Retinopathy

What is the best treatment for diabetic macular oedema?

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Diabetic macular oedema (DMO) affects around 7% of people with diabetes worldwide and is a major cause of visual impairment. Laser treatment has been the mainstay of treatment since its effectiveness was determined in the seminal studies in the 1980s (the Diabetic Retinopathy and Early Treatment Diabetic Retinopathy Studies). It remains the treatment of choice for diabetic retinopathy (DR) but has never been shown to be as effective in the treatment of DMO. Laser treatment is destructive and macular laser can be complicated by foveal burns, development of choroidal neovascular membranes, loss of colour vision and late visual loss due to enlargement of laser scars. This has led to a search for modifications (see Bressler et al [2013], summarised on the next page) and alternative therapies.

The article summarised alongside, by Mitchell and Wong, reviewed the evidence supporting the treatment modalities for DMO between 1985 and 2013, but focused on recent meta-analyses, systematic reviews and randomised controlled trials (RCTs), in order to provide guidance on management.

Optimal systemic management is well known to delay the development and progression of diabetic eye disease, and is crucial in its management, but there is emerging evidence that the risk factors for DR and DMO are different (see Tolonen et al [2013] and Kramer et al [2013], both summarised on the next page).

The emphasis latterly has been on the use of intravitreal agents – steroids and anti-vascular endothelial growth factor (anti-VEGF), formerly known as vascular permeability factor, agents. Both act to tighten the zonula occludens junctions between endothelial cells in the capillary bed. Both have been shown to be superior to laser in terms of improving visual acuity. However, it should be noted that all the recent RCTs have only compared intravitreal agents and laser treatment in individuals who had already lost vision (6/12 or worse).

Any intravitreal injection holds the risk of introducing an infection into the eye (endophthalmitis), although with strict infection control measures this should be minimal (less than 1% of cases). Anti-VEGF agents have been linked to a low risk of triggering arteriothrombotic episodes. Most of the evidence of risk comes from studies conducted in people with age-related macular degeneration and, therefore, caution should be exercised in individuals with diabetes, who are already at risk of a cardiovascular accident (CVA). They should not be used within 3 months of a CVA. There is also a risk of systemic absorption when intravitreal steroids are used, and this may be associated with cardiovascular episodes.

Anti-VEGF agents are given monthly for 3 months (loading dose) and then as required after monthly assessment. This is a significant time burden for people who already have multisystem disease and multiple appointments. Steroids are given every 4 to 6 months but are complicated by the inevitable development of cataract and a high risk of developing secondary glaucoma.

However, the evidence is very convincing that anti-VEGF agents are superior to laser treatment in the management of DMO, and that steroids are effective in individuals who have already had cataract surgery.

Mitchell and Wong conclude that anti-VEGF agents are indicated for centre-involving DMO with a vision of 6/12 or worse. For patients without centre involvement, or vision better than 6/12, laser treatment should be considered. For people with pseudophakia, combined treatment with intravitreal steroids and laser can be considered.

In the UK, two other bodies have also provided guidance. In December 2012, the Scottish Medicines Consortium (SMC) approved the use of ranibizumab (an anti-VEGF) in people whose vision was 6/12 or worse (SMC, 2012), and, in February 2013, NICE approved the use of the same agent for people with severe centre-involved DMO (NICE, 2013a). NICE also approved the use of the long-acting steroid implant, Iluvien (fluocinolone acetonide intravitreal implant), in November 2013 for individuals post-cataract surgery whose oedema had not responded to other treatment (NICE, 2013b). Evidence still needs to be collected on the efficacy of intravitreal agents versus laser therapy in people with good vision or minimal oedema as we still do not know how long these individuals will need to attend for monthly assessment. ■

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Am J Ophthalmol

Systematic review: Laser or anti-VEGF agents for the treatment of DMO

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓

1 Laser treatment has been the standard treatment for diabetic macular oedema (DMO) since the 1980s. This systematic review considered the alternative drug treatments of which anti-vascular endothelial growth factor (anti-VEGF) is at the forefront.

2 Literature searches of PubMed, Cochrane Library and ClinicalTrials.gov were conducted for meta-analyses, systematic reviews and randomised controlled trials published from January 1985 to July 2013.

3 From the review, the authors identified increasing evidence that anti-VEGF agents can provide superior outcomes compared with laser therapy for DMO treatment.

4 The anti-VEGF agent ranibizumab had the most robust evidence for its effectiveness to treat DMO with a favourable safety profile of up to 3 years.

5 The proportion of individuals gaining 10 or 15 ETDRS (Early Treatment Diabetic Retinopathy Study) letters after being treated with ranibizumab was two times higher than those that were treated with laser therapy.

6 Ranibizumab treatment resulted in fewer cases of visual loss and was well tolerated by participants in all studies.

7 Anti-VEGF therapy should be used instead of laser therapy for the treatment of moderate-to-severe visual impairment caused by DMO.

