The 7th Conference on Health Care of the Chinese in North America

Management of Diabetic Retinopathy

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Abstract

Introduction

Diabetic retinopathy (DR) has become the leading cause of blindness in the 20 to 74 years old age group in the U.S. In younger-onset patients (less than 30 years), the prevalence of DR increases from 17% to 98% when comparing disease duration of less than 5 years and more than 15 years, respectively. These prevalence figures are 29% and 78% when comparing the same disease duration in older-onset patients (30 years or older). Approximately 10% of diabetic patients have the most severe category of DR (proliferative); approximately 9.0% of diabetic patients have macular edema. Diabetic patients of Chinese American ancestry have not been identified to differ from this overall characterization.

Classification of diabetic retinopathy

The microvascular complications of DR can be subdivided into three main categories: nonproliferative, advanced nonproliferative, and proliferative retinopathy. Nonproliferative and advanced nonproliferative retinopathy consist of intraretinal abnormalities, whereas proliferative retinopathy includes both intraretinal and preretinal abnormalities.

Non-proliferative retinopathy

The intraretinal abnormalities of nonproliferative retinopathy consist of two main components: increased retinal vascular permeability and retinal ischemia. Clinically, the increased vascular permeability can be seen as:

- dot and blot retinal hemorrhages plus microaneurysms;
- retinal edema; and/ or
- exudates with surrounding microaneurysms

The retinal edema and exudates occur primarily in the central portion of the retina, known as the macula, and can cause decreased reading and driving vision due to macular edema. This break down of the "blood retinal barrier" occurs at the level of the retinal vascular endothelium. Histopathologically, the retinal capillaries show basement membrane thickening and loss of pericytes. The increased permeability of abnormal diabetic retinal

vessels can be demonstrated by leakage of dye into the retina during fluorescein angiography, whereas normal retinal vessels do not leak fluorescein.

The second component of the intraretinal abnormalities is retinal ischemia. This ischemia is secondary to occlusion of retinal vessels and is referred to as "capillary drop-out". The pathogenesis of these occlusions is not well understood but may be secondary to abnormal platelet aggregation and/or basement membrane thickening of the vessel wall. Nonperfusion of these abnormal retinal capillaries can be confirmed histopathologically by the presence of empty vessels and clinically during fluorescein angiography. If this "capillary drop-out" occurs in the macular region, the patient may experience decreased central vision secondary to macular edema. These macula abnormalities (edema and/or ischemia) may occur during any of the three categories of DR (nonproliferative, advanced nonproliferative, or proliferative).

Retinal ischemia in the periphery of the retina, away from the macula, does not result in decreased vision but is associated with proliferation of vascular and fibrous tissue on the retinal surface. This growth of fibrovascular tissue is the main component of the third category of diabetic retinopathy known as proliferative diabetic retinopathy (PDR). Warning signs that PDR may soon occur are known as advanced nonproliterative retinopathy (also referred to as preproliferative and moderate or severe nonproliferative retinopathy).

Advanced nonproliferative retinopathy

In addition to the nonproliferative findings mentioned above, patients with advanced nonproliferative retinopathy have:

1. venous beading;
2. IRMAs (intraretinal microvascular abnormalities),
3. severe retinal hemorrhage and microaneurysms (too many to count).

These vascular abnormalities occur as a response to local retinal ischemia. "Cotton wool spots" (nerve fiber layer infarcts) are located in the nerve fiber layer and are due to a blockage of axoplasmic transport at sites of capillary nonperfusion. Unlike the three lesions listed above, cotton wool spots, by themselves, are not signs that an eye may be rapidly progressing to the proliferative category of retinopathy.

Proliferative diabetic retinopath (PDR)

These abnormalities consist of the proliferation of fibrovascular tissue on the surface of the retina. The fibrous tissue and new vessels grow on the most anterior surface of the retina (the internal limiting membrane) and the most posterior surface of the vitreous (the posterior hyaloid). These vessels can bleed with resultant preretinal and vitreous hemorrhages which can markedly decrease vision. Also, the overlying vitreous can contract and pull on these abnormal vessels with consequent bleeding and/or traction detachment of the retina. Hemorrhages variably prevent light from reaching the retina, and vision may suddenly or gradually decrease to counting fingers or less. This often occurs in patients who are not aware of the presence of diabetic retinopathy. Patients with traction retinal

detachments also may be asymptomatic until the macula becomes involved in the detachment, at which time vision usually decreases to counting fingers. These patients may not be able to ambulate independently, particularly if both eyes are similarly affected.

