined and summarized in Table 1.

Before lasertherapy, all eyes had CSME. Among them, there was focal macular edema in 42.98% and diffuse macular edema in 57.02% of eyes.

Argon-laser was used for photocoagulation in all our patients. Total lasertherapy sessions including first and probable recurrent treatments was 141. In 60 (42.6%) eyes, the treatment method was focal, in 22 (15.6%) eyes, grid and in 59 (41.8%) eyes, modified grid laser photocoagulation was performed.

Considering all laser treatments, mean power was 309.292 mV, duration was 0.1 sec, spot size was 100 mic. and mean value for number of laser spots was 116.10 per eye. In 89 eyes (78.1%) only one session, in 23 eyes (20.2%) two and in 2 eyes (1.7%) three sessions of lasertherapy was performed. Visual acuity in each of the follow-up visits is recorded in Table 2 and the rates of moderate visual loss in each period is summarized in Table 3.

Visual acuity in each follow-up visit is compared with its baseline value. One-tailed paired t-student test was used for the comparison of visual acuity before and after treatment (Table 4).

The state of CSME in each follow-up visit is presented in Table 5. The effects of systemic disorders in the outcome of treatment either as background or as confounding factors has been assessed and the results are presented in Tables 6, 7 and 8. The rates of macular ischemia in each of the follow-up visits are summarized in Table 9.

Table 2. Frequency distribution of visual acuity in each follow-up visit of (FV).

Visual acuity	1st FV n(%)	2nd FV. n(%)	3rd FV. n(%)	4th FV. n(%)	5th FV. n(%)
Improved	26(22.8)	20(23)	18(25.7)	6(19.4)	4(16)
No change	37(32.5)	27(31)	19(27.2)	5(16.1)	2(9.5)
Worse	51(44.7)	40(46)	33(47.1)	20(64.5)	15(71.5)
Total	114(100)	87(100)	70(100)	31(100)	21(100)

FV= Follow-up Visit n = number

Table 3. Frequency distribution of moderate visual loss

Moderate visual loss	n	%
First FV	15	13.2
Second FV	14	16.1
Third FV	15	21.4
Fourth FV	7	22.6
Fifth FV	6	28.6.

Table 4. Statistical results of comparison between post and pre treatment visual acuity results in each follow-up visit

Number of FV	Mean of VA difference before and after therapy	Standard deviation	P-value	S/NS
First	-0.029	0.258	0.118	NS
Second	-0.050	0.260	0.037	S
Third	-0.044	0.266	0.083	NS
Fourth	-0.095	0.277	0.033	S
Fifth	-0.120	0.307	0.043	S

S=Significant NS=Non significant

Table 5. Frequency distribution of CSME in each follow-up visit

No. of follow up visit	Total no.of eye	No. of eyes with CSME	%
First	114	42	36.8
Second	87	35	40.2
Third	70	33	47.1
Fourth	31	20	64.5
Fifth	21	5	23.8

Complications of Lasertherapy

Visual scotoma, did not appear in any of the eyes during each of the follow-up periods. No sign of subretinal fibrosis or choroidal neovascula - rization appeared in our patients during these periods.

Table 6. Intervention of risk factors in VA response

Variant	FV-1 (P-value)	FV-2 (P-value)	FV-3 (P-value)	FV-4 (P-value)	FV-5 (P-value)
Basline VA	0.0003(S)	0.0133(S)	0.0030(S)	0.4337(NS)	0.3069(NS)
Baseline retinopathy severity	0.7006(NS)	0.6096(NS)	0.3558(NS)	0.7295(NS)	0.2804(NS)
No.of treatments	0.1877(NS)	0.2824(NS)	0.3147(NS)	0.3922(NS)	0.2853(NS)
Type of macular edema	0.5480(NS)	0.2265(NS)	0.9781(NS)	0.5769(NS)	0.0553 (S)
Digoxin	0.1419(NS)	0.0090(S)	0.0997(NS)	0.6452(NS)	*

* = Frequency is zero and statistical analysis is impossile; FV = Follow-up visit; NS = None significant; S = significant

