INDIRECT DIODE LASER TREATMENT FOR STAGE 3 RETINOPATHY OF PREMATURITY

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SUMMARY

Eight infants with stage 3+ retinopathy of prematurity (ROP) were treated using the diode laser through a binocular indirect ophthalmoscope. Two infants with zone I disease were treated prethreshold as soon as the signs of plus disease developed. Successful regression was achieved in all cases, though 3 infants required repeat treatment. All infants were followed up for a minimum of 3 months. Keeler acuity scores were in the normal range in 4 of the 8 infants.

Enhanced survival of very-low-birthweight infants with the introduction of new treatments in neonatal care has increased the incidence of blindness due to retinopathy of prematurity (ROP).[1,2]

Xenon arc photocoagulation for severe ROP was first used in 1968 by Nagata.[3] Subsequent work with the argon laser confirmed the efficacy of photocoagulation in the management of ROP.[4,5] Practical limitations of the argon laser delivery system in the treatment of neonates restricted its use and led to the common acceptance of cryotherapy. The American Multicenter Trial for Retinopathy of Prematurity (CryoROP)[6] confirmed previous clinical impressions by demonstrating a significant reduction in unfavourable outcome in the treatment of stage 3 threshold disease using this method. The advent of a delivery system on the indirect ophthalmoscope, and lightweight portable machines, has made laser treatment a practical alternative to cryotherapy, leading to a re-evaluation of this technique. Argon laser[7,8] and diode laser[9] have both been reported as being successful in treating stage 3 threshold disease. In this study the use of the diode laser was evaluated in 8 infants and the 3 month visual outcome described.

PATIENTS AND METHODS

Fifteen eyes of 8 infants were treated with a diode laser indirect ophthalmoscope between February 1992 and December 1992. Three infants were treated with the Nidek Laser Diode Photocoagulator DC-3000 (Cardiac Services, Dundee); for the remainder a prototype diode laser (Keeler UK, Windsor) was used. Both instruments were loaned from their respective manufacturers as needed. ROP findings were recorded according to the international classification.[10] All but 2 of the infants were treated at or beyond threshold disease. Threshold disease is defined as 5 or more contiguous (or 8 cumulative) clock-hours of stage 3 in zone I or zone II in the presence of plus disease. Two infants with zone I disease were treated prethreshold as soon as plus disease developed.

All infants of less than 32 weeks gestation and/or with a birthweight of less than or equal to 1500 g were screened for ROP as previously described.[11] Six of the infants were nursed in the Regional Neonatal Intensive Care Unit (NICU); 1 was referred for screening and treatment and 1 was referred for treatment from a peripheral unit having been screened by the local ophthalmologist.

Treatment was carried out as soon as was practically possible: within 48 hours in 5 cases and 72 hours in 3 cases. Infants were treated in a converted isolation room off the NICU. The pupils were dilated with 0.5% cyclopentolate and 2.5% phenylephrine drops prior to treatment. The infants were treated under a general anaesthetic administered by the neonatologist. They were paralysed with pancuronium, ventilated on an air/oxygen mixture and fentanyl 15μg/kg was used for analgesia.

Contiguous laser burns were placed just anterior to the ridge and in a scatter fashion throughout the rest of the avascular retina. A scleral depressor (Osbourne and Simmons, UK) designed by D.I.C. was used to facilitate treatment of the peripheral retina. Treatment was carried out using a diode laser with a wavelength of 800 nm (Nidek) or 810 nm (Keeler). A 28 dioptre lens was used, producing a spot size of about 600 μm diameter. Power sufficient to produce a dull grey/white reaction ranged from 390 to 1100 mW with a pulse duration of 0.1–0.2 seconds.

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Post-operatively the infants were kept ventilated until breathing spontaneously. Chloramphenicol ointment q.d.s. and homatropine 1% eye drops b.d. were administered post-operatively for 3 days. All infants were reviewed 10 days after treatment. If the disease showed signs of regressing the infants were then reviewed fortnightly for up to four visits.

Persistent plus disease was retreated within 48 hours. Retreatment was necessary in 3 infants, 2 because of failure to show signs of regression. These two infants had fill-in laser to the previously applied scatter treatment. The third case had initially shown complete regression but 32 days following treatment neovascular fronds were noted projecting into the vitreous at the vascular/avascular junction (Fig. 1). Cryotherapy was applied contiguously to the avascular retina as the laser was not available.

All infants were reviewed at 3 months from term for assessment of vision, orthoptic status, refraction and fundal examination. Grating acuity scores were recorded using Keeler acuity cards. The acuities were measured with both eyes open as the infants generally objected to occlusion of either eye. The infant in whom only one eye was treated was able to overcome a 10 baseout prism and we have assumed, with fusion present, that the uniocular visions would be equal. Refractions were carried out using 1% cyclopentolate.

