REVIEW ARTICLE

Principles of Laser Treatment and How to get Good Outcomes in a Patient with Diabetic Retinopathy

Subhadra Jalali

Diabetic Retinopathy is an emerging cause of treatable blindness in India. The urban population prevalence of diabetic retinopathy in the Andhra Pradesh Eye Disease Study (APEDS) was 7.8% (1). In a tertiary care diabetic centre 34.1% of diabetics had diabetic retinopathy (2). Laser treatment has revolutionized the treatment and prognosis of eyes with diabetic retinopathy. The judicious and timely use of this therapy can prevent significant visual loss in a significant number of eyes with diabetic retinopathy. The basic principles guiding the use and technique of laser treatment in eyes with diabetic retinopathy has been provided by large multicentric clinical trials i.e. Diabetic Retinopathy Study (DRS) (3), Early Treatment Diabetic Retinopathy Study (ETDRS) (4), Diabetes Control and Complications Trial (DCCT) (5) and the United Kingdom Prospective Diabetes Study (UKPDS) (6) trials. Various factors can influence outcome of retinal laser treatment. Some important issues are discussed in this article.

Promptness of Referral

A major reason why patients with diabetes lose vision from retinopathy is that they do not receive proper ophthalmic treatment at the proper time. Stross and Harlan (7) found that only 28% of family physicians and 46% of internists in a survey in USA were aware of the results of diabetic retinopathy study, 18 months after its publication, or knew that panretinal photocoagulation (PRP) was indicated for neovascularisation of the disc (NVD). Only 56% of physicians felt that IDDM patients should be evaluated routinely by an ophthalmologist.

There is a high risk of diabetic retinopathy being present shortly after diagnosis of NIDDM (8). It is the responsibility of all physicians to make sure that all newly diagnosed NIDDM patients and all patients with IDDM of more than 5 years duration are examined at least yearly by an ophthalmologist, irrespective of any visual complaints. A statutory message on all insulin vials and oral hypoglycemic tablets to 'Get your Retina checked' could be helpful in reminding this fact to patients and health care providers. Remember that diabetic retinopathy is asymptomatic in the treatable stages of the disease. Laser cannot improve vision but can prevent loss of vision if retinopathy is treated early. Laser treatment has to start before patient has any symptoms, to achieve good results. Many a times patients do not report visual complaints or there may be no complaints in initial stages, and so routine screening by dilated fundus examination can help in early diagnosis. The best method of screening for diabetic retinopathy is still debated. Fundus photography, direct ophthalmoscopy by ophthalmologists, general practitioners, hospital physicians, ophthalmic opticians, and trained optometrists has been advocated. The best method may involve one or more of these strategies depending on the environment and cost-effectiveness. It is the responsibility of the ophthalmologist to be familiar with the direct and indirect ophthalmoscopy and slit-lamp biomicroscopy methodology of retinal examination and criteria for photocoagulation. It is the responsibility of physicians to see that all diabetics have regular fundus examinations.

Patients get treated for cerebral strokes, cardiac complications, diabetic foot, inter-current infections, nephropathy, neuropathy, surgical problems etc. and all this time they are under regular care of a medical

From the Deptt. of Retina & Vitreous, Smt. Kannuri Santhamma Retina Vitreous Centre, LV Prasad Eye Institute, Hyderabad.
Correspondence to : Dr. Subhadra Jalali, Smt. Kannuri Santhamma Retina Vitreous Centre, LV Prasad Eye Institute, Hyderabad.

personnel. Patients have expressed their feelings time and again to us *'If only somebody in the medical field had told me to get a regular retinal examination done, I would not be blind today. I did not even know that diabetes could cause blindness and that this blindness could have been avoided by regular retinal examinations with early laser treatments. My physician who is seeing me for such a long time or even my optician who gives me optical glasses never told me about Retina and Retinopathy!.'*

Decision making and Laser Management Protocols in patients with Diabetic Retinopathy

On the basis of various clinical trials, it is clear that early diagnosis of retinopathy and proper follow-up of patients, simultaneously with good control of blood glucose levels can reduce the incidence and severity of visual loss from diabetic retinopathy. However, good control of blood sugar does not automatically mean absence of vision threatening retinopathy. Below is a summary of the indications and treatment protocols for laser in such patients.

Photocoagulation in diabetic Retinopathy (3,4,9)

Indications for scatter treatment (PRP):

