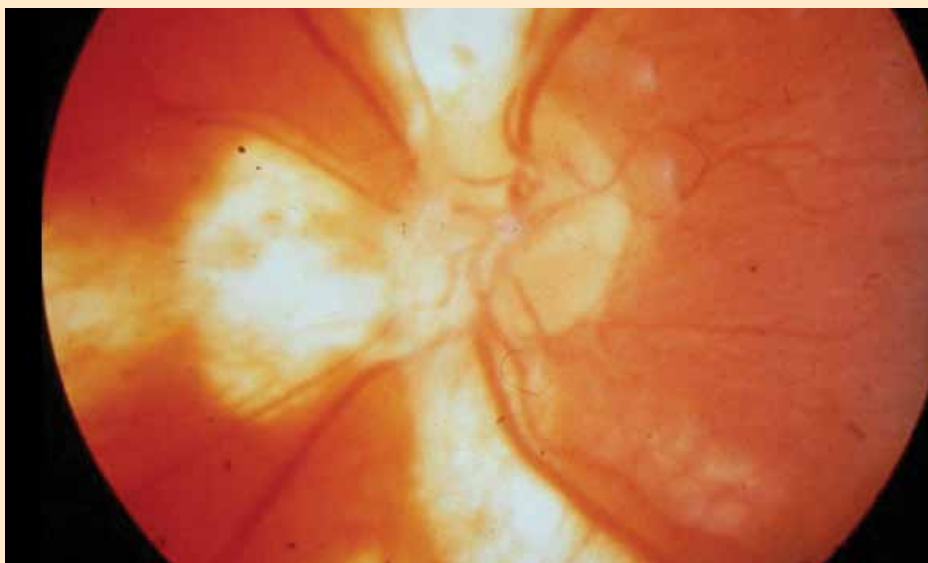


The management of diabetic retinopathy without laser

MODULE 13 PART 1: CLINICAL OPTOMETRY
COURSE CODE: C-12870/OD

34

15/01/10 CET



Jonathan Dowler MD FRCS FRCOphth Consultant Ophthalmic Surgeon, Moorfields Eye Hospital and the London Clinic

Before the advent of laser therapy, diabetic retinopathy was treated by pituitary ablation. This was undertaken either as a neurosurgical procedure involving craniotomy, or by implantation of radioactive seeds in the pituitary gland. This could only be carried out in a small proportion of patients because of the risks involved. The procedure induced regression of retinopathy in the majority of patients, but a significant proportion died of complications.¹

Benefits of laser therapy

In this context, the development of laser treatment was a major advance. The Diabetic Retinopathy Study (DRS) demonstrated that panretinal photocoagulation (PRP) halves the risk of severe visual loss (defined as visual acuity < 5/200 on three successive visits) in patients with high-risk proliferative diabetic retinopathy² (Table 1). The Early Treatment Diabetic Retinopathy Study (ETDRS)³ showed that macular laser therapy halved the risk of moderate visual loss (defined as a doubling of the visual angle) in patients with clinically significant macular oedema (CSMO)

(Table 2). These benefits were achieved by procedures that can be undertaken in the majority of patients who meet criteria for treatment. The treatment itself is well tolerated, and can be carried out in an outpatient setting under local anaesthesia. Once the objectives of treatment have been achieved, the effect of treatment is often of long duration, and may be permanent. Techniques of treatment have also evolved considerably over time; for example early photocoagulators produced intense burns with significant damage to the nerve fibre layer, with corresponding visual field defects (Figures 1a and b), but over

time gentler laser application, including technologies such as micropulse diode to limit collateral tissue damage, have lessened treatment side effects.

Prevention of visual loss vs. visual improvement with laser

Treatment with laser, is, however, directed principally at preventing visual loss. It rarely reverses it. For proliferative diabetic retinopathy it does not generally improve vision and macular laser therapy at most produces a modest benefit (less than one line Snellen improvement) in 40% of treated (versus 20% of untreated) patients with CSMO.³ Patients therefore must be treated before visual loss supervenes, at a point when they are frequently asymptomatic. This necessitates diabetic retinopathy screening programmes to identify patients at risk of visual loss to ensure that treatment is administered in a timely fashion. The St Vincent Declaration of 1989⁴ pledged to reduce new diabetic blindness by a third or more in five years. It is a measure of their success in identifying patients with diabetes at risk of visual loss that none of the countries signatory to the Declaration have succeeded in achieving this objective. Were treatments available which could reverse visual loss rather than occasionally averting it, prospects for reaching this target would be improved.

