Review

DIABETIC RETINOPATHY – RISK FACTORS AND STRATEGIES IN PREVENTION

Mala Dharmalingam

INTRODUCTION

Diabetes is a common cause of acquired blindness in developed and developing countries. In fact it is second only to cataract as a cause of blindness in India. This is indeed pathetic as it is a treatable cause and as more recent research has shown, to a certain extent, a preventable one also.

There are an incredibly large number of undiagnosed diabetic patients who are unaware of their disease, depriving them of appropriate diabetes care and placing them at a greater risk of complications with untreated diabetes. Recent advances in screening and treatment have not resulted in a significant reduction in sight-threatening retinopathy (1). Unfortunately, all persons with diabetes who would benefit from timely and appropriate retinal examination and sight-saving laser surgery do not have access to specialized eye care. Reasons for this lack of care and unnecessary loss of vision include (2):

1. Approximately 60% of persons requiring laser surgery do not receive or do not have access to expert eye care.

2. There is currently no known cure or method to prevent diabetic retinopathy.

DIABETIC RETINOPATHY AND CLASSIFICATION

Before we go on to the prevention of diabetic retinopathy it is important for us to know about its classification (Table 1). ETDRS classification is now universally accepted and is detailed below.

Table 1: Classification of Diabetic Retinopathy (3).

Early Treatment Diabetic Retinopathy Study Levels of Diabetic Retinopathy [ETDRS]

Nonproliferative Diabetic Retinopathy (NPDR)

A. Mild NPDR
- At least one microaneursym

B. Moderate NPDR
- Hemorrhages or microaneurysms (H/Ma)
- Soft exudates, Venous beading (VB), and intraretinal microvascular abnormalities (IRMAs) definitely present.

C. Severe NPDR
- H/Ma in all 4 quadrants
- VB in 2 or more quardrants
- IRMA in at least 1 quadrant

D. Very Severe NPDR
- Any two or more of C

Proliferative Diabetic Retinopathy

E. Early PDR
- New vessels on the retina
- Definition not met for F

F. High-Risk PDR
- New vessels on the disc (NVD) of 1/4 to 1/3 or more of the disc area or
- Any NV and vitreous or preretinal or vitreous hemorrhage

Clinically Significant Macular Edema (any ONE of the following)
- Thickening of the retina located 500 μm or less from the center of the macula
- Hard exudates at 500 μm or less from the center of the macula with thickening of the adjacent retina
- A zone of retinal thickening, one disc area or larger in size, any portion of which is one disc diameter or less from the center of the macula

Department of Endocrinology, M S Ramaiah Medical College, Bangalore-560054.

RISK FACTORS FOR THE DEVELOPMENT OF DIABETIC RETINOPATHY

Certain factors may influence the onset or progression of diabetes-related complications. Some of these factors, such as duration of disease, are clearly not modifiable, whereas others, including smoking, the degree of metabolic control achieved, or the presence of systemic hypertension, may be amenable to highly effective interventions.

Duration of Disease: Abnormalities may be detectable at the time of disease diagnosis, such as increased blood vessel permeability in the retina and a raised GFR. However, most of these defects are reversible within the first weeks to months after the initiation of insulin therapy.

Metabolic Control: The Diabetes Control and Complications Trial (DCCT) and other intervention trials, as well as epidemiologic studies, have demonstrated unequivocally that there is a close relationship between the degree of long term metabolic control achieved and the onset and progression of microvascular complications (4).

Hypertension: Hypertension is a risk factor for the development of diabetes-related complications.

Family History: Compelling data suggest that diabetes-related complications tend to cluster in families (5).

Hyperlipidemia: There is a close correlation between metabolic control and disturbances in lipid metabolism. In addition, patients with lipid abnormalities tend to be at increased risk not only for macrovascular disease but for microvascular complications. In the Berlin retinopathy study, there was some indication that elevated triglycerides and reduced HDL cholesterol may contribute to the development of retinopathy in adolescents (6).

Smoking: Persons with diabetes who are current smokers are at greater risk for the onset and progression of retinopathy.

Puberty: Early manifestations of microvascular complications (nephropathy and retinopathy) are rarely found in prepubertal children with type 1 diabetes (6, 7). In contrast, both retinopathy and nephropathy show an increasing prevalence during the pubertal and post pubertal years (8).

PRIMARY PREVENTION OF DIABETIC RETINOPATHY

The Diabetes Control and Complications Trial (DCCT) (1983-1993) (7) conclusively demonstrated that intensive control of blood glucose levels for type 1 diabetes, as demonstrated by reduction of glycated hemoglobin readings, substantially reduces the risk of onset and progression of retinopathy, and the need for laser surgery (9). Intensive control also had a beneficial effect in reducing the risk of kidney disease, neuropathy, and, to a lesser degree, large vessel disease. Similar results were established for type 2 diabetes in the United Kingdom Prospective Diabetes Study (UKPDS) (10, 11) (Table 2 and 3).

