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ORIGINAL ARTICLE

Role of laser peripheral iridotomy and treatment outcomes in patients of pigment dispersion syndrome, pigmentary ocular hypertension, and pigmentary glaucoma in North Indian population

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Abstract

Aim: This study aims to study the effectiveness of laser peripheral iridotomy and other treatment modalities in reducing intraocular pressure (IOP) in patients of pigment dispersion syndrome (PDS), pigmentary ocular hypertension (POH), and pigmentary glaucoma (PG).

Materials and Methods: Retrospective analysis of the records of patients diagnosed with PDS, POH, and PG was done in glaucoma clinic of tertiary eye care center. Patients of PG who underwent laser iridotomy (LI) were separately analyzed. Minimum follow-up was of 6 months.

Results: A total of 86 eyes of 43 patients were analyzed. Patients had a mean follow-up of 49.05 ± 49.68 months. There were 24 males and 19 females. The diagnosis was PDS in 24% (21/86) eyes, POH in 18% (15/86), and PG in 58% (50/86) eyes. Mean age was 51.5 ± 11.58 years, 52.42 ± 13.41 years, and 47.08 ± 17.81 years among PDS, POH, and PG group, respectively. LI was performed in 36.04% (31/86) eyes, of them 70.96% (22/31) eyes had PG. There was a significant difference in IOP before and after LI ($P < 0.05$) in all the groups. The number of antiglaucoma medicines (AGMs) also dropped significantly after LI ($P < 0.05$). There was no significant difference in IOP at final follow-up in LI-treated and no LI-treated PG group. Glaucoma surgery was required in 9.3% (8/86) eyes.

Conclusion: LI helps in reducing IOP and number of AGM in PG. Long-term prospective studies are required to evaluate the effectiveness of LI in PDS and PG.

Introduction

Pigment dispersion syndrome (PDS) and pigmentary glaucoma (PG) are two spectral ends of a pathological process characterized by the release and deposition of uveal pigment, particularly in the anterior chamber structures and the trabecular meshwork (TM).[1,2] This deposition of pigment may result in raised intraocular pressure (IOP) and optic nerve damage leading to PG.[3,4]

Various treatment options available for PG include antiglaucoma medications, laser iridotomy (LI), trabeculectomy with or without antimetabolites, and glaucoma drainage devices. According to the Campbell theory, the reverse pupillary block is a known etiopathology for causing PDS, especially in young male population.[5] The LI is hypothesized to alleviate the reverse pupillary block mechanism, leading to the equalization of the pressure between the anterior and posterior chambers. Moreover, this causes flattening of iris which reduces the irido-zonular contact, leading to decrease in the pigment release from the posterior iris surface.[6] However, the role of LI in preventing the development and progression of PG is not established as a mono or combination therapy.

PDS and PG have been studied at length among the Caucasians and have been reported from Latin America also. However, there is a paucity of literature on the natural course of this condition and its response to treatment modalities like laser

peripheral iridotomy from India. This study was carried out to have an insight into the treatment outcomes and effectiveness of LI in IOP reduction.

Materials and Methods

It was a retrospective case series recruiting patients of PDS, pigmentary ocular hypertension (POH), and PG, who presented to glaucoma clinic of our tertiary health care institute between January 2002 and June 2018, with follow-up of >6 months. The study was approved by the institutional review board. The patients were classified[1] into the following categories:

- PDS was diagnosed if two of the following inclusion criteria were present: Krukenberg's spindle [Figure 1], increased pigmentation of the TM [Figure 2] or other intraocular structures, radial slit-like transillumination defects in the midperipheral iris, without any signs of optic nerve damage or visual field defects.
- POH: PDS with elevated IOP (>22 mmHg) and no glaucomatous optic neuropathy.
- PG: Glaucomatous optic neuropathy and visual field changes in association with PDS.

Patients with other pathology of pigment release such as post-trauma, uveitis, pseudophakia, pseudoexfoliation, and other pathologies of decreased vision such as corneal opacity and retinal pathology were excluded from the study. Patients with follow-up of <6 months were excluded from the study. Information regarding age, gender, details of the ocular examination, and treatment were recorded for all patients. Informed written consent of each patient included in the study was obtained.

