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Anemia as a factor related to the progression of proliferative diabetic retinopathy after photocoagulation

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ABSTRACT

Objective: This study aimed to investigate factors that could be related to the progression of proliferative diabetic retinopathy in patients treated with photocoagulation.
Methods: In this case-control study, a total of 106 patients with diabetic retinopathy participated who were treated with photocoagulation. We analyzed glycaemia, serum cholesterol, triglycerides, hemoglobin, platelet levels, blood pressure measurement, diabetes duration, diabetes and hypertension treatment, sex, and age. The statistical analysis was done with *t* test, χ^2 test, odds ratio (OR), and simple linear regression.
Results: We found statistical significance in blood glucose level (P=.038), cholesterol level (P<.001), and hemoglobin level (P<.001). The simple linear regression was significant with blood glucose level (P<.05) and hemoglobin level (P=.001). Hemoglobin had a significant result: OR=2.432, 95% CI 1.902–3.115; Pearson χ^2=16.812; P<.001.
Conclusions: Anemia is an important finding in diabetic patients. Anemia is a relevant factor related to the progression of proliferative diabetic retinopathy, which can be treated with photocoagulation.

1. Introduction

Diabetic retinopathy is the leading cause of blindness among the diabetic population aged 20–74 years. During the first two decades of diabetic life, all patients with type I diabetes and about 60% of patients with type II diabetes will have some degree of diabetic retinopathy (DR) (Fong et al., 1994).

Since the 1980s, there are reports indicating that glycosylated heamoglobin (HbA_{1c}) is the most reliable marker of metabolic control in diabetes (Tayyeba & El-Remessy, 2009). In 1992, other reports - mentioned that elevated levels of HbA_{1c} were related to the severe stage of diabetic retinopathy (Sociedad Mexicana de Oftalmología, 2005). Up to 2000s, further studies confirmed the tendency of HbA_{1c} to serve as a predictor of the presence and severity of diabetic retinopathy (Lesso-Zamora et al., 2009; Janka, Warram, Rand, & Krolewski, 1989; Agardh, Eckert, & Agardh, 1992).

In the Early Treatment for Diabetic Retinopathy Study (ETDRS) which performed metabolic measurements in 2079 patients, it was found that there is a relationship between higher cholesterol and triglyceride levels, and the appearance of hard exudates in the macula of patients (P<.001). Also, loss of visual acuity was related to the extension of the exudates (Aiello, Cahill, & Wong, 2001).

A study conducted in 2005 showed that by decreasing HbA_{1c} levels, patients can undergo photocoagulation to improve diabetic retinopathy (Koutola, Koukolis, Zintzaras, Karabatsas, & Chatzoulis, 2005). But our question is: Are there metabolic parameters related to the progression of proliferative diabetic retinopathy after photocoagulation? Since the Diabetes Control and Complications Trial and Follow-Up Study, the elevated blood glucose level is always the major factor in the progression of diabetic retinopathy, as confirmed in later studies with the HbA_{1c}, as mentioned above. Nevertheless, other reports showed the fact that patients with low level of normocromic hemoglobin are more likely to have proliferative diabetic retinopathy. This study did not mention whether the patients previously underwent photocoagulation (Qiao, Keinanen-Kiukaanniemi, & Laara, 1997).

We conducted the following study under the premise of trying to find a parameter that could make a significant difference and which could be related to the progression of diabetic retinopathy after photocoagulation.

2. Material and methods

This case-control study was conducted from September to November 2009. The participants were recruited from diabetic patients who were attending the ophtalmology service from Unidad

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Médica de Atención Ambulatoria #7, Instituto Mexicano del Seguro Social. The inclusion criteria were that the participants (a) have diabetes, (b) were treated with photocoagulation, (c) have no opacities (cataracts, corneal scars) in the visual axis which could hinder in taking an eye fundus photograph. Also, all the patients underwent a laboratory screening and physical examination. All participants read and signed an informed consent form prior to their involvement in the study. The ethical aspects of the recruitment conformed to the Helsinki Declaration and to Mexican laws on public health.

Cases were defined as patients who showed progression of proliferative diabetic retinopathy with these complications: bleeding into the vitreous cavity, tractional or non-rhegmathogenous retinal detachment, macular edema, and optic nerve atrophy, regardless of the time elapsed since the last application of laser photocoagulation (Maa & Sullivan, 2007). It has been reported that, despite focal photocoagulation, poor metabolic control can lead to macular edema; and even after full panretinal photocoagulation, vitreous hemorrhage can occur and may need pars plana vitrectomy (Chantelau, 2001).

In our experience, we have also found that, in Hispanic patients with poor metabolic control, tractional retinal detachment will appear despite prior pan-phocoagulation. It has been reported that diabetic retinopathy has an effect on the glaucomatous or atrophic shape of the optic nerve and can be improved with photocoagulation (Lim et al., 2009).