Screening and follow-up of diabetic retinopathy - Different guidelines have been developed for screening of the diabetic population, depending upon visual symptoms, the length of diagnosis and type of diabetes. Follow-up intervals are based upon further findings upon retinal examination. These recommendations are based on statistical data from treatment trials (see references).

For patients with no diabetic retinopathy:

1. type I (juvenile-onset, age at diagnosis of diabetes mellitus less than 30 years); yearly retinal examination with ophthalmoscopy through dilated pupils after 5 years duration of diabetes.
2. type II (maturity-onset, age at diagnosis of diabetes mellitus 30 years or older): dilated retinal examination at time of initial diagnosis and yearly thereafter. With any vision problems, prompt retinal examination through dilated pupils is recommended.

For patients with diabetic retinopathy and no visual symptoms:

1. microaneurysms and/or retinal hemorrhag es only: dilated fundus examination every 6 to 12 months.
2. exudates in macular region (a four disc diameter area centered approximately two disc diameters temporal to the optic disc): dilated retinal examination by an ophthalmologist at 4 to 6 month intervals.
3. venous beading. IRMAs (intra-retinal microvascular abnormalities), severe retinal hemorrhages and microaneurysms (too many to count), new vessels on disc (NVD), and/or new vessels on retina (NVR): prompt dilated retinal examination by ophthalmologist and at least every 3 to 4 months thereafter.

As before, patients with visual symptoms should have prompt retinal examination through dilated pupils.

In diabetic patients who become pregnant (not patients with gestational diabetes). dilated retinal examination during the first trimester and every three months until delivery is recommended, because an accelerated progression of diabetic retinopathy is observed in some. After delivery, follow-up is recommended according to the above guidelines.

Treatment

Multicenter randomized clinical trials have established the place of treatment with laser photocoagulation for different manifestations of diabetic retinopathy. Clinically significant macular edema is one indication for laser in order to decrease vascular leakage. This is usually performed with topical anesthesia, and may reduce loss of reading and driving vision in treated patients by 60%.

For eyes with PDR and high risk of severe visual loss, panretinal photocoagulation (PRP) with 1200 to 1600 burns scattered throughout the periphery of the retina (sparing the macula and optic nerve) is indicated. This is administered as an outpatient procedure with topical or retrobulbar anesthesia. Through regression of proliferative changes and reduction of vitreous hemorrhage, PRP reduces loss of ambulatory vision by approximately 50%.

Vitrectomy surgery is considered for non clearing vitreous hemorrhage or traction retinal detachment involving the macula.

Prevention

As demonstrated in the Early Treatment of Diabetic Retinopathy Study, aspirin does not appear to be beneficial to the course of diabetic retinopathy. Conversely, aspirin does not increase the risk of preretinal or vitreous hemorrhages. There are thus no contraindications to the use of aspirin when required for cardiovascular disease or other medical conditions in diabetic patients.

The Diabetes Control and Complications Trial Research Group recently reported that intensive control of blood glucose concentrations close to the normal range in insulin-dependent patients can decrease the frequency and severity of microvascular complications of diabetes mellitus. The risk of developing retinopathy was reduced by 76%, and the progression of very early retinopathy was slowed by 54%. The development of proliferative or severe nonproliferative retinopathy was reduced by 47%. The chief adverse event associated with these favorable results of intensive therapy was a two-to-three fold increase in severe hypoglycemia.

A recent population-based study found systemic blood pressure to be a significant predictor of the incidence of diabetic retinopathy in patients younger than 30 years but not in patients 30 years or older. One study of Pima Indians suggests that control of blood pressure may reduce the incidence of retinal exudates in Type II diabetics not being treated with insulin.