


Cyclo-cryotherapy for the management of absolute glaucoma in rural areas

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Abstract**Introduction:** Ciliary body destruction has been performed with many techniques with considerable differences in efficacy and complication rates. Among these methods, cyclo-cryotherapy is noninvasive, Simple and very economical to treat uncontrolled IOP in refractory absolute glaucoma.**Objective:** To assess the efficacy of cyclo-cryotherapy, in painful blind refractory absolute glaucoma.**Methods:** Prospective study of 34 patients with blind refractory absolute glaucoma who were treated with Cyclo-cryotherapy. Cyclo-cryotherapy treatments were performed with retinal cryoprobe of 3.3 mm diameter. The temperature of each Cyclo-cryotherapy spot was -80°C and each spot was maintained in Place for 60 seconds. Four Cyclo-cryotherapy spots were placed in each quadrant. Repeated measures ANOVA was used to find the difference between preoperative and postoperative intraocular pressure.**Results:** The mean baseline pretreatment intraocular pressure (IOP) in all eyes was 59.76+/-5.14 mmHg, which was decreased to a mean IOP at last follow-up of 16.29 +/-2.42 mmHg.**Conclusions:** Cyclo-cryotherapy is a simple effective procedure to lower IOP and is a reasonable treatment option for refractory absolute glaucoma patients who experience with ocular pain and headaches, in rural health care setup.**Keywords:** Ciliary body², Absolute Glaucoma¹, Cyclo-cryotherapy³, intraocular pressure⁴

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Introduction

Destruction of the ciliary body has been used to treat glaucoma since 1930. In cyclo-destructive procedures, the secretory epithelium of the ciliary process are damaged, which leads to reduced aqueous humor secretion and lower intraocular pressure (IOP). Cyclo-cryotherapy was popularized by De Roeth Jr A¹ in late 1960s and reported a 73% of success rate in patients with uncontrolled IOP. However, Cyclo-cryotherapy was introduced by Bietti² in 1950. Various studies have reported success rate of 34% to 92%. In tertiary centres, Transscleral Nd: YAG and diode laser photocoagulations are replacing cryotherapy as the preferred form of cyclodestruction in advanced patients³⁻⁵. However till today in remote rural areas cryotherapy has a major role in the management of end-stage refractory glaucoma, where resources are poor. In the past, cyclodiathermy, retrobulbar injection of alcohol and enucleations were considered for refractory glaucoma management.

Objective: To assess the effect of cyclo-cryotherapy, in painful blind refractory absolute glaucoma.**Materials and Methods**

A prospective study was designed and conducted between Jan 2011 to Dec 2014. Thirty four eyes of thirty four patients were included in the study with the following inclusion and exclusion criteria's.

Inclusion criteria: The inclusion criteria's were presence of primary, secondary or neovascular glaucoma associated with high IOP that was unresponsive to other medical or surgical treatment for at least three months with no perception of light.**Exclusion criteria:** Patients who had less than six months of follow up, eye surgery less than three months and visual acuity of light perception or better were excluded.

Under peribulbar anesthesia retinal cryo-probe with a diameter of 3.3 mm was applied directly on the intact conjunctival surface, the centre of the tip being 4 mm from the limbus, for 45 seconds at about -80° thus being directly over the ciliary body. Probe was allowed to defrost completely before removing it from the tissue. In all cases the probe was applied in such a way that the margin of the ice-craters touched one another on each application, and the applications were given all round the limbus. Following cryosurgery the eyes were padded for 24 hours, using 1% Atropine eye ointment twice daily for 2 weeks and Ciprofloxacin + Dexamethasone eye ointment which was then continued 3 times a day for one week and tapered every week. Oral analgesics were given for 5 days. All patients continued pretreatment antiglaucoma medications for first two weeks and then tapered depending on the IOP. IOP were recorded at each

pre-procedure and post-procedure patient visit. IOP was measured using the Goldmann tonometer. Any observations of excessive anterior segment inflammation (corneal infiltrations, hypopyon, marked conjunctival edema, or injection) and post procedure pains were also noted. Criteria for successful outcome included were IOP between 5 and 21mmHg, relief from ocular pain, watering and headache. The post-operative IOP was checked on 1st, 2nd, 4th weeks, 2nd, 4th and 6th months after the Cyclo-cryotherapy procedure and all patients were followed up for minimum of 6 months.

