Management of diabetic retinopathy

An update

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Diabetic retinopathy is a leading cause of visual loss and the GP plays an important role in the prevention and management of the condition.

Diabetic retinopathy is the leading cause of visual loss in working-age adults in developed countries. Worldwide, it has been estimated that 93 million people with diabetes have diabetic retinopathy, of which 28 million have vision-threatening disease.[1] The Australian Diabetes, Obesity and Lifestyle (AusDiab) study reported that 15% of people with diabetes have diabetic retinopathy with 2.1% of those having proliferative retinopathy and 3.3% having diabetic macular oedema, which are vision-threatening complications of diabetic retinopathy.[2]

Pathology of vision-threatening diabetic retinopathy

Diabetes can cause visual loss by two distinct mechanisms.

The first mechanism of visual loss is proliferative retinopathy, secondary to retinal ischaemia, with subsequent formation of 'new' vessels on the retina (Figure 1). Increased levels of vascular endothelial growth factor (VEGF) play an important role in this process. The 'new' vessels do nothing to relieve the ischaemia, and they are fragile and bleed easily causing vitreous haemorrhage. They may also become fibrosed and contract causing retinal traction and detachment.

The second mechanism of visual loss is diabetic macular oedema, which is swelling of the central retina with consequent reduction in visual acuity. The underlying mechanism is incompletely understood but VEGF and other proinflammatory factors, which increase vascular leakage, appear to be involved.

Both of these processes can be identified at an early stage through screening, allowing for early treatment.

Screening and prevention

In Australia, optometrists and ophthalmologists screen patients with diabetes for the presence of diabetic retinopathy using wide-field fundus photography or slit-lamp ophthalmoscopy. The NHMRC recommends screening all people with diabetes for diabetic retinopathy; biennially for non-Indigenous patients and annually for Indigenous patients. Once mild nonproliferative diabetic retinopathy is seen, referral to an ophthalmologist is indicated. Screening of children with type 1 diabetes should start once they reach puberty. During pregnancy, an eye examination is recommended in the first trimester. This may be delayed if an eye examination has been performed in the three to six months before pregnancy, but must be completed as soon as possible when preconception eye examination has not taken place.

Treatment

Role of the GP

There is evidence that careful control of diabetes and its associated comorbidities (such as hypertension) and complications can significantly reduce the risk of visual loss from diabetic retinopathy. Optimising the cardiovascular risk factors as well as weight reduction can be beneficial and GPs can play a crucial role in these areas.

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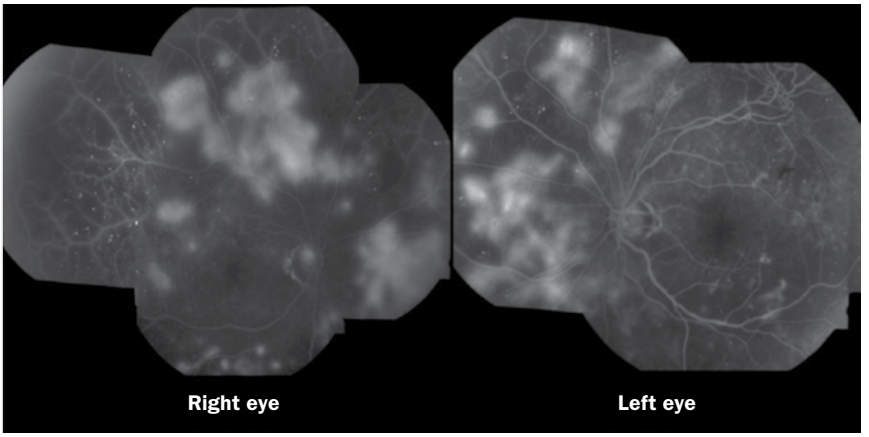


Figures 1a and b. Fluorescein angiograms of proliferative diabetic retinopathy. The new vessels fluoresce brightly and extensive neovascularisation is present in both eyes.

Glucose control

The Diabetes Control and Complications Trial (DCCT; in type 1 diabetes) and the UK Prospective Diabetes Study (UKPDS; in type 2 diabetes) showed that lowering the HbA_{1c} level to 7% led to a significant reduction in both the progression and development of retinopathy.[2] In simple terms, every 1% reduction in HbA_{1c} level reduces the risk of retinopathy by 30 to 40%. It is unclear whether there is any added benefit in reducing the HbA_{1c} level below 7%.[3]

Blood pressure

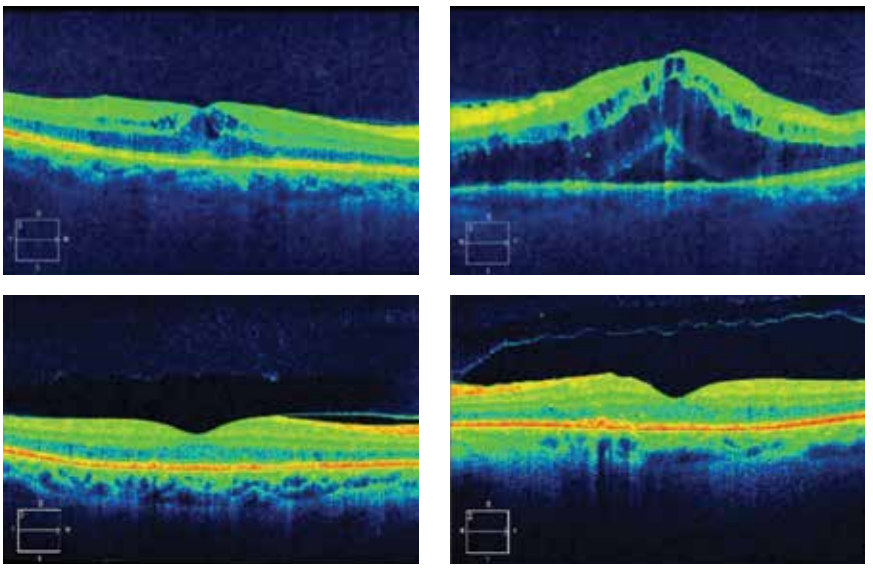
In the UKPDS, 'tight' blood pressure control (average, 144/82 mmHg) reduced the need for laser treatment by a third in patients with type 2 diabetes.[3] 'Intensive' blood pressure control (systolic, <120 mmHg) in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study did not confer any additional benefit beyond this.[3,4]

Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor inhibitors may offer protection against the development of diabetic retinopathy, which is in addition to their blood pressure-lowering effect. It remains unclear whether these drugs would be beneficial in normotensive people with diabetes and vision-threatening retinopathy.[3]

Fenofibrate

Two large studies (Fenofibrate Intervention and Event Lowering in Diabetes [FIELD] and ACCORD Lipid) have shown that fenofibrate has a beneficial effect on the progression of diabetic retinopathy in patients with type 2 diabetes.[5,6] This appears to be independent of its effects on lipid levels.

In the FIELD study, patients receiving fenofibrate had a 31% reduction in laser treatments for both proliferative retinopathy and maculopathy over five years.[6] The question as to whether all patients with diabetic retinopathy should receive fenofibrate is currently unresolved.[2,5,6] In the ACCORD trial, which compared fenofibrate with placebo in patients taking statins, the level of ocular protection was similar.



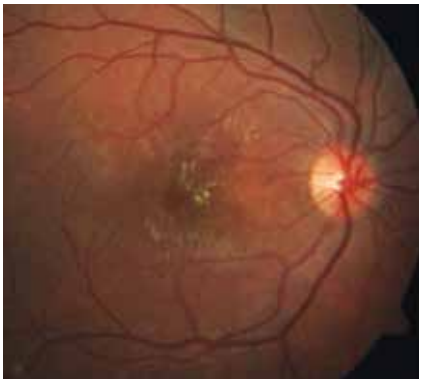
Figures 2a to d. a and b (top). Right and left diabetic macular oedema. Optical coherence tomography scans show the macular area in cross section. c and d (bottom). Following one year of treatment with intravitreal anti-VEGF therapy the macular oedema has resolved and the normal foveal contour has been restored.

Role of the ophthalmologist

Proliferative diabetic retinopathy

The risk of severe visual loss (defined as visual acuity worse than 6/120) is halved with the use of argon laser panretinal photocoagulation.[4] This technique is the application of multiple heavy laser burns to the peripheral retina to ablate the ischaemic retina, thereby reducing the VEGF drive for new vessel formation. Multiple sessions are typically required. The treatment can cause restriction of the peripheral visual field, which may affect night vision and, less often, driving vision.

Off-label use of anti-VEGF agents such as bevacizumab, ranibizumab and aflibercept, which cause rapid regression of the new vessels after intravitreal injection is useful to allow time to apply the




Figures 3a and b. Right and left fundus photographs of a 27-year-old woman with type 1 diabetes. Bilateral macular hard exudates and microaneurysms can be seen.

peripheral laser. However, their effect is temporary (usually four to six weeks).

Surgery is indicated for patients with recurrent or nonclearing vitreous haemorrhage, tractional retinal detachment, vitreomacular traction and premacular gliosis causing distorted vision. These conditions can all occur secondary to proliferative diabetic retinopathy.

Diabetic macular oedema

Until recently, macular laser was the mainstay of treatment for patients with diabetic macular oedema. This technique reduces the risk of moderate visual loss (doubling of visual angle, which is about equivalent to a decrease in visual acuity of three or more lines on the Snellen chart) but few patients gained vision.

In recent years, intravitreally administered anti-VEGF therapy has progressively replaced laser as the primary treatment for centre-involving diabetic macular oedema, with many eyes gaining two to three lines of vision (Figures 2 and 3).[6,7] There are two anti-VEGF agents available in Australia that are PBS listed for treatment of visual impairment due to diabetic macular oedema: ranibizumab (a fully humanised antigen-binding portion of an anti-VEGF-A monoclonal antibody) and aflibercept (a human recombinant fusion protein that functions as a decoy receptor by binding VEGF-A and B and placental growth factor).[7,8] Another anti-VEGF agent bevacizumab (off-label use) is used in some instances, such as when it is not possible to get PBS-funded medication as bevacizumab is much cheaper than the private cost of the on-label medications.[9,10]

Intravitreal corticosteroids (such as triamcinolone acetonide and dexamethasone intravitreal implant) have anti-inflammatory, antipermeability and angiostatic effects in treating patients with diabetic macular oedema. They can play a significant role in the management of diabetic macular oedema, particularly in refractory cases.[11,12] They tend to be used as second-line agents due to ocular side effects such as cataract formation, but may be considered first-line treatment after cataract surgery. There is also a risk of elevated ocular pressure (glaucoma).

Intravitreal therapy for diabetic macular oedema, especially with the anti-VEGF agents, is an ongoing treatment, with most patients requiring more aggressive and frequent injections during the first two years.

Conclusion

Recent advances in treating patients with diabetic eye disease in the eye clinic are exciting, but the role of the GP in preventing vision-threatening diabetic eye disease remains paramount. MT

COMPETING INTERESTS: None.

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