Treatment thresholds in laser therapy

Laser treatment is typically applied when certain thresholds of disease have been reached; high-risk proliferative diabetic retinopathy, and CSMO (Tables 1 and 2).^{2, 3} There is evidence of risk of visual loss at levels of disease less severe than these thresholds, as can be seen from data extracted from the DRS (Table 3).² The threshold is determined by the limits to the benefit of laser therapy, and the side effects of it. Were a treatment to be available which had fewer side effects or greater efficacy these thresholds might be lowered, with corresponding benefit to the patient.

Limitations to applicability of laser therapy

It is important to recognise the limitations to the applicability of laser therapy. Some forms of diabetic retinal disease do not respond to laser – for example, diabetic macular ischaemia. Some cannot readily be treated with laser therapy – for example, foveal cystoid oedema with perifoveal microvascular abnormalities, in which laser therapy risks foveal damage. Laser therapy also demands relatively clear ocular media, for recognition that the threshold for treatment has been reached, for imaging with fluorescein angiography and optical coherence tomography (OCT) in order to plan treatment, and for application of laser itself. Where cataract – far more common in patients with diabetes than in those without – prevents fundus visualisation, cataract extraction may worsen macular oedema or proliferative disease.^{5, 6} If vitreous haemorrhage obstructs fundus visualisation, proliferative retinopathy can progress unchecked (Table 4). Treatments applicable in eyes with opaque media, or in which laser is not appropriate are thus likely to provide benefit to patients with diabetes.

Complications of laser therapy

There are significant short and long term visual side effects of laser therapy (Table 5).⁷ PRP, despite improvements in the technique, may still damage the visual field sufficiently to result in loss of a driving license in approximately 20% of patients.⁸ Macular oedema can be detected with OCT a week after panretinal laser treatment in the majority of eyes,⁹ and although it commonly resolves spontaneously, it can take some months to do so. Macular laser therapy is associated with immediate reduction in indices of central retinal function¹⁰ and over time, contraction of sub-retinal fibrous membranes extending up to 900 microns from the site of laser application may result in scar enlargement and late visual loss.¹¹ Treatments without such complications clearly offer the prospect of improved visual prognosis.

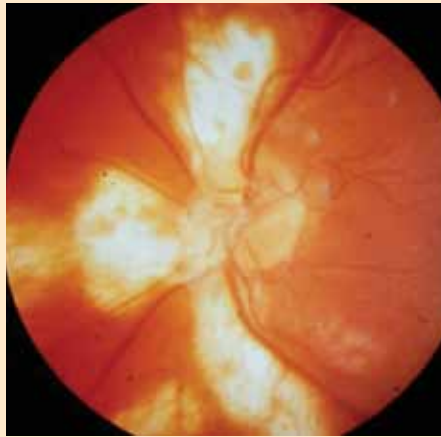


Figure 1a
Heavy laser burns around the optic disc

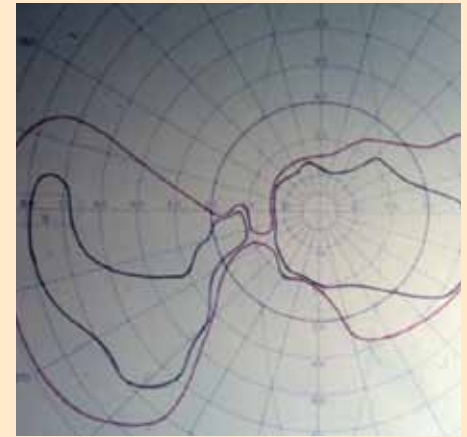


Figure 1b
Corresponding visual field defect

Re-evaluation of laser therapy

The first report of the DRS was published 34 years ago, and the first report of the ETDRS was published 25 years ago. The management of patients with diabetes has changed greatly in the interval. Some have argued that these classic studies are no longer applicable to their patients because of the disparity between the attributes of the patients studied and those of their patient population.¹² Should the trials be repeated? Perhaps not. Excellent though these studies are, they represent scientific evidence of efficacy of an empirically derived treatment, and, as can be seen from the foregoing discussion, one which has significant shortcomings. Our understanding of the pathogenesis of diabetic retinopathy has

also improved markedly in the interval since the publication of the ETDRS and DRS, in particular with regard to the role of vascular endothelial growth factor (VEGF) and the inflammatory component to diabetic retinopathy, and increasingly, treatments are being based on this better understanding rather than on historical empiricism. Two main groups of treatments fall into this category (i) intravitreal therapy and (ii) systemic therapy.

