Titrated Cyclocryopexy - A report on long term results

N SAEED* T F BABAR** S JAN** *I HUSSAIN** M D KHAN***
**Department of Ophthalmology, Khyber Teaching Hospital and Khyber Medical College, Peshawar*
***Khyber Institute of Ophthalmic Medical Sciences, Hayatabad Medical Complex, Peshawar*
Correspondence to Dr. Nasir Saeed, Associate Professor Ophthalmology

Objective: To determine the efficacy and safety of a titrated cyclocryopexy in advanced glaucomatous eyes in term of intraocular pressure control and complications. **Material and Methods:** Retrospective Cohort analysis of a titrated cyclocryopexy in 30 eyes of 25 patients with uncontrolled glaucoma during July 1996 to July 2003 at Hayatabad Medical Complex, Peshawar. Inclusion criteria applied was; patients having uncontrolled IOP with maximum medical therapy, previous trabeculectomy and a minimum follow-up of 2 years. All patients were assessed for glaucoma. Numbers of cryo-applications were determined according to the IOP. Four to 12 applications in one sitting were used. Repeat cryo-application were applied at least after six-weeks of previous therapy if IOP was not controlled. **Results:** A total of 30 eyes of 25 patients were studied. IOP control of less than 21 mm Hg was achieved in 83% of the eyes. Mean IOP was reduced from 29 ± 4.96 pre-op to 17 ± 7.36 at two years follow-up. Forty percent of the eyes needed single session, 40% received 2 sessions and other 20% needed 3 sessions. All the patients lost at least one line of Snellen chart at 2 years follow-up, 70% retained useful vision, 20% retained light perception and 10% lost perception of light. Serious complications included phthisis, persistent vitreous hemorrhage with retinal detachment, and total retinal detachment and persistent vitreous hemorrhage in 1 eye each. **Conclusion:** Cyclocryopexy appears to be an effective procedure in cases of advanced glaucoma with an acceptable risk / benefit ratio. If done in a titrated manner the number of complications are reduced in severity.
Key words: Advanced glaucoma, Titrated cyclocryopexy, Failed trabeculectomy.

Glaucoma is the second leading cause of world blindness, and is affecting more than 66.8 millions people worldwide[1]. The treatment of glaucoma is even complex. At present availability of new drugs like β-blockers, topical carbonic anhydrase inhibitors and prostaglandin analogue effectively control intra-ocular pressure (IOP) [2]. Surgical procedures have been improved and use of anti-metabolites intra-operatively has helped increasing the success rate[3]. New and safer drainage devices are helpful in difficult cases[4]. Still there are difficult situations where nothing works for example advanced congenital glaucoma, aphakic and pseudo-phakic glaucoma, traumatized eyes with distorted anterior segments, eyes with dislocated lenses, neo-vascular glaucoma (NVG), eyes with high risk of scarring and conjunctival fibrosis and eyes with repeated failed drainage surgeries[5].

If aqueous drainage cannot be improved in such cases, its production may be reduced. Ciliary body is the area of attention since long. In 1933, Weve first introduced surface diathermy to ciliary body to reduce IOP[6]. Other methods like penetrating diathermy[7], transpupillary cyclophotocoagulation by Argon Laser[8], Trans-scleral contact Nd: YAG laser photocoagulation [9], edoscopic cyclophotocoagulation [10], trans-scleral ultra-sonic destruction of ciliary body[11], and trans-scleral microwave destruction of ciliary body [12] have been reported to be effective but with a high rate of complications. The safety of trans-scleral diode laser photocoagulation is high enough that researchers advocate using them as primary procedure when maximum medical therapy fails to control IOP [13,14]. Cyclodestructive procedure can favorably be compared to aqueous shunts. In a retrospective Cohort analysis using Medicare data, it was found that eyes with an aqueous shunt were 3.8 times more likely to have an adverse out come than eyes with a cyclodestructive procedure[15].

