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Changes in Peripapillar Retinal Nerve Fiber Layer Analized by Td-Oct in Patients with Diabetic Retinopathy that Receive Panretinal Photocoagulation

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Abstract

Objective: Explain changes in peripapillar retinal nerve fiber layer in patients with diabetic retinopathy with criteria to receive panretinal photocoagulation, analyzed by td-oct (stratus) unit.

Material and Methods: A transversal retrospective and observational study was done to study peripapillar nerve fiber layers of 46 eyes from 33 patients using a td-oct (stratus) unit. according to laser application technique, time since application and day of the study, 4 groups of patients were set: the first with patients with less than 30 days since last laser application and day of study. The second with patients with 180 days since laser photocoagulation; the third and fourth groups received panretinal photocoagulation and macular selective laser with an Oct 30 and 180 days after administration of treatment.

Results: The clinically significant finding was in the comparation of the group that received panretinal photocoagulation with oct after 30 days, and the group that received panretinal photocoagulation and oct after 180 days. average thickness was less in the second group, with a statistical significant finding p=0.012 in inferior quadrant.

Conclusion: Administer laser photocoagulation makes changes in retina´s structure and function, there are many different results in accordance to equipment used to apply treatment and to take measurements. the patient must be informed about secondary and adverse effects after the treatment.

Keywords: Diabetic retinopathy; Panretinal photocoagulation; Macular laser; Time-Domain optic coherence tomography; Retinal nerve fiber layer

Introduction

Diabetic Retinopathy is one of first causes of blindness or severe visual impairment, in Mexico has been reported up to 8% of blindness cases because of diabetic retinopathy [1]. In other countries as England, data are 14.4% to 17.7% in causes of blindness [2]. In both cases CIE-10 classification considers severe visual impairment that one with far visual acuity best or equal to 20/400, but worse than 20/200, or blindness is diagnosed when visual field is restricted only to 10 grades from central point of fixation in anyone of eyes or worst than 20/400 [3].

Administration of laser in diabetic retinopathy had an important evidence in the Early Treatment Diabetic Retinopathy Study (ETDRS), published in 1976, and with subsequent reports through years, with evidence that extensive laser application in retina and focal zones with neovascularization can reduce at 50% the risk of visual lost, at least in a following of 2 years [4]. After aleatory studies, the ETDRS, through several subsequent reports from 1985, demonstrates that photocoagulation in patients with clinically significant diabetic macular edema reduces the risk of visual lost [5].

Indications for panretinal photocoagulation are: patients with proliferative diabetic retinopathy with or without high risk characteristics (optic disk neovascularization greater than a quarter of optic disk, or neovascularization not in optic disk but greater in size than a half disk diameter or with vitreous or preretinal hemorrhage) may be that the patient has or not central macular edema, or in patients with circumstances that difficult subsequent medical checkups such as severe diabetic retinopathy, a long distance home-laser unit, fast evolution disease, bad treatment accomplishment, or patients with mobilization problems [6].

In another way, the indication to administer macular selective laser is the presence of clinically significant macular edema, this particular pathology has specific characteristics: a) retinal thickening within 500 microns of the center of the fovea, b) hard exudates within 500 microns of the center of the fovea, with retinal thickening, c) one or more optic disc diameters of retinal thickening, part of which is within one disc diameter of the macula center. Just one of these criteria is enough to diagnostic. Additionally, there should be no vitreomacular traction [6].

Objective

Describe the changes in retinal nerve thickness after administer panretinal photocoagulation in different groups of patient, each group with a different time lapse between laser administration and

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Table 1: Nerve fiber layer thickness average in patient groups, in each quadrant, with average shots of laser.

Variables	PPC 30(SD)	PPC 180(SD)	MSL 30(SD)	MSL 180(SD)	
Average laser shots	1931.10 (±1019.05)	2426.3 (±613.9)	1595.7 (±1118.52)	495(±388.9)	P=
Fiber thicknes(micras)					
Superior	116.97 (±44.12) μ	88.10 (±14.7) μ	85.7 (±11.7) μ	104.5 (±4.9) μ	0.13
Nasal	84.2(±35.21) μ	63.8(±21.8) μ	75 (±13.39) μ	67.5(±13.43) μ	0.332
Inferior	120.23(±29.96) μ	93.5(±18.65) μ	111.5(±27.16) μ	129(±8.45) μ	0.65
Temporal	91.9(±45.4) μ	71.6(±23.01) μ	72.25(±25.39) μ	63(±21.21) μ	0.398

Kolmogorov-smirnov test was used for normality. To get "p" value, the mean was compared with ANOVA.
SD: Standard Deviation; μ: Microns

OCT study, the retinal nerve fiber layer thickness is compared with the data base of normal thickness that the OCT units has pre-installed [7].

