“Cyclodiode”: results of a standard protocol

Anne Fiona Spencer, Stephen A Vernon

Abstract

Aims—To analyse the results of intraocular pressure (IOP) reduction in refractory glaucoma following diode laser cyclophotocoagulation with a repeatable standard protocol.

Methods—58 eyes of 53 patients were followed for 6–37 months (mean 19 months) after initial cyclodiode treatment.

Results—Mean (SD) pretreatment IOP for the 58 eyes was 33.0 mm Hg (10.7) reducing at final index visit to 16.7 mm Hg (7.8) (p<0.0001). The mean antiglaucoma medication score per eye was significantly reduced from 2.4 (0.8) to 1.4 (1.0) at last index visit (p<0.0001) with 91% of patients able to stop oral acetazolamide. 45% of eyes required more than one treatment and the overall mean per eye was 1.6 (range 1–5). Of eyes with visual acuity 6/60 or better pretreatment, 12 (32%) lost more than two lines of Snellen acuity and two eyes with poorer acuity initially dropped to NPL. Poor visual outcome was associated with the presence of diabetic retinopathy. Hypotony (IOP <5 mm Hg) was noted in two eyes at the last index visit although neither had specific signs of the same. No phthisis was seen.

Conclusion—The simple treatment protocol, repeated if necessary, appears relatively safe and effective at lowering IOP in eyes with refractory glaucoma.

(Cr J Ophthalmol 1999;83:311–316)

Ciliary body ablation has been used effectively in the treatment of refractory glaucoma for many years. A number of methods have been described including cyclocryotherapy and laser photocoagulation using energy of different wavelengths.1–6 Until recently, most experience was obtained with the neodymium:YAG (Nd:YAG) laser utilising wavelengths.1–6 Until recently, most experience has been with the 1064 nm Nd:YAG laser.4–7–10

The advent of the 810 nm semiconductor diode laser appears to offer a better method of cycloablation with potentially fewer complications as there is better absorption of this wavelength by the pigmented tissues of the ciliary body than the 1064 nm Nd:YAG laser.11–12 Initial reports suggest a lower incidence of the complications seen with other cyclodestructive techniques—namely, phthisis, hypotony, uveitis, pain, and loss of visual acuity.13–15 These advantages, combined with the compact and portable nature of the diode, make it an attractive treatment modality. To date, published studies have either not used a standard protocol throughout or have not addressed the results of repeated treatments should the first treatment fail to lower intraocular pressure (IOP) effectively.15–17 We therefore report the results of the diode laser for cyclophotocoagulation (“cyclodiode”) for all eyes treated in our unit using a standard protocol.

Methods

All eyes treated between April 1994 and May 1997 (and therefore with a minimum follow up of 6 months) were entered into the study. Cyclophotocoagulation (“cyclodiode”) was performed using the Oculight Sx semiconductor diode 810 nm laser (Iris Medical Instruments) and the contact G-probe (Iris Medical Instruments).

Patients received cyclodiode treatment because either (a) they had medically uncontrollable glaucoma and had had previous failed filtering surgery and/or were unlikely to respond to or declined filtering surgery, or (b) we were attempting to discontinue medications to which they were intolerant, usually systemic carbonic anhydrase inhibitors (all but one of the patients were taking these before cyclodiode). All patients had given informed consent for cyclodiode treatment.

Each treatment session was performed either under local anaesthesia, using a peribulbar or retrobulbar injection, or under general anaesthesia at the patient’s request (including the only “child” treated). The laser energy was delivered through a 600 µm diameter quartz fibre oriented within the G-probe handpiece to centre treatment 1.2 mm behind the limbus. Transillumination was used to identify the ciliary body position in eyes with congenital glaucoma or where the limbal anatomy was distorted by previous surgery. The fibreoptic tip protrudes 0.7 mm from the G-probe contact surface in order to indent the conjunctiva and sclera thereby improving the laser transmission to the ciliary body. Care was taken to apply the G-probe to the limbus indenting as above as this ensured that the G-probe surface contour matched the scleral curvature and the posterior angulation was correctly oriented to protect the lens of phakic eyes from laser damage. Each laser application was spaced by half the width of the G-probe surface, easily guided by the visible indentations of the previous application and ensuring an equal separation of about 2 mm.

