Retinopathy

Laser treatment for maculopathy remains the standard treatment

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This important article (Aiello et al, 2010; summarised alongside) presents the results of one arm of a multicentre, randomised trial by the Diabetic Retinopathy Clinical Research Network (DRCRnet, 2008), comparing an intravitreal steroid with laser photocoagulation for the treatment of diabetic macular oedema (DMO).

Photocoagulation has long been established as an effective treatment for DMO, although the efficacy for maculopathy is not as substantial as laser treatment of retinopathy (ETDRS [Early Treatment Diabetic Retinopathy Study] Research Group, 1985; 1991). Laser treatment aims to stabilise retinal changes rather than to improve visual acuity (VA). Even after successful stabilisation of maculopathy with a laser, people with DMO may experience problems with daily living – although their vision may not be poor enough to be registered as visually impaired. Laser scars also spread with time, compromising the initial result.

Recent articles discuss the effectiveness of newer treatments, particularly intravitreal steroids and intravitreal anti-vascular endothelial growth factor agents, both of which have been shown to be effective in temporarily reducing DMO (Nguyen et al, 2009; Rudnisky et al, 2009). Evidence as to whether they should replace laser treatment as the treatment of choice has been lacking. Injections need to be repeated at regular intervals, possibly for life, and intravitreal steroid injection may be complicated by secondary glaucoma, cataracts and endophthalmitis.

The full DRCRnet (2008) trial aimed to determine whether VA at 2 years was better in eyes with central DMO in people treated with intravitreal triamcinolone (1 or 4 mg) compared with those undergoing focal/grid treatment according to a modified ETDRS protocol. Results for the laser arm of the trial have been published by Aiello et al (2010).

Numbers in the study were large and confidence intervals tight. In total, 82% of 330 people randomised to the laser arm of the study completed the 2-year follow-up. Re-treatment was performed every 4 months when necessary for persistent or recurrent oedema and, on average, participants underwent 2.9±1.4 treatments during follow-up. A total of 81% of participants showed no significant worsening of VA at 2 years, with almost one-third (32%) showing a significant improvement.

Interestingly, given the large number of epidemiological and morphological factors measured, the only significant factor associated with an improvement in VA at 2 years was baseline VA – worse VA at baseline was associated with greater improvement and, conversely, if VA was high at baseline there was an increased likelihood of worsening of VA. However, after adjusting for VA, unsurprisingly, thicker maculas at baseline were more likely to lose vision than thinner ones, probably reflecting more severe disease or longer standing, more refractory, oedema.

The authors conclude that, at this point in time, focal/grid photocoagulation remains an effective ocular treatment and the standard management for DMO.

Diabetic Retinopathy Clinical Research Network (2008) A randomized trial comparing intravitreal triamcinolone acetonide and focal/grid photocoagulation for diabetic macular edema. *Ophthalmology* **115**: 1447–9

ETDRS Research Group (1985) Photocoagulation for diabetic macular edema: ETDRS report number 1. *Arch Ophthalmol* **103**: 1796–806

EDTRS Research Group (1991) Early photocoagulation for diabetic retinopathy. ETDRS report number 9. *Ophthalmology* **98**: 766–85

Nguyen QD, Shah SM, Heier JS et al (2009) Primary End Point (Six Months) Results of the Ranibizumab for Edema of the mAcula in diabetes (READ-2) study. *Ophthalmology* **116**: 2175–81

Rudnisky CJ, Lavergne V, Katz D (2009) Visual acuity after intravitreal triamcinolone for diabetic macular edema refractory to laser treatment: a meta-analysis. *Can J Ophthalmol* **44**: 587–93

OPHTHALMOLOGY

Photocoagulation best treatment for macular oedema

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 This multicentre, randomised trial was undertaken to determine the factors associated with visual acuity outcome after focal/grid photocoagulation for diabetic macular oedema (DMO) in the focal/grid photocoagulation cohort from the DRCRnet (Diabetic Retinopathy Clinical Research Network) trial.

2 A total of 330 people with DMO (aged ≥18 years [mean age 63 years]; T1D or T2D [4% and 96%, respectively]; visual acuity 20/40 to 20/320; optical coherence tomography [OCT] central subfield thickness ≥250 microns) each had one eye assigned to focal/grid coagulation.

3 Focal/grid photocoagulation was performed at baseline and repeated at 4-month intervals for persistent or recurrent DMO.

4 Association of demographic, clinical, OCT and fundus photographic variables with visual acuity improvement or worsening (≥10 letters) from baseline to 2 years was evaluated.

5 Worse baseline visual acuity was the only factor found to be significantly associated with greater improvement ($P<0.001$). Greater retinal volume and improved visual acuity were associated with more frequent visual acuity worsening ($P=0.001$ and $P=0.009$, respectively).

6 Visual acuity outcome at 4 months was not a predictor of the subsequent treatment course, with many eyes that worsened to ≥10 letters from baseline to 4 months improving and many eyes that initially improved subsequently worsening.