RESULTS

In this study 8 infants were treated with diode laser. Asymmetrical disease occurred in 1 baby and symmetrical disease in the rest, resulting in 15 eyes being treated. The disease regressed completely in all 15 eyes, though 6 eyes required repeat treatment. The gestational ages ranged from 23 to 26 weeks and the birthweights from 576 to 1160 g (Table I). The median post-menstrual age at treatment was 36.3 weeks (range 34–43 weeks) and the median age at treatment 78 days (range 69–118 days). All the infants demonstrated plus disease and an average of 8 clock-hours of stage 3 was present. However, 2 patients (cases 4 and 8) had prethreshold zone I disease and were treated as soon as plus disease was noted. In 5 eyes the disease was located in anterior/mid zone II; in 6 eyes in posterior zone II (in these cases the disease dipped into zone I temporally); and 4 eyes had zone I disease. The average number of laser applications required was 845 (range 327–1441).

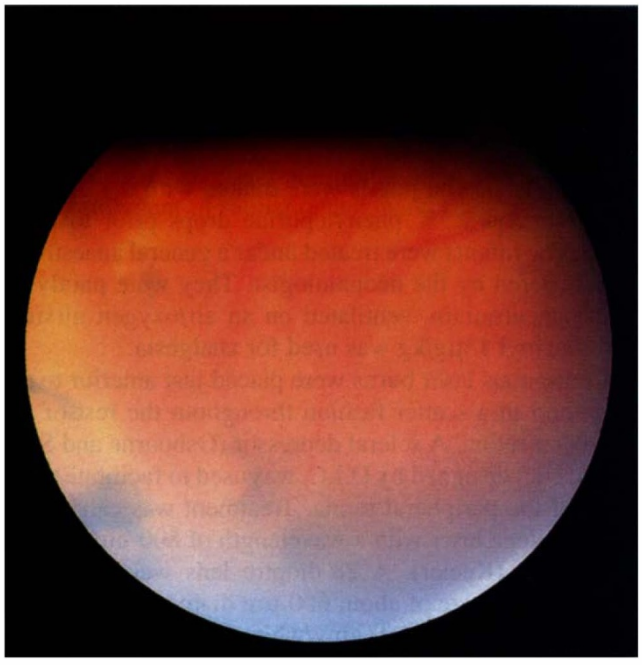

Fig. 1. *Case 3. There is recurrence of extraretinal fibrovascular proliferation in the presence of old laser scars*

The treatment was successful in all cases. In 2 patients (cases 6 and 7) retreatment was deemed necessary as there was no resolution of plus disease. In case 3 regression was thought to have occurred but 32 days following treatment neovascular fronds were visible extending into the vitreous (Fig. 1). The infant was successfully treated with cryotherapy, though one eye has developed macular ectopia.

Treatment complications were limited to variability of the burn intensity resulting in a rupture of Bruch's membrane associated with a faintly audible 'pop' in 2 patients. No systemic complications occurred during the procedure and the subsequent post-operative course was uneventful.

The grating acuity in 4 infants was at or above the lower limit of normal (Fig. 2). However, in the remaining 4 patients the acuities were below normal. Two infants (cases 2 and 4) had acuities of 0.18 and 0.65 cycles/degree respectively; both had had grade 4 intraventricular haemorrhages (IVH). The other 2 infants (cases 5 and 8) would not respond during the vision testing procedure though some level of vision was present; they had had grade 4 IVH and had required ventriculo-peritoneal shunts. The refractive errors ranged from +4.00 to −4.00 dioptres spherical equivalent (SE).

DISCUSSION

The Multicenter CryoROP Trial has shown the effectiveness of treating threshold ROP using cryotherapy.[6] The advent of portable lasers delivered through a binocular indirect ophthalmoscope facilitates treatment of this condition, using a modality that is currently used for other ischaemic retinal vascular conditions such as diabetes and vein occlusions. McNamara *et al.*,[8] in a prospective randomised trial of cryotherapy versus argon laser, demonstrated that laser treatment was as effective as cryotherapy. More recently Hunter *et al.*[9] in another randomised trial comparing diode laser with cryotherapy also found laser to be effective, though the numbers were too small for statistical analysis. In our study we have shown that diode laser was successful in causing regression of stage 3 threshold disease and prethreshold zone I disease.

Laser photocoagulation has a number of advantages over cryotherapy. In our own experience of treating infants using either method, laser is tolerated far better with no bradycardias or arrhythmias during the procedure. The treatment of posterior disease is far easier, avoiding the necessity of a conjunctival incision. Scleral indentation is

Table I. Characteristics of patients treated with diode laser

Patient no. and sex	Gestational age (weeks)	Birthweight (g)	PMA[a] at treatment	Eye	Clock-hours of stage 3	No. of laser burns	Zone
1 M	26	916	43	L	7	327	Ant. zone II
2 F	26	920	36	R	12	700	Post. zone II
				L	12	630	
3 F	23	662	34	R	10	786	Post. zone II
				L	10	659	
4 M	23	622	35	R	3	1263	Zone I
				L	3	1078	
5 M	26	1160	37	R	7	1241	Ant. zone II
				L	5	713	
6 F	23	576	38	R	8	749	Post. zone II
				L	7	540	
7 M	25	732	36	R	8	722	Mid zone II
				L	7	749	
8 M	24	672	34	R		1078	Zone I
				L		1441	

R, right; L, left; Ant., anterior; Post., posterior.
[a] Post-menstrual age at treatment (weeks).

minimal and used mainly to position the globe, and lid and conjunctival oedema is slight compared with cryo-treated infants.

