Clinical*DIGEST 6*

Retinopathy

Response to laser treatment is associated with good glycaemic control



Debotal Broadbent Director of Diabetic Eye Screening, Royal Liverpool University Hospital

he epidemiology of diabetic retinopathy, its pathogenesis, progression and risk factors have been the subject of many, many papers over the past 20–30 years. The

importance of metabolic control, particularly glycaemic and blood pressure control,

was identified as far back as the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), and subsequently confirmed in the Diabetes Control and Complications Trial (DCCT) in type 1 diabetes and the United Kingdom Prospective Diabetes Study (UKPDS) in type 2 diabetes. These studies have significantly influenced the modern management of diabetes.

The effectiveness of laser treatment in the treatment of both proliferative retinopathy and maculopathy was established in a number of highly important studies in the 1970s and 1980s, although there has been considerable research into the development of novel, non-destructive treatments for both over the past 10 years. It is well established that optimally timed laser treatment is effective in up to 95% of retinopathy cases, but in only around 60%

of maculopathy cases. There are many reasons why laser treatment should not be effective in all cases, but I am unaware of any previous studies specifically addressing the question of whether improved metabolic control not only slows progression of diabetic eye disease but also influences the outcome of laser treatment – a logical and intuitive consideration.

This prospective study on 115 eyes with high-risk proliferative retinopathy found that in only 56.5% of patients treated with panretinal photocoagulation by a single surgeon was there a satisfactory response, in terms of signs of regression, at 12 weeks. The authors found that the probability of a satisfactory response to laser treatment was related to better glycaemic control (plasma HbA_{1c} levels <8%) but not related to presence or absence of microalbuminuria.

This is only one study and numbers are small. Ophthalmologists now recognise the need for good metabolic control in their patients but the emphasis has been on the slowing of progression and the lessening of severity of complications. The implications for improved responses to laser treatment should persuade all ophthalmologists to become more active in the monitoring and management of metabolic control in their patients and in patient education.

INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE

Retinal vascular leakage lowered by ruboxistaurin

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

In this 18-month placebo-controlled double-masked trial the effect of ruboxistaurin mesylate (RBX; a protein kinase-C β inhibitor) on blood-retinal barrier permeability was examined in 41 people with diabetic macular oedema. The four study arms were RBX at 4, 16 and 32 mg/day or placebo.

2 Vitreous fluometry was used at baseline and 3, 12 and 18 months to assess retinal vascular leakage.

3 RBX, at all doses, was found to have a significant association with baseline permeability (P=0.032) demonstrating that RBX treatment is able to lower retinal vascular leakage in eyes with diabetic macular oedema. Visual acuity was normal at baseline and stayed so throughout the study.

The authors conclude that this significant effect suggests that future RBX-based trials will benefit from focusing on eyes with marked retinal vascular leakage at baseline.

Strom C, Sander B, Klemp K et al (2005) Effect of ruboxistaurin on blood-retinal barrier permeability in relation to severity of leakage in diabetic macular edema. *Investigative Ophthalmology and Visual Science* **46**(10): 3855–8



Good glycaemic control improves response to laser treatment

| Readability | 111 |
|---------------------------|------|
| Applicability to practice | 1111 |
| WOW! factor | 11 |

Previous studies have linked the progression of retinopathy to glycaemic control and noted an association between nephropathy and retinopathy but have never considered

the effect of metabolic control on the outcome of laser treatment.

2 The aim of this study was to assess the effect of the level of glycaemic control and microalbuminuria on the initial response to panretinal photocoagulation (PRP) in people with high-risk proliferative diabetic retinopathy (PDR) and type 2 diabetes.

3 Full-scattered PRP was used in this prospective cohort study of 115 eyes.

The participants were divided into four groups based on their level of glycaemic control and the presence or absence of microalbuminuria.

5 Sixty-five of the 115 eyes examined showed a successful initial response to PRP and 50 did not. Using a logistic regression model for data analysis, the authors demonstrated a significant association between low HbA_{1c} levels and a positive response to PRP (P<0.05).

6 The association between microalbuminuria and a positive response to PRP was not significant $(P \ge 0.05)$.

The authors are encouraged by findings that well-balanced glycaemic control appears to improve the outcome of treatment but say that further studies are required to confirm these data and elucidate the mechanisms involved.

Kotoula MG, Koukoulis GN, Zintzaras E et al (2005) Metabolic control of diabetes is associated with an improved response of diabetic retinopathy to panretinal photocoagulation. *Diabetes Care* **28**(10): 2454-7

Retinopathy

<u>Clinical *DIGEST*</u>

DIABETIC MEDICINE

Pregnancy is not a risk factor for microvascular complications

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

Seven hundred and ninety-three women, from the EURODIAB Prospective Complications Study, with type 1 diabetes and who were potentially childbearing were followed up for 7.3 years in order to examine the effect of pregnancy on the development and progression of microvascular complications.