Intravitreal therapy

The benefits of laser without the burn

Intravitreal therapy offers a new prospect: that of visual improvement. The mechanism of laser therapy is unknown, but possible mechanisms include a change in the growth factor and

High risk proliferative diabetic retinopathy

- New vessels on the optic disc greater than a quarter to a third disc area
- Any new vessels on the optic disc associated with vitreous or retrohyaloid haemorrhage
- Moderate to severe new vessels elsewhere associated with vitreous or retrohyaloid haemorrhage

Table 1

Clinically significant diabetic macular oedema

- Thickening of the retina at or within 500 microns of the fovea
- Hard exudates at or within 500 microns of the fovea if associated with retinal thickening
- A zone of retinal thickening one disc area or larger any part of which is within one disc diameter of fovea

Table 2

FREE CET

Approved for Optometrists ✓ Approved for DOs ✓

Grading of diabetic retinopathy	Laser treated	Untreated
Mild NVE, no H	3%	8%
Moderate to Severe NVE, no H	4%	5%
Mild NVE, H	0%	9%
Moderate to Severe NVE, H	10%	36%
Mild NVD no H	4%	13%
Moderate to severe NVD no H	9%	20%
Mild NVD, H	8%	22%
Moderate to Severe NVD, H	10%	40%

Table 3

Rates of severe visual loss at two years in the Diabetic Retinopathy Study; NVD=new vessels disc, NVE=new vessels elsewhere, H=retrohyaloid or vitreous haemorrhage

tissue milieu of the retina, stimulated by the repair mechanism in response to the injury of photocoagulation. Intravitreal therapy permits changes in the milieu without the antecedent injury, or with a lesser injury. In addition, the beneficial effects of intravitreal therapy are often of very rapid onset; for example iris neovascularisation can regress within 24 hours of intravitreal injection of Avastin, whereas laser response tends to be slower because its effect is less direct.

Treatment of patients ineligible for laser or as an adjunctive to laser

Intravitreal therapy offers the possibility of treatment in patients with diabetic retinopathy who are either unresponsive to or are unable to access laser therapy. Patients with disease below the threshold for laser therapy may also benefit. Although the effect of treatment has a limited duration, it may be of value as an adjunctive therapy, either to mitigate or eliminate transient

unwanted effects of other therapies such as macular oedema following PRP, or to arrest the process of disease, buying time for the application of other therapy, such as in proliferative diabetic retinopathy which cannot be treated with laser because of vitreous haemorrhage.

Benefits of local therapy in patients with diabetes

Intravitreal therapy has other advantages. Because the eye is a small structure, the doses of drug required are small, and unwanted systemic effects are correspondingly less frequent. This is important in patients with diabetes who often have associated co-morbidities. The presence of inner and outer blood retinal barriers, albeit with some compromise in diabetic retinopathy of the inner barrier, further reduces systemic dissemination of drug. This is important in relation both to anti-VEGF agents (which have been implicated in hypertension and an increased risk of arterial thrombotic events such as heart attack and stroke), and steroids (which compromise diabetic control and elevate blood pressure when administered systemically).

Disadvantages of intravitreal therapy

The principal disadvantage of intravitreal therapy is related to the limited duration of action of the agents used, and the need to continue therapy in order to maintain benefit: short term treatment for long term disease. This requires repeated injection, and there are fixed and cumulative risks associated with such a regimen. A secondary disadvantage is that many of the therapies outlined below lack the support from large scale randomised controlled trials afforded to laser treatment; and as such the data from the smaller series which are presented below must be interpreted with some caution. It also means that the threshold at which these treatments should be applied, how they should be monitored and ceased is still uncertain.



Figure 2

Topical anaesthesia

Indications for vitrectomy
Non-clearing vitreous haemorrhage
Tractional macular detachment
Active progressive posterior proliferative retinopathy

Table 4

Typical technique used in intravitreal injection

- 1) The pupil of the eye to be treated is dilated
- 2) The surgeon washes hands and dons sterile gloves
- 3) The eye is anaesthetised with topical anaesthetic such as g. Tetracaine (Figure 2)
- 4) Povidone iodine 5% is instilled into the conjunctival sac (Figure 3)
- 5) The skin around the eye is swabbed with Povidone iodine 5-10% (Figure 4)
- 6) The skin is dried and a sterile adhesive surgical drape placed
- 7) An eyelid speculum is placed (Figure 5)
- 8) The patient is asked to direct gaze away from the site of injection
- 9) The site of injection is marked (3.5mm from limbus in pseudophakic eyes and 4mm in phakic eyes) (Figure 6)
- 10) The injection is administered (Figure 7)
- 11) Topical antibiotic is administered (Figure 8)
- 12) Indirect ophthalmoscopy is used to check the posterior segment and in particular the perfusion of the optic nerve head (Figure 9)
- 13) Topical antibiotics may be used for five days post injection.

