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Sir,

Reply to Patel and Larkin

Thank you for your interest in our case and your insightful comments. Reaching a diagnosis of Eale's disease involves systematic exclusion of known causes of retinal vasculitis.[1] Although baseline investigations are important in all cases, individually tailored diagnostic testing based on patient symptoms and signs is recommended. Furthermore, in cases of diagnostic doubt, infection may be considered more likely if, after an initial improvement with therapy, the patient's disease rapidly becomes refractory to treatment.[2]

Our case did in fact undergo an extensive systemic work-up, which was not emphasised in the study. We also referred our patient to the physicians given the unusual nature of his presenting symptoms. A complete physical examination as well as medical, contact, and travel history did not reveal any abnormalities or risk factors. In addition to routine blood and urine testing, other investigations performed included fasting glucose and lipid profile, thyroid function tests, renal and liver function tests, serum homocysteine levels, coagulation screen, vitamin B12 and folate levels, serum ACE, CRP, ESR, full autoantibody screen, serum protein electrophoresis, and 72-h Mantoux testing. Radiological investigations performed comprised a chest X-ray, abdominal ultrasound, and carotid Doppler. All investigations completed did not reveal any systemic abnormality. We agree that prompt referral to the physicians and a full contact and travel history are important in ruling out other causes of retinal vasculitis, especially in cases with systemic features (eg, fever, weight loss, and altered bowel habit). In our case, the clinical effect of adjunctive treatment with pegaptanib was evidenced by the rapid regression of disc and retinal neovascularisation with no recurrence of vitreous haemorrhage for up to 9 months.

References

1 Biswas J, Gopal L, Madhavan HN, Sharma T, Sulochana KN, Ramakrishnan S. Eales disease—an update. *Surv Ophthalmol* 2002; **47**: 197–214.
2 Stanford MR, Verity DH. Diagnostic and therapeutic approach to patients with retinal vasculitis. *Int Ophthalmol Clin* 2000; **40**: 69–83.

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Sir,

Subthreshold diode micropulse panretinal photocoagulation for proliferative diabetic retinopathy

We read with interest the article 'Subthreshold diode micropulse panretinal photocoagulation for proliferative diabetic retinopathy' by Luttrull *et al*.[1]We would like to congratulate the authors for their work and cite a clarification.

The authors mention that the treatment parameters were designed to avoid the creation of clinically detectable photocoagulation lesions and that the effectiveness of subthreshold diode pan retinal photocoagulation (PRP) at this low irradiance level along with its efficacy in diabetic macular oedema is an evidence in favour of subthreshold laser in clinical practice. However, the mechanism of action of laser photocoagulation is thought to be different in these two conditions. The decrease in macular oedema is supposed to be mediated through the retinal pigment epithelium[2] for which even subthreshold energies may be sufficient. However, in proliferative diabetic retinopathy, destruction of the ischaemic retina thereby decreasing the angiogenic stimulus and improved oxygenation of the remaining retina are among the major hypotheses of the mechanism of action.[3] Keeping in mind these factors, the likely mechanism of action of subthreshold PRP stated by the authors needs clarification.

Also, is it justified to treat all the patients with the same energy levels and to titrate it with the pain threshold that has a wide variation independent of the energy required for producing a visible lesion? Titrating the energy for a visible spot and then reducing the power or the time of the laser beam will be a better method for doing subthreshold PRP, as it will provide the required subthreshold energy for a given patient and amount of retinal oedema.

References

1 Luttrull JK, Musch DC, Spink CA. Subthreshold diode micropulse panretinal photocoagulation for proliferative diabetic retinopathy. *Eye* 2008; **22**(5): 607–612.
2 Akduman L, Olk RJ. Laser photocoagulation of diabetic macular edema. *Ophthalmic Surg Lasers* 1997; **28**: 387–408.
3 Olk RJ, Lee CM. *Diabetic Retinopathy: Practical Management*. J.B. Lippincot company: Philadelphia, 1993: 93.

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This article has not been presented earlier

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Sir,

Reply to Dr Kumar *et al*

We thank Dr Kumar and his associates for their interest in our recent study entitled 'Subthreshold diode micropulse panretinal photocoagulation for proliferative diabetic retinopathy' and for the major concerns they have regarding the study.