A standard treatment protocol was used at each “session” to treat three quarters of the circumference of the ciliary body. This usually resulted in 14 applications (four eyes had 13 applications and one eye 12 applications), in order not to treat more than 270 degrees. An energy of 2.0 W was used for 2.0 seconds, resulting in a power delivery of 4.0 J per appli-
cation (56 J per session for 14 applications). This was not altered even if “pops” were heard during treatment. In the first treatment session the temporal 90 degrees was left untreated. A different 90 degrees was left untreated if further treatment sessions proved necessary. On subsequent treatments the 90 degrees untreated varied depending on the appearance of the sclera and conjunctiva at the limbus—that is, if an area of scleromalacia from previous surgery was present this area could be avoided. If one eye underwent more than two treatments, a different 90 degrees was left untreated on each subsequent occasion.

Oral acetazolamide, if prescribed before laser treatment, was continued for a period of 1 week after laser treatment. Topical antiglaucoma medications were discontinued if the IOP was <22 mm Hg on day 1 post-laser treatment. At 1 week post-laser treatment oral acetazolamide was discontinued if the IOP was <22 mm Hg, with reintroduction of topical IOP lowering medications at the discretion of the clinician. Topical steroids, usually dexamethasone 0.1% eye drops, were prescribed four times a day for 2–4 weeks after treatment. At further follow up, topical IOP lowering medications were reintroduced if IOP control required this. If an adequate response was not achieved, cycloidiode was repeated up to a maximum of five treatment sessions. IOP assessment was made using the Goldmann applanation tonometer in most cases with occasional use of the Tonopen where the corneal condition dictated.

Age, sex, diagnosis, length of follow up, IOP pretreatment, and post-treatment at 6, 12, 18, 24, 30, and 36 months, and at the last index visit was noted. Visual acuity, topical and oral medications pretreatment and at last index visit were noted as were the number of laser treatment sessions performed.

Treatment was defined as a success with respect to (a) IOP <22 mm Hg; (b) IOP <17 mm Hg; and (c) for a drop in IOP of greater than 30% (as used by Bloom et al18), despite the use of topical and/or oral medications. A further definition of success was used to identify the number of patients not requiring oral acetazolamide post-treatment as this is a practical consideration for many ophthalmologists using this treatment modality.

Statistical analysis was performed using a two tailed paired Student’s t-test where data approximated to normal distribution, and the Mann–Whitney U test when it did not.

### Results

Fifty-nine eyes of 54 patients were treated in the study period. Six month results are available for 58 eyes of 53 patients as one eye was eviscerated for bacterial endophthalmitis within 1 month. This eviscerated eye with bullous keratopathy had an IOP of 44 mm Hg before treatment, no reduction in IOP after treatment, and subsequently developed bacterial keratitis and endophthalmitis. The vision fell from bare hand movements to no perception of light, so the eye was eviscerated. Two eyes had further IOP lowering surgery for failure of a single cycloidiode treatment after 2–3 months. These eyes had been thought more likely to respond to the diode laser, before treatment, than to an enhanced trabeculectomy. As IOP was not controlled after cycloidiode, enhanced drainage surgery was performed at 2–3 months. In one of the two eyes, cataract surgery had been planned so a combined enhanced phacotrabeculectomy and intraocular lens implant was performed. These eyes were treated early on in our experience with the cyclodiode and had they occurred later in the series, they may have had further cycloidiode treatments in preference to filtration surgery.

Only one eye in the series had undergone previous cyclodestructive surgery—that is, cyclocryotherapy.