Non-agent specific complications of intravitreal injection

Complications of intravitreal injection independent of the agent used include



Figure 3
Povidone iodine plus further topical anaesthesia

endophthalmitis and injury to ocular structures. The incidence of endophthalmitis following intravitreal injection for neovascular age related macular degeneration (AMD) is often stated to be approximately 1:1000.¹³ It should be recalled, however, that following cataract surgery the incidence of endophthalmitis appears higher in patients with diabetes¹⁴ and this may prove to be the case following intravitreal therapy. Injury to ocular structures includes corneal abrasion, subconjunctival haemorrhage, vitreous haemorrhage, lens damage, and retinal detachment.

Agents used in intravitreal therapy

A. Anti-VEGF agents

VEGF-A

VEGF-A is a widely occurring agent which has a number of physiological roles including neuroprotection, embryogenesis and wound healing. Pathological roles include choroidal neovascularisation in AMD. Its effects include the stimulation of endothelial cell proliferation and increases in vascular permeability. VEGF-A occurs in several isoforms, one of which in particular, VEGF₁₆₅, appears to be involved in pathological as opposed to physiological neovascularisation.¹⁵

Rationale for use of anti-VEGF-A agents in diabetic retinopathy

There is considerable evidence linking diabetic retinopathy to VEGF-A. Intravitreal injection of VEGF-A into



Figure 4
Skin preparation

primate eyes results in retinal changes similar to diabetic retinopathy with microaneurysms, haemorrhages, venous beading, capillary closure, and increased vascular permeability.¹⁶ Blockage of VEGF-A in primate models inhibits iris and retinal neovascularisation.^{17, 18} Samples of ocular fluids from patients with proliferative diabetic retinopathy show elevated VEGF-A levels which decline following PRP.¹⁹ Finally, VEGF concentrations are significantly higher in diabetic patients with extensive macular leakage than in diabetic patients with minimal leakage.²⁰

Agents

There are three anti-VEGF-A agents currently available which have been used for the treatment of diabetic retinopathy, although of these Pegaptanib (Macugen) and Ranibizumab (Lucentis) were developed for the management of neovascular AMD, and Bevacizumab (Avastin) for colonic cancer. For ease of pronunciation, each will be referred to hereafter by its trade name.

Macugen

Macugen is an aptamer, a molecule designed specifically to bind to the target molecule, in this case, VEGF-A. It is different from the other two agents in that it is active only against VEGF₁₆₅ and larger isoforms of VEGF-A. This suggests that it may selectively block the pathological functions of VEGF-A without impairing physiological functions. This is of importance in

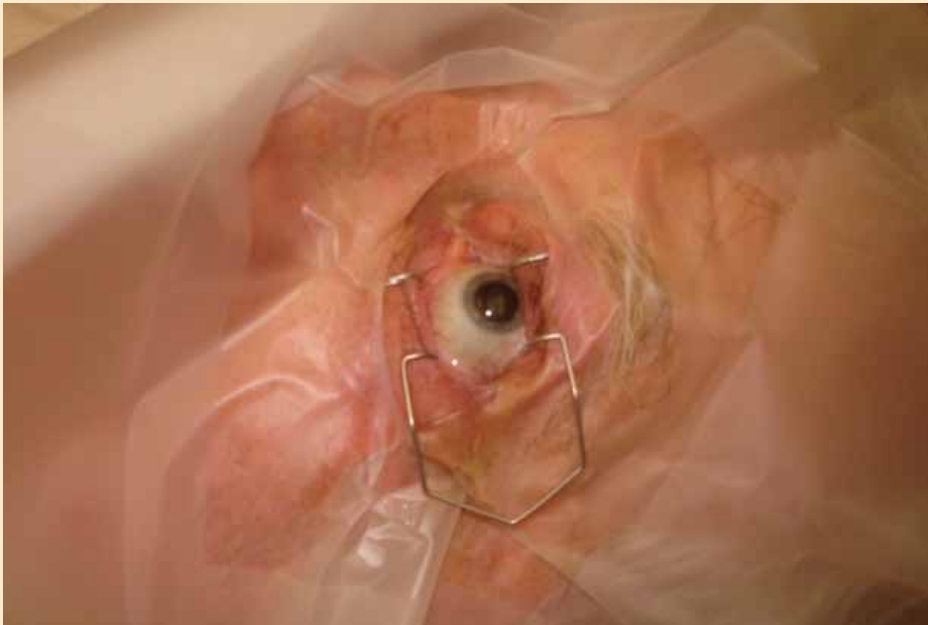


Figure 5
Sterile drape and lid speculum

diabetic retinopathy since some actions of VEGF-A in the retina may be protective. It may also limit systemic side effects, a feature important in patients with diabetes since they have in any case an increased risk of hypertension, stroke and heart attack.