Cyclocryotherapy in the treatment of glaucoma was first described by Bietti in 1950[16], since then a number of studies have been conducted using cyclocryotherapy in advanced cases of glaucoma[17,18,19]. The reported results have varied greatly probably due to differences in technique and to the hetero-genecity of the patients being treated [20]. Cyclocryopexy is not widely recommended because of reported high rate of complications[21,22,23], this may be because of non-availability of standard protocols. In spite of these facts, cyclocryopexy still have an important role in the treatment of difficult glaucoma in situations of non-availability of more safe equipment like contact diode laser cyclophotocoagulation.

We developed a form of titrated cyclocryopexy in an effort to minimize the complications of cyclocryopexy and still achieve the good results.

We report the results of long-term follow-up after titrated cyclocryotherapy in patients with advanced glaucoma in seeing eyes where other form of treatment failed.

Material and methods:

We carried out a retrospective Cohort analysis of a titrated cyclocryopexy in 30 eyes of 25 patients with uncontrolled glaucoma. The study was carried out at Hayatabad Medical Complex, Peshawar. Records of all the patients treated during the period, July 1996 to July 2003, were analyzed. Only those patients were selected for the study that had a minimum follow up of two years.

Only those patients were selected for cyclocryotherapy where maximum medical therapy could not control IOP and already had at least one failed drainage surgery and further surgery was either not possible or feasible. All the patients were evaluated and underwent slit lamp biomicroscopy, gonioscopy, applanation tonometry and fundoscopy when possible. Records were checked for previous ocular surgeries including drainage operation. Anti-glaucoma medications were assessed. Pre-operatively, patients were put on topical atropine, dexamethasone, β-blocker, oral acetazolamide and analgesics, for several days as to control intra-ocular pressure, inflammation and pain. All the patients were admitted to the hospital. Patients were treated under peri-bulbar anesthesia with a mixture of 2% Xylocain and 0.75% Bupivacain. Children were treated under general anesthesia. A cryoprobe of 2.5 mm diameter (ERBE-Germany) was used. Freezing temperature of 70° C to 90° C was achieved for a minimum of 60 seconds or when the ice-ball reached within one mm of limbus. The center of the probe was put 4 mm away from the limbus in a normal sized eye. If the globe was of abnormal size, ciliary body zone was located by trans-illumination. The number of applications were selected according to the IOP with maximum medical therapy as given in table I.

Up to 6 applications were applied in lower 180°. More than 6- applications were distributed in 360°. Applications were never made contiguous. Repeat cryo-applications were done if IOP was still unacceptably high with maximum medical therapy, after 6-weeks of previous therapy. In repeat therapy, numbers of application were put at 2/3 of original formula i.e. 4- applications for an IOP of 25-30 mm of IOP instead of 6 applications.

Patients were closely monitored for IOP post-operatively at 6 hours and 12 hours. Thereafter, every 24 hours for the first one-week and weekly for the first six weeks. The patients were continued with the same pre-op medical therapy and treatment adjusted accordingly.
The patients were followed regularly every 8-weeks for first year and thereafter every 8–12 weeks according to the response. On each follow-up visit, the patient was examined for level of IOP control and any complications.

Results:
A total 30 eyes of 25 patients were included in the study. Fifteen were males and 10 were females. Five patients were operated on both eyes. Twenty-four eyes (80%) had undergone two or more drainage surgery and 3 eyes (10%) had undergone 4 drainage surgeries each (Table II). Twenty eyes (66%) had at least one drainage surgery augmented with intra-operative local application of Mitomycin-C (MMC).