Material and Methods

A transversal, retrospective and observational study was done to analyze peripapillar nerve fiber layer in patients with diabetic retinopathy who received panretinal photocoagulation, measurements were made with a TD-OCT unit (time domain-optic coherence tomography). The number of patients was in base of convenience because of the patients had irregularities in subsequent medical checkups.

This study was under informed consent, developed in the ophthalmology department of Regional Hospital Valentin Gomez Farias, Jalisco, Mexico. With approval of the Etic and Investigation Committee of the hospital and in base of Helsinsky declaration. From April 4, to July 29 of 2016. Photocoagulation was done with Argon Carl Zeiss Visulass 532s LASER, and OCT was a Humphrey-Zeiss Stratus TD-OCT.

The inclusion criteria were patients with proliferative diabetic retinopathy with or without high risk criteria, in these patients photocoagulation was administered in the wider possible area; for such procedure, an Ocular 165 lens was used, with previous topical anesthesia, we put hypromellose 2% in the lens previous contact with the surface of the eye. In total, we require 3 or less sessions to complete treatment, with a difference of 1 week between each one.

Patients who receive macular selective laser had clinically significant macular edema without vitreomacular traction.

In a total of 40 patients we got 79 eyes to take OCT of peripapillar nerve fiber layers thickness, 1 patient had 1 eye secondary to ocular trauma; all of them received tropicamide plus epinephrine to get mydriasis, with 1 drop in the selected eye to study by OCT or to receive Laser.

Exclusion criteria were patients with glaucoma, high density cataract, hemovitreous, or a bad quality signal in OCT unit (less than 6); finally, we had 33 patients, with 46 eyes in total. We registered total laser shots received in each one, and average thickness of retinal nerve fiber layer in each quadrant displayed in OCT unit: superior, nasal, inferior, temporal.

These 46 eyes were segmented in 4 groups in accord of laser administration technique and elapsed time since last application. To simplify descriptions, abbreviations are used for each group:

Table 2: Eyes are assigned in 3 groups: low, normal, or high, considering retina nerve fiber layer thickness in each quadrant, and laser administration characteristics.

		PATIENTS GROUP				
Quadrant	Range according to thickness	PPC30[1] n=30;(%)	PPC180[2] n=10;(%)	LSM30[3] n=4;(%)	LSM80[4] n=2;(%)	P=
Superior	*Low*	12 (50)	7 (29.2)	4 (16.7)	1 (4.2)	0.244
	Normal	13 (76.5)	3 (17.6)	0 (0)	1 (5.9)	
	High	5 (100)	0 (0%)	0 (0%)	0 (0)	
Nasal	*Low*	19 (65.5)	8 (27.6)	1 (3.4)	1 (3.4)	0.278
	Normal	7 (53.8)	2 (15.4)	3 (23.1)	1 (7.7)	
	High	4 (100)	0 (0%)	0 (0%)	0 (0)	
Inferior	*Low*	8 (53.3)	6 (40)	1 (6.7)	0 (0%)	0.285
	Normal	17 (65.4)	4 (15.4)	3 (11.5)	2 (7.7)	
	High	5 (100)	0 (0%)	0 (0%)	0 (0)	
Temporal	*Low*	24 (70.6)	8 (23.5)	1 (2.9)	1 (2.9)	0.241
	Normal	4 (44.4)	2 (22.2)	2 (22.2)	1 (11.1)	
	High	2 (66.7)	0 (0%)	1 (33.3)	0 (0)	

Contingency tables were used, comparing groups with chi-square test, with confident interval of 95%, and a significative result a $p<0.05$. 1:Group with an OCT 30 days after panretinal photocoagulation. 2: Group with an OCT 180 days after panretinal photocoagulation. 3: Group with an OCT 30 days after panretinal photocoagulation plus macular selective laser. 4: Group with an OCT 180 days after panretinal photocoagulation plus macular selective laser. n: Number of Patients.

1.- The first group (PPC30) received panretinal photocoagulation within 30 days since the last session, getting 3 eyes, from 20 patients. Average laser shots were 1931, with 13 right eyes, 17 left eyes.

2.-The second group (PPC180) were patients that received panretinal photocoagulation 180 days previous OCT study, included 10 eyes from 8 patients.

3.- Third group (MSL30) included patients that received photocoagulation in retina plus macular selective laser, 180 days before OCT study, we got 3 patients, 3 right eyes and 1 left eye.