1. Full scatter treatment also known as `panretinal photocoagulation' (PRP) should be carried out promptly in all eyes with PDR having high-risk charateristics, (HRC) (10) i.e.(i) NVD more than or equal to 1/4-1/3 disc area or (ii) vitreous or pre-retinal haemorrhage with any amount of new vessels observed or assumed to be obscured by the haemorrhage.
2. Whenever HRC are present, PRP should be carried out inspite of presence of fibrous proliferation or TRD. Areas of fibrous proliferation and any tractional detachment should be avoided, and treatment intensity should be mild to moderate, as there is risk of extension of the localised TRD into the macula. A combination of vitrectomy and photocoagulation may be needed in some of these eyes.
3. Whenever iris or angle neovascularisation is seen, early PRP should be done irrespective of presence or absence of retinal HRC.
4. Consider systemic factors for decision regarding PRP for eyes approaching HRC i.e. eyes with very severe NPDR or eyes with PDR without HRC (see point 9 below). Role of PRP in such cases is uncertain (11,12) and individual decisions are to be made.
5. Eyes with severe ischaemia i.e. extensive retinal haemorrhages, capillary non-perfusion, multiple, prominent soft exudates have high risk of anterior segment neovascularisation and should be considered for PRP
6. Eyes with burnt out retinopathy or showing regression of retinopathy should not be treated with laser. They can be kept under observation. Similarly eyes with a single NVE without associated haemorrhage may be observed, provided patient comes for regular follow-up and has no other factors associated with worsening of retinopathy.
7. In eyes with PDR and maculopathy, macular treatment is preferably done first followed by PRP 2-4 weeks later.
8. If delay in PRP is undesirable due to high-risk characteristics (HRC), the focal macular treatment can be combined with nasal half PRP, followed 2-3 weeks later with completion of PRP.
9. Various factors known to worsen the retinopathy may influence the decision to initiate treatment in eyes with severe NPDR or PDR without HRC. These factors include pregnancy, nephropathy, cardiac failure, Carotid artery disorders, Cataract surgery and Yag laser capsulotomy, uncontrolled blood sugars, recent institution of Insulin in a patient of NIDDM with long-standing uncontrolled blood sugars, poor patient follow-up etc. For example, if laser is deferred in a patient till HRC develop, and this happens at a stage when patient needs dialysis/ renal transplant or is in later stages of pregnancy, these more pressing problems may interfere with optimal laser treatment schedule in such patients. This is important in our country where due to various social and economic factors patients cannot always come for regular follow-up or prompt treatment.

The decision to treat or not to treat hence has to take into account all these factors, besides the guidelines provided in

the randomized clinical trials. Remember that the randomized trials are done after careful selection of cases and excluding many patients who do not 'fit-in' into the inclusion criteria. When such patients present to a clinician, treatment has to be individualized, taking the trial results and retinopathy worsening risk factors into consideration.

Treatment Techniques

1. Panretinal photocoagulation (PRP)/ Full Scatter treatment

The pupils are fully dilated and topical anaesthesia is used. The commonest wavelengths used are Argon green, blue green, and 532 green laser, using the slit-lamp delivery system. In case of hazy media due to cataract or vitreous haemorrhage, Krypton red or diode red laser (814nm) can be used. In patients with poorly dilating pupils, poor cooperation, inability to sit at the slit-lamp, peripheral cortical cataract, vitreous haemorrhage, children etc one may need to use the indirect ophthalmoscope delivery mode for PRP. Various types of lenses are available to visualise different areas of the retina so as to cover as much area of retina as possible (13).

A total of 1600-3000 burns are placed in two or more sittings, carefully avoiding the macular area and any areas of tractional elevation of the retina. The burns are placed 2 to 3 disc diameters away from the macula and the disc i.e. usually outside the arcades and extended peripherally upto the equator and beyond. Typical initial settings on the Argon laser would be 500 μ spot size, a 0.1second exposure and 250-270 mw power. The power is gradually increased till a whitish reaction is obtained on the retina.

The lesions are placed one burn width apart. Local confluent treatment to small, flat NVE can be done in addition. Laser treatment should not be applied over major retinal veins, pre-retinal haemorrhages, darkly pigmented chorioretinal scars or within one DD of centre of macula, so as to avoid risk of haemorrhage or large scotomas (14). Burns along the long ciliary nerves can be painful. This can be decreased by premedication, using a mild tranquiliser 30 to 45 minutes before treatment or using lesser power, longer exposure time and smaller size burns i.e. 200 micron spot size, but this would require 6.25 times more number of burns to cover the same area of the retina. A final alternative is to give peribulbar anaesthesia.

Follow-up treatment after initial PRP (9,14, 15)

In about 25% of eyes that undergo complete PRP for DRS-High risk characteristics, enough new vessels persist or recur to justify additional photocoagulation. The ETDRS guidelines (14) for follow-up treatment after initial PRP are based on consideration of six factors. These are:

1. Change in new vessels since the last treatment/last visit.
2. Appearance of the new vessels (calibre, degree of network formation, extent of accompanying fibrous tissue).
3. Frequency and extent of vitreous haemorrhage
4. Status of vitreous detachment
5. Extent of photocoagulation scars
6. Extent of tractional retinal detachment and fibrous proliferation.

Factors favouring additional photocoagulation

1. Lack of regression within 6-8 weeks of the initial treatment.
2. Active new vessels (tight networks, little fibrous tissue, rapid growth in size).
3. Recurring vitreous haemorrhage, whether the source is visible or not.
4. Extensive intraretinal lesions (venous beading, IRMA, blot haemorrhages, retinal edema).
5. 'Skip areas' and room for more burns in between previous scars.

