

EDITORIAL: CURRENT MANAGEMENT OF DIABETIC MACULAR EDEMA

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The prevalence of Diabetes Mellitus (DM) is estimated to rise from 2.8% (2000) to 4.4% (2030). The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030¹. The prevalence is estimated to be 10% in Pakistan. With over 5.2 million people with diabetes Mellitus, it is the 6th country with the largest population of people with DM.

Diabetic Retinopathy is a progressive dysfunction of the retinal vasculature caused by chronic hyperglycemia. This leads to either microvascular occlusion or microvascular leakage. Occlusion of small blood vessels occurs due to multiple factors including thickening of capillary basement membrane, capillary endothelial cell damage and proliferation, changes in red blood cells, platelet stickiness and aggregation and vascular endothelial growth factor (VEGF) produced by hypoxic retina leading to growth of shunt & new vessels. Leakage occurs due to formation of microaneurysms, loss of pericytes and high blood pressure.

Successful management of diabetic retinopathy via a combination of glucose control, laser therapy and vitrectomy represents one of the most striking achievements of modern ophthalmology. By fundus examinations initiated prior to the development of significant retinopathy and initiating treatment according to early treatment of diabetic retinopathy (ETDRS) guidelines the risk of severe visual loss can be reduced to 50%. The vast majority of diabetic individuals who lose vision do so, not because of an inability to treat their disease but rather due to a delay in seeking medical attention.

The prevalence is highest among type 1 DM (40%) while it is 20% in type 2 DM and patients with DR are 25% more likely to go blind than non-diabetics. Patients with type 1 DM have very low risk of developing any diabetic retinopathy in the first five years while 5% patients have diabetic retinopathy on presentation in type 2 diabetics. Results of Diabetic Control and

complication trial (DCCT) showed that type I Diabetics with tight control of blood glucose (4 measurements / day) do far better than conventional therapy (1 measurement / day). Tight control group had 76% reduction in rate of development of any retinopathy and 54% reduction in progression of established retinopathy as compared to conventional treatment group. For advanced retinopathy even the most rigorous control of blood glucose may not prevent progression³. In the United Kingdom prospective Diabetic study (UKPDS) in Type II Diabetics there is 21% reduction in the 1 year rate of progression of retinopathy is seen with tighter blood pressure control⁴. There are 35% of patient with symptomatic retinopathy who develop proteinuria, elevated blood urea nitrogen values and elevated creatinine levels³. The risk factors determining the onset and severity of Diabetic retinopathy include duration of diabetes, poor control of diabetes, pregnancy, hypertension, nephropathy, obesity, hyperlipidemia and smoking.

Exudative Diabetic maculopathy is characterized by pockets of fluid in the outer plexiform layer, if large enough, can be seen as cystoid macular edema. Usually cystoid macular edema is seen in eyes that have other signs of severe NPDR such as numerous hemorrhages or exudates. In rare cases, cystoid macular edema due to generalized diffuse leakage from the entire capillary network can be seen in eyes that have very few other signs of diabetic retinopathy. Macular edema that meets predetermined criteria for extent or location is termed clinically significant macular edema (CSME). It includes macular thickening at or within 500 μ m of the fovea; associated with hard exudates that are at or within 500 μ m of the fovea; or one disc area in size or greater, with any part of the edema at or within 1500 μ m of the fovea. Photocoagulation of all leaking microaneurysms >500 μ m from the center of the macula is the treatment of choice in these patients. Yellow laser with micro pulse technology is the latest treatment strategy. EDTRS study showed that focal laser

photocoagulation for CSME decreased the risk of moderate visual loss, caused occasional moderate visual gain and decreased retinal thickening. The ETDRS also showed that PRP should not be given to eyes with CSME unless high risk characteristics are present. Patients with macular edema who have the best prognosis for improved vision have circinate retinopathy of recent duration, focal, well-defined leaking areas and good capillary perfusion surrounding the avascular zone of the retina. Patients with an especially poor prognosis have dense lipid exudates in the center of the foveola, diffuse edema with multiple leaking areas, extensive central capillary non-perfusion, increased blood pressure and cystoid macular edema. ETDRS found that even eyes with these adverse findings still benefited from treatment when compared with control eyes⁵.

VEGF Levels are increased in the vitreous of patients with DME and it is an ideal target to treat DME. It is up regulated in DME; it leads to hyper permeability, which leads to macular edema. Therefore VEGF blockade would be an ideal therapy to treat macular edema. Anti-VEGF agents available include Pegaptanib, Bevacizumab, Ranibizumab, Aflibercept and Brolucizumab. Steroids injected intravitreally are an alternative to this therapy and include triamcinolone, dexamethasone, fluocinolone implants. BOLT study comparing Bevacizumab versus laser for 12 months using Bevacizumab for 3 to 9 injections at 6 weekly intervals versus laser used 1 to 4 times showed that laser showed -0.5 line improvement in letters versus +6 lines for bevacizumab⁶. RISE and RIDE⁷ trial compared the efficacy of different concentration of Lucentis for the treatment of diabetic macular edema while VIVID and VISTA⁸ trial found the efficacy of Eyelea. Bevacizumab should be considered as first-line therapy in patients with a visual acuity of 20/40 or better according to DRCR Protocol T⁹. For patients who present with a visual acuity of 20/50 or worse, improvement in vision was greatest with aflibercept and similar between bevacizumab and ranibizumab. Aflibercept should be considered as first-line therapy in these patients, with bevacizumab as the alternative. Cost of Eyelea and Lucentis will have to come down more than 50% for them to become as cost effective as Avastin. Patients who are resistant to anti-VEGF therapy should be considered for intravitreal steroid therapy.

In conclusion the treatment of diabetic macular edema has evolved over the years with better visual outcomes for the patients. Careful evaluation of the patient is necessary to get the best results for which

Ocular coherence tomography (OCT) with angio OCT has become the standard of care.

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