European Journal of Ophthalmology / Vol. 13 no. 7, 2003 / pp. 648-652

Diabetes mellitus: A risk factor affecting visual outcome in branch retinal vein occlusion

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PURPOSE. *The prognosis of visual acuity (VA) after branch retinal vein occlusion (BRVO) in patients with diabetes mellitus is unknown compared to the VA in non-diabetic patients with BRVO. The aim of this study was to evaluate the visual outcome of BRVO in diabetic and non-diabetic patients.*
METHODS. *A retrospective case-control study of diabetic and non-diabetic patients with BRVO was performed. VA and commonly known risk factors and complications of BRVO were compared in a follow-up period of at least 1 year.*
RESULTS. *A total of 28 eyes of patients with diabetes and 49 eyes of non-diabetic patients with BRVO were included. One year after BRVO, the VA in the patients with diabetes decreased significantly more than that of the non-diabetic patients. During the second year after BRVO, the VA did not change significantly in either group. BRVO in patients with diabetes occurs at an earlier age. Diabetic patients needed more outpatient visits.*
CONCLUSIONS. *The VA 1 year after BRVO in patients with diabetes is worse compared to the VA in patients without diabetes. The VA stabilizes 1 year after onset in both groups. Diabetic patients tend to need more frequent follow-up in order to treat the sequelae of BRVO. (Eur J Ophthalmol 2003; 13: 648-52)*

KEY WORDS. *Branch retinal vein occlusion, Diabetes mellitus, Visual acuity, Vascular retinal occlusion*

Accepted: March 24, 2003

INTRODUCTION

Branch retinal vein occlusion (BRVO) is a common retinal vascular disease causing visual loss in adults, second in frequency only to diabetic retinopathy (1). Several systemic and ophthalmic conditions have been reported in association with BRVO. The most important systemic risk factor is hypertension (2-9). In some studies, diabetes mellitus is also found to be a risk factor for development of BRVO (1, 3-5). In patients with diabetes with retinal vein occlusion, a strikingly high prevalence of hypertension compared to patients with diabetes without retinal vein occlusion is present (10). The prevalence of diabetes mellitus in groups of patients with BRVO has been described in several studies, which showed that 2.5 to 33% of patients with BRVO also had diabetes mellitus (1, 2, 4, 6-11). In the ophthalmic literature, we only found one article in which visual acuity (VA) in patients with diabetes with BRVO was compared to VA in non-diabetic patients with BRVO, but a short follow-up was described (11).

The aim of this study was to evaluate the course of BRVO and visual prognosis in patients with diabetes mellitus as compared to patients without diabetes.

1120-6721/648-05$02.50/0
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METHODS

In this retrospective case-control study, patients were included if they had had BRVO for more than 1 year in the period from January 4, 1985, until January 4, 2002. To identify patients with BRVO, we used the records of the Department of Ophthalmology of the Vrije Universiteit Medical Centre in Amsterdam, the Elkerliek Hospital in Helmond, and Oogheelkunde Rijswijk in Rijswijk, all in the Netherlands. From this group we selected all patients with a major BRVO of a full temporal quadrant of the retina. We also selected all patients with a minor BRVO of a branch of the superior or inferior temporal vein in the foveal area. Patients with other occlusions or occlusions of the nasal veins were excluded, as they have no significant effect on VA. The most recent eyes with BRVO were included and not matched for age, sex, or other factors. These factors could give additional information concerning BRVO in patients with diabetes. In the selected group of patients, we identified those with diabetes mellitus. Diabetes was diagnosed if the patient reported having diabetes and was treated with diet, insulin, or oral antidiabetic agents. The diagnosis of diabetes mellitus had to be established before the occurrence of BRVO. From this group the 28 most recent eyes were included. Each center contributed an equal number of eyes.

