REVIEW

Blindness and microvascular complications of diabetes mellitus are preventable

MR Van Newkirk

This paper reviews the evidence of the Early Treatment Diabetic Retinopathy Study that with early retinal photocoagulation, blindness as a complication of diabetes mellitus is preventable. The evidence from the Diabetes Control and Complications Trial and the 10-year follow up report of the Wisconsin Epidemiologic Study of Diabetic Retinopathy that high blood sugar levels play a major role in the development of microvascular complications of diabetes mellitus in insulin-dependent and non–insulin-dependent diabetes mellitus are also reviewed. The screening methods used to detect diabetes mellitus and diabetic retinopathy and the cost-effectiveness of diabetic retinopathy screening are also discussed. The early diagnosis, proper treatment, and reduction of risk factors of diabetes mellitus can prevent the complications of the disease, avoid the need for expensive treatment, and decrease the morbidity and mortality associated with the disease. Investment in early diagnosis and education of patients in the effective management of their disease is cost-effective.

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Key words: Diabetes mellitus, insulin-dependent; Diabetes mellitus, non–insulin-dependent; Diabetes, gestational; Diabetic retinopathy

Introduction

Diabetic retinopathy (DR) is the most common cause of new cases of blindness among people of working age in the developed world.[1] Ninety-five per cent of visual loss from DR could be prevented with improved management of diabetes and early detection and treatment of DR.[2] The Early Treatment Diabetic Retinopathy Study (ETDRS) demonstrated in 1985 that severe visual loss can be nearly eliminated when proliferative DR and macular oedema are detected early and treated appropriately with laser retinal photocoagulation.[3] After 10 years, however, this knowledge has had little impact on the amount of blindness caused by diabetes mellitus (DM) in Asia and many other parts of the world. A recent vision survey in Melbourne, Australia, revealed that fewer than 50% of the people in that city with diabetes were receiving timely and appropriate eye examinations.[4]

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In Hong Kong, a recent study found that only 38% of the diabetic population had been previously diagnosed with diabetes.[5] These studies identify three major problems with DM: 1) The majority of people with non–insulin-dependent diabetes mellitus (NIDDM) may not yet have been diagnosed; 2) an alarming proportion of patients with DM are not sufficiently informed of the risk of complications, such as blindness, and do not take advantage of the available diagnostic opportunities to pursue timely and appropriate eye examinations and retinal laser treatment; and 3)the majority of those diagnosed with NIDDM do not have access to programmes giving patient education and ideal management of NIDDM.

Results

Historically, the most significant predictive factor for DR has been duration of the disease; after 20 years of diabetes, 98% of patients with Type I and more than 60% of patients with Type II have DR.[6] Two excellent studies have shown that hyperglycemia is also a major risk factor in the development and progression of DR. The Diabetes Control and Complications Trial (DCCT) has shown that intensive control of blood glucose levels in patients with diabetes can delay the onset and retard the progression of DR, neph-