7 The authors concluded that focal/grid photocoagulation remains the most effective treatment for DMO.

Aiello LP, Edwards AR, Beck RW et al (2010) Factors associated with improvement and worsening of visual acuity 2 years after focal/grid photocoagulation for diabetic macular edema. *Ophthalmology* **117**: 946–53

"The authors found no association between thiazolidinedione (TZD) therapy and diabetic macula oedema, but acknowledged that this might have been due to the short exposure to TZD and exclusion of people with previous laser therapy."

DIABETES

Importance of maintaining normal HbA_{1c} levels

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓

1 The EDIC (Epidemiology of Diabetes Interventions and Complications) study examined the differences between 1055 adults and 156 adolescents with T1D in the effect of prior intensive glycaemic therapy on the progression of retinopathy 10 years after the DCCT (Diabetes Control and Complications Trial).

2 At study year 10, adults in the original intensive (INT) group demonstrated slower progression of retinopathy than those in the former conventional treatment group (adjusted hazard reduction [AHR], 56%; $P<0.0001$). In the adolescent cohort this beneficial effect was not seen (AHR, 32%; $P=0.13$).

3 In total, 79% of the metabolic memory difference between adults and adolescents at year 10 ($P=0.0385$) was attributed to the difference in mean HbA_{1c} levels during DCCT (8.1 vs 8.9% [65 vs 74 mmol/mol], respectively), particularly in the INT groups (8.0 vs 8.4% [64 vs 68 mmol/mol], respectively).

4 The results show the importance of maintaining normal HbA_{1c} levels early, and for as long as possible.

White NH, Sun W, Cleary PA et al (2010) Effect of prior intensive therapy in type 1 diabetes on 10-year progression of retinopathy in the DCCT/EDIC: Comparison of adults and adolescents. *Diabetes* **59**: 1244–53

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Mecamylamine activity in DMO

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This trial investigated the safety and bioactivity of topical mecamylamine, a nicotinic acetylcholine (nACh) receptor antagonist, in 23 people with T1D with chronic diabetic macular oedema (DMO).

2 Participants received 1% mecamylamine twice daily for a total of 12 weeks. Drops were well tolerated and no drug-related safety problems were reported.

3 An improvement in best-corrected visual acuity was seen at 1, 4, 8, 12 and 16 weeks (2.8, 1.9, 2.4, 0.8 and 3.1 mean letter improvement, respectively), but little change occurred in mean excess foveal thickness.

4 The authors concluded that mecamylamine may have heterogeneous effects in people with DMO and that further study on the nACh receptor subtypes is warranted.

Campochiaro PA, Mahmood Shah S, Hafiz G (2010) Topical mecamylamine for diabetic macular edema. *Am J Ophthalmol* **149**: 839–51

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ADREV valid measurement of visual function

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓

1 Authors aimed to validate the ADREV (Assessment of Disability Relating to Vision) against the 25-Item National Eye Institute Visual Functioning Questionnaire (VFQ-25) scoring, both performance-based measures of visual function.

2 Visual function was measured by ophthalmic examination in 91 people with diabetic retinopathy.

3 Analyses showed that there was a stronger positive relationship between ADREV total and subscale scores and clinical measures of visual function compared with VFQ-25 total and subscale scores.

4 The authors concluded that the ADREV performance measure is a valid instrument for assessing visual function in people with diabetic retinopathy.

Warrian KJ, Lorenzana LL, Lankaranian D et al (2010) The assessment of disability related to vision performance-based measure in diabetic retinopathy. *Am J Ophthalmol* **149**: 852–60

ARCHIVES OF OPHTHALMOLOGY

Association between DMO and TZD use

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓

1 The ACCORD (Action to Control Cardiovascular Risk in Diabetes) Eye Substudy assessed the association of diabetic macular oedema (DMO) and visual acuity with thiazolidinedione (TZD) therapy in 9690 participants with T2D from the ACCORD trial through use of baseline fundus photographs and a standardised ETDRS (Early Treatment Diabetic Retinopathy Study) logarithmic chart. Cross-sectional data were reported.

2 Among the ACCORD subsample, 20% ($n=695$) of people were administered with TZD and 6.2% ($n=217$) had DMO.

3 TZD therapy was not associated with DMO in unadjusted (odds ratio [OR], 1.01; 95% confidence interval [CI], 0.71–1.44; $P=0.95$), or adjusted (OR, 0.97; 95% CI, 0.67–1.40; $P=0.86$), analyses.

4 Retinopathy severity ($P<0.001$) and age ($P=0.03$) were found to be significantly associated with DMO.

5 HbA_{1c} ($P=0.06$), diabetes duration ($P=0.65$), sex ($P=0.72$) and ethnicity ($P=0.20$) were not significantly associated with DMO.

6 TZD therapy was found to be associated with marginally better visual acuity (0.79 letters; 95% CI, 0.20–1.38; $P=0.009$).

7 The authors found no association between TZD therapy and DMO, but acknowledged that this might have been due to the short exposure to TZD and exclusion of people with previous laser therapy. A longitudinal study measuring incident oedema are more likely to determine whether an association exists.

Ambrosius WT, Davis RP, Goff DC et al (2010) Lack of association between thiazolidinediones and macular edema in type 2 diabetes: the ACCORD eye substudy. *Arch Ophthalmol* **128**: 312–8