Table 7. Intervention of risk factors in CSME response

Varient	FV-1 (P-value)	FV-2 (P-value)	FV-3 (P-value)	FV-4 (P-value)	FV-5 (P-value)
Baseline VA	0.0522(S)	0.0256(S)	0.1385(NS)	0.3301(NS)	0.3442(NS)
Baseline retinopathy severity	0.2943(NS)	0.0343(S)	0.0695(S)	0.3710(NS)	0.5613(NS)
No. of treatments	0.0032(S)	0.0056(S)	0.0171(S)	0.8442(NS)	0.1700(NS)
Type of macular edema	0.8607(NS)	0.4357(NS)	0.3514(NS)	0.0140(S)	0.0984(NS)
Digoxin	0.4880(NS)	0.5434(NS)	0.5434(NS)	0.3548(NS)	*

Table 8. Statistical results of risk factors intervention

Variant Relation	FV-1 (P-value)	FV-2 (P-value)	FV-3 (P-value)	FV-4 (P-value)	FV-5 (P-value)
Macular ischemia and VA response to lasertherapy	0.1932(NS)	0.3391(NS)	0.8344(NS)	0.4684(NS)	0.0936(NS)
Macular ischemia and CSME response to lasertherapy	0.004(S)	0.00008(S)	0.0001(S)	0.0519(S)	0.5497(NS)
Digoxin and baseline retinopathy severity	0.0401(S)	0.0128(S)	0.1725(NS)	0.5340(NS)	*
Macular edema and baseline VA	0.0008(S)	0.0118(S)	0.0322(S)	0.1693(NS)	0.7010(NS)
Macular edema and baseline retinopathy severtiy	0.0195(S)	0.0060(S)	0.9497(S)	0.2592(NS)	0.4143(NS)
Macular edema and macular ischemia	0.4999(NS)	0.1774(NS)	0.4645(NS)	0.2121(NS)	0.4381(NS)
Baseline VA and VA response to lasertherapy	0.5845(NS)	0.4285(NS)	0.1253(NS)	0.7314(NS)	0.3665(NS)

Table 9. Frequency distribution of macular ischemia in each follow-up visit

No. of follow-up visit	Total No. of eye	No. of eyes with macular ischemia	%
First	114	28	24.6
Second	87	26	29.9
Third	70	21	30.0
Fourth	31	13	41.9
Fifth	21	10	47.6

DISCUSSION

Among all the researches, concerning the effects of laser photocoagulation in diabetic macular edema, ETDRS and Olk's studies are most prominent. After one year of ETDRS research, the rate of occurence of moderate visual loss was 5% in treated and 8% in untreated group (14). In our study, after a similar period, the rate of moderate visual loss has been estimated 21.4%. Compared with controlled group in ETDRS (natural course of diabetic macular edema), lasertherapy was not a successful method in our patients (P-value=0.0001). In ETDRS, the rate of moderate visual loss was 7% in the treated group, and 16% in the untreated group after two years (14). After a similar period in our study the rate of moderate visual loss came about 28.6%, therefore laser photocoagulation has not effectively decreased the rate of moderate visual loss after two years (P-value=0.0571). After one year of following-up ETDRS patients, the rate of remaining CSME was 35% in treated and 63% in untreated group (14). In our study, 52.9% of the patients showed CSME after one year of follow-up. Although the comparison of our results with untreated ETDRS patients shows that our laser photocoagulation was effective in treatment of CSME (P-value=0.040), there is a significant difference between our patients and ETDRS treated group. Another important study which should be taken in mind is Olk's research. As his patients were very similar to ours in age, sex, visual acuity (VA), and severity of

retinopathy, his results are important for comparison (13). In Olk's research, after one year, the rate of moderate visual loss was 27% in the untreated and 4% in the treated eyes. After a similar period in our study, 21.4% of our patients were afflicted with moderate visual loss, which is not significantly different from Olk's controlled group (P-value=0.2180). After two years of follow-up the rate of moderate visual loss was 43% in the untreated and 10% in the treated group in Olk's study. In our patients, after similar period, 28.6% of the eyes were afflicted with moderate visual loss which has no significant difference with the natural course of macular edema. Therefore in contrast with Olk's results, lasertherapy has not been effective in treating our patients as far as visual acuity is concerned. In accordance with Olk's results CSME was resolved in all treated eyes but in the untreated group no resolution of CSME occured. In our reserch, CSME resolved in 47.1% of the eyes after one year and in 23.8% after two years. These results show that laser photocoagulation is effective in treatment of CSME, but it is not useful in prevention of visual loss in our patients, which is due to several different factors. Macular ischemia is the most prominent factor (25). In most cases, macular ischemia is in concordance with macular edema and it is impossible to differentiate their roles in visual impairment. According to our statistical analysis macular ischemia has been a contributing factor in decreased response of CSME to lasertherapy (Table 8), but there has been no significant relationship between macular ischemia and visual acuity response to lasertherapy (Table 8), therefore we should consider macular ischemia as a major cause in failure of photocoagulation, in the treatment of CSME, but there are other factors responsible for ineffectiveness of lasertherapy in preventing the occurence of visual loss.