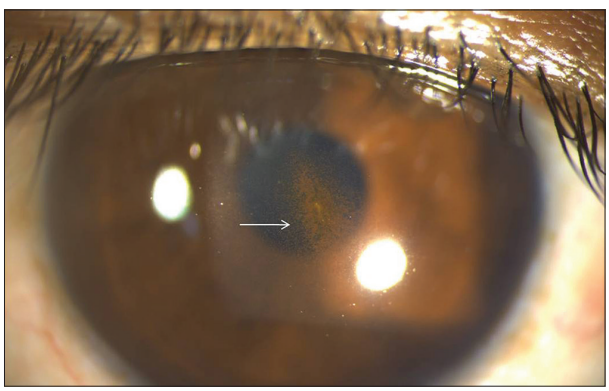

Figure 1: Pigment deposits on the endothelium layer of cornea (Krukenberg's spindle)

Figure 2: Gonioscopic image of inferior angle showing pigment around Schwalbe's line (Sampaolesi line), pigmented trabecular meshwork, and scleral spur

IOP at presentation and during follow-up, number of antiglaucoma drugs at presentation and during follow-up, and details of any intervention such as laser peripheral iridotomy (LI), glaucoma filtration surgery, and laser trabeculoplasty performed were extracted from records. Clinical details were reviewed with respect to IOP by Goldmann applanation tonometer (Haag-Streit AG, Bern, Switzerland), Gonioscopy (with Zeiss 4-mirror goniolens), optic nerve head examination, and visual field analysis (with Swedish interactive threshold algorithm strategy) (Humphrey Instruments Inc., San Leandro, CA).

Neodymium:yttrium-aluminum-garnet (Nd:YAG) LI was performed with Abraham lens. Trabeculectomy with Mitomycin-C (0.2 mg/ml) was done in patients with PG whose IOP was uncontrolled on maximum IOP lowering medication. One patient with advanced field defect and uncontrolled IOP on maximum IOP lowering medication underwent glaucoma drainage device implantation (Aurolab aqueous drainage implant).

The primary outcome measure was the difference in IOP at presentation and at final follow-up in the eyes which underwent LI and in those in which no LI was performed. The secondary outcome measure was, change in the number of antiglaucoma medications and requirement for surgical intervention for control of IOP.

The statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS Version 22, IBM, New York, USA). Normality of the quantitative data was checked by Kolmogorov–Smirnov test. Distributions were summarized using proportions, mean ± standard deviation, or medians/interquartile range as appropriate. The change in parameters such as IOP at baseline and final visit was analyzed using the Wilcoxon signed-rank test. $P < 0.05$ is considered statistically significant. We have not aimed to perform intergroup analysis of LI versus non-LI eyes.

Results

A total of 86 eyes of 43 patients were analyzed. There were 24 males and 19 females. The diagnosis was PDS in 24% (21/86) eyes, POH in 18% (15/86), and PG in 58% (50/86) eyes. Mean age at the time of presentation was 51.5 ± 11.58 years, 52.42 ± 13.41 years, 47.08 ± 17.81 years among PDS, POH, and PG group, respectively. A family history of glaucoma was present in 14% (6/43) patients. Of these six eyes with positive family history, five were diagnosed as PG (83.3%) while one patient (16.7%) presented with POH. The patients had a mean follow-up of 49.05 ± 49.68 months.

The mean IOP at presentation was higher in POH group followed by PG and PDS groups as mentioned in Table 1. There was a significant reduction in IOP in the POH and PG group ($P < 0.05$ at last follow-up [Table 1]. Topical antiglaucoma

Table 1: Mean intraocular pressure at presentation and last follow-up in all the three groups

Mean intraocular pressure	Pigment dispersion syndrome	Pigmentary ocular hypertension	Pigmentary glaucoma
At presentation	15±2.68	29±6.86	21±5.55
At last follow-up	15.14±2.49	16.93±3.45	13.96±3.82
P value	0.90	0.001	<0.001

Table 2: Mean intraocular pressure and number of medicines before and after laser iridotomy in all groups, i.e., pigment dispersion syndrome, pigmentary ocular hypertension, and pigmentary glaucoma

All groups	Baseline	Final follow-up	*P* value
Mean intraocular pressure	24±6.49	15.90±3.95	<0.001
Number of medicines	2.16±0.93	1.48±1.23	0.003

Table 3: Mean intraocular pressure and number of medication at baseline and final follow-up in both the groups of pigmentary glaucoma patients

