EXTENDED REPORT

Transscleral diode laser cyclophotocoagulation as primary surgical treatment for secondary glaucoma in juvenile idiopathic arthritis: high failure rate after short term follow up

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Aim: To evaluate the success rates of transscleral diode cyclophotocoagulation (TD-CPC) for secondary glaucoma in patients with juvenile idiopathic arthritis (JIA) as primary surgical treatment.

Methods: Retrospective chart review of 12 paediatric patients with JIA associated uveitis and secondary open angle glaucoma.

Results: 21 eyes of the 12 patients had chronic anterior uveitis, 21 eyes had secondary open angle glaucoma, and 19 eyes were treated 41 times with TD-CPC. Patients underwent a mean of 2.15 treatment sessions per eye. Pretreatment intraocular pressure (IOP) was 30.2 (5.5) mm Hg before the first treatment, 30.5 (5.7) mm Hg before the second treatment, and 28.7 (6.3) mm Hg before the third treatment. Reduction of IOP 6 weeks after treatment was highest after the second and third treatments with 9.4 (8.8) and 8.7 (5.8) mm Hg, respectively and 5.2 (10.7) mm Hg after the first treatment. Qualified success (IOP $\leq$ 21 mm Hg with glaucoma medication) was achieved at the end of follow up in six of 19 eyes (32%, follow up time 10.1 (9.3) months).

Conclusion: TD-CPC as a primary surgical treatment in JIA patients, is often unsatisfactory in eyes with uveitic glaucoma.

Chronic anterior uveitis is a challenging manifestation of juvenile idiopathic arthritis (JIA).¹ Uveitis occurs in up to 48% of the patients and is a typical cause of visual loss.² Many patients (42–48%) develop secondary glaucoma.^{2–3} Usually, secondary glaucoma occurs late in the clinical course after the acute inflammation is controlled with immunosuppressive drugs.⁴ Visual prognosis is generally poor in patients with early onset glaucoma.³

Surgical therapies, such as trabeculectomy with or without antiproliferatives, and goniotomy are commonly used as primary surgery and glaucoma drainage devices are often used if one of the previous treatment has failed. All these procedures may have major complications such as, for example, scarring of the filtering bleb, hypotony, or cataract formation.^{1–5}

Transscleral diode laser cyclophotocoagulation (TD-CPC) is an established and relatively safe treatment strategy in secondary open angle glaucoma.^{6–7} Only a limited series on uveitis patients has been previously published with heterogeneous aetiologies.⁸

The aim of this retrospective analysis was to quantify the success rate of TD-CPC with primary surgery in a homogeneous group of patients with secondary glaucoma caused by anterior uveitis associated with JIA. The major outcome was intraocular pressure (IOP) reduction. Secondly, the progression of optic neuropathy was examined. Additionally, the effect on visual acuity, reduction of topical and systemic glaucoma medication, and treatment complications were determined.

PATIENTS AND METHODS

The medical records of all patients with uveitis seen between 1999 and 2005 at the Department of Ophthalmology at St Franziskus Hospital in Muenster were reviewed for secondary glaucoma in association with JIA and TD-CPC.

Our institution does not require institutional review board approval for chart review studies.

Overall, 1761 patients with uveitis were found in the database. A total of 116 had JIA associated uveitis with a minimal follow up of 6 months. JIA was classified according to the ILAR classification system.⁹ All patients had antinuclear antibody positive oligoarthritis or polyarthritis. All patients in this series had secondary open angle glaucoma or ocular hypertension without pupillary block mechanisms and no previous glaucoma surgery. Secondary open angle glaucoma was defined as the presence of typical glaucomatous disc cupping measured by biomicroscopy. Sustained IOP above 24 mm Hg without pathological disc cupping was defined as ocular hypertension.

Laser cyclophotocoagulation was performed after topical antiglaucomatous and/or systemic acetazolamide therapy failed to reduce IOP sufficiently or had to be reduced because of side effects, mainly the result of the systemic medication, or glaucomatous optic neuropathy was found to have progressed or IOP increased permanently despite initiation or increase of antiglaucomatous therapy without notable disc changes. Visual field testing was not used as a marker for glaucoma progression in this analysis because of a lack of availability in all of the children. Visual field testing is difficult in JIA patients because of the young age and the additional visual disturbance such as, for example, cataract or macular oedema. The same restriction applies for objective optic nerve assessment as a marker for glaucoma progression. A combination of up to four different topical glaucoma medications was accepted before TD-CPC was considered. If possible, TD-CPC treatment was postponed until quiescence of uveal inflammation could be achieved without any

Abbreviations: IOP, intraocular pressure; JIA, juvenile idiopathic arthritis; TD-CPC, transscleral diode cyclophotocoagulation

inflammatory cells in the anterior chamber. All patients were on immunosuppressive drugs (table 1) because of their uveitis and arthritis and were therefore seen regularly by their paediatric rheumatologist.

