Diode laser for retinopathy of prematurity – early outcome

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Abstract

Diode laser treatment for retinopathy of prematurity was successful in 81% of 21 eyes with 'threshold' (zone 2, stage 3+) disease. This compares favourably with cryotherapy and argon laser photocoagulation. The retinal outcome and technique are discussed.

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Retinopathy of prematurity (ROP) is one of the leading causes of blindness among children in the developed world.[1,2] It is the commonest cause of blindness arising in the perinatal period and leads to 11% of childhood blindness in the Republic of Ireland.[3]

The multicentre North American cryotherapy study (Cryo-ROP) demonstrated a significant decrease in the incidence of blinding disease by treatment of 'threshold' disease.[4–6]

Photocoagulation for ROP has been described in the past.[7–12] Recent studies suggest that argon laser[13] and diode laser[14] photocoagulation, with indirect ophthalmoscope delivery systems, is at least as effective as cryotherapy in preventing adverse outcome in 'threshold' ROP. Laser photocoagulation of the retina without the use of a contact lens and slit-lamp has long been possible. With advances in indirect ophthalmoscope delivery systems and the advent of the highly portable diode laser, it is now possible to deliver this treatment in the neonatal intensive care unit.

The outcome and clinical course of 12 consecutive premature infants (21 eyes) treated with diode laser retinal photocoagulation for threshold ROP or more severe disease is described.

Method

Twelve consecutive premature infants (eight male and four female) with 'threshold' (stage 3+ disease over 5 or more contiguous clock house (30° sectors) or 8 cumulative clock hours) or more severe ROP in 23 eyes diagnosed during routine ROP screening in three neonatal units were included in this study. Twenty one eyes received diode laser retinal photocoagulation between February 1992 and November 1992 using an Iris OcuLight SL diode laser system. This produces a laser emission at 810 nm.

All infants born at less than 30 weeks' gestation and/or 1500 grams birth weight are screened at 6 weeks postnatal age. For those without ROP, routine follow up examinations are carried out on a monthly basis until vascularisation of the temporal periphery is complete. More frequent examinations are carried out on those who develop stage 2 or subthreshold stage 3 disease (the frequency depending on the severity of the disease). Examinations are carried out through dilated pupils with the use of a speculum and indentation. Treatment was undertaken within 36 hours of the observation of threshold disease in all cases described.

The treatment was delivered in a darkened room in the neonatal unit at the cotside with the infants' monitors undisturbed and oxygen delivered as required in each case. A nurse assisted the operator by holding the patient's head. Sedation was required for larger, healthier neonates, using chloral hydrate under the supervision of a neonatologist. Topical anaesthesia was required for those cases requiring indentation and the pupils were fully dilated in all cases with cyclopentolate 0·5% and phenylephrine 2·5% applied at 1 hour and 30 minutes before treatment. There was only one exception to this protocol in that one infant required general anaesthesia (case 8, Table 1) because she was too mobile for safe application of laser therapy while awake.

Burns were placed, with only two exceptions, on the avascular retina anterior to the mesenchymal shunt, avoiding the ridge, up to the ora serrata, a half burn diameter apart. The therapeutic end point was a grey 'blanching' of the burn site. Subsequent therapy consisted of a 'fill in' pattern of burns in the gaps between those applied on previous occasions. In the two exceptions to this protocol burns were applied behind the ridge. In case 5 (left eye), this was required to arrest rapidly progressive disease that had failed to respond to two previous laser treatment sessions to the avascular retina. In case 8, stage 5 disease, present at the first examination, prevented treatment in the left eye and laser in the

Table 1 Severity of ROP, mean laser power, burn duration, total number of burns, and retinal outcome (all treated eyes had 'plus' disease in zone 2)