As a control group, we included patients who were not diagnosed with diabetes. In these patients, blood glucose measurement was performed to confirm absence of diabetes. Diagnosis of BRVO was made by fundus examination and fluorescein angiography. Patients were excluded if the first presentation occurred later than 8 weeks after onset of the BRVO. Follow-up after diagnosis had to be at least one year. Patient data were retrospectively evaluated from patient records by one single observer. Data collected concerned general findings such as patient age and sex and presence of hypertension or cardiovascular disease. Cardiovascular disease was considered present when a patient reported having a disease such as angina pectoris, cardiac decompensation, myocardial infarction, or peripheral vascular disease (i.e., carotid stenosis, transient ischemic attack, or cerebral vascular attack).

Data evaluated were diagnosis of glaucoma and best-corrected Snellen VA before BRVO (if known), at diagnosis, after 1 year, and, when available, 2 years after BRVO. We also registered the number of outpatient clinic appointments in the first year after diagnosis; the status of the diabetic retinopathy, if present, according to the Early Treatment Diabetic Retinopathy Study (ETDRS) scale; and the number of argon laser burns given to treat sequelae of BRVO in the first year after diagnosis. A patient was considered to have hypertension when the diagnosis was made by a physician or if the patient used medication to control hypertension. Data were statistically evaluated with the unpaired t-test or Fisher exact test whenever applicable. A p value <0.05 was considered to indicate a statistically significant difference.

RESULTS

Twenty-eight eyes of 28 patients with diabetes with a recent BRVO in the macular area had a follow-up of at least 1 year. There were only five eyes with diminished VA as a result of background diabetic retinopathy with macular edema before the BRVO developed. According to the ETDRS scale, intraretinal hemorrhages and microaneurysms in two or three quadrants were present in all five patients; retinal edema was located within 500 µm of the centre of the macula. The visual outcome in this subgroup was not significantly different from that of patients with diabetes without diabetic retinopathy. Two of these patients needed panretinal photocoagulation because of advanced diabetic retinopathy in the following year. Four patients with diabetes without pre-existing diabetic retinopathy needed panretinal photocoagulation due to advanced diabetic retinopathy.

Forty-nine eyes of 49 non-diabetic patients with a recent BRVO followed for at least 1 year could be identified from the same sources, and were considered as control subjects. The distribution of general patient characteristics and comorbidity in patients with diabetes and control subjects is described in Table I. No significant differences in sex, number of patients with major or minor BRVO, high cholesterol, or presence of glaucoma could be detected (Tab. I).

The mean age in the patients with diabetes was significantly lower as compared to non-diabetic patients: 64 (range 41-81) versus 71 years (range 48-85, $p< 0.01$). In both groups the prevalence of hypertension was almost equal, in contrast to another report (10). In the

TABLE I - GENERAL PATIENT CHARACTERISTICS AFTER BRANCH RETINAL VEIN OCCLUSION (BRVO)

Characteristics	Diabetes, n=28 eyes	No diabetes, n=49 eyes	p value
Male/female	16/12	30/19	NS*
Age, yr, mean ± SD	64 ± 9	71 ± 9	<0.01†
Hypertension, %	64	65	NS*
Cardiovascular disease, %	50	28	<0.05*
Glaucoma, %	11	10	NS*
High cholesterol, %	14	10	NS*
Major BRVO, %	89	89	NS*
Minor BRVO, %	11	11	NS*

*= Fisher exact test; †= Unpaired t-test; NS= Not significant

TABLE II - VISUAL ACUITY IN PATIENTS WITH BRANCH RETINAL VEIN OCCLUSION (BRVO)

Visual acuity	Diabetes, n=28	No diabetes, n=49	p value
Before BRVO	0.7 (22)	0.7 (13)	NS*
After BRVO	0.4 (28)	0.4 (49)	NS*
1 year after BRVO	0.3 (28)	0.5 (49)	<0.01*
2 years after BRVO	0.3 (16)	0.5 (28)	<0.01*

Values are mean (n); *Unpaired t-test; NS = Not significant

TABLE III - INTENSITY OF LASER TREATMENT AND NUMBER OF OUTPATIENT APPOINTMENTS IN THE FIRST YEAR AFTER BRANCH RETINAL VEIN OCCLUSION

Treatment or appointments	Diabetes, n=30	No diabetes, n=50	p value
Number of argon laser burns in first year	449	264	0.11*
Outpatient appointments in first year	9.6	8.6	0.14*

Values are mean (n); *Unpaired t-test; NS = Not significant

glaucoma patients, only minor visual field defects were detected, without influence on visual function. Cardiovascular disease was found in 50% of patients with diabetes and in 28% of non-diabetic patients.

