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Review Article

Diabetic retinopathy prevention and treatment options

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ABSTRACT

The objective of this review article was to mention the prevalence and risk factors for diabetic retinopathy to occur. Also, mention and compare the best ways to prevent this complication. Adding also a comparison of the best currently available treatments for diabetic retinopathy. Diabetic retinopathy is the first cause of visual impairment in working-age adults worldwide. Duration of diabetes is a major risk factor associated with the development of diabetic retinopathy. Due to the large number of patients with type 2 diabetes, this group comprises a larger proportion of the disease burden in patients with visual impairment from diabetic retinopathy compared to patients with type 1 diabetes. Diabetic retinopathy is the most common cause of visual impairment and blindness in patients aged 20-74 years. Approximately 80% of the patients with type 1 diabetes will develop retinopathy after 15 years after the onset of the pathology. In the case of type 2 diabetes will develop retinopathy after 30 years of history with the disease. Some important factor that can accelerate the process is the use or not of insulin for treatment. The most important for the treatment of diabetic retinopathy is the prevention of the diabetes in healthy people that have the risk factor to develop this pathology. The best options of treatment continued to be the combination of anti-VEFG/panphotocoagulation depending the stage of the complication. Improvement of the early detection of this type of microvascular complication for give them an early treatment and improve the evolution in positive way. We believed that is need to investigate more techniques for early detections of microvascular complications of diabetes mellitus, like imagen or biomarkers.

Keywords: Diabetes mellitus, Retinopathy, Hb1AC, Anti-vascular endothelial growth factor, Panretinal photocoagulation, Prevention

INTRODUCTION

Diabetic retinopathy is one of all the chronic complications of diabetes mellitus, that mostly quality of life for patient living with diabetes, which end loss of the vision of the patient for the rest of their live. Affecting them their social background, economy and mental health. In the view of above, in this article we are going to review the natural progression like first symptoms, screening methods for early detection, and early treatment with better outcome for the quality of life of the patients. Diabetes mellitus describes a group of metabolic diseases that are characterized by chronic hyperglycemia.

Type 1 diabetes mellitus is the result of an autoimmune response that triggers the destruction of insulin-producing β cells in the pancreas and results in an absolute insulin deficiency. It often develops during childhood, manifesting with an acute onset. Type 2 diabetes mellitus, which is much more common, has a strong genetic component as well as a significant association with obesity and a sedentary lifestyle. T2DM is characterized by insulin

resistance and impaired insulin secretion due to pancreatic β-cell dysfunction, resulting in relative insulin deficiency.

Diabetic retinopathy is the first cause of visual impairment in working-age adults worldwide. Duration of diabetes is a major risk factor associated with the development of diabetic retinopathy. Due to the large number of patients with type 2 diabetes, this group comprises a larger proportion of the disease burden in patients with visual impairment from diabetic retinopathy compared to patients with type 1 diabetes.[1]

Epidemiology

Diabetic retinopathy is the most common cause of visual impairment and blindness in patients aged 20-74 years. Approximately 80% of the patients with type 1 diabetes will develop retinopathy after 15 years after the onset of the pathology. In the case of type 2 diabetes will develop retinopathy after 30 years of history with the disease. Some important factor that can accelerate the process is the use or not of insulin for treatment.

In the view of above, the principal action and the most important is the early diagnosis firstly of diabetes mellitus. The indications listed below are consistent with the 2023 ADA guidelines. The 2021 USPSTF guideline recommends screening in adults aged 35-70 years with overweight or obesity.[2,3]

The screening for diabetic retinopathy are the following modalities dilated comprehensive eye examination performed by an ophthalmologist/optometrist and retinal photography. This should done after the onset of type 1 DM: within 5 years and type 2 DM at the time of diagnosis with an interval every year.[1,4] Diagnostic for diabetic retinopathy totally is made by retinal finding that's why is so important the screen in the next graphic we are going to show to most retinal findings. Treatment is made by multidisciplinary team based primarily in the good glycemic control and lifestyle recommendations. Early detection and treatment of diabetic retinopathy can prevent 90% of blindness.[1]

Treatment by retinopathy subtype depend if the patient has non-proliferative retinopathy or proliferative retinopathy. Non-proliferative retinopathy in the casa of mild NPDR to moderate NPDR, observation only is indicated; repeat dilated comprehensive eye examination every 6-12 months.

Severe NPDR should treat as proliferative retinopathy with panretinal laser photocoagulation (PRP) and/or anti-VEGF therapy.