No	Stage	Extent clock hours	Laser power (mW)	Duration (ms)	No of burns	Retinal outcome
1	3	5 Contig	300	200	85	Flat
	3	5 Contig	300	200	273	Flat
2	3	12	475	500	684	Flat
	3	12	475	500	805	Flat
3	3	5 Contig	300	500	173	Flat
4	3	5 Contig	300	200	320	Flat
	3	12	300	200	785	Flat
5	4	12	300	200	683	Stage 5
	4	12	550	200	1204	Flat
6	3	8 Contig	300	200	761	Flat
	3	8 Contig	300	200	646	Stage 4A
7	3	6 Contig	300	200	211	Flat
	3	6 Contig	300	200	127	Flat
8	4A	7 Contig	650	350	1000	Stage 4B
9	3	8 Cumul	350	200	900	Flat
	3	12	450	200	900	Stage 4B
10	3	6 Contig	350	200	687	Flat
	3	8 Cumul	300	200	478	Flat
11	3	12	350	250	518	Stage 5
12	3	5 Contig	300	200	237	Flat
	3	5 Contig	300	200	100	Flat

Contig=contiguous, cumul=cumulative.

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temporal periphery was prevented by tractional detachment in the right with stage 4A disease. The only option in this latter eye was to treat the attached retina to try to limit extension of the traction and ablate ischaemic retina wherever possible.

Follow up examination was carried out by 1 week after laser treatment and later frequency of examination depended on the response to treatment. Where further laser treatment was deemed necessary it was applied within the first 2 weeks.

Results

Twenty one eyes were treated with diode laser retinal photocoagulation in 12 infants. Table 1 contains a summary of the severity of the disease at the time of treatment in these eyes, the laser parameters used, and the final retinal outcome. One fellow eye did not reach threshold disease level (case 3), one was too far advanced for laser therapy (stage 5) at the time of first examination (case 8), and a third was treated with cryotherapy and eventual encirclement because a rigid pupil prevented adequate viewing of the posterior segment for the application of laser therapy (case 11).

In seven children ROP was present at the first screening examination. In the other five children in whom the ROP was not present at first sighting the mean postconceptual age of onset was 34·6 weeks (range 34–36). In 10 cases the progression to threshold disease was observed after the first examination during routine follow up and the mean postconceptual age of the development of threshold disease was 35·7 weeks (range 33–40). In two cases (8 and 9) it was at threshold level at the first examination.

Seventeen eyes (81%) of the 21 treated had favourable outcomes as defined by the Cryo-ROP group – that is, a flat posterior pole after regression of active ROP. Case 6 had stage 4A disease (extramacular tractional detachment) with only a very limited area in the extreme periphery remaining detached. In the four with unfavourable outcome, two developed stage 5 disease (one eye in case 5 and the only laser treated eye in case 11) and two stage 4B (cases 8 and 9). Case 5 developed very aggressive ROP with progression to stage 4 in zone 2 bilaterally over a period of less than 1 week from diagnosis of the onset of ROP but was successfully treated in one eye with the greatest number of burns used in any one eye in this series. Case 8 had suprathreshold disease in both eyes at first sighting. The left was untreatable, having already developed stage 5. The right had stage 4A and, despite laser behind the ridge to attached retina as well as avascular retina and early apparent arrest of the disease, progressed eventually to stage 4B. Case 9, who also developed stage 4B, had advanced stage 3 in that eye at the first examination and progressed despite extensive laser therapy. Rigid pupils prevented laser therapy altogether in the right eye in case 11, as described above, and also made application in the left eye difficult, with eventual progression to stage 5.

Ten eyes received one treatment only; seven eyes, two; and four eyes, three. The mean total number of burns required was 551 (range 850–1204) applied in all but two cases outside the ridge in the vicinity of the threshold ROP. Mean burn duration was 252 ms (range 200 ms to 500 ms), and the mean power used was 359 mW (range 300 mW to 1000 mW). (See Table 1 for details of laser treatment parameters in individual cases.)

Regression was noted, on average, 5 days after application of adequate laser therapy (range 2–14).