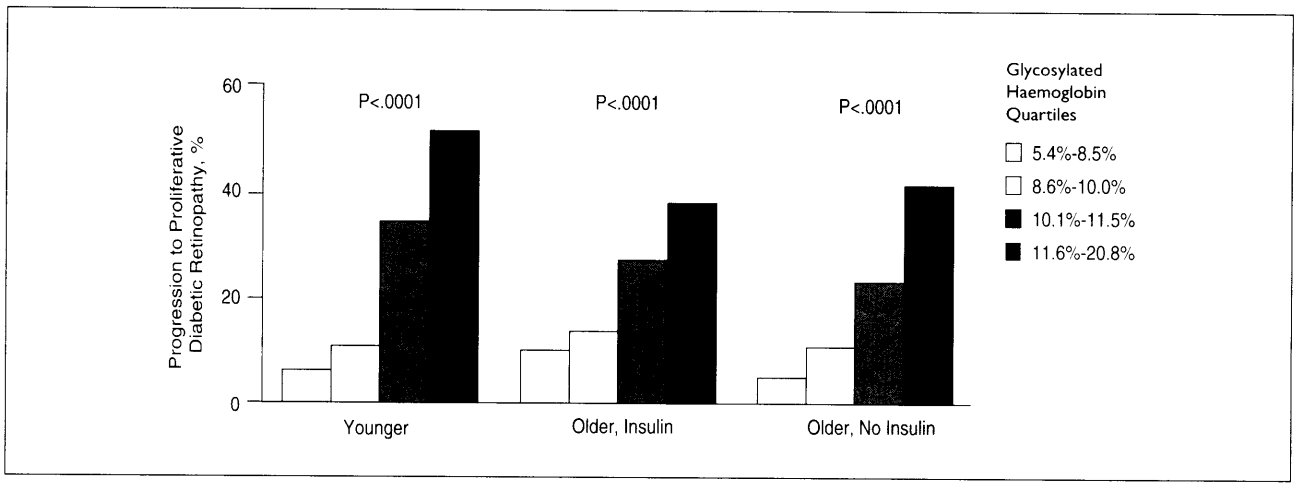

Fig 1. Proliferative diabetic retinopathy is the ocular complication most significantly related to severe visual loss. These data make it very clear that patients with normal levels of glycated haemoglobin have significantly lower risk of progressing to proliferative diabetic retinopathy at the 10 year follow-up period.[8] (Reproduced with permission of the Archives of Internal Medicine. Taken from: Klein R, Klein BE, Moss SE, Cruickshanks KJ. Relationship of hyperglycemia to the long-term incidence and progression of diabetic retinopathy. Arch Intern Med 1994;154:2169-78).

ropathy, and neuropathy.[7] The DCCT was limited to those with insulin-dependent diabetes mellitus (IDDM) and many health care providers have been reluctant to apply this important data to NIDDM patients.

The 10-year follow up report of the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR),[8] which included both IDDM and NIDDM groups, strongly suggests that the glycated haemoglobin level is related to the incidence and progression of DR and to the incidence of gross proteinuria. In the WESDR study, the glycated haemoglobin A1 (HbA_1, A_{1a}, A_{1b}, and A_{1c}) was measured using a microcolumn technique[9] at baseline, four-year follow up, and 10-year follow up. The WESDR HbA1 results were compared with the DCCT HbA1c results using the formula: DCCT = 0.003 + 0.935 (WESDR). Figures 1 and 2 depict the baseline results of glycated haemoglobin levels of the three groups of patients and the incidence % of progression of retinopathy to proliferative DR (Fig 1) and macular oedema (Fig 2).

The most common causes of severe vision loss in DR are proliferative DR and macular oedema. The WESDR evaluated the progression of retinopathy to proliferative DR, as measured by standardised stereoscopic fundus photography, which is a modification of the ETDRS adaptation of the modified Airlie House Classification scheme of DR.[10] The WESDR findings clearly show that patients in all three groups with low levels of glycated haemoglobin at baseline have significantly less proliferative DR and macular oedema. The younger-onset group taking insulin at baseline had a mean age of 29.3 years, a mean duration of diabetes of 14.7 years, and a mean glycated haemoglobin level of 10.8%. The older-onset group taking insulin at baseline had a mean age of 65.2 years, a mean duration of diabetes of 15.0 years, and a mean glycated haemoglobin of 10.2%. The older-onset group not taking insulin at baseline had a mean age of 68.0 years, a mean duration of diabetes of 8.8 years, and a mean glycated hemoglobin of 8.9%.

The important findings in the WESDR were not limited to diabetic retinopathy, but also include renal complications. An increasing incidence of gross proteinuria for all three groups was noted, which was significant in the younger IDDM group (Fig 3).

Discussion

Non–insulin-dependent diabetes mellitus accounts for 85% to 90% of all diabetes cases. In 1994,[11] it was estimated that 51.4 million people in Asia had DM, and by the year 2010 that number is projected to increase to 139.2 million people.[10] The health risks of NIDDM are grossly underestimated in most parts of Asia; there is a significant lack of public awareness education and diabetes support groups in Asia.

Diabetes mellitus screening

Screening for a chronic disease such as DM is most cost-effective when a selective approach is used.[12] The public health approach should focus on the

identification and education of the following high risk individuals: the obese (especially those with increased intra-abdominal fat),[13] persons older than 60 years, anyone with a positive family history of DM, and pregnant women who are at risk for gestational diabetes. Some debate exists regarding the best screening methods and there has been movement away from mass screening using blood glucose tests. However, a 2-hour post-load glucose test has a reported specificity of 93.3% and a 47.9% predictive value for NIDDM confirmed by a full oral glucose tolerance test (OGTT),[14] compared with values of 64.5% and 9.5%, respectively, for glycohaemoglobin screening. Recently, a study of non-fasting finger stick glycated haemoglobin has been shown to be a useful screening tool for detecting DM and to also be helpful in predicting who will develop DR.[15]

Diabetic retinopathy screening

A successful screening programme should target high risk patients. The most important risk factors for developing DR are duration of disease and glycated haemoglobin levels. The following patients with diabetes should be screened for DR: all post-pubescent patients with IDDM of more than 5 years' duration; all patients diagnosed with NIDDM; all women with IDDM who are planning a pregnancy. Screening should consist of assessment of visual acuity, direct or indirect ophthalmoscopy with dilation of the pupils, and measurement of intra-ocular pressure.