Avastin

Avastin is a full-length recombinant humanised antibody active against all isoforms of VEGF. One particular advantage is that being a larger molecule, it persists longer in the vitreous than does the similar but smaller molecule of Lucentis, which may allow a greater interval between injections. Its longer half-life may be a disadvantage in relation to systemic side effects, however.

Lucentis

Lucentis is a recombinant humanised antibody fragment active against all forms of VEGF-A. It is a smaller molecule than Avastin, which enhances retinal penetration, and because of its shorter half-life, is more rapidly cleared and thus may have fewer systemic side effects. Lacking the potentially

immunogenic murine segment of the Avastin molecule, Lucentis may be less inclined to cause inflammation.

Agent-specific complications

Local

VEGF-A, in addition to its presumed pathological role in diabetic retinopathy, has a role as a retinal

Visual complications of photocoagulation

- Reduced visual acuity
- Reduced contrast sensitivity
- Reduced colour vision
- Reduced night vision
- Reduced visual field

Table 5

neuron survival factor, and plays a critical neuroprotectant part in the adaptive response to ischaemic injury.²¹ It follows that generalised blockade of VEGF-A such as occurs with Avastin and Lucentis, whilst reducing the increase in vascular permeability and vasoproliferation seen in diabetic retinopathy, may nonetheless reduce retinal neuronal survival. Interestingly, the neuroprotective effect of VEGF-A does appear to persist when only the VEGF₁₆₅ isoform is blocked as with Macugen. Furthermore, pan-VEGF-A blockade inhibits physiological revascularisation and neovascularisation,¹⁵ which raises the concern that for example macular ischaemia may be exacerbated.

Systemic

In original studies on Avastin as a

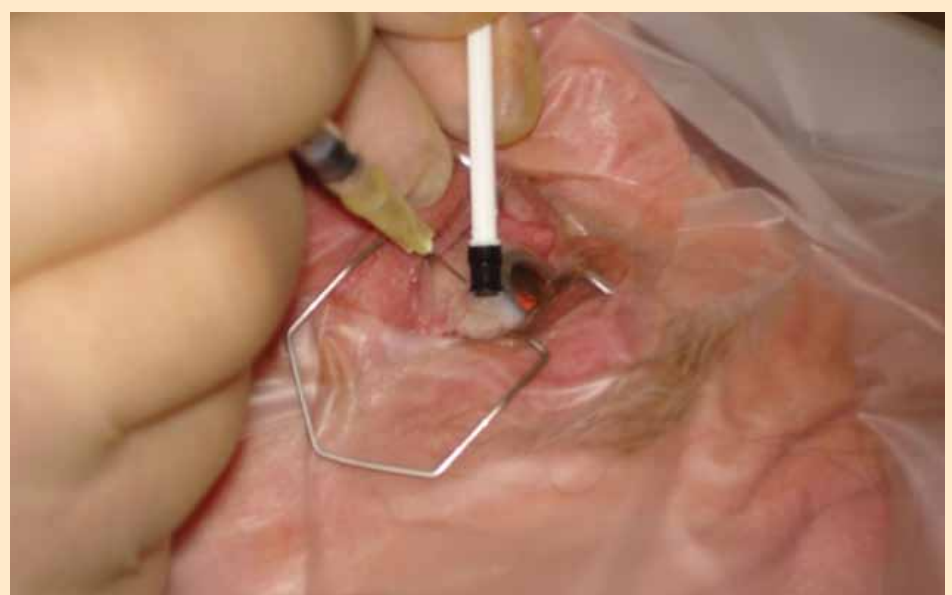


Figure 6
Measuring distance from limbus

treatment for metastatic colon cancer, rates of vascular events such as strokes and heart attacks were higher in those treated with Avastin than in those not.²² In this study, the drug was administered intravenously, rather than intravitreally, at a dose 400 times that used in the eye, and the patients were by definition unwell. Nonetheless, the possibility of such side effects is of concern in patients with diabetes who are in any case more prone to vascular events. For these reasons, despite reassuring safety data in patients treated with anti-VEGF agents for AMD,²³ careful surveillance of treated patients is indicated.

Treatment of diabetic macular oedema

Macugen

In a prospective, randomised, double-masked, controlled multi-centre phase II trial, Macugen at three different doses versus sham injection (the surgeon prepares and anaesthetises the patient's eye but does not perform an injection) was administered at six-week intervals via intravitreal injection in 172 patients with CSMO. Eyes treated with Macugen 0.3mg were more likely than sham injected eyes to show a two line visual acuity improvement (34% vs. 10%), were less likely to require photocoagulation (25% vs. 48%), and showed a reduction in OCT measured central retinal thickness of 68µm compared to essentially unchanged thickness in sham treated eyes.²⁴

Lucentis

Two small phase I studies, each of 10 patients, have demonstrated improvement in visual acuity of approximately two lines, and a reduction in OCT measured central retinal thickness in patients with CSMO treated with Lucentis.^{25,26} A larger phase II study with 126 patients randomised to Lucentis, laser or both showed better visual outcome at six months in Lucentis-treated compared to laser-treated patients; combination therapy was not significantly different to single therapy. Excess foveal thickness was



Figure 7

Intravitreal injection

reduced the most in Lucentis-treated patients.²⁷ Phase III studies are planned.