4.- The fourth and last group (MSL180) were patients with photocoagulation in retina plus macular selective laser administered 180 days before OCT study. Included 2 eyes, from 1 patient

The computer program used for analysis of patients was SPSS v.20 for MAC. Chi-squared test and contingency table were used for categorical variables, with confidence intervals within 95%, taking a

statistically significant value a p<0.05. Non-parametric Kolmogorov-Smirnov test for normality was calculated in case of numerical variables. Also, were compared statistical mean with ANOVA and t-test according to situation.

Results

There were 33 patients, 24 men, 9 women, with average age of 60.03 years old for women and 56.5 for men, a total average of 58.9 years old for both genders. In each patient was compared mean value of each quadrant with the thickness of retinal nerve fiber layer in base of the OCT manual from the unit software. First were compared mean thickness of all the groups with non-parametric Kolmogorov-Smirnov test for normality. The mean values were compared with ANOVA test. There were not statistically significant P values (Table 1).

Comparing each quadrant of each patient with the TD-OCT data base, they were grouped in low, normal, or high, this process was made in all the 4 groups. In the final result there was not a significant p (Table 2). Contingence tables were used in group comparison, using chi-square test.

A non-parametric Kolmogorov-Smirnov test for normality was made to compare the mean thickness of each quadrant in PPC30 and PPC180 groups. In this case there was a statistical significant result of p=0.012 in inferior quadrant; In PFC180 group was found a low mean in the nasal quadrant (Table 3) situation that will be analyzed in the discussion.

A comparison between thickness of MSL30 and MSL180 group was realized. Using non parametric Kolmogorov-Smirnov test for normality, and t-test for mean values, without results statistically significant (Table 4).

Discussion

Secondary effects after photocoagulation in retina have been described, including defects in campimetries from 15 to 30 grades within central vision field, with most of affection if the laser spots are near of peripapillar zone 8; a thicker central macular area may originates edema, and vitreous hemorrhage [9]; peripheral and night vision loss are significant effects, as well as a decrement in 1 to 4 lines of central vision in 10% of patients, this secondary effect is seen more frequently in patients with high risk criteria, and not so common in persons with epiretinal membrane, cataract, neovascular glaucoma, and macular degeneration [10].

Histological effects of laser are the result of retinal pigment epithelium and photoreceptors destruction and sometimes, even choriocapillaris damage. The resulting scare is formed by glia, with a few mitochondria and a consecutive low energy use, which lets oxygen a free flow to adjacent photoreceptors, the hydrostatic pressure decrements in capillary and venule secondary to capillary constriction, therefore edema decreases, because of best oxygenation and less capillary diameter [11].

Structurally, it has been corroborated with SD-OCT focal necrosis areas that include inner nuclear layer and outer nuclear layer, an edema area is created a few hours after administered energy, with reabsorption in a couple of days. An atrophic scare will be formed

Table 3: Comparison of nerve fiber layer thickness between PFC30 and PFC180 group, both without macular selective laser.

	PPC30[1] (SD3)	PPC180[2] (SD)	P
Average laser shots	1931.10 (±1019.05)	2426.3 (±613.9)	
Quadrant			
Superior	116.97 (±44.12) μ	88.10 (±14.7) μ	0.051
Nasal	84.2 (±35.21) μ	63.8 (±21.8) μ	0.094
Inferior	120.23 (±29.96) μ	93.5 (±18.65) μ	0.012
Temporal	91.9 (±45.4) μ	71.6 (±23.01) μ	0.185

In case of numerical variables, Kolmogorov-Smirnov test for normality was used. The mean was compared with t-test. 1: Group with an OCT 30 days after panretinal photocoagulation. 2: Group with an OCT 180 days after panretinal photocoagulation . 3: Standard deviation. μ: Microns.

Table 4: Comparison of retinal nerve fiber thickness of MSL30 y MSL180 group.

	LSM30[1] (SD[3])	LSM180[2] (SD)	P=
Averages laser shots	1595.7 (±1118.52)	495(±388.9)	-
Quadrant			
Superior	85.7 (±11.7) μ	104.5 (±4.9) μ	0.107
Nasal	75 (±13.39) μ	67.5 (±13.43) μ	0.553
Inferior	111.5 (±27.16) μ	129 (±8.45) μ	0.445
Temporal	72.25 (±25.39) μ	63 (±21.21) μ	0.684

In case of numerical variables, Kolmogorov-Smirnov test for normality was used. The mean was compared with t-test. 1: Group with an OCT 30 days after panretinal photocoagulation plus macular selective laser. 2: Group with an OCT 180 days after panretinal photocoagulation plus macular selective laser. 3: Standard deviation. μ: microns.

with higher density in retinal pigment epithelium [12]. One month after a misaligned patron can be observed in any retina layer, that gradually will be homogeneous again, at least partially, but the scare will be thicker; is notable the direct relation between laser power and retinal damage in many studies by SD-OCT [13].