Primary care physicians play an important role in the diagnosis and management of complications of DM. Improved diagnosis and referral of patients with DR can result from an education programme directed at primary care physicians.[16] After 10 primary care physicians were given a four-hour course on the recognition of diabetic retinopathy, ophthalmoscopy of diabetic fundi, and instruction in the management of various stages of retinopathy, scores on a written examination increased from a mean of 49% to 78%. Failure to detect and refer proliferative or pre-proeiferative retinopathy decreased from 60% to 15%. In addition, recognition of maculopathy improved significantly. These results emphasise the value in continuing education for primary care physicians in the diagnosis and management of complications of DM.

The diagnosis and management of diabetic retinopathy

A slide script has been produced by the American Academy of Ophthalmology, specifically designed to help the primary care physician learn to screen for this disease.[17] Various screening methods for the detection of DR have been studied. The "gold standard" technique that has repeatedly shown superior sensitivity and specificity over all other methods is seven-field stereoscopic fundus photography. In the Diabetic Retinopathy Study (DRS), dilated ophthalmoscopy by ophthalmologists was found to be less sensitive and specific than colour stereoscopic fundus photographic grading in detection and staging of DR.[18] The ETDRS found stereoscopic fundus photographic grading superior to dilated ophthalmoscopy with contact lens biomicroscopy when performed by retinal specialists.[19] Non-mydriatic fundus photography has been used as a

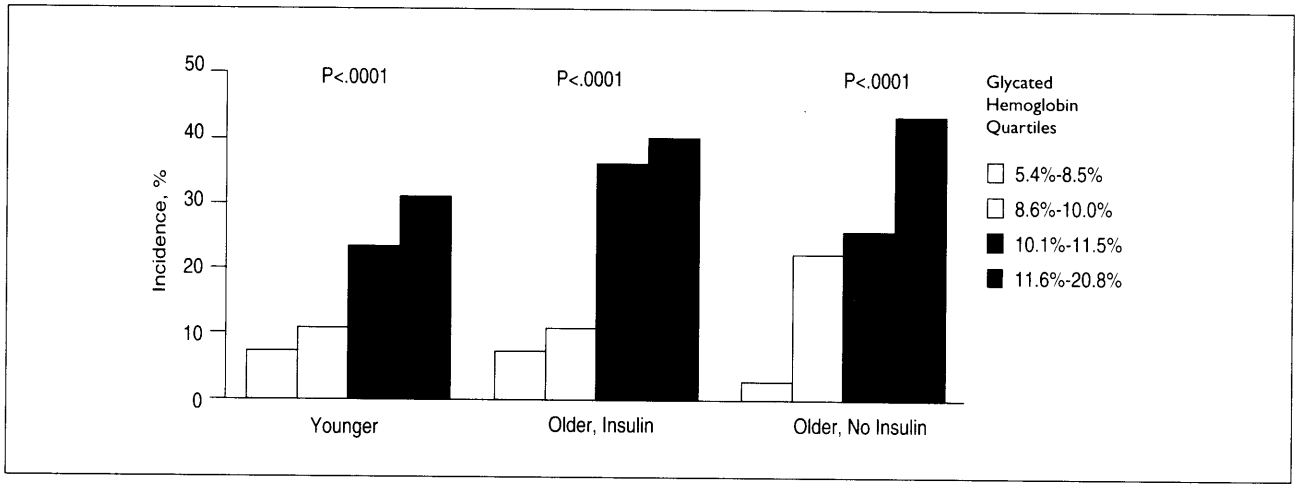

Fig 2. Macular edema is a very important mechanism causing severe visual loss in the diabetic population. These data indicate clearly the increased risk of macular edema in all groups of diabetics when the glycated haemoglobin levels are in the high range.[7] (Reproduced with permission of the Annals of Internal Medicine. Taken from: Klein, et al. Relation of glycemic control to diabetic microvascular complications in Diabetes mellitus. Ann Intern Med 1996;124:90-6).

