THE FORMATION OF THE PERIPHERAL RETINAL SCAR DUE TO CRYORETINOPEXY IN NONPROLIFERATIVE DIABETIC RETINOPATHY TO MAINTAIN THE CENTRAL AUTOREGULATION RETINA SYSTEM

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ABSTRACT

Diabetic retinopathy is one of serious problems for ophthalmologist, because in western countries diabetic retinopathy is a leading cause of blindness. The gold standard treatment of diabetic retinopathy is Argon laser photocoagulation, but this laser is very expensive in developing countries. ***Objective:*** *To study the influence of peripheral retinal scar due to cryoretinopexy to maintain the central autoregulation retina system.* ***Materials and methods:*** *The prospective study of the pretest - posttest control group experimental design was conducted for 25 patients of non-insulin dependent diabetes mellitus. Every patient had nonproliferative diabetic retinopathy of both eyes. One eye was photocoagulated by Argon laser and the fellow eye was subjected to cryoretinopexy.* ***Results:*** *The study showed that the central autoregulation retina system had no significant difference before and after cryoretinopexy. The central autoregulation retina system showed had significant difference between that after cryoretinopexy and that after laser.* ***Conclusion:*** *Peripheral retinal scar due to cryoretinopexy can maintain the central autoregulation retina system.*

Keywords: *autoregulation retina, cryoretinopexy, laser, non proliferative diabetic retinopathy, peripheral retinal scar*

INTRODUCTION

Blindness due to diabetic retinopathy is the leading cause in patients aged 20 - 64 years in the United Stated and in western countries. The gold standard treatment of diabetic retinopathy is the photocoagulation of Argon laser (Klein R, Klein RB, 1984). In East Java with 34 million inhabitants there are only 4 laser photocoagulation machines. It is therefore not possible to treat diabetic retinopathy by the photocoagulation of Argon laser. An ophthalmologist can perform cryotreatment for the diseased eye. Due to this reason this study suggests a new technology for the treatment of diabetic retinopathy by cryosurgery.

This paper discusses a new method for the treatment of diabetic retinopathy by cryoretinopexy. The objective of this research was to study the influence of the peripheral retinal scar due to cryoretinopexy to maintain central autoregulation retinal system. The population of this research was non-insulin dependent diabetes mellitus patients with nonproliferative diabetic retinopathy in both eyes at Dr. Soetomo Hospital and Undaan Eye Hospital Surabaya. The formation of peripheral retinal scar (cicatric) was performed by cryoretinopexy and peripheral retinal scar (PRS) by indirect ophthalmoscope examination was noted. The central autoregulation retina system was determined by the fundal fluorescein angiography, which consisted of microaneurysms, soft and hard exudates, retinal hemorrhage, retinal and macular edema, and the new vessel.

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MATERIALS AND METHODS

This study used pretest - posttest control group experimental design, and this was a prospective study of non-insulin dependent diabetes mellitus with the complication of non proliferative diabetic retinopathy in both eyes. During 2 years period from April, 1997 to March 1999 at Dr. Soetomo Hospital and Undaan Eye Hospital Surabaya, the author enrolled a number of 30 patients with non proliferative diabetic retinopathy (NPRD) of both eyes with a similar condition of the retina. The author randomized the each patient for Argon laser photocoagulation of one eye and the fellow eye was subjected to cryoretinopexy to make the peripheral retinal scar.

Before treatment with cryoretinopexy and Argon laser photocoagulation, these patients were examined in the laboratory and underwent standard eye examination. The patients enrolled in this study were male and female, aged 40 - 65 years. The diagnosis of diabetes mellitus (DM) was based on Perkeni consensus 1998, while the criteria of non insulin dependent diabetes mellitus (NIDDM) was confirmed if the fasting C-peptide level was > 0.8 mg/ml (Tjokroprawiro A, 1995). Blood glucose regulation was decided by the fasting and two hours postprandial plasma glucose and the glycosylated haemoglobin A (HbA1c) and the marker of the vascular genetic risk factor was seen by Lipoprotein

(a). If this vascular genetic risk factor Lipoprotein (a) / Lp(a) > 20 mg/dl, the patient had predisposition to stroke and coronary heart diseases. The blood pressure before and after treatment were < 140/90 mmHg.

The central auto regulation retina system was determined with the changes of the macular area and the posterior pole of the retina. The fundal fluorescein angiography (FFA) changes are micro aneurysm, retinal hypoxia (non perfusion retina = soft exudates), hard exudates, macular edema, retinal edema, retinal hemorrhage, neovascularization of retina (NVE) and neovascularization of optic disc (NVD). The dependent variables in this study were micro aneurysm and soft exudates, and the independent variables were laser photocoagulation and the fellow eye underwent PRS by cryoretinopexy. The confounding variables were HbA1c and Lp(a). The time schedule of laboratory and eye examination was twice, prior to and six months after laser photocoagulation and the formation of PRS by cryoretinopexy.