Analysis: Results were presented in percentages, mean and standard deviation (SD). Pre-operative IOP and Postoperative IOP at multiple intervals was expressed in mean and SD. Difference in means between baseline and post operatives IOP was assessed by repeated measures ANOVA by using R statistical software.

Results

Thirty four eyes with uncontrolled refractory glaucoma on maximum antiglaucoma medications were treated with Cyclo-cryotherapy at each quadrant. The mean age of the subjects was 55.79+/-11.67(SD) years, 19 men and 15 women. The average follow-up time was 12 months (range 6 to 18 months).

Major Symptoms, leading patients to seek Cyclo-cryotherapy treatment was ocular pain and headache in twenty six patients. The most common pre-procedure diagnosis was neovascular glaucoma in twenty six (76.5%) eyes, followed by angle closure glaucoma in four (11.8%) eyes, and open angle glaucoma in four (11.8%) eyes. Causes of neovascular glaucoma were central retinal vein occlusion in 18 (52.9%) eyes, diabetic retinopathy in 12 (35.3%) eyes and ocular injuries in 3 (8.8%) eyes. Prior ocular surgeries had been performed in nine eyes, pan retinal photocoagulation done in

thirteen eyes, trabeculectomy in four eyes, and vitrectomy was performed in one eye because of vitreous haemorrhage. For the remaining eyes, no procedure was performed prior to Cyclo-cryotherapy.

The mean IOP in all patients was 59.76±5.14 mmHg pretreatment and 16.29±2.4mmHg at the last follow-up. The mean IOP at last follow-up was significantly reduced by 43.47mmHg. Four eyes required repeat cyclotherapy at 2 months.

Overall, the success rate of Cyclo-cryotherapy in this study was 94%. Postoperative complications like hyphema and severe uveitis developed in 6 (17.6%) eyes. Hyphema and severe uveitis gradually resolved using topical antibiotics and steroids. Phthisis bulbi was seen in two cases at the 6 months.

Table 1: Demographic details of patients

Characteristics		Number (Percentage)
Total Number of eyes		34
Gender	Male	19 (55.9%)
	Female	15 (44.1%)
Eyes	Right	18 (52.9%)
	Left	16 (47%)
Below 60 years		20 (58.8%)
Above 60 Years		14 (41.2%)
Mean Age	55.79 ± 11.67 SD	

Table 2: Distribution as per type of glaucoma

Type	Number	Percent
Neovascular glaucoma	26	76.5
Angle closure glaucoma	4	11.8
Open angle glaucoma	4	11.8

Table 3: Intraocular pressure pre and post procedure follow-up periods

Intraocular pressure	Pre-operative	1 st week	2nd week	1 month	2 month	4 month	6 month	1 year
Mean	59.76	37.71	24.18	18.82	18.82	15.94	15.76	16.29
SD	5.135	6.789	4.628	6.478	9.305	3.209	2.547	2.419

Repeated Measure ANOVA $F = 175.8, P < 0.001$ ($P < 0.05 =$ statistically significant)

Discussion

We analyzed the clinical outcome of reduction of Intraocular pressure in thirty four eyes treated with Cyclo-cryotherapy performed at in all quadrants. The mean IOP at six month follow-up was significantly reduced by 44 mmHg from the baseline IOP and the mean number patients using antiglaucoma medications decreased to five at 6 months follow-up. After treatment, acute complications like hyphema and uveitis developed in six eyes, but these complications gradually resolved with medications. Four patients continue to use cycloplegic and steroids due to recurrence of pain on stopping the medicines, in spite of normal IOP. The ocular pain may be due to cyclitis and ciliary muscle spasm. Phthisis bulbi occurred in two eyes (5.9%) but patients were free from symptoms. The overall success rate was approximately 94%. Ciliary body destruction is a treatment reserved for eyes that does not respond to other forms of surgical or medical treatment.

