

Retinopathy

THE LANCET

Can fenofibrate reduce retinopathy treatment?

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

1 A sub-analysis based on the data from the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study, aimed to assess whether long-term fenofibrate therapy could reduce the need for laser treatment and the progression of retinopathy in people with type 2 diabetes.

2 FIELD was a randomised controlled trial of 9795 people aged 50–75 years.

3 Eligible people were assigned into one of two groups: receive fenofibrate 200mg/day (n=4895), or receive a matching placebo (n=4900). Information concerning laser treatment was gathered at each clinic visit.

4 To determine the cumulative incidence of diabetic retinopathy, a sub-analysis of 1012 people was carried out using standardised retinal photography and Early Treatment Diabetic Retinopathy Study (ETDRS) grading.

5 The requirement for first laser treatment for all retinopathy was significantly lower in the fenofibrate group than in the placebo group (3.4% vs 4.9% respectively, $P=0.0002$).

6 In this sub-analysis, there was no significant difference in the primary endpoint of two-step progression of retinopathy grade between the two groups (9.6% fenofibrate group vs 12.3% placebo group, $P=0.19$).

7 The authors conclude that fenofibrate therapy reduces the need for laser treatment for diabetic retinopathy, but the mechanism of this effect does not seem to be related to plasma concentrations of lipids.

Keech AC, Mitchell P, Summanen PA et al (2007) Effect of Fenofibrate on the Need for Laser Treatment for Diabetic Retinopathy (FIELD study): a Randomised Controlled Trial. *The Lancet* **370**: 1687–97

Adding to the polypharmacy in type 2 diabetes?



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Statins are routinely administered as lipid lowering agents, producing a protective effect for the macrovascular complications of diabetes. A small number of studies suggest that lipid lowering may also have a beneficial effect on the development

and progression of diabetic eye changes, particularly diabetic maculopathy, but results are inconclusive and the mechanisms are unclear. Does the clearing of retinal exudates seen on statin treatment merely reflect a reduction in the plasma load or a direct effect on the underlying mechanisms at play in the development of maculopathy?

Fibrates have also been proposed as a treatment for hyperlipidaemia in type 2 diabetes. The FIELD study aimed to assess the effect of long-term treatment with fenofibrate on the macro and microvascular outcomes in people with type 2 diabetes.

Unfortunately, the study was not designed to detect an effect on ophthalmic complications – laser treatment being only a tertiary endpoint in the study design. In the main study (9795 patients randomised to drug or placebo) the initial baseline was based on patients self-reporting pre-existing diabetic retinopathy (DR) rather than on photographic or biomicroscopy documentation, and there was no standardisation of decision to treat, relying instead on the averaging effect of clinical discretion. The subgroup did incorporate photography but this arm of the study was under-powered (10.3% of the total population).

Despite this, the results are very interesting!

At the end of the study there was a significant difference in outcomes between the treated and placebo groups.

In the main study 402 (4.1%) patients required laser treatment. In patients undergoing laser treatment for the first time significantly more were on placebo – 4.9% compared to 3.4% on fenofibrate. A visible separation in the cumulative incidence (CI) curves between the treated and placebo groups was seen as early as 8 months into the trial and showed increasing benefit with time. The relative effects of fenofibrate seemed to be larger in patients without DR at baseline.

This subgroup analysis only showed a significant reduction in a composite endpoint of 2-step progression of DR or development of clinically significant macular oedema or requirement of laser treatment. Conversely, most benefit was shown in people with pre-existing retinopathy. However, it should be remembered that despite the limitations of small numbers in this analysis the presence of retinopathy at baseline was accurately documented in this group.

The authors conclude that the effect of fenofibrate treatment goes beyond its effect on lipid concentration and propose a number of possible and plausible mechanisms for its action. Including protection against endothelial cell death, thus maintaining the blood–retinal barrier, and an inhibition of VEGF, the effects of which could certainly explain the reduction in the need for laser treatment.

Although it is not clear whether fenofibrate treatment should commence at diagnosis of diabetes or on development of DR, evidence for the addition of fenofibrate for people with type 2 diabetes is compelling, although not conclusive.

‘Areas of capillary nonperfusion show morphologic changes of retinal structure which may lead to a loss of sensitivity.’

AMERICAN JOURNAL OF OPHTHALMOLOGY

Incidence of PDME higher after laser treatment

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

1 The purpose of this prospective, observational case series was to examine the optical coherence tomography (OCT) characteristics in a series of eyes with persistent clinically significant diabetic macular oedema (PDME) after focal macular laser therapy.