RESULTS

A number of 30 cases, consisting of 25 patients with NPRD of both eyes, were included in this study. From those patients, 19 patients were female and 6 patients male. The mean age was 51.12 ± 4.45 years and the youngest was 44 years and the oldest was 65 years. The author enrolled 50 eyes with NPRD of both eyes and 25 eyes were photocoagulated by Argon laser and 25 the fellow eyes were performed cryoretinopexy to make the peripheral retinal scar. Five patients dropped-out. One patient died and 4 others were excluded due to loss of follow-up after treatment.

Statistical analyses to compare the results before and after treatment, and to compare laser photocoagulation eyes to cryoretinopexy eyes were chi-square test, student t test and Anova test. The statistical analysis was conducted by the Statistical Package for Social Sciences 7.5 for Windows 95 program. The significant level of this study was 0.05. Ttable 4 to table 11 showed no significant difference of the result between the laser photocoagulation and cryoretinopexy treatment, and Table 6 notes a good result after cryoretinopexy in the group of a low risk vascular genetic factor.

Table 1. Distribution of age and sex

Age (years)	Sex		Total	Percentage (%)
	Male	Female		
41 — 45	0	1	1	4
46 — 50	2	6	8	32
51 — 55	2	7	9	36
56 — 60	2	2	4	16
61 — 65	0	3	3	12
Total	6 (24%)	19 (76%)	25	100%

The study shows that the frequency of female (76%) is higher than that of male (24%), and the highest age incidence is 51 – 55 years (36%).

Table 2. Eye distribution with Cryoretinopexy and Laser according to HbA_{1c} level

HbA_{1c} level	Cryoretinopexy		Laser		Total
	Right eye	Left eye	Right eye	Left eye	Eyes
≤ 8.4 %	8	5	5	8	26
> 8.4 %	6	6	6	6	24
Total eyes	14	11	11	14	50

There is similar incidence of the sample between a good regulation of blood glucose ($HbA_{1c} \leq 8.4\%$) and a bad regulation of blood glucose ($HbA_{1c} > 8.4\%$).

Table 3. Eyes distribution with Cryoretinopexy and Laser according to Lp(a) level

Lp(a) level mg/dl	Cryoretinopexy		Laser		Total eyes
	Right eye	Left eye	Right eye	Left eye	
Lp(a) ≤ 20	8	5	5	8	26
Lp(a) > 20	6	6	6	6	24
Total eyes	14	11	11	14	50

The similar incidence of samples between a low risk of the marker vascular genetic factor (Lp(a) ≤ 20 mg/dl) and a high risk of marker vascular genetic factor (Lp(a) > 20 mg/dl).

Table 4. The microaneurysm before and after Cryoretinopexy and Laser photocoagulation of the group HbA_{1c} ≤ 8,4%.

Treatment	Before	After	Statistical test	
			p	significance
Cryoretinopexy	20.46	19.46	0.121	NS
Laser	22.08	24.92	0.183	NS
Statistical test				
p	0.686	0.218		
significance	NS	NS		

Table 5. The microaneurysm before and after Cryoretinopexy and Laser photocoagulation of the group HbA_{1c} > 8.4%.

Treatment	Before	After	Statistical test	
			p	significance
Cryoretinopexy	29.67	29.00	0.347	NS
Laser	28.67	29.50	0.339	NS
Statistical test				
p	0.884	0.941		
significance	NS	NS		

Table 6. The microaneurysm before and after Cryoretinopexy and Laser photocoagulation of the group Lp(a) ≤ 20 mg/dl

Treatment	Before	After	Statistical test p	significance
Cryoretinopexy	26.06	24.38	0.041	S
Laser	25.38	26.38	0.500	NS
Statistical test p	0.879	0.688		
significance	NS	NS		

Table 7. The microaneurysm before and after Cryoretinopexy and Laser photocoagulation of the group Lp(a) > 20 mg/dl

Treatment	Before	After	Statistical test p	significance
Cryoretinopexy	23.58	23.67	0.795	NS
Laser	25.08	27.92	0.134	NS
Statistical test p	0.827	0.527		
significance	NS	NS		

Table 8. The soft exudates before and after Cryoretinopexy and Laser photocoagulation of the group $HbA_{1c} \leq 8.4$ %

Treatment	Before	After	Statistical test p	significance
Cryoretinopexy	0.15	0.15	1.00	NS
Laser	0.15	0.15	1.00	NS
Statistical test p	1.00	1.00		
significance	NS	NS		

Table 9. The soft exudates before and after Cryoretinopexy and Laser photocoagulation of the group HbA_{1c} > 8.4 %

Treatment	Before	After	Statistical test p	significance
Cryoretinopathy	0.50	0.58	0.338	NS
Laser	0.25	0.42	0.339	NS
Statistical test				
p	0.573	0.775		
significance	NS	NS		

