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DIABETIC RETINOPATHY UPDATE

Advances in the treatment of diabetic retinopathy

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Abstract Diabetic retinopathy, the most common long-term complication of diabetes mellitus, remains one of the leading causes of blindness worldwide. Strict metabolic control, tight blood pressure control, laser photocoagulation, and vitrectomy remain the standard care for diabetic retinopathy. Focal/grid photocoagulation is a better treatment than intravitreal triamcinolone acetonide in eyes with diabetic macular edema and should be considered as the first-line therapeutic option. The current evidence suggests that intravitreal triamcinolone acetonide or anti-vascular endothelial growth factor agents result in a temporary improvement of visual acuity and a short-term reduction in central macular thickness in patients with refractory diabetic macular edema and are an effective adjunctive treatments to laser photocoagulation or vitrectomy. However, triamcinolone is associated with risks of elevated intraocular pressure and cataract. Vitrectomy with the removal of the posterior hyaloid without internal limiting membrane peeling seems to be effective in eyes with persistent diffuse diabetic macular edema, particularly in eyes with associated vitreomacular traction. Emerging therapies include islet cell transplantation, fenofibrate, ruboxistaurin, pharmacologic vitreolysis, rennin-angiotensin system blockers, and peroxisome proliferator-activated receptor gamma agonists.

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1. Introduction

Diabetic retinopathy is the most common microvascular complication of diabetes and remains one of the leading causes of blindness worldwide among adults aged 20–74 years. The two most important visual complications of diabetic retinopathy are diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR). The prevalence of diabetic retinopathy increases with duration of diabetes, and nearly all persons with type 1 diabetes and more than 60% of those with type 2 have some retinopathy after 20 years. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), 3.6% of younger-onset patients (type 1 diabetes) and 1.6% of older-onset patients (type 2 diabetes) were legally blind (Fong et al., 2003).

2. Evidence-based patient care

Five large randomized controlled trials provide the scientific basis for care in the diabetic patient to preserve vision.

2.1. The diabetes control and complications trial (DCCT)

The DCCT randomized 1441 patients with type 1 diabetes to receive intensive glycemic or conventional therapy. Over 6.5 years of follow-up, intensive treatment [median HbA1c (glycosylated hemoglobin A1c), 7.2%] reduced the incidence of diabetic retinopathy by 76% and progression of diabetic retinopathy by 54%, as compared with the conventional treatment (DCCT, 1993). Long-term observational DCCT data showed that despite gradual equalization of HbA1c values after study termination, the rate of diabetic retinopathy progression in the former intensively treated group remained significantly lower than in the former conventional group (“metabolic memory”) (White et al., 2008), emphasizing the importance of instituting tight glycemic control early in the course of diabetes.

Tight glycemic control has two clinically important adverse effects. First, there is risk of early worsening of diabetic retinopathy. In the DCCT, this occurred in 13.1% of the intensive versus 7.6% of the conventional treatment group. However, this effect was reversed by the 18th month, and no case of early worsening resulted in serious visual loss. In the DCCT, the long-term benefits of intensive insulin treatment greatly outweighted the risks of early worsening of diabetic retinopathy. Therefore, ophthalmoscopic monitoring before initiation of intensive treatment and at 3-month intervals for 6–12 months thereafter seems to be appropriate when intensive treatment is initiated in patients with long-standing poor glycemic control, particularly if retinopathy is at or past the moderate non-proliferative stage. In patients whose retinopathy is already approaching the high-risk stage, it may be prudent to delay the initiation of intensive treatment until photocoagulation can be completed, particularly if the HbA1c level is high (DCCT, 1998). Second, tight glycemic control was associated with more frequent severe hypoglycemic episodes compared to the conventional group (DCCT, 1993).

2.2. The United Kingdom prospective diabetes study (UKPDS)

The UKPDS randomized 3867 patients with newly diagnosed type 2 diabetes to receive intensive or conventional therapy. After 12 years of follow-up, the progression of diabetic retinopathy was reduced by 21% and the need for laser photocoagulation by 29% in the intensive versus the conventional treatment group (UKPDS Group 33, 1998). The UKPDS also investigated the influence of tight blood pressure control. A