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Short Communication

Current Ideas to Prevent Diabetic Retinopathy (DR) in Diabetes Mellitus (DM)

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Diabetes is a global epidemic. In the USA, the Center for Disease Control and Prevention (CDC) reported in 1994 that only one state (State of Missouri) had > 6% prevalence of diabetes mellitus (DM). In 2015, the CDC showed that the prevalence of > 9% of DM was in found in more than 36 states. In 2015, there are over 30 million adults diagnosed with diabetes in the USA, with additional 84 million diagnosed as pre-diabetes. The health cost related to diabetes now stands at over $245 billion (2012). This is 2.3 times higher costs for diabetics versus non-diabetics.

Diabetic Retinopathy (DR) is the most common microvascular complication of Diabetes Mellitus (DM). It is considered the leading cause of vision loss and blindness among the adult population. Unfortunately, diagnostic screening is still considered inadequate, since only 60% of diabetics attend yearly screening. It is unfortunate, considering the major advancements in recent years in the assessment and treatment of DR. Research continues to increase our understanding of the pathogenesis of DR and provides valuable information about modifiable risk factors. Many studies have led to changes in the management paradigm of diabetes, with new therapies and expanded treatment options that allow more individualized treatment.

Achievement of glycemic control in non-pregnant adults with Type 2 Diabetes can be challenging. The Hemoglobin A1c (HbA1c) goals, once considered to be global and equal to all patients are now recommended to be personalized for DM patients. Treatment is now based on discussions of benefits and harms of pharmacotherapy; patient preferences, health and life expectancy; treatment burden; and costs of care. Nowadays, physicians aim for an HbA1c level between 7% and 8% in most patients with type 2 diabetes. De-intensifying pharmacologic therapy is considered in patients with DM and HbA1C levels less than 6.5%. Treatment is adjusted so it minimizes hyperglycemia symptoms only and used cautiously, if at all, when treating patients with a life expectancy of less than 10 years due to advanced age, nursing home residence, or end-stage chronic conditions.

A year ago, the American College of Physicians (ACP) released a guidance statement update regarding the HbA1c targets for glycemic control with pharmacologic therapy for DM. This statement conjoined recommendations from many societies, including the American Diabetes Association, the Department of Veterans Affairs/US Department of Defense, and many more. The ACP emphasized that the strict reduction in HbA1c levels in regards to surrogate microvascular outcomes (e.g. albuminuria) and clinically significant microvascular outcomes (e.g. end-stage renal disease) still remains unclear. Furthermore, most (70%) American adults have other co-morbidities that limit their achievement of levels lower than 6.5%. The ACP also mentions the increased mortality among patients randomized to intensive treatments in ACCORD study and a greater risk of severe hypoglycemia without mortality benefit among patients randomized to intensive treatments in ADVANCE study. In young patients, however, this is not the case, and these may still benefit from intensive control. The idea is to find the right balance, but not to send the wrong message.

The pathogenesis of diabetic retinopathy is complex and includes both genetic and environmental factors. Many Genome-Wide Association Studies (GWAS) for diabetic macular edema and proliferative diabetic retinopathy have been published so far. The META-EYE Study (2012) is a pooled analysis of 35 population-based studies that included data from 22,896 individuals with diabetes to determine

global prevalence of and major risk factors for diabetic retinopathy. The study nominated the following factors as the most influential on retinopathy progression: diabetes duration; Hb A1c; blood pressure; dyslipidemia; and obesity.

It makes sense that as a patient has more years of diabetes, their risk to develop diabetic retinopathy increases exponentially. The Wisconsin Epidemiologic Study found, that the prevalence of diabetic retinopathy at 5, 10, and 15 years after diagnosis of diabetes was made was 25%, 60%, and 80%, respectively.

The HbA1c levels are traditionally measured every 3 months (120 days of red blood cell cycle). It is recommended to be measured at least twice per year if reached treatment goal. Each 1% decrease in HbA1c level is associated with a decreased risk of any diabetes-related endpoint by 21%; myocardial infarct by 14%; stroke by 12%; and any microvascular complication by 37% (when diabetic retinopathy risk is reduced by 40%). In the Diabetic Control and Complication Trial (DCCT) intensive glycemic control therapy reduced the risk to develop DR in 76% compared with conventional therapy and halved the number of patients requiring treatment for DR. Nowadays- ADA recommendations, as above-mentioned, have changed, and are individually planned.

In the META-EYE analysis, diabetes was associated with hypertension more often. In the UKPDS trial - more than one third of patients had reduced risk to develop DR if they were under tight blood pressure control. The ADA recommends that most patients with DM and hypertension should be treated to a blood pressure goal of < 140/90 mmHg. Patients with high risk for cardiovascular disease may benefit from lower target (130/80). The American Association of Clinical Endocrinologists recommends individualized treatment.

Strict treatment of dyslipidemia is still studied. A large study that investigated the effects of treatment with Fenofibrate for treatment and reduction of cardiovascular events (FIELD study in 2006) and its sub-study for eye disease (ACCORD) showed, that there was no reduced number of cardiovascular events with this treatment, though other effects were shown (such as neuroprotection, antioxidant quality, anti-inflammatory and more). In the case of DR - the risk to get laser treatment due to DR was significantly reduced. Unfortunately, no future collaboration was done in further investigation of the drug.

Obesity is a well-known known risk factor for type 2 DM. It is also considered a world-wide epidemic. In the USA, the number of states with over 20% of population diagnosed with obesity has also increased even in past 5 years. Nowadays, at least 26% of the population is considered to be obese in 32 states. However, not all obese patients will develop DM.

Obstructive sleep apnea was also investigated to be one of the risk factors for worsening DR and specifically diabetic macular edema. Several studies support this statement, yet others failed to find the connection. The assumption is that the associated ischemia may contribute to further deterioration with the DR status [1-10].

To summarize, there are well-known risk factors that if managed successfully, are able to prevent, or at least to stop the progression of diabetic retinopathy. The management of these patients should be a joined effort of all treating personnel, including optometrists and ophthalmologists, and therefore knowledge of the current paradigms is important.

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