Ciliary body destruction has been performed with many techniques, including ciliary body excision, penetrating cyclodiathermy, Cyclo-cryotherapy, microwave cyclodestruction, and trans-scleral and endoscopic cyclophotocoagulations. There are considerable differences in efficacy and complication rates between these different procedures^{1,6-10}. Among these methods, Cyclo-cryotherapy is noninvasive, Simple and very economical to treat uncontrolled IOP in eyes of patients with refractory glaucoma. However, success rates vary widely from 34% reported by Krupin et al⁵ to 92% reported by Bellows and Grant¹¹ After performing Cyclo-cryotherapy on 68 eyes in 64 patients, Benson and Nelson¹² reported a 29.4% success rate. Hennekes and Belgrado¹³ reported a 58.3% success rate from 56 cases, while Goldenberg-Cohen et al¹⁴ achieved a 60.5% success rate from 38 cases. Complications that may develop after performing Cyclo-cryotherapy include temporary IOP increase, uveitis, pain, hyphema, choroidal detachment, vitreous hemorrhage, anterior segment ischemia, subretinal fibrosis, subluxated lens, vision loss, low IOP, and phthisis bulbi. Some of the most serious complications include vision loss, low IOP, and phthisis bulbi. Benson and Nelson¹² reported phthisis bulbi in 11.8% of their cases (follow-up range of 2.6 to 6.3 years), while Caprioli et al.¹⁵ reported 12% and 6% of their patients developed phthisis bulbi after Cyclo-cryotherapy was performed in 360 degrees and 180 degrees, respectively (follow-up period of 29 months for both therapy protocol). In 1998, Heuring et al.¹⁶ reported a 6.7% rate of phthisis bulbi development in 76 eyes from 75 patients (follow-up range of 12 to 36 months). The

success rate of this study (94%) was higher than that of previous studies. Our study mean follow-up time was 12 months. Because our study included only four Cyclo-cryotherapy applications in each quadrant, we had fewer complications than other studies. We avoided other complications (vision loss) because we only selected blind patients. With these results, we conclude that four Cyclo-cryotherapy applications in all quadrants are effective to control IOP in blind painful refractory glaucoma. Cyclo-cryotherapy decreases aqueous production by damaging the ciliary epithelium with a freezing technique and cut off the vascular supply to the ciliary body¹⁷. Upon completion of Cyclo-cryotherapy, the blood supply in the ciliary epithelium and ciliary body is reduced, resulting in reduction of aqueous fluid production. The effectiveness of Cyclo-cryotherapy is dependent on the tissue temperature at the moment of performing the procedure. Intracellular ice crystals begin to form at temperatures below -15°C . To induce permanent cell damage by intracellular changes, a freezing time of 30 seconds or longer is necessary.

For most cases, a 60-second freezing time at -80°C has been found to be optimal^{15,18,20}. According to previous studies, performing cryotherapy on 180° or more of the eye at once is not recommended, and application to the 3-o'clock and 9-o'clock positions, where the long posterior ciliary artery is located, should be avoided^{11,12}. These are recommendations from the association of Cyclo-cryotherapy with the development of complications, such as phthisis bulbi. According to that study, a mean IOP reduction of 38.5 mmHg was achieved at the time of the last follow-up, and 19 out of the total 20 had an IOP of 21 mmHg or lower at their last follow-up.

In our study, most common type glaucoma was neovascular glaucoma in 76.5% (26 eyes), while neovascular glaucoma accounted for 51% of cases in the study by Brindley and Shields²⁰ and only 21% of the cases reported by Caprioli et al.¹⁵ Because of the natural history of neovascular glaucoma and its poor prognosis, success rates following treatment are lower and the recurrence and retreatment rates are higher than for other types of glaucoma^{12,16}. Benson and Nelson¹² reported that Cyclo-cryotherapy rendered 71.4% of painful eyes, comfortable despite poor prior IOP control. They suggested that pain relief from Cyclo-cryotherapy was not due solely to pressure control. In this study, relief from ocular pain and headaches was achieved in all cases. Four patients continue to use cycloplegic and steroids due to recurrence of pain on stopping the

medicines, in spite of normal IOP. The ocular pain may be due to cyclitis and ciliary muscle spasm.

In summary, this simple, noninvasive, and very economical Cyclo-cryotherapy results in good intra ocular pressure control and relief of pain in refractory absolute glaucoma there by reducing the agony of poor rural patients. We selected subjects only with refractory absolute glaucoma eyes and no vision, leading to a possibility of selection bias. Our study includes a small number of subjects, which decreases our statistical power. We recommend confirmation of the reliability of our results with well-designed studies which have a control groups.

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Conflict of Interest

We are here by declared that, the present study conducted on prospective basis. During the study period we have not been supported financial resource from private or government agency.

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