One of the main factors is the status of visual acuity before treatment. According to ETDRS (14) and many other studies (26, 27), lasertherapy has been more successful in preventing visual loss in eyes with better VA. Our research confirms this, (Tables 6 and 7); there has been a significant relation between primary VA state and VA response to photocoagulation. The VA of our patients was worse than the ETDRS cases (14), which can be responsible for the poorer therapeutic results of our study. Another important factor is the severity of diabetic retinopathy. In ETDRS research, the effect of treatment appeared similar in all retinopathy severity subgroups (except for the moderate nonproliferative retinopathy group)(14). According to our study, there was not a significant relation between retinopathy severity and visual acuity response to lasetherapy in any of the follow-up visits (Table 6), but we found that the relation between this factor and CSME response to laser photocoagulation was statistically significant (Table 7). On the other hand, retinopathy was more severe in our patients as compared to the ETDRS cases (14), which can account for our relative failure in the treatment of CSME.

In our research, there was a statistically significant relation between the number of treatment sessions and CSME response to lasertherapy, but the relation between this factor and VA response to lasertherapy was not statistically significant (Tables 6 and 7). Comparing the number of treatment sessions in our patients and Olk's indicates that in our study, the number of treatments per eye is much less than Olk's research. As our patients are relatively similar to Olk's patients, decreased number of lasertherapies should be considered as one of the reasons of our relative failure in treating CSME. All of our patients participated in the first follow-up visit. About 76.31% of the eyes had two, 61.40% had three, 27.19% had four and only 18.42% of the eyes had five follow-up visits during the study which shows that our patients have not completely participated in follow-up visits (Tables 3 and 5). In addition, CSME

resolution and VA improvement rate have decreased progressively in the follow-up of treated cases. Moderate visual loss may have forced cur patients to participate in follow-up visits (P-value=0.0764). This means that the patients, who had regular follow-up visits, were those with worse VA state, and this can be considered a major reason for progressive decrease in the rate of CSME resolution and VA improvement after lasertheray in follow-up treatments.

According to ETDRS, eyes with diffuse macular edema, had a less favorable response to laser treatment (14). In our study, only in the last follow-up visit, was there a statistically significant relation between the state of macular edema and visual response to lasertherapy (Table 6). In our study only in the fourth follow-up visit for VA and only in the last follow-up visit for CSME, there was a significant relation between the state of macular edema (focal or diffuse) and response to photocoagulation (Tables 6 and 7). As in the above periods, the state of macular edema, is an independent factor (Table 8), we may conclude that in long term, the state of macular edema can influence the response to laser photocoagulation.

As background variants, we evaluated the effects of the age and sex on the results of treatment. Confirming other studies, there has been no significant relation between the latter and response to lasertherapy. In addition, the effect of several risk factors such as the side of involvement (right or left), type of diabetes, method of blood sugar control, duration of diabetes, hyperlipidemia, hypertension, cardiovascular disease, antihypertensive drugs, aspirin intake, diuretics, neuropathy and nephropathy did not affect our treatment results. We should note that in the patients using digoxin, VA did not respond to treatment (Table 6). Table 8 indicates that there is a significant relation between digoxin and the severity of baseline retinopathy, which may be the main cause. Non of our patients complained of paracentral scotomata, however, this is based on subjective reports and may not be precise. In addition we did not have any case with sub-retinal fibrosis and choroidal neovascularization.

Although lasertherapy is an effective modality in the treatment of diabetic macular edema, delay in ophthalmologic visits inadequate attention to follow-up visits reduce the effectiveness of photocoagulation. Therefore, general practitioners, internists and endocrinologists should refer these patients for timely ophthalmologic examination. Type one patients should be referred 5 years after the onset of diabetes, while type two patients should see an ophthalmologist at the time of diagnosis. The latter is recommended because many type two patients have had their disease for years before the diagnosis is made. It is also necessary to educate the patients about the importance of follow-up visits and the primary goal of lasertherapy, which is stability of vision and not visual improvement.

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