The mean (SD) number of applications per treatment session was 13.9 (0.36) and the total amount of energy delivered per treatment

<table>
<thead>
<tr>
<th>Table 1: The diagnostic groups of glaucomatous eyes which had cyclodiode</th>
</tr>
</thead>
<tbody>
<tr>
<td>POAG</td>
</tr>
<tr>
<td>No of patients</td>
</tr>
<tr>
<td>Percentage of total</td>
</tr>
<tr>
<td>Mean IOP pretreatment</td>
</tr>
<tr>
<td>SD of IOP pretreatment</td>
</tr>
<tr>
<td>Mean IOP last index visit</td>
</tr>
<tr>
<td>SD of IOP last index visit</td>
</tr>
<tr>
<td>Percentage IOP reduction</td>
</tr>
<tr>
<td>Mean No treatment sessions</td>
</tr>
<tr>
<td>Mean follow up (months)</td>
</tr>
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</table>

POAG = primary open angle glaucoma, CCAG = chronic closed angle glaucoma, IOP = intraocular pressure, SD = standard deviation.
Table 2  Intraocular pressure at each time interval from initial treatment

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>At 6 months</th>
<th>At 12 months</th>
<th>At 18 months</th>
<th>At 24 months</th>
<th>At last index visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of eyes</td>
<td>58</td>
<td>58</td>
<td>49</td>
<td>34</td>
<td>21</td>
</tr>
<tr>
<td>Mean</td>
<td>33.0</td>
<td>20.0</td>
<td>17.9</td>
<td>18.6</td>
<td>14.6</td>
</tr>
<tr>
<td>SD</td>
<td>10.7</td>
<td>6.5</td>
<td>6.3</td>
<td>6.2</td>
<td>6.6</td>
</tr>
</tbody>
</table>

The mean number of treatment sessions was 1.6 (0.9) with a range of 1–5. Thirty-two (55%) eyes had one treatment, 18 had two, six had three, one had four, and one had five treatments. The aphakic eyes had a higher number of treatment sessions and those with uveitis had a lower number of treatment sessions, on average, than the overall group (Table 1), although not reaching statistical significance.

The mean IOP before treatment was 33.0 mm Hg (10.7) and at last index visit this had fallen to 16.7 mm Hg (7.8) (p<0.0001). This is demonstrated in Figure 1 which shows a scattergram of IOP before treatment and at the last index visit. Only two eyes had higher IOP at last index visit than pretreatment and both had been on oral acetazolamide pre-treatment which was later withdrawn. The eye with an IOP of 44 mm Hg had additional IOP lowering medication prescribed at the last index visit and the eye with an IOP of 26 mm Hg was awaiting visual field analysis before a decision about further treatment. Both eyes had had an initial reduction in IOP after the first cyclodiode treatment.

Seven more eyes had an IOP higher than 22 mm Hg at the last index visit; two eyes were awaiting further diode treatment; two eyes were awaiting visual field assessment before a further decision; in one eye the IOP had reduced to 24 mm Hg in a 93 year old and so observation was planned; in one eye the IOP was 42 mm Hg but the eye's acuity was no perception of light (NPL) and as it was no longer painful further treatment was not instigated. In the last of the seven eyes further treatment was refused as the acuity was only hand movements (HM).

From Table 1 it is apparent that the cyclodiode gives a mean reduction of at least 33% in all the diagnostic groups, excluding the one eye with chronic closed angle glaucoma (CCAG). The commonest subgroups requiring cyclodiode in our unit (including referrals from other units) were glaucoma in aphakic eyes (19%), followed by primary open angle glaucoma (POAG 17%), uveitic glaucoma (15%), and glaucoma secondary to corneal disease (12%).

Table 2 shows the results of IOP pre- and post-treatment at each time interval compared with pretreatment IOP. The reduction in IOP compared with pretreatment IOP is statistically significant at each time point (p<0.001 by Mann–Whitney U test). The group IOPs at 6, 12, 18, and 24 months did not differ significantly from each other by the Kruskal–Wallis ANOVA by ranks test (p=0.01).

It should be noted that only six eyes underwent further treatment after 1 year in order to maintain a reduced IOP; two eyes had a second, one eye a third, two eyes a fourth, and one eye a fifth treatment session.

