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CLINICAL REPORT

Screening for Retinopathy in the Pediatric Patient with Type 1 Diabetes Mellitus

ABSTRACT. Diabetic retinopathy (DR) is the leading cause of blindness in young adults in the United States. Early identification and treatment of DR can decrease the risk of vision loss in affected patients. This clinical report reviews the risk factors for the development of DR and screening guidance for pediatric patients with type 1 diabetes mellitus.

Key words: type 1 diabetes mellitus, diabetic retinopathy, ophthalmic screening.

ABBREVIATIONS: DR, diabetic retinopathy; DCCT, Diabetes Control and Complications Trial

BACKGROUND

Type 1 diabetes mellitus is one of the most common metabolic disorders in children, with a prevalence of approximately 2 per 1000 school-aged children in the United States. The prevalence of type 1 diabetes mellitus increases with age, and the overall incidence of the disease may be increasing. Although the incidence of type 2 diabetes in children is increasing, there are no data or guidelines regarding ophthalmic screening in children with this disorder. Diabetic retinopathy (DR) is one of the most important complications of type 1 diabetes mellitus, representing the leading cause of blindness in young adults. There are 3 main components of a strategy to minimize the risk of visual loss attributable to DR:

1) provide the most effective treatment of the underlying metabolic disorder and its comorbidities;
2) develop optimal treatment modalities for patients with ocular disease;
3) identify risk factors for the development of ocular disease and implement effective screening programs to identify at-risk patients. The first 2 have been evaluated in well-conducted, large, prospective trials.

Optimizing Metabolic Control

The efficacy of providing intensive treatment of the underlying metabolic disorder was evaluated by the Diabetes Control and Complications Trial (DCCT),[1] which clearly demonstrated the benefits of improving glycemic control and decreasing hemoglobin A1c concentrations in decreasing the complication rate. In this study, patients who received intensive treatment with either an insulin pump or 3 or more daily insulin injections, frequent phone calls and clinic visits, and self-management education

substantially decreased their risk of both onset and progression of retinopathy, compared with patients treated with conventional therapy. The risk of retinopathy was decreased by 53% in children 13 to 17 years of age and with no retinopathy at study entry, and the risk of retinopathy progression was decreased by 70% in those who had retinopathy at the beginning of the study.[2]

One of the concerns regarding the institution of intensive metabolic control had been the potential for the acceleration of DR, on the basis of a report by Daneman et al [3] of 4 patients with poorly controlled diabetes mellitus and short stature who developed macular edema and severe proliferative diabetic retinopathy shortly after initiation of appropriate insulin therapy. This complication was evaluated in patients enrolled in the DCCT, and early worsening over the first 6 to 12 months was found to be more prevalent in patients with intensive treatment (13.1%) compared with patients with conventional treatment (7.6%).[4] However, the long-term outcomes in the patients with early worsening were the same or better than those treated with conventional therapy. The Kroc Collaborative Study Group also found that early worsening of DR was not sustained and was not associated with a worse long-term outcome.[5] Additionally, the benefits of intensive therapy continued to be evident 7 years after the end of the DCCT as demonstrated in the Epidemiology of Diabetes Interventions and Complications study.[6-8] Thus, in most cases the potential for early worsening should not restrict institution of intensive glycemic control.

Optimizing Treatment of Retinopathy

The development of optimal treatment modalities for ocular disease has also been evaluated in several studies; one of the most important is the Early Treatment of Diabetic Retinopathy Study.[9] This large study evaluated the benefit of early treatment for 2 ocular complications of type 1 diabetes mellitus, diabetic macular edema and proliferative diabetic retinopathy. Studies clearly demonstrated that patients with high-risk characteristics of these disorders experienced a marked improvement in outcome after laser therapy.[9,10] The risk of moderate vision loss (e.g., a doubling of the visual angle or 20/20 vision reduced to 20/40) from diabetic macular edema was decreased by approximately 50% with appropriate focal laser photocoagulation for clinically significant macular edema (from approx 25% without treatment to approx 12% with treatment). The risk of severe vision loss (best corrected vision of 5/200 or worse) from proliferative diabetic retinopathy was decreased to less than 2% with appropriate scatter (panretinal) laser photocoagulation.

Identification of Risk Factors for Ocular Disease

DR typically follows a predictable progression.[11] Early nonproliferative DR is characterized by changes in retinal blood flow and other microvascular changes, which may lead to ischemia, small retinal hemorrhages, and leakage of exudative fluid within the retina. More severe nonproliferative DR is characterized by intraretinal microvascular abnormalities, more extensive hemorrhages and microaneurysms, and changes in venous caliber and tortuosity, reflecting progressive capillary closure and retinal ischemia. Proliferative diabetic retinopathy is marked by fibrovascular proliferations on either the optic disc (new vessels on the disc) or new vessels

elsewhere on the retina. Proliferative diabetic retinopathy may cause vision loss by vitreous hemorrhage or contraction of fibrovascular tissue with subsequent retinal detachment. Laser surgery is promptly indicated when an eye approaches or reaches high-risk proliferative diabetic retinopathy. High-risk proliferative diabetic retinopathy is clearly defined and characterized by one or more of the following lesions:

1) new vessels on the optic disc approximately one fourth to one third disc area or more in size;
2) new vessels on the optic disc less than one fourth the disc area in size when fresh vitreous hemorrhage or preretinal hemorrhage is present; or
3) new vessels elsewhere on the retina greater than or equal to one half the disc area in size when fresh vitreous hemorrhage or preretinal hemorrhage is present.

The goal of regular eye examination is to identify and treat patients before the development of vision-threatening complications. Diabetic macular edema can be present with any level of nonproliferative or proliferative diabetic retinopathy. The role of ophthalmologic screening programs for DR will be the focus of this report.