Avastin

In one prospective case series,⁵¹ patients with chronic diffuse diabetic macular oedema unresponsive to laser, intravitreal triamcinolone or vitrectomy underwent 1.25 mg intravitreal Avastin injection; 70% of patients underwent a second injection at six weeks.²⁸ A three-line visual acuity improvement occurred in 26% patients by 12 weeks (the study end point), and OCT measured central retinal thickness declined by a third.

A second study, a multi-centre, retrospective analysis followed for an average of six months, 78 eyes of patients treated with Avastin for CSMO. A second and third injection was required in 20% and 8% of eyes respectively. 55% of treated eyes showed a two-line visual acuity improvement, and 41% were stable at six months; OCT measured central retinal thickness declined by approximately a quarter.²⁹

A randomised prospective phase II trial of 121 patients examined dosage, dose frequency and the effect of photocoagulation on the response to intravitreal Avastin for diabetic macular oedema. There appeared to be no benefit in increasing the Avastin dose from 1.25mg to 2.5mg, nor of adjunctive photocoagulation. It appeared that a dosage frequency of less than six weeks was desirable.³⁰

An additional study recruited

126 patients into a non-comparative prospective study of intravitreal injection of Avastin in patients with diffuse diabetic macular oedema which had persisted despite prior therapy. Of these patients, 44% had severe macular ischaemia. At 12 months, mean visual acuity had improved a line and there was a 20% reduction in central foveal thickness.³¹

Treatment of proliferative diabetic retinopathy

Macugen

The previously quoted study of Macugen for diabetic macular oedema was subjected to a post-hoc analysis to determine its effect on retinal neovascularisation. Sixteen patients had neovascularisation of the retina at baseline, had follow up photographs, and had not received PRP prior to entry into the trial. Of these, one had PRP during study follow up. Of Macugen treated eyes, 8 out of 13 (62%) showed regression of neovascularisation, compared to 0 out of 3 in the sham treatment arm.³²

A further randomised pilot study compared intravitreal Macugen administered six weekly for 30 weeks with PRP in 16 patients with high-risk proliferative diabetic retinopathy. All Macugen treated eyes showed complete regression of new vessels, whereas 75% of laser treated eyes manifested residual disease activity.³³

Avastin

Following early case series demonstrating regression of neovascularisation with intravitreal Avastin injection,^{34,35} later studies have demonstrated a variety of possible roles for Avastin in the management of proliferative diabetic retinopathy, which include: 1) Management of active progressive proliferative diabetic retinopathy. In a study of 38 patients with proliferative diabetic retinopathy, intravitreal Avastin treatment was associated with significant clearance of vitreous haemorrhage, and regression of the vascular component of fibrovascular proliferation. The area of fibrous

FREE CET

Approved for Optometrists ✓ Approved for DOs ✓

40 15/01/10 CET



Figure 8

Cotton bud and topical antibiotic

proliferation did not change, and two patients suffered tractional retinal detachment.³⁶

2) Adjunctive treatment to PRP.

Adjunctive use of intravitreal Avastin with PRP was associated with a greater reduction in the area of active leaking new vessels than PRP alone in patients with high-risk PDR.^{37, 38}

3) Treatment for persistent vitreous haemorrhage in patients unwilling or unfit for vitrectomy.³⁹

4) Treatment for iris neovascularisation where vitreous haemorrhage precludes proliferative diabetic retinopathy.³⁴

5) Treatment of proliferative diabetic retinopathy where vitreous haemorrhage precludes PRP.⁴⁰

6) Treatment for persistent new vessels following PRP.⁴¹

7) Enhancing the outcome of surgery for neovascular glaucoma by causing regression of iris new vessels.⁴²

8) Preoperative/intraoperative treatment for patients undergoing diabetic vitrectomy, to reduce intraoperative and postoperative bleeding.^{43, 44}

Lucentis

There is as yet no clinical trial demonstrating efficacy of Lucentis in proliferative diabetic retinopathy.