2 In order to characterise the condition further, this study concentrated on the vitreomacular interface (VMI) characteristics of the eyes.

3 Fifty eyes with PDME were analysed prospectively, after at least one focal laser photocoagulation session.

4 Methods employed were slit-lamp biomicroscopy, stereoscopic fundus photography, fundus fluorescein angiography (FFA).

5 Due to incomplete data, 2 of 50 eyes were excluded. For the remaining 48 eyes, 25 eyes (52.1%) demonstrated definite VMI abnormalities (VMIA), including anomalous vitreal adhesions, epiretinal membrane or both. Six eyes (12.5%) had questionable VMIA.

6 At detecting VMIA, OCT was 1.94 times more sensitive than traditional techniques combined ($P=0.00003$). There was no association between the number of focal laser sessions and diffuse leakage demonstrated on FFA and an increased prevalence of VMIA ($P=0.13$ and $P=0.47$, respectively).

7 This study shows that there was a high prevalence of VMIA in eyes with PDME after focal laser treatment, and that OCT is a superior detection method.

Ghazi NG, Ciralsky JB et al (2007) Optical Coherence Tomography Findings in Persistent Diabetic Macular Edema: The Vitreomacular Interface. *American Journal of Ophthalmology* **144**: 747–54

AMERICAN JOURNAL OF OPHTHALMOLOGY

Nonperfusion and loss of sensitivity

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

1 This prospective, observational cross-sectional study aimed to assess light sensitivity and morphologic changes of capillary nonperfused areas in diabetic retinopathy.

2 Twenty eyes underwent fundus-related microperimetry and

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No correlation between HbA_{1c} and retinopathy

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

1 The authors of this study set out to determine a possible correlation between HbA_{1c} levels and the presence and severity of retinopathy during eye screening for people with T2D.

2 This was a retrospective medical record review of all new patients examined in a Veteran Affairs Medical

INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE

Sensitivity and specificity of OCT

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

1 The authors systematically reviewed the sensitivity and specificity of optical coherence tomography (OCT) for diagnosing macular oedema due to diabetic retinopathy compared with more well-established tests.

2 Electronic databases and six major ophthalmic journals were searched

fluorescent angiography. Non-perfused areas were scanned with OCT.

3 Areas of capillary non-perfusion were associated with the loss of retinal sensitivity, in all eyes. OCT highlighted a structural disturbance of the inner retina and high-reflectivity deposition in the areas of capillary non-perfusion.

4 In conclusion, areas of capillary nonperfusion show morphologic changes of retinal structure which may lead to a loss of sensitivity.

Unoki N, Nishijima K, Sakamoto T, et al (2007) Retinal Sensitivity Loss and Structural Disturbance in Areas of Capillary Nonperfusion of Eyes with Diabetic Retinopathy. *American Journal of Ophthalmology* **144**: 755–60

Center diabetic screening clinic in 2005.

3 Six hundred and seven people out of the 1316 people examined during that year were included. People were excluded if they had T1D, prior diabetic screening within the previous 3 years, or incomplete data.

4 Data collected: HbA_{1c} levels and grade of diabetic retinopathy.

5 Regression calculations revealed no correlation between HbA_{1c} level and presence of retinopathy.

6 The authors conclude that HbA_{1c} appears to have little predictive value for the presence or severity of retinopathy.

Maa AY, Sullivan BR (2007) Relationship of Hemoglobin A1C With the Presence and severity of Retinopathy Upon Initial Screening of Type II Diabetes Mellitus *American Journal of Ophthalmology* **144**: 456–457

including studies from 1998–2006. Quality was assessed using Quality Assessment of Diagnostic Accuracy Studies (QUADAS) and data extracted. Fifteen studies were reviewed.

3 A bivariate model was used to obtain summary estimates and fit a summary receiver operating characteristic (ROC) curve.

4 Using ROC, OCT had a sensitivity of 0.79 (95% CI) and a specificity of 0.88 (95% CI), which suggests good overall performance of OCT.

Virgili G, Menchini F, Dimastrogiovanni AF et al (2007) Optical Coherence Tomography versus Stereoscopic Fundus Photography or Biomicroscopy for Diagnosing Diabetic Macular Edema: A Systematic Review. *Investigative Ophthalmology & Visual Science* **48**: 4963–72