Most common type of glaucoma treated was congenital glaucoma (8 eyes), aphakic glaucoma (6 eyes), pseudo-phakic glaucoma (4 eyes), NVG (4 eyes) and primary open angle glaucoma (3 eyes) (Table III). The initial IOP before treatment and final IOP after 2 years of follow up are given in Figure I. Mean IOP was reduced from 29 ± 4.96 mm Hg pre-op to 17 ± 7.36 mm Hg at two years follow-up. IOP was reduced to less than 21 mm Hg in 25 eyes (83%) of the eyes at two years of follow-up. IOP could not be brought down below 21 mm of Hg in 3 eyes (10%). In two eyes (6.7%) of neo-vascular glaucoma, the eyes develop hypotony after 3rd session of cyclocryopexy; one of it went into phthisis. The visual acuity at the time of presentation and at two years follow up is given in Figure I. All the eyes lost at least one line of Snellen's chart at 2 years follow-up. Three eyes (10%) lost perception of light two of these were cases of NVG while another 6 eyes (20%) retained vision of only perception of light to hand movements one of this was a case of NVG. Twelve eyes (40%) achieved the desired IOP with single session; another 12 eyes (40%) required two sessions of cyclocryopexy while remaining 6 eyes (20%) required 3 sessions of cyclocryopexy(Figure II).

The most common complication noted at 2-year follow-up was, increasing in the opacification of lens in 7 eyes (23.3%), two of them had to be operated for cataract surgery. Two eyes (6.7%) developed macular edema due to concurrent diabetic retinopathy. One eye (3.3%) developed cystoid macular edema the patient was aphakic with an A/C IOL secondary to trauma. One eye (3.3%) developed macular gliosis without any apparent reason. Two eyes (6.7%) developed persistent intraocular hemorrhage with total retinal detachment, one of which occurred in a patient who was treated for glaucoma secondary to R/D surgery with vitrectomy and intra-vitreal silicon oil. Corneal de-compensation occurred in two eyes (6.7%) of aphakic glaucoma where vitreous was in anterior chamber, both of them were posttraumatic eyes. Two eyes (6.7%) developed sublaxated / posterior dislocated lenses; both of these eyes were buphthalmic due to congenital glaucoma (Table IV). All eyes developed some degree of inflammation and experienced postoperative pain, which responded promptly to the treatment. No case of immediate postoperative elevation of IOP occurred requiring any further treatment.

Table I: Number of applications selected according to the presenting intraocular pressure

Pre Op-IOP	Number of applications
20 – 25 mm of Hg	04
26 – 30 mm of Hg	06
31 – 40 mm of Hg	08
> 40 mm of Hg	12

Table II: Number of failed procedures before cyclocryopexy was advised

Number of failed procedures (Trabeculectomy with /without MMC)	No. of eyes
One time	06(20%)
Two times	15(50%)
Three times	06 (20%)
Four times	03 (10%)

Table III: Types of glaucoma treated

Types of glaucoma	No. of eyes
Congenital glaucoma	08 (26.66%)
Aphakic glaucoma	06 (20%)
Pseudo-phakic glaucoma	04 (13.3%)
Neo-vascular glaucoma	04 (13.3%)
Primary open angle glaucoma	03 (10%)
Primary angle closure glaucoma	02 (6.7%)
Aniridia with glaucoma	02 (6.7%)
Post retinal detachment surgery	01 (3.3%)

Table IV: Complications recorded at 2 years follow up after cyclocryopexy

Complications	No. of eyes
Developed cataract	07
Maculopathy with diabetic retinopathy	02
Corneal de-compensation	02
Persistent vitreous hemorrhage with retinal detachment	01
Dislocated lens with retinal detachment	01
Cystoid macular edema with aphakia with A/C IOL	01
Persistent hypotony with choroidal detachment	01
Phthisis bulbi	01
Sublaxated lens with buphthalmos	01
Persistent vitreous hemorrhage in an eye with NVG	01

