

Current Management of Diabetic Maculopathy

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Introduction

Diabetic Mellitus is now considered a pandemic disease. The World Health Organization reported that about 195 million people worldwide suffer from diabetes and that about two third of them are in the developing countries [1]. By the year 2030, the number of people living with the disease will be more than double [2]. In the past, diabetes was thought to be foreign, but now, there is a global trend towards increase of the incidence and prevalence of diabetes in Africans [3].

Diabetic retinopathy is a major cause of blindness in the developed world. However, the changing lifestyle of people in developing countries is bringing this disease to the fore. Diabetic retinopathy is now a significant cause of blindness in developing countries such as India [4] and Nigeria [5,6].

Diabetic Maculopathy

Majority of diabetic maculopathy occur in Non Insulin Dependent Diabetes Mellitus (NIDDM) [7], Macular ischemia is more frequent in Insulin Dependent Diabetes Mellitus (IDDM) [8], after 20 years of known diabetes, the prevalence of diabetic macular edema (DME) is approximately 28% in both type 1 and type 2 diabetes [9].

Diabetic maculopathy consist of macular edema and ischemia. The edema occur as a result of breakdown in blood retinal barrier at the level of the perifoveal vessels. It consists of non- clinically significant macular edema, clinically significant macular edema which could be focal or diffuse. The use of Optical Coherence Tomography will further

help in classifying into spongiform, foveal detachment and vitreo macular traction.

Diabetic Macular edema (DME) is the leading cause of moderate visual loss in people with diabetes. Visual loss from DME is five times more than that from proliferative diabetic retinopathy (PDR) [7].

Pathophysiology of diabetic macular edema [10]

The pathophysiology of diabetic macular edema is explained by micro angiopathies that occur in diabetics. This includes retinal microvascular change, thickening of retinal capillary basement membranes and reduction in the number of pericytes. There is loss of autoregulation, increased permeability, incompetence of retinal vasculature and edema. The above mechanisms produce impaired oxygen diffusion, which stimulate the production of vascular endothelial growth factor (VEGF) [11]. VEGF may induce retinal vascular permeability through phosphorylation of the tight junctional protein occludin, resulting in the dissolution of the junctional complex [12].

Other pathogenetic mechanisms include endothelial cell apoptosis and retinal endothelial cell intercellular adhesion molecule-1 and CD 18 induced Inflammation.

All the above mechanisms results in retinal vascular permeability and compromise of blood-retinal barrier leading to leakage of fluid and plasma constituents in the surrounding retina especially in diffuse macular edema (Figure 1, 2).

Macular ischemia

Macular ischemia is a devastating condition that causes irreversible visual loss. It occur more in type I diabetes [13]. Pathogenesis of macular Ischemia include basement membrane thickening, increased viscosity of blood and endothelial cell damage. This result in closure of perifoveal capillaries as evidenced by irregular widening of fovea avascular zone (FAZ) and budding of capillaries into FAZ on fundus fluorescein angiography (FFA) (Figure 3).

Diagnosis of diabetic maculopathy

Clinical examination of the retina with the slit lamp biomicroscopy using the 78 or 90 diopter non contact fundus lens will show retinal elevation and swelling. This method of examination offer stereoscopic and magnified view of the retina. Fundus fluorescein angiography



Figure1: Clinically significant macular edema (Hard exudates and edema within 500microns to center of fovea).

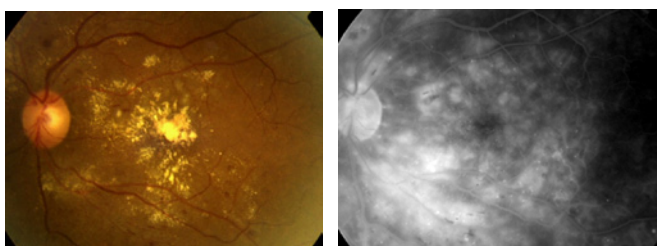


Figure 2: Hard exudates and diffuse macular edema, fundus fluorescein angiography showing diffuse leakage and cystoids macular edema.