B. Steroids

Rationale for the use of steroids in diabetic retinopathy

In experimental models of diabetes, early features include the adhesion of white

blood cells (leukocytes) to vascular endothelial cells, and migration of leukocytes into the retina – essentially, histological evidence of inflammation. This coincides with the onset of vascular dysfunction, and leads to breakdown of the blood retinal barrier, and premature endothelial cell death. Leukocytes appear to be key to this process, and if their adhesion to endothelial cells is blocked, blood retinal barrier breakdown and premature endothelial cell death are prevented.⁴⁵ VEGF itself has shown to be pro-inflammatory.⁴⁶ By stabilising the blood retinal barrier,⁴⁷ blocking VEGF production,⁴⁸ reducing leukocyte adhesion and suppressing retinal neovascularisation,⁴⁹ steroid therapy may be beneficial in diabetic retinopathy.

Agents

There exists a significant number of formulations of intravitreal steroid, but the most commonly used is triamcinolone acetonide. This drug is in fact not licensed for intraocular use, but as with Avastin, this has provided no barrier to widespread use.

Complications of intravitreal steroid injection

Local

Intravitreal steroid causes cataract and raised intraocular pressure. One study demonstrated that in triamcinolone treated eyes, at two years, 44% of patients required treatment for raised intraocular pressure and 54% had required cataract surgery compared to 10% and 0% respectively in the placebo group.⁵⁰

Systemic

It is not thought that there are significant systemic effects of intravitreal triamcinolone.

Treatment of diabetic macular oedema

A well controlled randomised trial of intravitreal triamcinolone in diabetic macular oedema demonstrated in treated eyes at two years a one line visual acuity

improvement compared to placebo and a one seventh reduction in central foveal thickness compared to baseline.⁵⁰

Treatment of proliferative diabetic retinopathy

Whereas there are case reports of neovascularisation responding to intravitreal steroid,⁵¹ the principal use of steroid in proliferative diabetic retinopathy appears to be the limitation of post treatment macular oedema.⁵²

Systemic therapy

Glycaemic control

In one study, 1,441 patients with Type 1 diabetes and either no retinopathy or mild to moderate non-proliferative retinopathy were recruited into a trial to assess whether intensive blood glucose control was beneficial to retinopathy development or progression when compared to conventional treatment. It was found that there was a 76% reduction in the risk of developing retinopathy, and a 54% reduction in the risk of progression. The effect was proportionate to the improvement in blood sugar control, and increased over time. 22% of intensively treated patients with retinopathy at baseline showed an initial worsening of retinopathy compared to 13% in the conventionally treated group; but by 18 months this effect had largely disappeared.⁵³ In another study, 3,867 patients with Type 2 diabetes were recruited into a study to determine the effect of intensive blood glucose control on diabetic retinopathy. There was a 29% reduction in the risk that photocoagulation would be required, and a 21% reduction in the risk of retinopathy progression. Visual acuity was unaffected. The effect was proportionate to the improvement in blood glucose control.⁵⁴

Hypertensive control

In this study, 1,148 hypertensive Type 2 diabetic patients were randomised to intensive or conventional treatment of blood pressure in a study

designed to determine the impact of blood pressure control on diabetic retinopathy. Although there was only a small difference in mean blood pressure between the two groups (144/82 vs. 154/87) there was a risk reduction of 34% for retinopathy progression, 35% for retinal photocoagulation, and 47% for moderate visual loss (doubling of the visual angle). The effect was proportionate to the reduction in blood pressure, and synergistic with the effect on blood sugar control.⁵⁵ Patients with Type 1 diabetes show some tendency for systolic and diastolic blood pressure to predict retinopathy but the effect seems small.⁵⁶

Other treatments

Fenofibrate

A large scale randomised controlled trial of the drug Fenofibrate, a cholesterol lowering agent, demonstrated that patients with Type 2 diabetes treated with the drug tended to have a reduced risk of retinopathy progression and of requiring laser, although the effect did not appear to be related to blood lipid levels.⁵⁷

Ruboxistaurin

Ruboxistaurin, a protein kinase C (PKC) beta inhibitor, exhibits significant anti-angiogenic activity by reducing the response of vascular endothelial cells to stimulation by VEGF. Oral Ruboxistaurin treatment of patients with Type 1 or 2 diabetes reduces (i) vision loss, (ii) need for laser treatment, and (iii) macular oedema progression, while increasing occurrence of visual improvement in patients with non-proliferative retinopathy.⁵⁸ It does not, however, appear to retard progression of retinopathy.

Losartan and Enalapril

Data recently published suggests that patients with Type 1 diabetes treated with these two drugs, which block the renin-angiotensin system in the kidney, show a 65-70% reduction in the risk of two-stage progression of diabetic retinopathy. The effect seems unrelated to blood pressure.⁵⁹



Figure 9

Indirect ophthalmoscopy to check fundus and optic disc perfusion

Conclusion

Optometrists should be aware that newer therapies with potential for visual improvement are emerging for the management of diabetic retinopathy, and that the paradigm of identifying diabetic patients at risk of visual loss and then referring for destructive laser treatment is likely to shift.