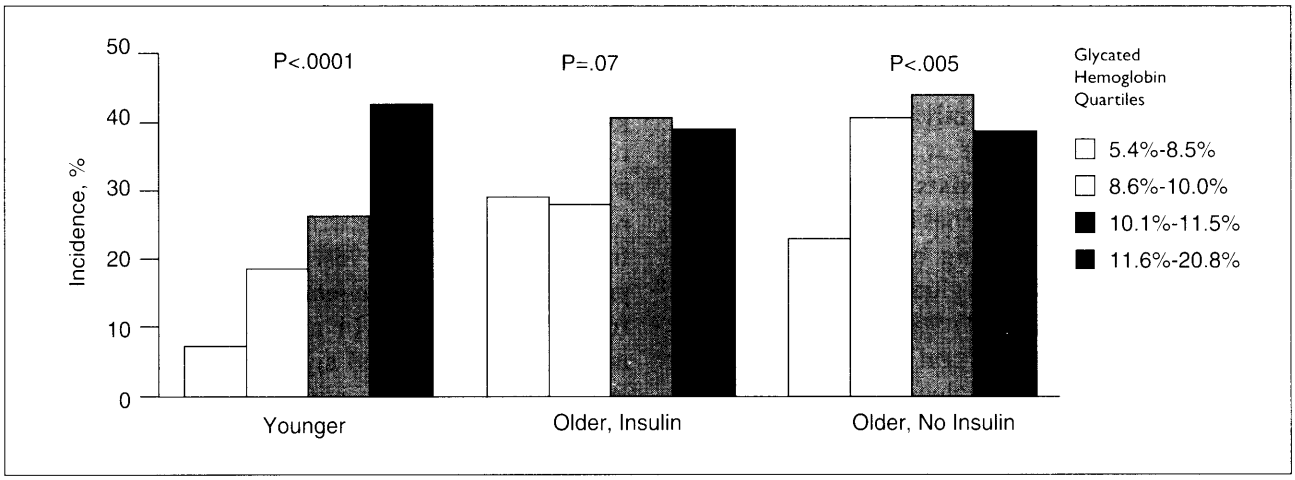

Fig 3. The important findings in the WESDR were not limited to diabetic retinopathy, but also include renal complications. An increasing incidence of gross proteinuria for all three groups was noted, which was significant in the younger IDDM group. (Reproduced with permission of the Annals of Internal Medicine. Taken from: Klein, et al. Relation of glycemic control to diabetic microvascular complications in Diabetes mellitus. Ann Intern Med 1996;124:90-6).

tool for mass screening, especially in rural areas. In about 10%, the photographic quality of the non-mydriatic camera does not allow grading of the fundus findings, especially in older people with small pupils or cataracts. The non-mydriatic photography was, however, superior to undilated fundus examinations performed by trained ophthalmologists.[20] The sensitivity for recognising DR increases from 14% to 43% when the pupil is dilated in conjunction with the use of the non-mydriatic camera.[21]

At the University of Oklahoma, Franzen reported on the transmission of digitised retinal images of diabetic patients at the Carl Albert Indian Hospital to the Department of Ophthalmology in Oklahoma City, 82 miles away. This enables the screening of diabetic patients for retinopathy by an ophthalmologist who views stereoscopic retinal images without the need to transport the patient or the physician. With satellite technology and fiber optic cables, digitised images can be transmitted from most places on the earth to another. This technology could save resources and correct the problem of the maldistribution of physicians, and may represent the screening mechanism for the future.

Patients with diabetes should be referred to an ophthalmologist as soon as they are diagnosed with either moderate background DR, any proliferative DR, or any DR with elevated Hg A_{1c} levels. In addition, all IDDM patients in the first trimester of pregnancy and any patient with reduced corrected visual acuity or whose retina can not be visualised need to be referred.

Diabetes education

There are few effective preventive education programmes on DM in most parts of Asia. The International Diabetes Federation (IDF) has begun to promote the diagnosis, treatment, care, and education of individuals with diabetes in Asia; and many hospitals are developing diabetes education units. However, much more needs to be done. All complications of DM should be addressed. Methods to empower the patient to decrease the risk of complications should be presented. Good presentation techniques and effective language must be used to enable each patient to understand their disease.