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will show leakage and capillary non perfused areas and is indicated in diabetics with unexplained visual loss to rule out macular ischemia. Optical coherence tomography is a non invasive diagnostic tool used to quantify macula edema. It is also useful in patient education and monitoring follow up response to treatment.

Treatment of diabetic maculopathy

The standard of treatment for diabetic macular edema should include glycemic control and optimal blood pressure control as demonstrated by the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) [14,15]. Anemia and nephropathy should also be controlled.

Laser photocoagulation

The Early Treatment Diabetic Retinopathy Study (ETDRS) set the guidelines for the treatment of diabetic macular edema. The study found that laser reduced the risk of moderate visual loss from diabetic macular edema by 50% [16].

Laser spot of 100microns, Power of 100Mw, and at duration of 100ms is recommended. The slit lamp delivery method with a macular contact lens is preferred. The laser spots are placed as shown in (Figure 4). The fovea avascular zone is spared.

Complications of laser treatment include transient retina edema, accidental foveolar burns, paracentral scotomas, laser scar expansion, subretinal fibrosis and choroidal new vessels.

The complications associated with laser treatment can be devastating hence the need for alternative therapy. For microaneurisms and macular edema affecting the center of fovea, laser treatment is not suitable. Corticosteroids such as Triamcinolone has been given intravitreally (at a dose of 4mg in 0.1mls) with success [17].

Recently slow release steroids such as fluocinolone acetonide

has been implanted into the vitreous cavity with reduction in the macular edema and improvement in vision [18]. Complications of steroids such as cataract and raised intraocular pressure have limited their use. The Diabetic Clinical Research Network (DCRNet) in a randomised trial found that laser was superior to triamcinolone in the treatment of diabetic macular edema on the long term [19]. In June 2010, DCRNet compared the anti VEGF ranibizumab with laser and triamcinolone in a randomised trial and found ranibizumab(at a dose of 0.3mg) to be superior to both laser and triamcinolone either alone or in combination with laser [20]. The RESTORE study showed that Ranibizumab monotherapy or combined with laser provided superior visual acuity gain over standard laser in patients with visual impairment due to diabetic macular edema (DME) [21]. The RESOLVE Study and the READ 2 study also clearly showed that ranibizumab is effective in producing visual gain [22,23]. Bevacizumab(at a dose of 1.25mg) , an antiVEGF similar to ranibizumab has also been found to be superior to laser in The BOLT study [24].

In developing nations like Nigeria, bevacizumab is preferred to ranibizumab, in view of the prohibitive cost of the latter. However, the former is used as an off label drug. The recent CATT trial (Comparism of Age related maculopathy Treatment Trial) has demonstrated that both medications have equal efficacy [25].

Injection risk such as endophthalmitis should be borne in mind when intravitreal injection is administered.

Macular edema with vitreomacular traction has been shown by the DCRNet to benefit from vitrectomy [26].

The treatment of macular ischemia has been disappointing. AntiVEGF and laser treatments are contraindicated [27,28].

Conclusion

Diabetic maculopathy is an important cause of visual loss in diabetics. Therefore all newly diagnosed diabetics should have dilated fundoscopy with 78 or 90D examination of their macula. All diabetic patients with unexplained visual loss should have flourescein angiography to rule out macular ischemia. Early recognition and prompt management of macular edema will prevent irreversible visual loss.

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Figure 3: Macular ischemia (note occluded vessel, arrow), FFA showing enlarged fovea avascular zone arrow, and capillary non perfused areas, blue arrow.

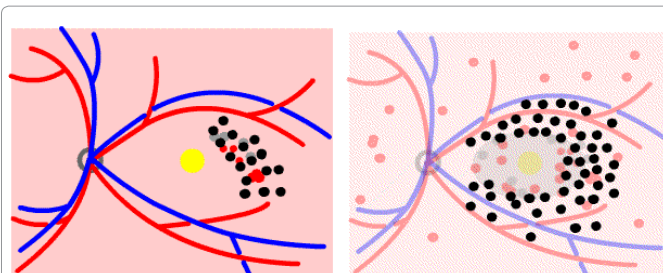


Figure 4: Focal laser (black spots) around microaneurysms (red dots); Grid laser along a 'C' pattern sparing the FAZ(fovea avascular zone) and the papillo- macular bundle.

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