Note: Multiple complications occurred in few eyes

Fig. I: Pre-op and two years post-op visual acuity after cyclocryopexy

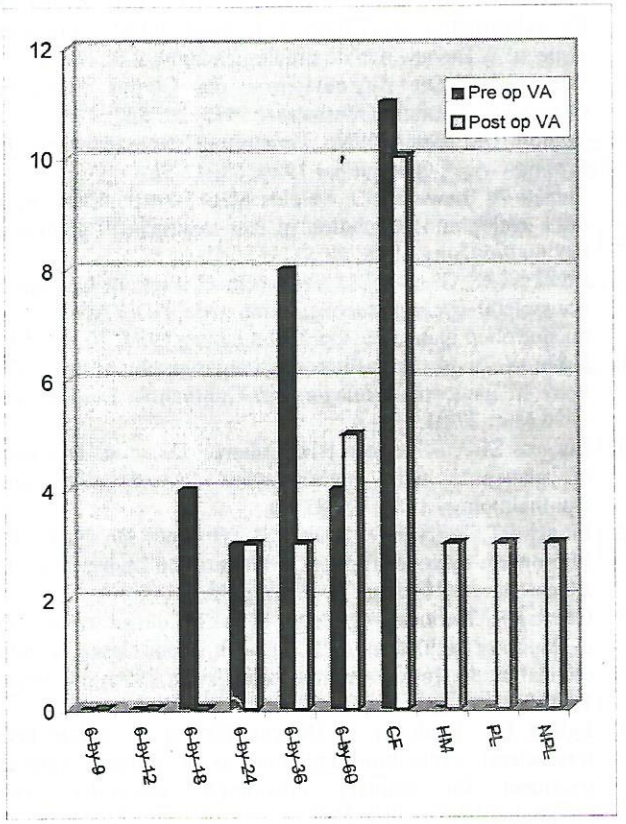
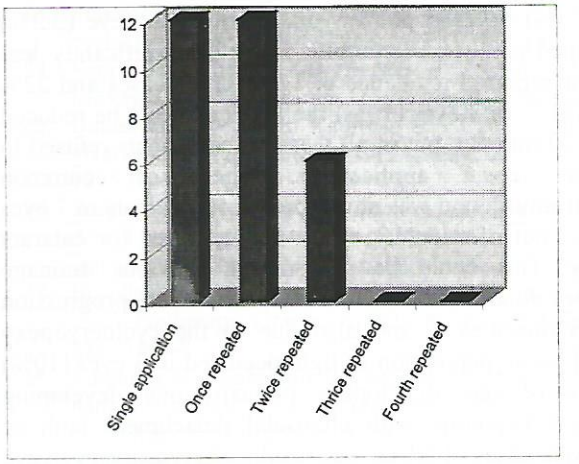


Fig. II: Number of repetitions required to achieve the desired IOP after cyclocryopexy



Discussion

Cryosurgery of the ciliary body has been used in the treatment of advanced open-angle glaucoma[17], glaucoma in a aphakic eyes[19], NVG[24], glaucoma after penetrating keratoplasty[25] and in congenital glaucoma[26]. de Roetth reported the results of cyclocryopexy in the treatment of advanced open-angle glaucoma[17]; 141 eyes were treated with one session of cyclocryopexy which resulted in a postoperative IOP less than 20 mm Hg in 57%. An additional 60 eyes required more than one treatment, of which 73% achieved a postoperative IOP less than 20 mm Hg. Preoperative IOP data and visual results were not reported. Bellows and Grant [18] reported the results of cyclocryopexy on 61 eyes with advanced uncontrolled glaucoma of various types, including open-angel glaucoma (OAG), secondary glaucoma, NVG, childhood glaucoma (including congenital glaucoma), and angle closure glaucoma (ACG). Overall, 59% of eyes had a reduction of IOP to less than 20 mm Hg. The NVG group had the lowest frequency of IOP control and the highest frequency of complications among the groups. In 1978, Bellows and Grant [19] reported the long-term follow-up of cyclocryopexy in 25 patients with OAG. Control was defined as a postoperative pressure of < 20 mm Hg and was achieved in 92% of the eyes. Complications were reported in 27% of the patients and included retinal detachment, vitreous hemorrhage, macular edema, persistent uveitis, transient elevation of IOP, and posterior synecchiae. Visual field data were not reported.