The mean follow up in these cases is 13·5 weeks (range 1 week to 32 weeks) from the time of treatment.

Discussion

Cryotherapy has been shown to be effective in treating threshold ROP.[4-6] The rationale behind this method of treatment is the ablation of presumed ischaemic retina, thus reducing the metabolic demand on the immature vasculature and removing the putative stimulus to fibrovascular proliferation. If this hypothesis is correct, it would appear that any treatment that has the same effect on the peripheral retina should be equally successful. The portable diode laser is ideal for use in the neonatal unit. The retinal lesion produced by the diode laser is deeper than that produced by the argon laser.[15,16] A report of a small randomised series comparing diode laser with cryotherapy for ROP showed encouraging results,[17] and the results of a larger, prospective, randomised trial suggest that diode laser photocoagulation is as effective as cryotherapy with a laser failure rate of 12%.[14] The failure rate (19%) of diode laser photocoagulation in our series compares favourably with the Cryo-ROP study (1 year outcome) figure of 25·7%.[6] However, the small number of eyes treated with diode laser in these studies means final conclusions cannot be reached.

With regard to the four laser treated eyes with an unfavourable outcome (detachment of the macula or worse) in this series one case (case 5, Table 1) had rapidly progressive disease bilaterally and it proved possible to apply enough laser to arrest the condition in only the left eye, the retina of the right eye detaching before this could be achieved. In fact the left eye in this case received more laser treatment than any one eye in the series (1204 burns). Case 8 had suprathreshold disease bilaterally at first sighting, untreatable stage 5 in the left, and stage 4A in the right. Progression in this latter eye was briefly halted by laser to avascular retina and to attached retina behind the peripheral detachment at the temporal edge of the macula, only to progress later to stage 4B. In case 9 severe stage 3 disease about 360° was present at first assessment in the left eye and this eye progressed to stage 4B. Rigid pupils in case 11 precluded laser treatment in the right eye which was unsuccessfully treated with cryotherapy and eventual encirclement. The same problem was present on the left to a lesser extent and progression to stage 5 took place bilaterally. This latter case demonstrates one disadvantage of laser therapy for ROP, in that a clear, wide view is essential for adequate treat-

ment. The alternative to laser therapy in cases where adequate mydriasis cannot be achieved is, of course, cryotherapy. However, recent experience in this unit, with this type of case, suggests that even if the view at the first treatment session is poor, if a partial treatment can be administered at that time, subsequent pupil dilatation improves in some cases.

The technique of application of diode laser to infantile eyes in the awake patient differs little from that of application of argon laser via the indirect ophthalmoscope in the adult. With an experienced assistant adequate stability of the patient's head can be ensured and indentation under topical anaesthesia can provide a stable eye. Regression of the disease within the first few days after successful treatment (compared with 10 days or more after cryotherapy) and the ease of repeat treatment means that the therapy can be more closely tailored to the individual case. In fact, it has been our observation that treatment to the avascular retina in the vicinity of the threshold disease alone (and not to the whole peripheral retina as mentioned by McNamara *et al*[13 14]) is successful. Other studies have described this technique.[18–21]

The clinical findings in three cases in this series raise the question, long discussed, of the optimum siting of treatment on the retina.[9 18 22 23] These observations include the short lived success with unconventional treatment of stage 4 disease mentioned above in case 8 (where laser was applied behind the mesenchymal shunt), the more lasting success with the same technique in the left eye in case 5, and the lack of success with more conventional treatment of the same level of disease in the fellow eye in case 5 where the treatment was applied only anterior to the ridge. Should the ridge be treated, or even the anterior shunt bearing vascularised retina, on a routine basis? It has been our experience that where laser treatment was inadvertently applied directly to the ridge it caused vitreous and retinal haemorrhage from the abnormal, friable new vessels.