Mitchell P, Wong TY (2013) Management paradigms for diabetic macular edema. *Am J Ophthalmol* 19 Nov [Epub ahead of print]

Diabetic Med

Association between retinopathy and nephropathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 Using data from participants of the DCCT (Diabetes Control and Complications Trial), the authors set out to investigate the concordance of retinopathy and nephropathy over time.

2 Over the mean 6.5-year follow-up, the progression of retinopathy and nephropathy was mapped in 1365 participants. Retinopathy was measured using the ETDRS (Early Treatment Diabetic Retinopathy Study) score, and nephropathy development was defined as a urinary albuminuria excretion rate ≥40 mg/24 h on annual evaluation.

3 In total, 69% had neither developed retinopathy or nephropathy; 12.9% had developed nephropathy but not retinopathy; 10.7% had retinopathy but not nephropathy; and 7.3% had developed both.

4 The incidence of retinopathy progression was higher in those that had developed nephropathy than those that had not ($P<0.001$). The presence of nephropathy independently increased the risk of developing retinopathy (hazard ratio [HR] 1.62; 95% confidence interval [CI] 1.23–2.13; $P=0.001$).

5 The incidence of nephropathy progression was higher in those that had developed retinopathy than those that had not ($P<0.001$). The presence of retinopathy independently increased the risk of developing nephropathy (HR 1.72; 95% CI 1.30–2.27; $P<0.001$).

6 The authors showed that one quarter of people with T1D have discordant progression of diabetic retinopathy and nephropathy; however, the presence of retinopathy or nephropathy both increase the risk for the incidence of the other. This suggests they have a shared aetiology.

Kramer CK, Retnakaran R (2013) Concordance of retinopathy and nephropathy over time in type 1 diabetes. *Diabet Med* **30**: 1333–41

J Intern Med

Lipid profiles, nephropathy and retinopathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 This study in Finland investigated the association between lipid profiles, retinopathy and nephropathy in people with T1D. Data from 1465 people from the FinnDiane Study were used, and the extent of their retinopathy was measured.

2 The authors found that HDL-cholesterol was associated with proliferative retinopathy and triglycerides were associated with mild non-proliferative retinopathy independent of nephropathy ($P<0.01$).

3 The albumin excretion rate, retinopathy status and lipid parameters were found to have a significant association ($P<0.001$).

4 Nephropathy had a strong effect on the associations between lipid parameters and retinopathy.

Tolonen N, Hietala K, Forsblom C et al (2013) Associations and interactions between lipid profiles, retinopathy and nephropathy in patients with type 1 diabetes. *J Intern Med* **274**: 469–79

Retina

Comparing green and yellow lasers for DMO treatment

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓

1 Green and yellow lasers can be used for the treatment of diabetic macular oedema (DMO), but the green wavelength is more commonly used.

2 As part of the Diabetic Retinopathy Clinical Research Network, authors compared data from two studies (the LRT-DME trial and the IVT trial) to investigate if there was a significant clinical difference between using the green or yellow wavelength.

3 In both trials, there was no significant difference in the average 1 year improvement in visual acuity, or retinal volume between the wavelength colours. By the second year of treatment in the LRT-DME trial, eyes that had been solely treated with green laser received fewer after care treatment sessions than those solely treated with yellow laser ($P=0.02$).

4 However, the authors conclude there is no need for a change in current practice to choose one wavelength over the other.

Bressler SB, Almukhtar T, Aiello LP et al (2013) Green or yellow laser treatment for diabetic macular edema. *Retina* **33**: 2080–8

PLoS One

Sleep apnoea and diabetic retinopathy

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 In a cohort of 93 severely obese people with T2D, the association between obstructive sleep apnoea (OSA) and diabetic retinopathy (DR) was investigated.

2 Participants underwent a routine clinical retinal screening and an overnight respiratory sleep monitoring.

3 In total, 46 people were characterised with OSA. This group was more hypoxemic than those without OSA, but there was no difference in the number of people with DR between those with and without OSA ($P=0.77$).

4 A high prevalence of diabetic maculopathy was found in participants with moderate to severe OSA.

5 There was no significant association found between OSA and DR complications. But the level of hypoxemia could be a factor which contributes to the hypothesis.

Banerjee D, Leong WB, Arora T et al (2013) The potential association between obstructive sleep apnea and diabetic retinopathy in severe obesity-the role of hypoxemia. *PLoS One* **8**: e79521

"Anti-VEGF therapy should be used instead of laser therapy for the treatment of moderate-to-severe visual impairment caused by diabetic macular oedema."

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NICE (2013b) NICE, London. Available at: www.nice.org.uk/ta301 (accessed 19.02.14)
Scottish Medicines Consortium (2012) SMC, Glasgow. Available at: http://bit.ly/KCmsLv (accessed 21.01.14)