The success rate of 83% for achieving an IOP control below 20 mm Hg after titrated cyclocryopexy in our study, was much better than reported by de Roetth (57%) [17] and Grant (59%) [18] but less than as reported by Bellows and Grant (92%)[19].

We selected only those eyes for cyclocryopexy, which had some level of vision, at least one failed drainage procedure and the IOP was not controlled with maximum medical therapy. Most of these were difficult cases with

structural abnormalities. We still were able to achieve reduction of IOP below 20 mm Hg in 25 eyes (83%). One eye (3.3%) develop phthisis and another one eye (3.3%) developed persistent hypotony which is significantly less than the reported incidence of 12% for all cases and 22% for NVG [27]. In 3 eyes (10%) the IOP could not be reduced below 20 mm Hg, but in all these cases patients refused to undergo repeat applications. The most common complication found was development of cataracts in 7 eyes (23.3%) out of which 2 eyes were operated for cataract surgery. This could be due to the previous drainage surgeries done which are known to accelerate progression of lens opacities [28] and also due to the cyclocryopexy itself. Loss of perception of light occurred in 3 eyes (10%) because of one developing phthisis, one developing persistent hypotony with choroidal detachment both of them were cases of NVG. The results of cryosurgery in eye with NVG were poor in accordance with previous reports [18,27]. One eye developed total retinal detachment with vitreous hemorrhage in an eye, which was previously, operated for total retinal detachment with vitrectomy and intra-vitreal silicon oil injection. This has already been reported in the literature [22]. One patient developed cystoid macular edema in an eye, which previously trauma with vitreous in wound and a secondary A/C IOL. Two eyes developed macular edema, which were also suffering from diabetic retinopathy. One eye developed macular gliosis for which no other cause except cyclocryopexy could be determined.

The eyes which were structurally normal responded much better to cyclocryopexy in term of final IOP control and visual preservation as compared to eyes which were structurally abnormal like traumatized eyes and aphakic eyes with vitreous in wound, large buphthalmic eyes with repeated drainage surgery and NVG. Both the eyes having aniridia with glaucoma responded very well against the reported poor results by Wagle et al [26] in which 50% of the eyes with aniridia developed phthisis.

In our series, two eyes developed sublaxated / dislocated lenses. This complication has already been reported[29]. This occurred in eyes suffering from congenital glaucoma, in which case the eyeball size was 16 mm and we believe that it was more for the structural abnormality of the eye rather than the effect of cyclocryopexy.

Taking in view the advanced nature of glaucomatous eyes selected for cyclocryopexy with so many structural abnormalities and repeated failed drainage surgery; the preservation of useful vision in 70% of eyes at 2 years follow-up is rather encouraging. We believe that if cyclocryopexy were not done to these eyes, most of them would have lost useful vision due to uncontrolled IOP.

Mechanism for reduction of IOP after cyclocryopexy is believed to be due to destruction of the ciliary epithelium, which in turn reduces production of aqueous humor and thus leading to reduction in IOP [23]. We also believe that cryo application to sclera in ciliary body region leads to some changes in permeability of the sclera of ciliary body region, which facilitate aqueous outflow. This is evident from our cases number 2, 9,19 and 22 as given in Figure 1, where only 4 applications of cryo in a single sitting brought the IOP from 24-25 mm Hg to 14 mm Hg and maintained that level at 2 years follow-up.

Conclusion:

Cyclocryopexy appears to be an effective procedure in cases of advanced glaucoma with an acceptable risk / benefit ratio. If done in a titrated manner, the number of complications are much less. In the present study the procedure was used in complex cases and only as a last measure. The author recommend that if it is used in the early course of glaucoma, the results can even be better and the complications less severe.

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