Diabetic Macular Oedema

BY P ALAGHBAND

Diabetes mellitus is a metabolic disorder that affects the metabolism of all three categories of carbohydrates, lipids and proteins. This condition is characterised by chronic hyperglycaemia [1]. This can cause end organ damage. The estimated worldwide diabetes prevalence for 2010 is 285 million and it is expected to affect 438 million people by 2030. There are 2.6 million people who have been diagnosed with diabetes in the UK (2009). By 2025, there will be more than four million people with diabetes in the UK (key statistics on diabetes UK 2010). People with diabetes are 10 to 20 times more likely to go blind than people without. Diabetes is the leading cause of blindness in people of working age in the UK. It is estimated that there are 4,200 people in England who are blind due to diabetic retinopathy. This increases by 1,280 each year.

Diabetic retinopathy is a chronic, progressive and potentially sight-threatening condition, which affects microvasculature of the retina.

Diabetic retinopathy can cause visual loss through two main mechanisms: generalised damage to the retina (retinopathy) or localised damage to the macula / fovea (maculopathy).

Diabetic maculopathy (DM) can be further classified to:

1. focal oedema
2. diffuse oedema
3. ischaemic
4. mixed.

DM can also be tractional due to the background vitreoretinpathy or non-tractional (intraretinal).

There are several means of documenting and assessing diabetic retinopathy:

Digital photograph

This is the best way of documenting the diabetic retinopathy.

Fluorescine patterns of macular leakage

1. Focal leakage: early leakage in the transit phase of fluorescine angiogram (FFA) which may be focal (discrete) followed by progressive leakage from the microaneurysm. These patients usually have circulating exudates. Such focal leakage responds well to macular laser (especially those with extrafoveal leakage).
2. Indeterminate leakage: usually seen in patients with diffuse macular oedema with indeterminate leakage in the late phase of FFA. These patients usually have retinal thickening, intraretinal cysts (cystoid macular oedema) and often without accompanying exudates. They usually respond poorly to macular laser (particulary the subfoveal lesions).
3. Mixed leakage: seen in the majority of the patients.
4. Macular ischaemia: capillary occlusions are associated with areas of capillary drop out in the macula. Macular ischaemia patterns could be central (involving the foveal avascular zone (FAZ)) or peripheral (involving the temporal vascular arcade or extrafoveal regions).

If the perifoveal vessels are involved, it carries poor visual prognosis and laser is not effective.

Optical coherence tomography (OCT)

OCT has revolutionised our understanding of maculopathy. It is mostly useful in selecting the type of treatment modality that is most suited for each patient. Cases with central involvement (fluid collection) might benefit from intravitreal injection, whereas in extrafoveal involvement macular laser might be more prudent. OCT is very useful in assessing vitreomacular traction. However, the shortcoming of OCT is that it cannot detect the source of leakage nor the capillary drop out.

Fundus autofluorescence

It is a form of functional imaging. It gives more information about retinal pigment epithelium function. This imaging modality might have a role in sub-threshold macular laser where the laser burns are not readily visible. Also in longstanding macular oedema (by assessing the underlying retinal pigment epithelium (RPE)) can infer the health of the adjacent photoreceptors. Hence, it can assess the visual potential in these patients.

Control of systemic risk factors

Patients with diabetic maculopathy should work towards optimum glycaemic and blood pressure control. In such patients statin administration should be considered; in DM type 2 patients this could be complemented with fenofibrates.

Laser photocoagulation

Laser photocoagulation has been the mainstay treatment for diabetic macular oedema since the 1980s. The Early Treatment Diabetic Retinopathy Study (ETDRS) was a landmark trial that confirmed the effectiveness of laser photocoagulation in managing diabetic maculopathy [2]. The study showed that in eyes with clinically significant macular oedema (CSMO), the rate of moderate visual loss was significantly reduced. CSMO was defined as the presence of one or more of the criteria below:

1. Retinal thickening at / or within 500µm of the fovea.
2. Hard exudates at / or within 500µm of the fovea if associated with adjacent retinal thickening.
3. An area or areas of retinal thickening one disc area in size, at least part of which is within one disc diameter of the fovea.

The most beneficial effect (delay in progression of visual loss) of treatment in patients with CSMO was seen when vision was between 6/12 and 6/24.

"Diabetes is the leading cause of blindness in people of working age in the UK."

Subthresholds laser

This type of laser has been developed to avoid neurosensory damage, hence reducing the potential complications such as paracentral scotoma and enlargement of laser scars. Even though photocoagulation reduces the risk of blindness in diabetic patients, new treatment options including intravitreal steroid and anti-vascular endothelial growth factor have unravelled new horizons in this field.

Intravitreal steroid injection

The DRCRnet showed that at one year follow-up the effect of intravitreal preservative free triamcinolone 4mg (IVTA) is superior to laser treatment. However, in the longer term follow-ups, laser was more effective to preserve vision [3,4]. The IVTA with laser is inferior to ranibizumab, except in pseudophakic patients. The longer acting steroids are of particular interest.

Intravitreal anti-VEGF treatment

It is shown that the VEGF level in the vitreous and the retina of diabetic retinopathy patients is elevated. The first anti-VEGF was pegaptanib (macugen) to be used in diabetic macular oedema (DMO). It showed some benefits. The READ-2 (Ranibizumab for Edema of the macula in Diabetes) study showed that at three year follow-up, ranibizumab 0.5mg group maintained the visual outcomes in comparison to the laser group [5,6]. Further studies showed promising effects of ranibizumab in DMO. In fact, the National Institute for Health and Care Excellence (NICE) has approved this as a treatment option for diabetic maculopathy with more than 400 micron central retinal thickening on OCT.

Bevacizumab is not licensed for intraocular use; however, it has been used extensively for retinal vasculopathies. Different dosages (1.25 or 2.5mg) have been used. Based on current evidence, the effect of bevacizumab on DMO is superior to laser only. However, there is not enough data on the level of efficacy of bevacizumab and also comparison studies between ranibizumab and bevacizumab [7].

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TAKE HOME MESSAGE

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