Using the criteria for success defined above then, at the last index visit 81% (47 eyes) had an IOP of <22 mm Hg; 59% (34 eyes) had an IOP of <17 mm Hg; and the IOP had dropped by more than 30% in 45 eyes (78%). Ninety-one per cent (48) of patients were able to discontinue oral acetazolamide after cyclodiode. Therefore, only five patients were receiving this agent at the last index visit (representing six eyes of five patients), the dosage being halved in four of the five patients. It should be noted that one patient (two eyes in the study) was being treated with oral acetazolamide in preference to topical medications as her ocular pemphigoid was considered secondary to IOP lowering medications. Twelve of the 13 patients where IOP had reduced by less than 30% were no longer taking oral acetazolamide.

The mean (SD) medication score per eye (each agent counting one) used before treatment was 2.4 (0.8) and ranged from 0 to 4. At the last index visit, this had fallen to a mean of 1.4 (1.0) range 0 to 3 (p<0.0001). Examining topical medications alone before treatment, a mean of 1.5 (0.8) were used (range 0 to 3), which reduced in a statistically significant manner to 1.2 (1.0), (range 0 to 3), (p = 0.037). Before the first cyclodiode, the most frequently used drops were β blockers (49 eyes), then pilocarpine (21 eyes), dorzolamide (eight eyes), Propine (dipivefrine, Allergan) (five eyes), and in one eye each aproclonidine 0.5%, adrenaline 1.0%, and Ganda (guanethidine, Chauvin) (2+0.5). At the last index visit, the topical medication profile had changed because new agents were available. β Blockers were the most commonly used drop, followed by β blockers and pilocarpine.

Figure 2  Visual acuity pretreatment compared with final follow up. The solid line represents no change in acuity, the broken lines above and below represent a change of two Snellen lines or grades of acuity. The number next to each point is the number of eyes at each point.
Table 3: The 12 patients with visual acuity (VA) of at least 6/60 whose acuity fell more than one Snellen line on follow up.

<table>
<thead>
<tr>
<th>Pre-treatment index VA</th>
<th>VA at last visit</th>
<th>Diagnosis</th>
<th>Cause of visual loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/5</td>
<td>6/9</td>
<td>Pseudophakia</td>
<td>Mild ARMD</td>
</tr>
<tr>
<td>6/9</td>
<td>6/18</td>
<td>Uveitis (sympathetic)</td>
<td>Corneal oedema</td>
</tr>
<tr>
<td>6/9</td>
<td>6/36</td>
<td>Aphakia</td>
<td>Cystoid macular oedema</td>
</tr>
<tr>
<td>6/9</td>
<td>2/60</td>
<td>POAG</td>
<td>Glaucoma progression</td>
</tr>
<tr>
<td>6/9</td>
<td>2/60</td>
<td>POAG (in diabetic patient)</td>
<td>Ischaemic maculopathy (diabetic)</td>
</tr>
<tr>
<td>6/18</td>
<td>6/60</td>
<td>POAG</td>
<td>ARMD</td>
</tr>
<tr>
<td>6/18</td>
<td>1/60</td>
<td>Cornea (penetrating keratoplasty)</td>
<td>Corneal oedema</td>
</tr>
<tr>
<td>6/18</td>
<td>1/60</td>
<td>Rubotic (diabetic)</td>
<td>Ischaemic maculopathy (diabetic)</td>
</tr>
<tr>
<td>6/24</td>
<td>6/60</td>
<td>Pseudophakia</td>
<td>Glaucoma progression</td>
</tr>
<tr>
<td>6/24</td>
<td>6/60</td>
<td>Pseudophakia (in diabetic patient)</td>
<td>Maculopathy (diabetic)</td>
</tr>
<tr>
<td>6/36</td>
<td>CF</td>
<td>Pseudophakia (in diabetic patient)</td>
<td>Diabetic traction detachment</td>
</tr>
<tr>
<td>6/36</td>
<td>PL</td>
<td>Cornea</td>
<td>Microbial keratitis</td>
</tr>
</tbody>
</table>

POAG = primary open angle glaucoma, ARMD = age related macular degeneration.

Changes in visual acuity are demonstrated in Figure 2. Visual acuity before treatment was 6/60 or better in 37 out of 58 eyes (64%). Considering these 37 eyes, acuity fell more than one Snellen line in 12 eyes (32%), improved by more than one line in one eye (3%), and stayed within one line of initial acuity in 24 eyes (65%). The causes of visual loss and diagnostic category are listed in Table 3.