Pigmentary glaucoma patients	Baseline	Final follow-up	*P* value
Group 1 (with laser iridotomy)			
Intraocular pressure	22±4.35	15.04±4.16	<0.001
Antiglaucoma medication	1.86±0.77	1.40±1.25	0.05
Group 2 (without laser iridotomy)			
Intraocular pressure	20±6.21	13.10±3.37	<0.001
Antiglaucoma medication	2.03±1.10	1.46±1.23	0.03

medications were used for treatment in 77.9% (67/86) eyes at presentation and decreased to 61.62% (53/86) last follow-up. LI was performed in 36.04% (31/86) eyes, of them 70.96% (22/31) eyes had PG. Cataract extraction was done in 10 eyes, of them two had also undergone LI.

Glaucoma surgery was required in 9.3% (8/86) eyes for IOP control. All the eight eyes which required surgery belonged to the PG group. Seven eyes underwent trabeculectomy. One eye underwent glaucoma drainage device implantation as a primary procedure to avoid the risk of wipeout phenomenon in view of the advanced visual field defect. Of these eight eyes, two eyes had preexisting LI.

Response to LI

LI was performed in two patients with PDS, seven patients with POH, and 22 patients with PG. Of the 31 eyes that underwent LI, 70.96% (22/31) eyes required additional treatment for control of IOP during the follow-up period. There was a significant difference in IOP before and after LI ($P < 0.05$). The number of antiglaucoma medicines (AGM) also dropped significantly after LI ($P < 0.05$) as mentioned in Table 2.

Patients with PG, i.e., 58% (50/86) eyes were analyzed separately. There were 17 males and 11 females in the PG group. Mean IOP at presentation and last follow-up was 21 ± 5.55 and 13.96 ± 3.82, respectively, in the PG group. Of 50 eyes, 22 eyes underwent LI (Group1) and 28 were managed without LI (Group 2). There was a significant difference in baseline and final follow-up IOP in both the groups. In LI-treated group, IOP decreased from 22 ± 4.35 to 15.04 ± 4.16 ($P < 0.05$) while in a group with no LI, IOP decreased from 20 ± 6.21 to 13.10 ± 3.37 ($P < 0.05$) at final follow-up. There was no significant difference in IOP at final follow-up in LI-treated and no LI-treated group. The number of AGM also decreased significantly at final follow-up [Table 3]. AGMs were used in 96% (48/50) PG eyes. Iridotomy and medications were used for treatment in 42% (21/50) PG eyes. After iridotomy, seven PG eyes could be weaned off drugs.

Discussion

The diagnosis of PDS and PG is often being missed during routine evaluation due to the subtle presenting signs. Various risk factors such as male gender, Afro-american race, high myopia, and Krukenberg spindles increase the incidence of conversion from PDS to PG.[2]

LI is a commonly performed procedure in our setup in patients with angle closure disease (ACD). However, the role of LI is not well established in the spectrum of PDS and PG as it is in ACD, due to the rarity of the condition. In our study, the patients with PG who underwent LI, i.e., 22 eyes of 50 eyes, have significant ($P < 0.05$) reduction in IOP at final follow-up; however, we could not found a significant difference in IOP at final follow-up among LI-treated and no LI-treated patients with PG. However, our study has found a significant reduction in the number of antiglaucoma medication after LI, as discussed in results, seven patients could be weaned off drugs after LI. Hence, LI could be a beneficial adjunct in decreasing IOP and number of antiglaucoma medication, thereby decreasing the burden of putting antiglaucoma medication in patients with poor compliance.

Various studies have discussed the outcome of LI in patients with PG. In a randomized controlled trial of 21 patients, Gandolfi and Vecchi[7] showed that Nd:YAG LI reduced the incidence of ocular hypertension (OHT) in PDS, but patients with PG were not included in the study. This study concluded that IOP difference between treated and untreated eyes is inversely related to the age of the patient and LI is more beneficial in young patients with active pigment release. Reistad *et al.*[8] found a significant decrease in IOP in LI-treated eyes versus non-treated eyes of 46 patients with PG in a 2-year follow-up study, but the IOP in 14 patients who were followed up for <2 years was high in LI-treated eyes than non-LI-treated eyes. This study concluded that high baseline IOP in treated eyes could have an