Table 10. The soft exudates before and after Cryoretinopexy and Laser photocoagulation of the group Lp(a) ≤ 20 mg/dl

Treatment	Before	After	Statistical test p	significance
Cryoretinopexy	0.31	0.31	1.00	NS
Laser	0.31	0.31	1.00	NS
Statistical test				
p	1.00	1.00		
significance	NS	NS		

Table 11. The soft exudates before and after Cryoretinopexy and Laser photocoagulation of the group Lp(a) > 20 mg/dl

Treatment	Before	After	Statistical test p	significance
Cryoretinopexy	0.33	0.42	0.339	NS
Laser	0.42	0.58	0.339	NS
Statistical test				
p	0.822	0.752		
significance	NS	NS		

DISCUSSION

Diabetic retinopathy has been and probably remains one of the four major causes of blindness in the western countries. Without treatment the eyes with proliferative diabetic retinopathy have at least a 50% chance of becoming blind within 5 years. Appropriate application of treatment that have been developed in the last three decades can reduce this risk of blindness to less than 5%.

The modalities of diabetic retinopathy treatment are medical treatment, laser photocoagulation and surgical treatment (vitrectomy). According to Olk RJ and Lee CM (1991) laser photocoagulation treatment is effective for diabetic retinopathy. However, laser photocoagulation is very expensive in developing countries because it needs a laser lamp during every four years to maintain the power of laser.

Medical treatment has revealed no good result to cure diabetic retinopathy. The current medical management of diabetic retinopathy is primarily preventive. Most patients with diabetes mellitus are coming in the ophthalmologic department, thus they had a visual disturbance due to diabetic retinopathy. Diabetic retinopathy is a irreversible process. This means that diabetic retinopathy patients had a problem to cure the diabetic retinopathy. Most effects of medical treatment are not yet proven clinically in reliable way. The best control of blood glucose including assessment of HbA1c and lipoprotein (a) as a marker of vascular diseases and blood pressure control are still of major importance. This study found the HbA1c and Lp(a) as the confounding variable, and the blood pressure as an inclusion criteria.

The available surgical treatment is vitrectomy especially for the advanced proliferative diabetic retinopathy. Blindness due to the diabetic retinopathy became a more serious public problem in 1960s. Meyer-Schwickerath introduced the photocoagulation for new vessels on the surface of the retina. Since 1970 the laser photocoagulation is used very extensively in diabetic retinopathy (Ivanisevic, 1992).

The Diabetic Retinopathy Study and the Early Treatment Diabetic Retinopathy Study had given clinicians excellent guidelines for the management of the diabetic macular edema and the early proliferative diabetic retinopathy. Not all diabetic patients are alike. Clinicians must balance the guidelines with their own clinical judgment. Now the Argon laser photocoagulation is a gold standard treatment for the diabetic retinopathy (ETDRS, 1988).

Unfortunately, in developing countries the price and maintenance cost of a laser machine is highly expensive. Ophthalmologists who can operate the laser machine in this country is very limited. In this study the author suggests a new technique for the treatment of non proliferative diabetic retinopathy. It is expected that this new technique can be used by all ophthalmologists, as this technique is very easy to do and not expensive. This technique is entitled as the cryoretinopexy of peripheral retina. The concept of the research was a formation of the peripheral retinal scar by cryoretinopexy to maintain the autoregulation of central retina system.

Table 1 shows that the frequency of this disease in female is larger than that in male. According to the Wisconcin Epidemology Study Diabetic Retinopathy sex was not associated with incidence of diabetic retinopathy. This study shows that the incidence in female (76%) is larger than in male. This result is different from that of the Wisconsin Epidemiology Study of Diabetic Retinopathy. In the Early Treatment Diabetic Retinopathy Study Research (1985), sex was not associated with 10-year incidence of diabetic retinopathy. In this study, the incidence of the female diabetic retinopathy was high. The explanation of this result may come from the fact that the population of female was larger than male in this study. The second reason was the small sample of the study and the observation of the study was too short. However, the small sample used in this study showed balanced result between left and right eye, and so did the same total sample between eye with Argon laser photocoagulation and eye with cryoretinopexy.

Table 4 - 11 show no significant difference between the eyes photocoagulated by Argon laser and the eyes subjected to cryoretinopexy. This study found that microaneurism and soft exudates before and after Argon laser photocoagulation or cryoretinopexy were not significantly different. This result showed that the variable of the autoregulation of the central retinal system could be maintained by cryoretinopexy. The signs of diabetic retinopathy were not significantly different between laser photocoagulation and peripheral cryoretinopexy, and Table 6 even shows that microaneurisms decreases after cryoretinopexy.

CONCLUSION

Based on the results and a statistical analysis, it can be concluded that cryoretinopexy of peripheral retina can maintain the autoregulation of a central retinal system.

The cryoretinopxy of the peripheral retina can be performed as an alternative treatment for diabetic retinopathy.

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