A good example of the benefits of preventive education for patients with diabetes is illustrated by a comparison of an intensive foot care education programme with a conventional foot care programme in Sydney, Australia.[22] The intensive foot care education programme consisted of an extended timespan, featured greater contact between the patient and the educators, included training sessions on practical foot care, and used cognitive motivational techniques. The intensive group, when compared with a conventional group showed significantly greater foot care knowledge ($P \leq 0.001$) and greater compliance with the recommended foot care routine ($P \leq 0.012$), and a significantly greater percentage sought a recommended consultation with foot care specialists ($P \leq 0.008$).

Patient glucose management education

Intensive public diabetes education programmes are needed on a large scale to achieve effective treatment

and compliance in patients with DM. Effective programmes include a teamwork approach that involves the patient, family, nurses, exercise therapists, diet counselors, and physicians. The ultimate responsibility, however, rests with the individual. It is important for each patient to be educated in the basic metabolic mechanisms of blood sugar and the interactions of diet, exercise, illness, and medicines as well as in the psychosocial aspects of living with DM. While diet and exercise education is changing with IDDM patients, diet and exercise therapy are extremely important in the establishment of near-normal blood sugar levels in patients with NIDDM. The DCCT has demonstrated the value of intensive short-acting insulin usage to keep near-normal levels of blood glucose in IDDM.[7] As a result of the DCCT study, the use of long-acting insulin agents has decreased in the management of IDDM patients.

The concept of relative insulin resistance in NIDDM is intimately linked to diet and exercise. Obviously, food intake is important, both in terms of caloric and nutritional value; diet must be included in all NIDDM education programmes. Exercise plays an important role in diabetes management because muscle tissue is the major target for insulin-stimulated glucose disposal and because a high muscle mass improves glucose use.[23] Obese individuals with NIDDM, especially those with intra-abdominal obesity, have greater insulin resistance involving hepatic glucose production and peripheral glucose utilisation,[24] hence, weight loss instruction and exercise programmes are critical for this group. Insulin resistance is commonly acquired in NIDDM as a result of hyperglycemia and glucose toxicity, and any intervention that lowers plasma glucose concentrations improves insulin sensitivity.[25] Insulin resistance is also a result of smoking[26] and hypertension,[27] so patients with NIDDM should be encouraged to stop smoking and to manage their hypertension closely.

It is appropriate for the patient to control the main day-to-day variables of blood glucose levels. Home finger stick blood glucose monitoring is required for the accurate assessment of blood glucose levels. This self-monitoring method is an essential part of the DM education programme and should be included in all therapy.

Cost-effectiveness of diabetic retinopathy screening and treatment

Javitt and Aiello[28] used the PROPHET (Prospective Population Health Event Tabulation) Modeling System to calculate the cost of screening and treatment per person-year of vision saved and the cost of screening and treatment per quality-adjusted life-year (QALY) saved for the average person. Based on 1986 US dollars, the costs of providing screening and treatment for DR is US$1757 per person-year of vision saved. This cost is higher for NIDDM, being US$2898 per person-year of vision saved. However, compared with the cost of coronary artery bypass surgery for left main coronary artery disease at US$5100, neonatal intensive care (birthweight, 1000-1499 g) at US$5460, and liver transplant at US$250 000, the screening and treatment of DR is very cost-effective. It is not as cost-effective to concentrate health care funds on complications of DM in the late stages of the disease, where the prognosis is poor, and the morbidity and mortality of affected patients is high. Health care dollars would be better spent by developing an improved system for the early diagnosis of DR and on patient education.

Conclusion

The knowledge that early retinal photocoagulation can prevent severe visual loss from the retinal microvascular complications of DM has had little impact on blindness from DM in Asia. Recent evidence that maintaining near normal blood sugar levels in patients with DM can prevent the microvascular complications of diabetes provides new hope. The pathological explanation of the damaging effects of hyperglycemia is not known at this time, however, with improved diagnosis of DM and management of blood sugar levels, most microvascular complications of diabetes, including blindness, can be prevented.

A teamwork approach that involves patients, family, and all levels of health care providers offers a mechanism for major improvement in the quality and productivity of the lives of the 139.2 million Asians projected to have the disease by the year 2010. Such an approach must educate about the roles of diet, exercise, major risk factors, and medication; it must stress the need for accurate diagnosis and treatment early in the disease process. This would enable patients to manage their disease effectively by maintaining their blood glucose at near-normal levels. Many of the expensive and catastrophic complications of DM could thereby be prevented.

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