References

See www.optometry.co.uk/references

MSc in Clinical Optometry

CITY UNIVERSITY and OT have joined forces allowing readers to achieve CET points through to a

full Masters in Clinical Optometry. By completing the MCQs that follow each article you can achieve:

- Two CET points (free)
- The opportunity of achieving 10 PG credits by completing an examination based on all the articles in the CET series (runs in May of each year).

The content of this article is part of the forthcoming Diabetic Eye Disease module running April 18-20 2010. For further information see www.city.ac.uk/optometry/msc. Contact Dr Michelle L Hennelly by emailing (m.hennelly@city.ac.uk) or call 0207 040 8352.

FREE CET

Approved for Optometrists ✓ Approved for DOs ✓

Module questions

Course code- C-12870/OD

1. Which one of the following is true regarding laser therapy for diabetic retinopathy?

- a. the effect of treatment is often of short duration
- b. it cannot be applied where there is significant media opacity
- c. the treatment is often intolerable
- d. it usually results in improved visual acuity

2. Which one of the following is false regarding macular laser therapy?

- a. it is effective in the presence of marked macular ischaemia
- b. the scars produced may enlarge over time
- c. it is associated with immediate reduction in indices of central visual function
- d. it is applied when a specific threshold of disease is present

3. Which one of the following is false regarding panretinal laser therapy?

- a. it may cause a reduction in visual field
- b. it may result in the loss of a driving license
- c. it may improve macular oedema
- d. it is applied when a specific threshold of disease is present

4. Which one of the following agents is not used in intravitreal therapy?

- a. Triamcinolone acetonide
- b. Lucentis
- c. Losartan
- d. Macugen

5. Which one of the following is true regarding intravitreal injection?

- a. it results in endophthalmitis in 1 in 100 cases
- b. it is administered through the limbus
- c. it requires an operating theatre
- d. it is carried out using sterile equipment

6. Which one of the following is false regarding VEGF-A (vascular endothelial growth factor A)?

- a. it causes endothelial cell proliferation
- b. it causes decreased vascular permeability
- c. it is involved in wound healing
- d. it is a retinal neuron survival factor

7. Which one of the following is false regarding Macugen?

- a. it was developed for the treatment of neovascular AMD
- b. it blocks all isoforms of VEGF-A
- c. when administered to diabetics with CSMO, it may reduce foveal thickness
- d. when administered to diabetics with CSMO it may improve visual acuity

8. Which one of the following is false regarding Lucentis?

- a. it was developed for the management of colon cancer
- b. it is a smaller molecule than Avastin
- c. it has been shown to reduce foveal thickness in diabetics with CSMO
- d. it has a shorter half-life than Avastin

9. Which one of the following is false regarding Avastin?

- a. there is evidence for effectiveness in treating diabetic macular oedema
- b. it can promote iris neovascularisation
- c. it may be of value in reducing intra and postoperative bleeding in diabetic patients undergoing vitrectomy
- d. it may improve the outcome of surgery for neovascular glaucoma

10. Which one of the following is not a feature of intravitreal steroid injection?

- a. it has no effect on the blood retinal barrier
- b. it inhibits leukocyte adhesion and migration
- c. it may cause cataract and elevation of intraocular pressure
- d. it may reduce foveal thickness in patients with diabetic macular oedema

11. Which one of the following is false regarding tight blood sugar control?

- a. in patients with Type 1 diabetes, it delays the onset and slow the progression of retinopathy
- b. in patients with Type 1 diabetes, its beneficial effect is proportional to the tightness of control
- c. in patients with Type 2 diabetes, blood sugar control has no effect on retinopathy progression
- d. in patients with Type 2 diabetes, tight blood sugar control improves visual acuity

12. Which one of the following statements is true?

- a. Fenofibrate reduces progression of retinopathy by lowering blood lipid levels
- b. Losartan reduces progression of retinopathy by lowering blood pressure
- c. Tight blood pressure control reduces the risk of visual loss and retinopathy progression in patients with Type 2 diabetes
- d. Ruboxistaurin reduces the rate of progression of diabetic retinopathy

PLEASE NOTE There is only one correct answer. All CET is now FREE. Enter online. Please complete online by midnight on February 17 2010 - You will be unable to submit exams after this date – answers to the module will be published on www.optometry.co.uk



EDUCATION NEVER STOPS

Looking to grow your business, enhance your clinical skills or gain FREE CET points?

Then visit the Academy for Eyecare Excellence™ - one central hub for all the latest developments, learnings, insights and advice.

www.cibavisionacademy.co.uk





ACADEMY
FOR EYECARE
EXCELLENCE.
CIBAVISION.