Severe complications have been reported during cryotherapy.[6] Brown *et al.*[12] reported 3 cases of respiratory arrest and 1 of cardio-pulmonary arrest when cryotherapy was carried out under local anaesthesia. Laser treatment is less stressful and relatively pain-free so would be more suitable than cryotherapy for local anaesthesia, though the preference of our paediatricians is to use a general anaesthetic.

The resultant large scars produced by cryotherapy may lead to adverse consequences later in life. Greven and Tasman[13] reported retinal detachments occurring 3 years after cryotherapy with the tear located at the junction of treated/untreated retina. They postulate the tear was due to the continued growth of the posterior segment in an eye with severe chorioretinal adhesions. It is not yet known whether such complications will occur in laser-treated eyes but the diode laser burns have been shown to be less destructive than cryotherapy.[14]

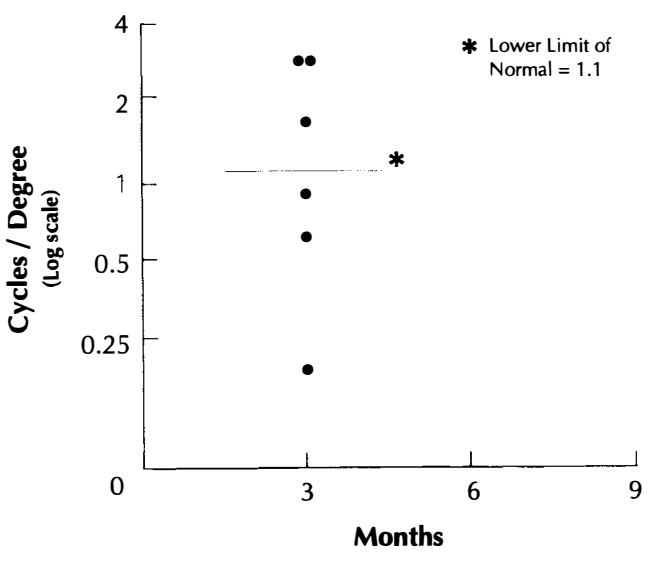

Fig. 2. *Keeler acuity at 3 months in diode-laser-treated infants.*

Iris clipping has been described as a complication of some types of diode laser but did not occur in our series.[15] Persistence of the tunica vasculosa lentis is often found in severe posterior ROP and absorption of argon laser by haemoglobin may lead to a lens burn. The longer wavelength of the diode makes this unlikely. No lens burns occurred in our babies. The only complication encountered during laser treatment was rupture of Bruch's membrane in 2 cases. The diode laser requires a consistent working distance to maintain identical burn intensities.[15] We recommend the laser energy is reduced as the treatment becomes more peripheral to reduce the risk of excessively heavy burns resulting in rupture of Bruch's membrane.

Two infants with zone I disease were treated prethreshold. The results of the CryoROP trial demonstrated a 75% unfavourable outcome if the disease was located in zone I.[6] Zone I disease does not progress in the sequential step-by-step manner of ROP occurring more peripherally; rather it is characterised by the development of arteriovenous anastomoses at the distal ends of the vessels[16] that subsequently join, leading to a 360° shunt from which fibrovascular proliferation develops.[17] This rapidly progresses to a retinal detachment. It is the opinion of Tasman[18] and Sternberg *et al.*[19] that waiting until threshold disease develops in zone I before intervening leads to an unacceptably high failure rate. Fleming *et al.*[20] have shown that the earlier treatment of 4 infants with posteriorly located disease resulted in complete regression of the disease. We agree that treatment for zone I disease should be given as soon as plus disease develops. Cases 4 and 8 had zone I prethreshold disease at treatment and had a successful outcome.

The visual results of treating stage 3 threshold ROP depend not only on regression of the retinopathy with normal posterior retinal anatomy but also on the neurological status of the infant. In 4 of our cases severe neurological abnormalities were present and in each case the visual responses were reduced. This is in accordance with the results of Luna *et al.*[21] who reported a delay in visual

development in patients with a history of grade 3 or 4 IVH. However, in our other 4 cases with no neurological sequelae the visual acuities were normal. Longitudinal data reported by Birch and Spencer[22] have suggested that the early grating acuity is predictive of the long-term visual outcome. The CryoROP 3½ Year Outcome has shown no significant change in the percentage of eyes with a favourable structural outcome at 1 year and 3½ years, but the functional results were different.[23] At 1 year the grating acuity showed a 37.8% reduction in unfavourable outcome but at 3½ years this had fallen to 20.1%. This is because at 1 year lower acuity values are still in the normal range. It is thus too early to predict what the final visual results will be from diode laser treatment.

In conclusion, although the numbers in the study are small, we have demonstrated that diode laser treatment for stage 3 ROP is successful in causing regression of the disease. The procedure is well tolerated, easy to administer and laser is now our preferred method of treatment.

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Key words: Grating acuity. Indirect diode laser. Retinopathy of prematurity.

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