Controls were defined as patients who showed no progression of proliferative or pre-proliferative diabetic retinopathy after treatment with laser photocoagulation. This included patients who were stabilized with the laser treatment.

The size of the population to be studied was estimated using the Epi-Info software. With a confidence interval of 95%, we obtained a population of 67 patients for each group for a total of 134 patients.

Because HbA_{1c} has been widely studied and its relation with the progression of proliferative diabetic retinopathy recorded, we decided to change this variable and, instead, introduced to the study the number of platelets (Demirtunc et al., 2009).

There was a need to relate the parameters with the progression of proliferative diabetic retinopathy. Systemic control was related to the parameters regarding glucose, serum cholesterol, triglycerides, HbA_{1c}, and blood pressure measurements. Other parameters were related to the duration of diabetes mellitus: heart disease, nephropathy, diabetes and antihypertensive treatment, sex, and age (Hudson, 2008).

A routine ophthalmologic examination was performed in every patient, recording the visual acuity, intraocular pressure, and clinical findings of the eye fundus. The diagnosis of the type and severity of the diabetic retinopathy was based on the San Luis Valley Diabetes Study, Colorado (1998). This classification is as follows:

(a) Nonproliferative diabetic retinopathy.
(b) Pre-proliferative diabetic retinopathy, subdivided into:
   1. Mild.
   2. Moderate.
   3. Severe.
(c) Proliferative diabetic retinopathy.

In all patients, fundoscopic photographs were taken with a Zeiss fundoscopic camera to confirm the diagnosis.

The statistical analysis was performed with the SPSS software version 15. The statistical analysis used *t* test, chi-squared distribution, odds ratio (OR), and simple linear regression.

3. Results

Each group consisted of 53 patients of the 63 originally estimated. The total population was 106 patients [54 men (50.9%) and 52 women (49.1%)]. Table 1 describes the behavior of the metabolic parameters studied, as well as the percentages of the data obtained from each parameter.

The mean age of the population was 59.8 years (±9.8, range 36–85). Duration of diabetes was 18 years (±8.2, range 1–40). Mean blood glucose level was 162 mg/dl (±74.14, range 47-451). Hemoglobin level had a mean of 12.8 g/dl (±1.64, range 8.40–15.90). Platelet level had a mean of 275.39 kU/l (±70.71, range 105–468). Cholesterol level had a mean of 214.5 mg/dl (±50.4, range 131–386). Triglyceride level showed a mean of 214.67 mg/dl (±136.5, range 60–1012). Systolic blood pressure level had a mean of 138.4 mmHg (±23.13 mmHg, range 110–220). Diastolic blood pressure level had a mean of 80.2 mmHg (±11.85, range 60–140). Intraocular pressure level had a mean of 17.6 mmHg (±2.19, range 12–27). This will be addressed in the Discussion section.

Table 2 shows the percentages of the pathologies that appear as a complication of proliferative diabetic retinopathy. All these complications were exclusive of the cases in this study.

We have to note the fact that, in our patients, besides macular edema, we found an important number of cases with alteration of the optic nerve, perhaps of low blood perfusion nature. There are other

Table 1
Description of metabolic parameters.

Variable (%)	Mean	Standard deviation	Range
Age, years (100)	59.8	9.8	36–85
Duration of DM, years (93.4)	18	8.2	1–40
Blood glucose (98.1)	162 mg/dl	74.14 mg/dl	47–451
Hemoglobine (98.1)	12.8 g/dl	1.64 g/dl	8.40–15.90
Platelets (92.5)	276.39 KU/L	70.71 KU/L	105–468
Cholesterol (86.8)	214.5 mg/dl	50.4 mg/dl	131–386
Triglycerides (71.7)	214.67 mg/dl	136.5 mg/dl	60–1012
Systolic BP (94.3)	138.4 mmHg	23.13 mmHg	110–220
Dyastolic BP (94.3)	80.2 mmHg	11.85 mmHg	60–140
IOP (82.1)	17.6 mmHg	2.19 mmHg	12–27

BP=Blood pressure; IOP=intraocular pressure; DM=diabetes mellitus.

Table 2
Description of the complications found in diabetic retinopathy patients.

	n (%)
Blood into vitreous cavity	31 (29.2)
Macular edema	15 (14.2)
Tractional retinal detachment	22 (20.8)
Isquemic optic atrophy	29 (27.4)

Table 3
Chi-squared distribution (non-parametrical studies).

		n (%)	
Sex	Men	54 (50.9)	*P*=.439
	Women	52 (49.1)	
DM Treatment	OHG	55 (51.9)	*P*=.005
	Insulin	30 (28.3)	
	Combine	9 (8.5)	
	None	7 (6.6)	
Other pathologies	Cardiac type	11 (10.4)	*P*=.145
	Renal type	14 (13.2)	
	PVI	5 (4.7)	
	Glaucoma	10 (9.4)	
	None	66 (62.2)	

PVI=Peripherical vascular insufficiency; OHG=oral hypoglycemic agents.