In Table II, the VA before the BRVO, after the BRVO, and 1 and 2 years after the occlusion is described. Before and directly after the occurrence of BRVO, there was no significant difference in VA between diabetic and non-diabetic patients. After 1 year of follow-up, VA was 0.3 in patients with diabetes with BRVO versus 0.5 in the non-diabetic patients ($p<0.01$). Two years after diagnosis of BRVO, the VA did not change significantly from the 1-year value in either group.

In Table III, data concerning frequency of follow-up and treatment are shown. Patients with diabetes required 9.6 outpatient clinic appointments, including laser treatment sessions in the first year of follow-up, compared to 8.6 appointments for patients without diabetes. Patients with diabetes received on average 449 argon laser burns, whereas the non-diabetic patients received only 264 laser burns. The fluorescein angiograms revealed more disc diameters of is-

chemia in the macula as well as more prominent macular edema in the diabetic group. However, no final conclusions can be drawn, as each time point for each angiogram was different. Some angiograms were made on the day of diagnosis; some were made 6 to 8 months later or even after laser coagulation. Differentiating between ischemic and edematous occlusions is therefore difficult. Sometimes the angiograms were obscured by hemorrhages. Also, diabetes in itself can cause ischemia and edema.

DISCUSSION

Diabetes mellitus is a well-known risk factor for cardiovascular disease, as in venous occlusions of the eye. Ample data have been published about the prevalence of diabetes mellitus in patients with BRVO (1, 2, 4, 6-11). However, there is little information about the visual outcome in patients with diabetes with BRVO compared to non-diabetic patients (11). The current study was performed to evaluate the course and prognosis of BRVO in patients with diabetes compared to patients without diabetes mellitus. One year after BRVO, patients with diabetes had a significantly lower VA than patients without diabetes. This in contrast to the study of Funderburk and Feinberg (11), who did not find a significant difference in visual outcome between patients with and without diabetes mellitus. In their study, follow-up was variable, with an average of 7.6 months. Therefore, the difference between the visual outcome in our study and the latter may be explained by a difference in follow-up. Furthermore, in the article by Funderburk and Feinberg, no information was given on general patient characteristics or ophthalmologic data. A relatively favorable risk profile may have influenced their results. An explanation for the worse visual outcome and greater need for laser treatment in eyes of patients with diabetes in our study could be a vascular compromise by diabetes mellitus. As a result of that, compensatory mechanisms of the vascular bed, such as dilatation of preexistent vascular channels and shunt formation to divert venous blood away from the occlusion site, may be less effective in patients with diabetes than in nondiabetic patients with BRVO. It is unlikely that preexistent diabetic retinopathy is the cause of the difference in course and visual outcome between diabetic and non-diabetic patients in our study, because in the 28 patients with diabetes mellitus, there were only 5 with diabetic retinopathy and macular edema. In these patients, VA before and after BRVO was comparable to that of the other patients with diabetes without significant pre-existing diabetic retinopathy. The VA in our study did not change to a significant degree after 1 year in either group. This indicates that the VA in BRVO is stable after 1 year. Cardiovascular morbidity occurred more frequently in diabetic BRVO patients compared to the patients without diabetes. This is probably a consequence of vascular changes due to diabetes. Laser treatment was more intense in patients with diabetes compared to non-diabetic patients owing to more frequent ischemia and macular edema. Moreover, an increased number of reviews were necessary for patients with diabetes with BRVO owing to complications and treatment of diabetes and the BRVO. This indicates a more serious disease course in patients with diabetes. Occlusions occur at an earlier age in patients with diabetes. We therefore recommend more frequent follow-up of patients with diabetes with BRVO to recognize and treat complications at an early stage.

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