Because of the age of the patients, TD-CPC was performed under general anaesthesia. In each treatment, 25 applications (not more than 180° of the globe) of 2000 mW for 2 seconds were used. Energy was delivered through a contact fibreoptic G probe (Iris endoprobe) attached to the Oculight SLx semiconductor diode laser (Iris Medical Instruments, CA, USA). Procedures were repeated up to three times when the IOP was uncontrolled. When the IOP did not drop (≤ 2 mm Hg) and progression of optic neuropathy (measured by change of cup to disc ratio) was obvious, other surgical procedures were performed even if TD-CPC was not performed three times.

Preoperative therapy consisted of continuing the systemic immunosuppression medication, and administering topical prednisolone acetate 1% eye drops five times daily 1 week before surgery. Postoperative treatment consisted of the continued systemic anti-inflammatory medications and of topical prednisolone acetate 1% eye drops five times daily for 1 week, and the latter was subsequently tapered off as adjusted to the individual inflammation.

Baseline information included age, sex, duration of uveitis and arthritis, duration of secondary glaucoma, and any other complications of uveitis. At each visit, the best corrected visual acuity, slit lamp examination, IOP (Goldmann applanation tonometry), binocular ophthalmoscopy for evaluation of glaucomatous optic neuropathy, and the systemic and topical medications were assessed. Six weeks after each laser treatment, the patients were examined to quantify the success of the treatment. Further visits were scheduled at 3 month intervals or more frequently on an individual basis with regard to inflammatory activity or IOP regulation. End results are considered at the last follow up (at least 3 month after the last TD-CPC) or directly before additional surgery in these patients.

An IOP of 21 mm Hg or lower without glaucoma medication was defined as a success. An IOP of 21 mm Hg or lower with a requirement for medication was defined as a qualified success; all other IOPs were defined as failures. When three TD-CPC have been performed without obtaining qualified success or when progression of the optic nerve damage occurred, a trabeculectomy was planned.

Table 1 Patient demographics

Demographics	Number
Number of patients	12
Sex	
Female	10
Male	2
Number of patients with immunosuppression	11
Methotrexate	9
Etanercept	2
Ciclosporin	3
Number of eyes with uveitis	21
Number of eyes with glaucoma	21
Number of TD-CPC treated eyes	19
Number of phakic eyes	10
Age (years) (SD) (range)	
Diagnosis of uveitis	4.7 (1.8) (3–7)
Diagnosis of arthritis	4.7 (1.8) (2–7)
First TD-CPC	10.9 (3.4) (6.2–19.5)
Duration of uveitis glaucoma (years) (SD) (range)	5.9 (3.3) (2–12)
Duration of glaucoma, first TD-CPC (months) (SD) (range)	11.7 (7.4) (1–26)

TD-CPC, transscleral diode cyclophotocoagulation.

Figure 1 Intraocular pressure (IOP) before and after laser cyclophotocoagulation with statistical significant reduction of mean IOP after each treatment.

RESULTS

The study group included 12 patients with JIA (oligoarthritis or polyarthritis, antinuclear antibody positive, all white). All 21 eyes with uveitis developed also secondary glaucoma. The time between manifestation of the uveitis and the onset of secondary glaucoma was 5.9 years (range 2–12 years). The period between the diagnosis of glaucoma and the first cyclophotocoagulation was 11.7 months (range 1–26 months) (table 1).

Compared with this, the intervals between the first and the second, and the second and third treatments were shorter, with 4.4 months (range 1–24 months) and 7.3 months (range 1–26 months), respectively.