Low intensity/high density subthreshold diode micropulse panretinal photocoagulation (SDM PRP) is a laser procedure that allows the management of patients with proliferative and preproliferative diabetic retinopathy without harming the retina or visual function. The desired clinical effect is obtained with low intensity laser applications that do not produce a visible intraoperative burn end point or thermal lesions detectable at any time postoperatively either by clinical examination, fundus photography, fluorescein angiography, or time-domain optical coherence tomography (OCT) as reported by Luttrull *et al*[1–3]; or by fundus autofluorescence photography, indocyanine green angiography, or fourier-domain OCT (JKL, unpublished data).[1–3] In the absence of iatrogenic thermal retinal damage, no complications, side effects, or inflammatory reaction of any kind are observed.

Dr Kumar points out that thermal retinal ablation to decrease angiogenic stimuli and improve retinal oxygenation is a widely accepted hypothesis proposed to explain the action of conventional photocoagulation.[4] However, we remember that thermal retinal destruction has never been shown to be therapeutically necessary. Our results, documenting effective treatment in the complete absence of laser-induced retinal damage counter the claim that tissue ablation is necessary for effective treatment.[1–3] Thus, by exclusion, we believe that high density/low intensity SDM for both diabetic macular oedema and proliferative retinopathy operates by the same mechanism, that is, by inducing the exposed and affected, but unharmed, RPE cell to alter its expression of key cytokines in a way which is clinically advantageous.[1,3,5]

We do not use the titration approach enquired by Dr Kumar as reports from studies employing such titration approaches document a high incidence of retinal burns, which may not appear clinically until sometime after treatment.[6–8] Alteration of SDM parameters based on retinal thickness is unnecessary due to the excellent retinal penetration and minimal scatter of the 810 nm wavelength.[9] However, the primary author's 9 years of clinical experience using SDM as the exclusive laser modality for treatment of retinal vascular disease has taught him that certain alterations in treatment parameters based on fundus pigmentation are necessary to minimize the risk of inadvertent burns, as reported by Luttrull *et al*.[1–3] We agree with Dr Kumar that pain thresholds are subjective and widely variable. However, the pain threshold with SDM PRP is much lower than the visible burn threshold, in contradistinction to conventional PRP. Thus, we find that patients' pain sensation can provide helpful feedback in the absence of a visible treatment end point. We believe that the wide therapeutic window of SDM permits us this welcome accommodation to patient comfort.[1,3]

To date, all reports of various approaches to SDM for treatment of retinal vascular disease describe clinical effectiveness comparable to conventional photocoagulation with less retinal injury. We have reported effective SDM without any retinal injury at all. These are substantive reasons to pursue further study. We thank Dr Kumar and his associates for their pertinent questions and the Editor for this opportunity to respond.

References

1 Luttrull JK, Musch DC, Mainster MA. Subthreshold diode micropulse photocoagulation for the treatment of clinically significant diabetic macular edema. *Br J Ophthalmol* 2005; **89**: 74–80.
2 Luttrull JK, Spink CJ. Serial optical coherence tomography of subthreshold diode micropulse photocoagulation for diabetic macular edema. *Ophthalmic Surg Lasers Imaging* 2006; **37**: 370–377.
3 Luttrull JK, Musch DC, Spink CJ. Subthreshold diode micropulse pan retinal photocoagulation for proliferative diabetic retinopathy. *Eye* 2008; **22**: 607–612.
4 Olk RJ, Lee CM. *Diabetic Retinopathy: Practical Management*. J.B.Lippincot company: Philadelphia, 1993 93.
5 Flaxel C, Bradle J, Acott T, Samples JR. Retinal pigment epithelium produces matrix metalloproteinases after laser treatment. *Retina* 2007; **27**: 629–634.
6 Laursen ML, Moeller F, Sander B, Sjoelie AK. Subthreshold micropulse diode laser treatment in diabetic macular oedema. *Br J Ophthalmol* 2004; **88**: 1173–1179.
7 Bhagat N, Zarbin MA. Diode subthreshold micropulse laser for diabetic macular edema. *Retinal Physician* 2006; **3**: 53–56.
8 Sivaprasad S, Chong V, Cunha-Vaz JG, Faria de Ahreu, Rosa A, Nunes S *et al*. Prospective randomized controlled trial comparing subthreshold micropulse diode laser photocoagulation and conventional green laser for clinically significant diabetic macular edema. *Br J Ophthalmol* 2008; **92**, [e-pub ahead of print].
9 Moorman CM, Hamilton AMP. Clinical applications of the MicroPulse diode laser. *Eye* 1999; **13**: 145–150.

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