2 Of these women 163 gave birth during the follow-up period; 425 were childless at baseline and 102 of this group gave birth during the follow-up period.

3 Risk factors (such as duration of diabetes, HbA_{1c}, systolic blood pressure, mean age and giving birth) were compared between participants who did or did not develop microvascular complications.

The authors demonstrate a significant link between raised HbA_{1c} levels and progression to microalbuminuria (P=0.0003); the other risk factors appeared not to be significant.

5 A high HbA_{1c} level and duration of diabetes showed a significant association with developing proliferative retinopathy (P=0.008 for both). Similar conclusions were drawn for any retinopathy.

6 Progressing to giving birth and neuropathy.

The data presented in this paper agree with previously published Diabetes Control and Complications Trial data in that a first or subsequent pregnancy has no effect on developing microvascular complications.

Verier-Mine O, Chaturvedi N, Webb D, Fuller JH (2005) Is pregnancy a risk factor for microvascular complications? The EURODIAB Prospective Complications Study. *Diabetic Medicine* **22**(11): 1503–9

AMERICAN JOURNAL OF OPHTHALMOLOGY

Diabetic retinopathy screening before the age of 10 not needed

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

In this observational case series the ophthalmic screening results of 51 children, from the authors' department, were analysed to see if any correlation existed between an early diagnosis of type 1 diabetes (before the age of 2) and the onset of diabetic retinopathy (DR). All

ARCHIVES OF OPHTHALMOLOGY

Which patients benefit most from triamcinolone?

Readability✓Applicability to practice✓WOW! factor✓

A prospective clinical interventional study was carried out on 53 eyes with diffuse diabetic macular oedema to see which factors have an effect on best-corrected visual acuity (BCVA) after treatment with an intravitreal injection of 20 mg triamcinolone acetonide.

Multiple linear regression analysis revealed that a maximum gain in

OPHTHALMOLOGICA

One-field photography inadequate for screening

Readability✓Applicability to practice✓WOW! factor✓

The eyes of 100 consecutive patients with diabetes (200 eyes) undergoing digital fundus photography were included in this retrospective study.

2 Images obtained using onefield, non-mydriatic, 45° digital photography were independently children were followed up for at least 5 years post-diagnosis, 33 for more than 8 years.

No children developed DR, indicating that children have an insignificant risk of developing DR up to the age of 10 years, even if they are diagnosed with type 1 diabetes before the age of 2 years.
The authors conclude that screening for DR before the age of 10 years is not needed; this conclusion is supported by a review of other trials, which included more than 900 children under the age of

10 years with type 1 diabetes, none of whom required treatment for DR, they say.

Lueder GT, Pradhan S, White NH (2005) Risk of retinopathy in children with type 1 diabetes mellitus before 2 years of age. *American Journal of Ophthalmology* **140**(5): 930–1

BCVA, after triamcinolone injection, was significantly (P=0.001) and positively correlated with an increased degree of macular oedema.

3 Observed changes in BCVA were statistically independent (P>0.15) of age, sex, pseudophakia and macular grid laser treatment prior to the start of the study.

The authors conclude that, after triamcinolone injection in eyes with diffuse diabetic macular oedema, an improvement in BCVA is influenced by a high level of pre-intervention macular oedema, a low level of macular ischaemia and low pre-intervention visual acuity.

Jonas JB, Martus P, Degenring RF et al (2005) Predictive factors for visual acuity after intravitreal triamcinolone treatment for diabetic macular edema. *Archives of Ophthalmology* **123**(10): 1338–43

graded by endocrinologists and a retinal specialist. The patients' eyes also had complete standard ocular examinations, which were used as the reference method of ascertaining diabetic retinopathy.

3 The false negative rates were 22% and 21.5%, and the sensitivities 45% and 53.8% for the endocrinologists and retinal specialist, respectively.

4 The authors conclude that onefield, non-mydriatic, 45° digital photography is an inadequate method for diabetic retinopathy screening.

Kuo HK, Hsieh HH, Liu RT (2005) Screening for diabetic retinopathy by one-field, non-mydriatic, 45 degrees digital photography is inadequate. *Ophthalmologica* **219**(5): 292–6 ⁶Screening for diabetic retinopathy before the age of 10 years is not needed.⁹

⁶One-field, non-mydriatic, 45° digital photography is an inadequate method for diabetic retinopathy screening.⁷