For the eyes with an initial acuity of less than 6/60, we defined one grade of acuity to be the difference between 6/60 and counting fingers (CF), between CF and hand movements (HM), between HM and perception of light (PL), and between PL and NPL. The visual acuity grade fell in three eyes by one grade and in two eyes by two grades (24%). In two eyes (9%) acuity improved; one improved one grade and the other two grades. The same acuity grade was retained in the remaining 14 eyes (67%). Two eyes had no perception of light at the last index visit; one eye was rubeotic following a central retinal vein occlusion, with PL vision pretreatment, and the other eye had chronic angle closure glaucoma with pretreatment acuity of HM (that is, a drop of two grades of acuity). The other eye that dropped by two acuity grades was also a rubeotic eye after a central retinal vein occlusion. Both of the rubeotic eyes had had their IOP controlled by the cyclodiode, after two and one treatments respectively. The eye with chronic angle closure failed to respond after three treatments.

No phthisis was observed throughout the study although two eyes had chronic hypotony as defined by an IOP of <5 mm Hg for over 3 months. However, neither eye showed any clinical signs associated with hypotony (namely, choroidal folds, choroidal detachments, optic disc oedema) and both eyes retained their pretreatment acuity—one eye that had glaucoma secondary to trauma retaining an acuity of 6/6 and one eye with glaucoma secondary to penetrating keratoplasty retaining HM.

Discussion

Diode laser photocoagulation is developing an acceptable track record for the treatment of complicated secondary glaucomas and primary open angle glaucoma refractory to treatment. The treatment is associated with only minor degrees of pain and inflammation in most eyes and, although not formally recorded in our study, our experience parallels that of other authors. The primary aim of therapy in these difficult eyes is to lower IOP to a level considered satisfactory for the eye in question while preserving visual function at pretreatment levels. For many patients discontinuation of oral acetazolamide is an important consideration and if IOP can be controlled on topical medications, this is acceptable.

In eyes with limited outflow facility, reducing aqueous production to a level that produces a “normal” IOP on no medication runs the risk of hypotony or phthisis. This has been well recognised in ciliary body ablation with cyclophotocoagulation or Nd:YAG laser therapy. We therefore chose a standard protocol, using information available at the commencement of the study, which we considered unlikely to result in phthisis after a single treatment in eyes that had not undergone previous cycloablative procedures. An internal audit of the results of the first 30 eyes with at least 6 months’ follow up provided encouraging data and resulted in a continuance of the protocol.

Direct comparisons are always difficult between studies with complex patients in view of referral practice, population demographics, and inclusion/exclusion criteria. As background information to our study, it is relevant that the glaucoma firm did not perform any seton procedures during the study period; all patients formerly considered for this treatment underwent cyclodiode. This may have resulted in a larger population of eyes with relatively good acuity being treated in comparison with other studies.

The literature to date is difficult to interpret concerning the optimal treatment settings and number of applications per session for an eye with uncontrolled refractory glaucoma when utilising the Iris diode laser with the G-probe. Kosoko et al delivered between 17 and 19 applications to 270 degrees of the ciliary body for a 2.0 second period and commencing at 1.75 W increasing to 2.0 W if no “pops” or “snaps” were heard. However, their protocol allowed for a further reduction in energy delivered by reducing the power setting if consecutive “pops” were heard. This resulted in a mean energy delivery of 63.3 J (7.2) over 17.6 applications per session compared with our mean of 55.5 J (about 12% less). The theory behind reducing the energy so as not to hear “pops” at each application is that these are indicative of tissue disruption, and that a response of this nature to each application might induce more destruction in the ciliary body than desired and also result in more inflammation. It was not our experience that “pops” were heard consistently with a consistent energy level, nor did we have any eyes with marked inflammation post-laser. We did not find a particular association between race and hearing “pops”. No eyes in Kosoko and others’ multicentre study
of 27 eyes had had a previous cyclodestructive procedure and only two eyes had repeat treatment (after 9 and 13 months). About 60% of eyes were controlled (IOP <22 mm Hg) which is less than the figure of 81% from our study. The difference is likely to be due to the fact that the cycloidiode was not repeated in most of their study eyes, perhaps to avoid the risk of phthisis or hypotony. Follow up was nearly identical to ours but the mean number of glaucoma medications at the last index visit was greater than in our study (2.1 versus 1.4) and no mention was made of the use of systemic carbonic anhydrase inhibitors.