Table 2: Major DCCT Findings (7)

Complications	Risk reduction with intensive therapy (%) [a]	
	After 6.5 yr in DCCT [b]	After 4 additional yr in EDIC[c]
Retinopathy		
3-step worsening	63	77
Macular edema	26	72
Proliferative or severe Non proliferative	47	75
Laser therapy	51	77

[a] Risk reduction of intensive versus conventional therapy, all P < 0.04, except for macular edema during DCCT (P=NS).

[b] Results from DCCT for combined primary prevention and secondary intervention. During 6.5 yr mean follow-up, intensive therapy achieved average HbA_{1c} of 7.2%, and conventional therapy achieved average HbA_{1c} of 9.1%.

[c] Results from DCCT/EDIC follow-up of DCCT cohort. DCCT subjects were followed for an additional 4 yr after DCCT, during which all subjects were encouraged to use former intensive therapy and median HbA_{1c} levels were 7.9% and 8.2% in the intensive and conventional treatment groups, respectively.

TABLE 3: Results of UKPDS (10)

Complications	Risk reduction (%) with Intensive glycemic therapy	Intensive anti-hypertensive therapy
All cause mortality	6	18
All microvascular	25	37
Retinopathy, laser therapy	29	35

SECONDARY PREVENTION

Present treatment modalities and understanding of diabetic retinopathy substantially reduces the risk of vision loss from diabetic retinopathy and diabetic macular edema. Multicentric national clinical trials over the past 30 years have led to precise clinical algorithms for diagnosis, management, follow-up, and treatment of diabetic retinopathy. The Diabetic Retinopathy Study (DRS) (1971-1975) established the benefits of scatter (panretinal) laser photocoagulation for reducing the risk of vision loss from proliferative diabetic retinopathy (3, 12). The Early Treatment Diabetic Retinopathy Study (ETDRS) (1979-1990) elucidated the natural history of diabetic retinopathy, provided insight into the optimal timing for scatter laser photocoagulation for diabetic retinopathy, and established the benefit of focal laser surgery for diabetic macular edema (13, 14). The Diabetic Retinopathy Vitrectomy Study (DRVS) (1977-1987) demonstrated the value of vitrectomy surgery for restoring useful vision in some eyes that have suffered vision loss from diabetes and clarified the optimal timing for vitrectomy for eyes with non-resolving vitreous hemorrhage or traction retinal detachment (15). Collectively, these clinical studies have provided the data that establishes current clinical management of diabetic eye disease.

TODAY'S CHALLENGES IN DIABETES CARE

The challenges for the twenty-first century are to eliminate the complications of diabetes and to find a cure for the disease. Until these challenges are met, the present task is to apply the knowledge gained in the twentieth century to reduce the mortality and morbidity associated with diabetes (16). To accomplish this task, the immediate challenges are to identify all persons with diabetes mellitus; diagnose the level of diabetic retinopathy yearly or as recommended [Table 4] for all patients by providing cost-effective, accessible, quality eye care, apply the standards of eye care established by the ETDRS by increasing access for the diagnosis and treatment of diabetic retinopathy. We should also apply the standards of care for diabetes control established by the DCCT; and create data bases for further study of diabetes, until there is a cure.

Table 4: Clinical Follow-up Based on Level of Diabetic Retinopathy

Level of DR	Follow-up
No DR	12 months
Mild nonproliferative DR	12 months
Moderate nonproliferative DR	4 months
Severe to very severe nonproliferative DR	1 week
Proliferative DR less than high risk	1 week
High risk proliferative DR	Immediate
Macular edema	1 week

TYPE 1 DIABETES AND RETINOPATHY

Sight-threatening diabetic retinopathy is rarely found in prepubertal children and is exceedingly uncommon before the age of 15 years (8). Furthermore, there is little likelihood of the presence of significant retinopathy before 5 years' duration of diabetes. In adults, retinopathy is frequently associated with diabetic nephropathy; however, in adolescents, studies report a similar prevalence of retinopathy in patients with and without microalbuminuria (26% versus 25%) (17).

Some instances of acceleration of diabetic retinopathy have been associated with significant improvements in metabolic control (18). The mechanism responsible for this deterioration is uncertain. Clinicians should be aware of this possibility as attempts are made to stabilize patients whose diabetes has been poorly controlled for a long time or as intensive diabetes management is begun. Fortunately, the deterioration seems self-limited and rarely causes impairment of vision.

SUMMARY

The current strategies for the prevention of diabetic retinopathy should be mainly aimed at identifying risk factors in the patient and counseling for the same. Patients should be discouraged from smoking. They should be encouraged to keep a close watch on their blood pressure and to achieve as good a glycemic control as possible. Today we can be certain that with these measures it is possible to prevent / delay diabetic retinopathy to a great extent.

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