Proliferative retinopathy[1] always is indicate PRP and/or anti-VEGF therapy, both PRP and anti-VEGF therapy are equally effective. PRP is usually preferred as treatment occurs in a single session.[1] Anti-VEGF injections alone can be considered for patients who are highly motivated and have no barriers to follow-up.

Additional treatments should be utilized if after initial treatment, any of the following are present a new vitreous hemorrhage or neovascularization or failure of existing neovascularization to regress.

Table 1: Features of different types of diabetic retinopathy.

Findings in diabetic retinopathy[1]	Features
Non-proliferative diabetic retinopathy	
Mild	- ≥1 capillary microaneurysms
Moderate	- ≥1 of the following: - Capillary microaneurysms (to a greater extent than in mild NPDR) - Intraretinal hemorrhages - Hard exudates[2] - Cotton wool spots - Mild intraretinal microvascular abnormalities or signs of ischemia
Severe	- ≥1 of the following: - In all 4 retinal quadrants: capillary microaneurysms, dot intraretinal hemorrhages - In ≥2 retinal quadrants: signs of ischemia (e.g., venous beading) - In ≥1 retinal quadrant: moderate intraretinal microvascular abnormalities
Proliferative diabetic retinopathy	
Non-high risk	- Neovascularization - Criteria for high-risk PDR not met
High risk	- Neovascularization - On the optic disc or within 1 disc diameter - Or elsewhere in the eye, if accompanied by vitreous and/or preretinal hemorrhage

Continued.

Findings in diabetic retinopathy[1]	Features
Macular edema	- Within 500 µ of the center of the macula - Retinal thickening - Hard exudates (if associated with adjacent retinal thickening) - Within 1 disc diameter of the center of the macula: any zone of retinal thickening ≥1 disc size in any area - If OCT has been performed, can be further categorized into[7] - Center-involving DME: ≥1 mm diameter retinal thickening in a central subfield - Non-center-involving DME: ≥1 mm diameter retinal thickening that does not involve a central subfield

DISCUSSION

Talking about the progression of the diabetic retinopathy in one article that follow up 3-year retrospective cohort study of 604 patients with type 2 diabetes mellitus.

They found that the patients that along the study, had elevated Hb1AC in mean had a worse progression of complications principally diabetic retinopathy and diabetic renal disease. Other factor that they found was the use of insulin for get an adequate glucose blood levels. In contrast the patients with a lower mean of Hb1 AC levels, low triglycerides and good control glucose blood levels with treatment options other than insulin. This patient stop the progressions of the diabetic retinopathy.[5]

In other article mentioned that the most important risk factor for diabetic retinopathy was high levels of Hb1AC and the presence of hypertension. Other associated risk factors were a high BMI, cataract surgery, puberty and pregnancy. Also, they mentioned that stronger risk mark could be the measurement of nontraditional lipid panel like levels of apolipoproteins A and B.[6]

In a review article found the use of systemic biomarkers of inflammation and noninvasive Imaging retinal biomarkers of inflammation could make the treatment and prevention of diabetic retinopathy more predictable and have more clinical outcomes for the patients with less complications.[7]

In this article mentioned that high level of TNF-a, IL-6 and retinol binding protein 4 are high associated in patients with diabetic retinopathy. Also, they associated to be elevate in patients that will progress in microvascular complications if the patient does not get good control levels glucose; principal the retinol binding protein 4 has been associated in patients with pre-diabetes and obesity or overweight. And if they progress to diabetes will have higher risk to have microvascular complications principal diabetic retinopathy.[7] In the case of the noninvasive imaging retinal biomarkers of inflammation consisted in sing different imaging modalities, but mostly spectral-domain (SD)-OCT and fundus autofluorescence. These imaging biomarkers include subfoveal neuroretinal detachment (SND) and hyperreflective retinal spots/foci (HRS) evaluated on SD-OCT, and foveal hyperautofluorescence (FAF) evaluated on fundus autofluorescence.[7]

The findings that can be detected with this type of images study could predicted and improve the management of diabetic retinopathy. Like found the precise moment when to use therapies like Anti-VEGF and surgery therapies options.[7]

In one randomized clinical trial of 305 patients made at 2018 they compare the use of PRP vs intra-ocular injection of ranibizumab in patients with proliferative retinopathy and they follow up the patients for 5 years. The result showed no important difference between the both options of treatment. Both groups maintained a mean visual acuity of 20/25.[8]