Bloom et al 18 allowed more than one treatment session but 18% of their eyes had cyclodestructive procedures before cyclodiode and the mean follow up was only 10 months. In addition, the treatment protocol varied considerably between eyes, from 20 to 40 applications of 1.5 W and 1.5 seconds “titrated against risk of phthisis”. The mean energy delivered is not stated and therefore their results may be difficult to reproduce in another setting. In Bloom and others’ series systemic carbonic anhydrase inhibitors were “spared” in 93% of cases which is similar to the 90% in our series despite our longer mean follow up. The mean number of treatment sessions was 1.75 in Bloom and others’ study which is similar to our 1.6, suggesting that by 1 year after the first treatment most patients will have been stabilised.

Brancato et al 17 and Bock et al 21 had a higher retreatment rate of 65% and 70% respectively than our 45%. This is probably due to patient group differences as Bock et al treated refractory paediatric glaucoma eyes and 10/48 patients in Brancato’s series had “paediatric glaucoma”. Although the numbers in each diagnostic category in our study are small, it appears that with our protocol, all of our groups respond well to the treatment (with the possible exception of the lone chronic angle closure eye). The rubeotic eyes, those with silicone oil glaucoma, those with glaucoma related to corneal disease (including post-keratoplasty glaucoma), and those with chronic post-traumatic glaucoma had the greatest percentage drop in IOP (56.7% to 65.6%). These groups, however, had the highest pretreatment IOPs and therefore would have required a larger drop to achieve the target pressure. It is interesting that the eyes with uveitis had an initial IOP similar to the aphakic eyes but required fewer treatment sessions (mean 1.2 compared with 2.0) to achieve a similar target pressure. Owing to the relatively small numbers of eyes, these figures just failed to reach significance but it suggests that these patients may be particularly sensitive to our cyclodiode protocol.

The results of this study indicate that with our protocol it is not necessary to change power/time settings as neither excessive uveitis or hypotony/phthisis is common. Our IOP results can be expected to be repeatable in a similar cohort of eyes provided our simple protocol is followed. We did not exclude uveitic eyes (compare Kosoko et al 16) or eyes with good acuity, or vary our treatment significantly from one eye to another, preferring to consider cycloidiode as a course of treatment in which multiple sessions are acceptable.

In view of this we consider Kaplan–Meier survival curves inappropriate for assessing the results of IOP control. Analysis is inevitably a “snapshot in time” with eyes at various stages in their “course”. This is substantiated by the status of our eyes with IOP >22 mm Hg at the last index visit. The above does not, of course, apply to visual function as the results of our eyes with relatively good acuity (64%) provide useful data for counselling patients before this therapy (Fig 2), particularly when the causes of significant decrease in acuity are taken into account (Table 3). These results indicate that in the absence of diabetic retinopathy, the visual prognosis for most eyes with good acuity is acceptable over the course of the first 18 months of treatment. In particular, the incidence of cystoid macular oedema appears low with our protocol, even with repeated treatments. Visual loss was common when treatments were repeated in Bloom’s series with 50% of those having three or more treatments losing vision. This may be related to each full treatment being a total of 90 J compared with 56 J in our protocol.

To date no study has compared cycloidiode with seton tube surgery. However, our “success” rate of 81% <21 mm Hg at a mean follow up of 19 months for cycloidiode compares favourably with 87% at a mean of 8 months in Noureddin and others’ study 22 for seton surgery, particularly as no seton procedures were performed by the glaucoma firm during the period of review. Cycloidiode has therefore rapidly become the treatment of preference in our unit for refractory glaucomas.

1 Bietti G. Surgical interventions on the ciliary body. New trends for the relief of glaucoma. XAMA 1980;142:809–11.