Of the 21 eyes with secondary glaucoma, 19 eyes were treated with TD-CPC. In seven patients, two eyes were laser treated, and in another five patients one eye was treated. Overall, 41 treatments were performed. Four eyes were treated only once, eight eyes twice, and another seven eyes three times. The mean IOP before the first and the second surgery were nearly equal with 30.2 (5.5) mm Hg (range 21–40) and 30.5 (5.7) mm Hg (range 24–41, $p = 0.89$), respectively. Before the third treatment, mean IOP was reduced to 28.7 (6.4) mm Hg (range 17–38, $p = 0.56$). The mean IOP reduction was more pronounced after the second and third treatment (fig 1), being statistically significant after the second (9.4 mm Hg, $p = 0.001$) and third (8.8 mm Hg, $p = 0.018$) coagulation, while IOP reduction after the first treatment was 5.2 mm Hg ($p = 0.09$). The mean IOP after treatment was measured 6 weeks later.

The reduction of topical medications was statistically significant after each treatment ($p = 0.13$). Systemic acetazolamide could only be discontinued after the second and third treatment in four and three cases, respectively. Reduction of acetazolamide dosage was possible after the first treatment in three eyes, after the second in four, and in two eyes after the third treatment (table 2).

Table 3 shows the outcome results 6 weeks after laser treatment. The treatment failed in 12 (63%) after the first, six (43%) after the second, and two (29%) after the third cyclophotocoagulation treatments.

Looking at the end results with an average follow up time of 10.1 (9.3) months (range 3–30 months), 13 failures in 19 (68%) treated eyes were found. Qualified success (follow up time 9.3 (9.8) month, range 3–31 months) was achieved in one eye with one treatment, in two eyes with two treatments, and in another three eyes with three treatments. Laser cyclophotocoagulation failed in three eyes after the first coagulation, in six eyes after the second coagulation, and in another four eyes after the third coagulation.

Table 2 Topical antiglaucomatous and systemic acetazolamide before and after the three TD-CPC treatments

	Treatment		
	1	2	3
Average of topical medication before treatment	3.7 (0.5)	–	–
Average of topical medication after treatment	3.3 (0.7)	3.0 (0.6)	2.7 (1.6)
	p=0.05	p=0.017	p=0.022
Number of patients with systemic acetazolamide before treatment	12/19	–	–
Number of patients with systemic acetazolamide after treatment	12/19	8/15	2/7

Seven eyes with failure after laser treatment were consequently operated on with trabeculectomy with intraoperative use of mitomycin C. In another six eyes filtering surgery is planned. Looking at six of the seven trabeculectomy eyes (follow up time of number 7 is below 3 months) with a mean follow up of 21.4 (15.8) months (range 9–44.4 months) four are classified as successes and two as failures. The two failed eyes underwent revision of the filtering bleb because of scarring and one had a glaucoma drainage device implantation.

The lens status did not correlate with the success rates, as three aphakic eyes were in the failure group and two in the qualified success group ($p = 0.5$). The numbers of confounding uveitic complications, such as band keratopathy, posterior synechiae, cataract formation, cystoid macular oedema or vitreous opacification, were very similar in both groups, with an average number of complications of 2.1 in the qualified success group and 2.2 in the failure group. The presence of any of the other complications and the treatment with immunosuppression did not correlate with success. In the qualified success group, one eye was being treated with etanercept in combination with methotrexate, two eyes with methotrexate alone, another two with methotrexate in combination with ciclosporin, and one without therapy. In the failure group, eight patients were on methotrexate alone, two in combination with ciclosporin, and two on etanercept. It was not necessary to change this immunosuppressive medication after one of the treatments, and uveitis remission was maintained in all.

Pop effects (overheating of the ciliary body leading to formation of small gas bubbles) from TD-CPC occurred in six (14.6%) treatments. Other intraoperative complications, such as conjunctival burns, did not occur in any of the patients. Postoperatively, a change in pupil configuration as permanent enlargement or loss of roundness was found in four (21%) eyes. No severe increase of inflammatory activity was seen in the patients, or any other severe adverse effects, such as retinal detachment, haemorrhage, or hypotony. Before treatment 10 eyes had best corrected visual acuity of 20/32 and better, six eyes had 20/100–20/40, and three were even worse. Visual acuity remained unchanged or improved in 16 eyes and one eye lost two Snellen lines and another two eyes three or more. Cataract formation in two patients and an

increase of vitreous opacification were primarily responsible for this change.

Progression of optic neuropathy, as determined by an increased cup to disc ratio, was noted in nine eyes, which all belong to the failure group after TD-CPC, and are consequently being treated or are planned to be treated with filtering surgery.