In other study made at 2018 in 394 patients having proliferative retinopathy without prior panretinal photocoagulation. Intravitreous ranibizumab (0.5 mg) versus PRP for proliferative retinopathy. Ranibizumab-assigned eyes (n=191) received monthly injections for 6 months unless resolution was achieved after 4 injections. They founded that at 1 month 16% of the patients with ranibizumab had complete neovascularization resolution and an additional 60% (113) showed improvement. At 6 months, 52% (80 of 153) showed neovascularization resolution, 3% (4) were improved, 37% (56) were stable, and 8% (13) had worsened since the last visit. In conclusion, they mentioned that the use of anti-VEGF 2 years before panretinal photocoagulation got better clinical outcomes for the patients.[9]

For the management phase and a correct treatment of diabetic retinopathy, it must be considered that it is a multidisciplinary treatment accompanied by a correct metabolic and lipid control, as well as a strict control of blood pressure figures along with a balanced diet and adequate to the health or comorbidities of the patient.

It is believed that laser therapy works by cauterizing and occluding the microaneurysms with leakage and risk of the same but there is not much information on this method, you can use the use of oral antidiabetic drugs to try to maintain metabolic control and then perform the standard procedure, which is considered as definitive treatment called laser panphotocoagulation. For the procedure, light energy is applied to the retina, this is absorbed by the retinal pigments that raise its temperature and cause protein denaturation, coagulation and tissue death in the outer layers of the retina which is useful in various

pathologies such as; diabetic retinopathy, central retinal vein occlusion, central retinal artery occlusion, sickle cell disease.[10]

Panphotocoagulation is a laser treatment that improves visual prognosis in patients with severe nonproliferative diabetic retinopathy and proliferative diabetic retinopathy. However, pain is frequently reported by patients undergoing this treatment. Panphotocoagulation has its advantages as well as disadvantages, some of the disadvantages and possible complications include patient discomfort during the procedure, pain, permanent retinal scarring, prolonged time to complete the treatment due to multiple sessions, elevated intraocular pressure, and slightly decreased peripheral vision.[11]

The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that a 1% reduction in glycosylated hemoglobin (HbA1c) level can reduce the risk of microvascular complications by 37%. According to the "Diagnostic standards for diabetes medicine" issued by the American Diabetes Association (ADA) in 2020, oral hypoglycemic drugs of the SGLT2 type are recommended as first-line treatment in patients with chronic heart failure and long-standing diabetes mellitus. In the first week of treatment they can rapidly reduce glucose by approximately 1.5 mmol/l and effectively reduce HbA1c by 1.5%, which is equivalent to the efficacy of metformin at a dose of 2000 mg per day.[12]

From the findings of the various articles used for this work, 50 millisecond pulse panphotocoagulation was found to be significantly less painful for patients with severe non-proliferative and proliferative diabetic retinopathy when compared to 200 millisecond pulse panphotocoagulation. The efficacy of laser photocoagulation in proliferative diabetic retinopathy for the prevention of visual loss has been demonstrated. A study confirmed that this procedure reduces the risk of extreme visual loss by 50.00%, especially in patients with high-risk proliferative diabetic retinopathy. It was corroborated that early treatment is beneficial in preventing progression of visual loss but does not reverse vision loss. This is often due to retinal and vitreous hemorrhages, or tractional retinal detachment that occurs in many patients. Many of them may become blind or require vitrectomy. In case of retinopathy progression, further photocoagulation may be applied. If proliferative retinopathy progresses, despite complete panphotocoagulation, referral to a vitreoretinal surgeon for surgical treatment should be made.[13]

CONCLUSION

In the view of above, the most important for the treatment of diabetic retinopathy is the prevention of the diabetes in healthy people that have the risk factor to develop this pathology. So, the governments and non-governmental institute of health should need to improve first level prevention policy, like campaigns for general population for changing their risk factor for develop diabetes mellitus type 2 primarily. Second they should improve the early detection of this type of microvascular complication for give them an early treatment and improve the evolution in positive way. Talking about treatment like we reviewed in the different articles mentioned above had evolved thanks to the technology and had few side effects and better's clinical outcome for the patients, preventing the loss of visual acuity in its entirety, if given an early moment in the evolution of the disease. The best options of treatment continued to be the combination of anti-VEFG/panphotocoagulation depending the stage of the complication. For the end, we believed that is need to investigate more techniques for early detections of microvascular complications of diabetes mellitus, like imagen or biomarkers.

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