In this study, data analysis shows nerve fiber layer thickness changes in the group with panretinal phocoagulation within 30 days compared with the group that had more than 180 days at the OCT study time, with a lower thickness in this last group. Even if the mean thickness was lower in every quadrant, the significant difference was lesser in the inferior zone with a p=0.012. In the referred bibliography is found that 1 to 3 months post laser photocoagulation in patients with diabetic retinopathy the biggest change is a thicker retina [13,14] although this characteristics were observable with Pascal Laser system, which has less effects in retina because of advantages with automatization in administered power and its distribution in an area; in this study Argon Laser was used.

Similarly, several studies demonstrate that peripapillar nerve fiber layer get thinner in 3 months [15,16]. But this results were investigated in patients treated with PASCAL laser, also there is an article where Argon Laser was used (the same used in this article) and after a month a thinner layer is founded [17], just as our finding in our patients.

In this study, 10 eyes with panretinal photocoagulation within 180 days since laser treatment had a tendency to be grouped in lower nerve fiber layer thickness; when these were compared with OCT data base, a total of 7 eyes had a lower thickness in superior quadrant,

8 eyes in nasal, 6 eyes in inferior, and 8 eyes in temporal, in spite of the statistically results were not significative, we can observe that total of eyes with lower thickness is greater than normal eyes, and there were not high thickness values. In reviewed articles, there was a significant statistically thinning in mean thickness of eyes with panretinal photocoagulation, but again, with Laser PASCAL unit. In the studies that used Argon Laser unit [17,18], tendency to thinning of nerve fiber layers is confirmed.

Respect to comparison between panretinal photocoagulation with OCT study at 30 days (PFC30) and panretinal photocoagulation plus macular selective laser with OCT study at 30 days (LSM30), the patients of the first group had tendency to stay with normal mean values, and the other group had tendency to mean thinner values, especially in superior quadrant. In the review of previous articles, it is told that if macular selective laser is administered, the most important changes are in inferior and superior quadrants [15,19].

Comparing PFC30 group with PFC 180 group the mean of thickness was lower in this last group, all quadrants had a lower mean, but the significant difference was found in the inferior quadrant with a p=0.012. In reviewed bibliography, 1 to 3 months after laser administration in patients with diabetic retinopathy the more relevant change is a thicker retina nerve fiber layer, but this result are found with PASCAL Laser unit, and as mentioned before, there are less secondary effects because of power and distribution of this automatized system; in the same way, may progress to thinner layer at long term, being more frequent in superior and inferior quadrant [15,18]. There are many results in the following of the patients, either by the laser system, or by evolution time, even by specific patient conditions.

To analyze results of this study must be considered the Laser system unit and the results with previous investigations, because in some cases Pascal Laser unit is used, this system has the option to administer a time shot near 10 to 30 milliseconds, in a quantity of 1 to 56 in each pedal activation, and the Argon Laser system has longer times of administration, near 100 to 200 milliseconds, and only one shot at the time, in both cases is possible graduate the level of power in accord the spot size, this is under medical criteria [19]. Just a little variation has been seen in macular thickness in 6 months in patients that received laser with PASCAL system, because of less absorbed energy [20], nevertheless in revision articles final results suggest a tendency to be similar in retinal nerve fiber layer thickness in both laser system after 6 months of administration [21].

A limitation to compare this study with the ones in named bibliography is that we use TD-OCT, while in the most articles the SD-OCT is used, and even some of those units are high definition; in the TD-OCT unit, the data obtained are fewer because of hardware limitations and a basic analysis logarithm [22].

Other articles point to the development of thinner nerve fiber layer in diabetic patients without photocoagulation compared with non diabetic patients, but photocoagulated patients have even thinner nerve fiber layer, that means that there is a tendency to thinner nerve fiber layer in diabetic patients [19].

Conclusion

Bibliography particularize that anatomical results are variable. Most cases the nerve fiber layer get thicker at 10 weeks, and thinner at 6 months after laser photocoagulation. Must be considered that some articles (just a few) explain that there is no difference between retinal thickness pre and post treatment, this evidences that results may vary.

In this study, the results are alike bibliography taking in count adverse anatomy effects in retina in the PFC30 and the PFC180 group. Also, must be considered geography condition and patients attitude in the region to get subsequent revisions, because of irregularity.

Must be taken in count secondary anatomical and functional changes described after energy administration in retina, which include a visual health problem, specially at long term, plus natural history of diabetic retinopathy even under treatment, so the patient must be informed about these adverse effects.

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