DISCUSSION

Intraocular pressure in patients with uveitis and JIA cannot be controlled with topical antiglaucomatous medication and/or systemic acetazolamide in the majority of cases.³ Surgical treatments include trabeculectomy with mitomycin C, goniotomy, trabeculodialysis, and implantation of drainage devices.^{3 10–12} Success rates at the end of follow up time ranged from 60% to 90% with these techniques. To the best of our knowledge, our study is the first to evaluate the outcome of contact diode laser photocoagulation as primary surgical treatment of uveitic glaucoma in a homogeneous group of patients with JIA. Our qualified success rate with TD-CPC was limited to 32%. Taking into account that our follow up time is limited to an average of 10.1 months, it might be speculated that the success rate may even decrease over time; CPC, when repeated several times, might increase the risk for ocular hypotony in the long term.

All of the previous studies investigating TD-CPC included a heterogeneous study group concerning age and aetiology of uveitis. There is only one other study focusing on refractory glaucoma caused by inflammatory eye disease reporting a success rate of 72.2%.⁸ In this report, only three eyes with JIA uveitis were included, and one of these failed after three treatments.⁸ The other studies on cyclophotocoagulation included only a few inflammatory glaucoma patients, precluding meaningful conclusions. Most of these studies were performed in adults. The overall success rate was 81% after TD-CPC in a recent investigation, and the group of nine uveitis eyes was not different from other groups.⁷ In probably the largest study on cyclophotocoagulation with 210 eyes, only nine eyes had uveitic glaucoma. In this study, no differences were seen compared with the general success rate of 66%.⁶ In another study on adults, success was obtained in two of five eyes with uveitic glaucoma.¹³

Table 3 Success rates 6 weeks after each of the three laser cyclophotocoagulation sessions and at the last visit, 19 eyes with 41 treatments

	Treatment			End of follow up
	1	2	3	
Qualified success	7	8	5	6
Failure	12	6	2	13

Looking at the published data on paediatric refractory glaucoma, there are only limited numbers of patients with "uveitic glaucoma." These studies are difficult to compare, as success has been defined differently. Kirwan and co-workers reported on three eyes (not further classified) of 77 in their study group, with an overall success rate of 72%.¹⁴ In another investigation, 11 eyes of 69 treated with cyclophotocoagulation had a success rate of 66% initially, and this dropped to 41% after 1 year. The success rate after re-treatment increased in the total group to 79%.¹⁵ The lowest success rate has been reported by Bock *et al*, with an overall success rate of 50% after 6 months in paediatric glaucoma.¹⁶ Neely and Plager chose another approach with endocyclophotocoagulation in difficult paediatric glaucoma. In their work, the success rate dropped down to 43% after 19 months of follow up with severe complications in four (all aphakic) of the 29 treated eyes.¹⁷ In all of these studies, origin (infectious or non-infectious) or anatomical classification of the uveitis, which is critical for success, has not been specified.

Our number of re-treatments was 78.9% (mean 2.15 treatments), and this is in accordance with the other studies in inflammatory glaucoma.⁸ In the work of Kirwan *et al*, the number of treatments was 2.3 in the whole group with paediatric glaucoma.¹⁴

In other studies, aphakia appeared to be a risk factor for severe adverse effects, including retinal detachment or phthisis bulbi after cyclophotocoagulation.^{14 15} In none of our patients, however, was severe treatment associated adverse effects noted. Differences in the success rates of cyclophotocoagulation in children or adults are controversial in the literature.^{14 18}

In conclusion, transscleral laser cyclophotocoagulation has a much lower success rate in the treatment of secondary glaucoma in children with chronic anterior uveitis in JIA than is reported in adult glaucoma. Although the number of patients in this study appears to be fairly small, JIA associated uveitis is a rare disease and this is the largest collection of such patients studied so long after TD-CPC. TD-CPC has also a much lower success rate as a primary surgical treatment compared to other surgical techniques such as trabeculectomy or goniotomy: In our series TD-CPC had no severe adverse effects. In a limited number of patients mean IOP is reduced and after TD-CPC a reduction of antiglaucomatous therapy is often possible. Cyclophotocoagulation might therefore be useful to gain time before further surgical therapy is performed, but it has to be kept in mind that progression of glaucomatous damage might occur in the meantime. Overall, the results after TD-CPC in the difficult group of JIA associated uveitis with secondary glaucoma as primary surgical treatment strategy are not satisfactory in many patients.

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All the authors confirm herewith that there are no competing interests.

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