FACTORS THAT AFFECT ONSET OF DR

Several epidemiologic studies have evaluated risk factors for development of DR. Some of these factors are amenable to treatment, resulting in a decreased risk of DR, such as optimizing metabolic control as reported in the DCCT, discontinuing smoking, avoiding obesity, and monitoring blood pressure. Other factors such as patient age, duration of disease, and the effects of puberty and pregnancy are not modifiable. The impact of the individual risk factors may be difficult to isolate, as they are not independent of one another (i.e., the longer the duration of the disease, the older the patient will be).

Duration of Disease

The duration of diabetes is unequivocally one of the most important risk factors for the development of DR. Essentially all studies demonstrate that the risk of DR increases with time in individuals with diabetes. In a study of 996 patients who had been diagnosed with type 1 diabetes mellitus when they were younger than 30 years, Klein et al.,[12] found that the prevalence of DR increased from 17% for patients with diabetes for fewer than 5 years to 98% for patients with diabetes for 15 or more years. The prevalence of proliferative diabetic retinopathy increased from 1% in patients with diabetes for fewer than 10 years to 67% in patients with diabetes for 35 or more years. A few studies have reported mild DR in children with duration of disease as short as 1 to 2 years,[13,14] but in most studies, the duration is 3 or more years, with typical durations of 8 to 10 years before development of DR.[15,16]

Age

The effect of age on the development of DR is linked to the duration of the disease (patients with longer durations are typically older). What is clear is that young children (younger than 10 years) with type 1 diabetes mellitus are at minimal risk of the development of significant ocular complications. The presence of any DR before 10 years of age has been reported rarely,[13,14] and these cases have been mild. In a series

of 996 patients with type 1 diabetes mellitus who had been diagnosed before age 30 years, Klein et al.,[12] found that mild DR was identified in only 1 patient in the first decade of life, and moderate DR was identified in 1 patient between 10 and 14 years of age. Neither of these patients required treatment. In a follow-up study of 634 patients by Klein et al,[17] no patient who was younger than 10 years at the time of diagnosis of type 1 diabetes mellitus developed proliferative diabetic retinopathy within 10 years of diagnosis. In a comprehensive review of the literature, no report of proliferative diabetic retinopathy could be found in a patient in the first decade of life.

Puberty

The effect of puberty on the development of DR has been difficult to clearly elucidate. Although the duration of diabetes before puberty affects the onset of DR,[14,18] there is good evidence that the hormonal changes associated with puberty exert an effect that is independent of age and duration of disease. Rogers et al,[19] in a study of 76 patients, found a significantly higher prevalence of DR in late pubertal subjects compared with prepubertal subjects, despite similar duration of disease and similar glycosylated hemoglobin concentrations. Murphy et al.,[20] in a similar study, found the relative risk of having DR in a pubescent group of children compared with a prepubescent group was 4.8.

Pregnancy

Pregnancy represents another well-established risk factor for DR. Several studies have demonstrated progression of DR during pregnancy.[21-24] Factors that exacerbate the acceleration of DR during pregnancy include poor metabolic control, hypertension, and a baseline degree of retinopathy. The large studies of pregnancy and DR do not include pediatric patients, and we are unaware of any study that specifically addresses the effects of pregnancy in adolescent patients with type 1 diabetes mellitus.

GUIDELINES FOR OPHTHALMIC SCREENING FOR DR

Screening guidelines for DR have been published previously by the American Academy of Pediatrics[25]; by the American Academy of Ophthalmology[26]; and by the American Diabetes Association.[27] The recommendations regarding pediatric patients with type 1 diabetes mellitus are similar. The American Academy of Ophthalmology recommends annual screening beginning 5 years after the onset of diabetes.[26] The guidelines from the American Diabetes Association include annual screening beginning 3 to 5 years after diagnosis of diabetes once the patient is 10 years or older.[27] The American Academy of Pediatrics recommends an initial examination 3 to 5 years after diagnosis if older than 9 years, with annual follow-up thereafter.[25]

The recommendations reflect the fact that the incidence of DR in young children is negligibly small, and therefore, children younger than 9 years do not require screening for DR. The incidence of retinopathy in young adolescents is also very low, particularly for proliferative diabetic retinopathy. Although the risk of DR typically does not increase

significantly until 8 to 10 years after diagnosis, the recommendation for annual screening beginning 3 to 5 years after diagnosis (in children who are older than 9 years) is reasonable, given that DR has occasionally been reported within this time.

Because children with type 1 diabetes mellitus are at a greatly increased risk of visual loss over the course of their lives, special attention should be given to identifying other causes of visual loss in these patients. Screening for potentially treatable visual disorders, such as amblyopia, is recommended for all children[28] and should be performed with particular care in children with type 1 diabetes mellitus. Patient and parent education regarding the benefits of optimal metabolic control is also beneficial early in the course of the disease.

IMPLEMENTATION

The development of appropriate screening strategies for detecting DR in patients with type 1 diabetes mellitus is important, but guidelines are of little use if they are not implemented. Unfortunately, studies that evaluate this aspect of care have been discouraging. In a study by Witkin and Klein[29] that included 902 young patients with type 1 diabetes mellitus, 26% had never had an ophthalmologic examination, including 11% of patients at high-risk of visual loss. In an Australian study that was performed before and one year after distribution of ophthalmic screening guidelines, McCarty et al[30] found that the guidelines had been successfully distributed, but there was no significant change in management practice. The usefulness of digital photography in detecting retinopathy has been demonstrated.[31] This technology holds great promise but is unlikely to become widely used until it can be performed rapidly, simply, and at a reasonable cost. Studies that evaluate methods to improve implementation of guidelines could potentially provide great benefit to patients with type 1 diabetes mellitus.

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