Some cases reported here raise further questions about the techniques currently in use for treatment of ROP. Perhaps a quarter of the cases of threshold disease go on to an unfavourable outcome according to the Cryo-ROP study,[6] and two eyes in this series had unfavourable outcomes from stage 3 disease at the time of first treatment (case 9 left eye and case 11 right eye). The criteria for threshold disease were established on the basis of clinical experience in the main and were not the subject of a controlled study. Recent reports are encouraging regarding the treatment of early disease in some circumstances.[24 25] It will also be important to assess critically the visual function of those children with macular traction long term, since clinical experience would suggest that a proportion of these children have useful visual function that distinguishes them from those more severely affected and raises a question over the appropriateness of their inclusion in the formally defined 'unfavourable outcome' category.[4] These categories were defined on the basis of structural outcome (that is, 'unfavourable' designates macular retinal detachment or worse) irrespective of function. It is now appropriate that categorisation of outcome should include functional criteria in the light of a recent paper on this topic.[6]

Individual outcome in this series raises a number of questions regarding the screening of at risk neonates. It is the policy of this unit to screen all neonates born at 30 weeks' gestation or less and/or a birth weight of 1500 grams or less. The first examination takes place at 6 weeks' postnatal age. The British College of Ophthalmologists and the British College of Perinatal Medicine recommended screening of all neonates under 32 weeks' gestation and/or 1500 grams in 1990. They recommended that the first examination should take place 7 weeks postnatally. However, Fielder *et al* have shown that the onset of ROP is related to postconceptual age (occurring between 32·5 and 38·5 weeks)[26] as is the development of threshold disease (at 34 to 42 weeks).[27] Case 8 was first seen at 35 weeks of postconceptual age (having been born at 29 weeks) as dictated by the unit screening protocol. This child already had severe ROP at this first review with stage 4A in one eye and stage 5 in the other. She had had minimal oxygen and had been relatively well during her first 6 weeks of life. Similarly, case 9 had bilateral threshold disease at the first review at 6 weeks of postnatal age resulting in an unfavourable outcome in the more seriously affected eye. In those cases where commencement of the disease was observed the mean age of onset was 34·6 weeks' postconceptual age with a narrow range, and probably more importantly the average age of onset of threshold disease was 35·7 weeks (range 33–40 weeks). This has led us to change the unit screening policy to include a first screen at 33 weeks of postconceptual age in those cases born before that stage of gestation even if this falls before 6 weeks of postnatal age.

Laser therapy does not require general anaesthesia. The Cryo-ROP group report the use of a general anaesthetic in 27% of cases. Complications such as bradycardia and apnoea occur in those cases treated under local anaesthesia.[28] The practice in this unit is to use general anaesthesia in all cases treated with cryotherapy since we have concluded that this gives better pain relief, allows for better control of these complications, and makes the application of cryotherapy easier.[29] Further advantages of laser therapy may be summarised as the rapid response to adequate treatment, or conversely, rapid diagnosis of inadequate treatment, the ease of repeat treatment, application in the neonatal unit (with the diode laser) facilitating rapid treatment after diagnosis of threshold disease, avoidance of lesions to the eye wall and external eye that are part of transconjunctival cryotherapy, and cryotherapy applied direct to the sclera and probable minimisation of inflammation and vitreous traction.

The disadvantages are confined to inadvertent burns to structures other than avascular retina including the fovea, the difficulty of use with hazy media and small pupils, and the lack of long term experience with this modality. Furthermore, the authors have seen apnoea occur, on rare occasions, following diode laser photocoagulation, and there is also the comparative

painfulness of diode laser treatment compared with argon or krypton.[15] The extra capital and maintenance costs of a diode laser system are not inconsiderable.

This series confirms that diode laser photocoagulation is an effective treatment for threshold ROP and further controlled trials are needed to refine it.

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Diode laser for retinopathy of prematurity--early outcome.

M Goggin and M O'Keefe

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Notes