Additional photocoagulation may be less urgent if

a. The caliber of new vessels has decreased and fibrous proliferation is developing.

b. There is a single episode of vitreous haemorrhage coincident with a posterior vitreous detachment and no recurrent haemorrhage thereafter.

c. There is extensive or almost complete posterior vitreous detachment.

d. If there is no space in between scars, and additional treatment will require confluent treatment, clear indications are necessary before additional treatment is given as it can lead to extensive field loss. In some cases, especially with vitreous traction, vitrectomy surgery is a better alternative.

Technique

1. Add burns in between scars of initial treatment.
2. Add burns farther peripherally (if needed with the indirect ophthalmoscope laser delivery mode) and also at the posterior pole, sparing the area within 500-1500 μ from the centre.
3. Favour quadrants with active new vessels and/or severe intraretinal lesions, areas where scars are more widely spaced, and areas of severe ischaemia not previously treated, such as the temporal part of the posterior pole.
4. Direct treatment of small, new, active patches of NVE in between scars.The number of additional burns may be as high as 1500 to 12,000 divided in repeated sessions to cause significant regression of the retinopathy and decrease the incidence of visual loss (15).

If vitreous haemorrhage prevents additional photocoagulation, choice between vitrectomy with endophotocoagulation and observation is influenced more towards observation if:

1. Extensive scatter treatment has been applied.
2. Intraretinal lesions are not active.
3. Posterior vitreous has detached from the macula and temporal vascular arcades.
4. Past ophthalmoscopy and present ultrasonography. does not show any traction on the macula.
5. Blood is mostly behind the detached vitreous.
6. Useful vision is present in the fellow eye.

If new vessels continue to proliferate and patient has recurrent vitreous hemorrhage or increasing vitreous traction, inspite of extensive photocoagulation, early vitreous surgery is useful in preventing irreversible visual loss.

Indications for macular treatment

1. Eyes with CSME with centre involved should be considered for immediate treatment.
2. Eyes with CSME without centre involved and even with good vision, should also be considered for immediate laser treatment.
3. Eyes with macular edema that is not clinically significant should generally be watched without treatment.

Technique

Once the CSME is detected clinically, usually (though not essentially), a fluorescein angiography is done prior to the laser treatment, so as to identify the treatable lesions, according to the ETDRS protocol (16).

'Focal' macular treatment includes focal laser treatment of microaneurysms and grid treatment of areas of diffuse leakage and focal non-perfusion within 2DD of centre of the macula (16). No treatment is applied to lesions closer than 300 nm from the centre of the macula. Laser parameters used are a 200 or 100 micron spot size, 120 to 150 mW energy and very light gray intensity of the burn. Care is taken to demarcate and avoid the foveal avascular zone. If CSME is associated with large areas of macular ischemia, only the areas of retinal thickening are treated. Patient must be explained that treatment is useful only in stabilisation of the vision and may not improve what vision is already lost. Areas of non-thickened retina including outside the arcades should not be treated as that worsens the macular edema (12).

Clinically Significant Macular edema (CSME)

Macular lesions in diabetes are evaluated by stereoscopic slit-lamp biomicroscopy fundus examination, using a fundus- viewing lens such as a 90 Dioptre lens. The ETDRS defined CSME (4) as the presence of one or more of the following criteria:

Retinal thickening involving or within 500 of the centre of the macula (2).Hard exudate(s) at or within 500 of the centre of the macula, if associated with thickening of the adjacent retina (but not hard exudates remaining after disappearance of the retinal thickening) (3) and A zone(s) of retinal thickening one disc area or larger in size, any part of which is located within one DD of the centre of the macula. In recent years, Ocular coherence tomography (OCT) is being increasingly used to evaluate diabetic macular diseases (17).

Precaution

If patient has NPDR with Diabetic CSME, especially of the diffuse type, sometimes the edema can worsen after laser therapy. The visual acuity can decrease markedly from subretinal fibrosis (18) or lipid migration under the fovea following laser (19). Hence, before

starting laser treatment, especially in eyes with diffuse macular edema and extensive hard exudates, systemic evaluation and control of various abnormalities promptly is essential. These include correction of not only the random blood sugar to less than at least 200 mgm%, but also hemoglobin, serum lipids (including triglycerides) and renal functions like serum creatinine and urea levels besides reduction of albuminuria. In case of PDR especially with HRC, risk of rapid and substantial visual loss is very high and here the systemic control is carried out along with prompt laser treatment, without waiting for complete control.

Results

Laser treatment in PDR with HRC can reduce risk of severe visual loss (defined as visual acuity of less than 5/200 or 5/60) by 50% or more. Macular photocoagulation also reduces risk of visual loss in treated than in untreated eyes (16). Further refinements in treatment techniques and improved understanding of the underlying pathology and its response to laser treatments, has in recent times further improved visual outcomes over the last two decades, since the laser treatment trials of diabetic retinopathy were published.

Summary

Every diabetic patient must be informed by their physicians/ opticians/ ophthalmologists about risk of retinopathy and need for periodic dilated eye retinal examinations. Proper and prompt classification and laser management of the condition goes a long way in allowing preservation of vision in many of these patients. In eyes not amenable to laser treatment or where the retinopathy progresses even after laser treatment, very early and appropriate vitreoretinal surgery is also highly successful in regaining some of the lost vision.

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