account for apparent treatment effect after LI. Hence, they could not found the benefit of LI in a long-term IOP control in patients with PG and influence of age was also not taken into account as 36% of patients were >40 years in the study. Scott *et al.*[9] discussed the benefits of laser peripheral iridotomy in preventing progression from PDS with OHT to PG in a 3-year follow-up study and found no significant difference in both LI-treated and no LI-treated groups. The patients included in the study have IOP >have IOPr we know persistently raised IOP can damage the TM so no benefit of LI was found in preventing conversion to PG. LI helps to equalize the pressure between anterior and posterior chamber and will have no benefit if TM will already be damaged. In old age due to increased ocular rigidity with less pigment release[10] and already damaged TM in PG patients, so less benefit of LI is seen if pigment release is not a contributory factor to glaucoma progression.[7] Similarly, in this study, the patients showing VF conversion were slightly older than non-converters in either arm of the study. According to Gandolfi *et al.*,[11] reduction in IOP elevation was found to be same in LI-treated high-risk eyes (positive phenylephrine test) and in low-risk eyes in which LI was not done in a 10-year follow-up study in PDS patients, without involving POH and PG patients. Hence, various studies discussed above have included either PDS patients only or PG patients [Table 4]. We tried to include all the three groups, i.e., PDS, POH, and PG in our retrospective analysis to see the effect of LI in reducing IOP and antiglaucoma medication.

Karickhoff[12] described flap valve mechanism of iris against the anterior lens surface, allowing forward flow of aqueous which acts by pushing the peripheral iris backward against the lens zonules by increasing anterior chamber pressure, thereby causing a further shedding of pigment. Laser peripheral iridotomy helps to equalize the pressure in both chambers by restoring the planar configuration of the iris, thus, preventing the further pigment dispersion by reducing the irido-zonular contact.

LI may not be as effective if pigment release is no longer a contributory factor to progression to glaucoma.[9] Richardson[13] proposed two pathogenic stages to explain the PDS without glaucoma and its conversion to PG. Trabecular endothelial cells help to remove pigment granules from the TM by phagocytosing them.[14-16] In the irreversible stage of disease, IOP rises due to loss of pigment-laden cells, the fusion of lamellae and loss of intertrabecular spaces, thus any intervention at this stage like Nd:YAG LI, may be ineffective.[13,15] Hence, identification of disease process may help to decide whether LI will help to control IOP or not.

Other age-related factors such as decrease pigmentation[10] and accommodation[17] and increase in ocular rigidity[18] should also be considered while interpreting disease progression. In our study, the number of medication at presentation and last follow-up in patients >40 years of age (58/86 eyes) was 1.70 ± 1.27 and 1.13 ± 1.26, respectively, and in patients <40 years of age (28/86 eyes) was 1.5 ± 1.07 and 1.39 ± 1.25, respectively. The decrease in the number of medicines at last follow-up, in patients >40 years of age may be attributed to burnt out nature of the disease.

Table 4: Outcome of various studies and their inclusion criterion

Study	Number of patients	Age	Type of patients	Race	Effect on IOP reduction and conclusion	Limitations	Follow-up (years)
Gandolfi and vecchi[7]	21 (42 eyes)	19–60	PDS	-	IOP elevation in 1 (4.7%) treated versus 11 (52.3%) untreated eyes and LI is less beneficial for IOP reduction after 40 years	-	2
Reistad *et al.*[8]	60 (46 with >2 years FU were analyzed)	38±9.9	PG	Caucasian	Mean IOP reduction -2.07±1.415 (P = 0.005)	Baseline IOP was high	2
Scott *et al.*[9]	116 (57 - LI and 59 in untreated eyes)	48.3 in LI, 49.1 in untreated eyes	PDS and OHT	110 - Caucasian, 5 - Indian/Asian, 1 - Afro-Caribbean	No benefit of LI to prevent progression from PDS with OHT to PG	Baseline IOP >21	3
Gandolfi *et al.*[11]	72 (117 eyes)	34 in high- and 31 in low-risk eyes	PDS	-	Same level of IOP reduction after LI in both high- and low-risk eyes after 10 years	-	10

OHT: Ocular hypertension, IOP: Intraocular pressure, PDS: Pigment dispersion syndrome, PG: Pigmentary glaucoma, LI: Laser iridotomy, PDS with elevated IOP (>22 mmHg) and no glaucomatous optic neuropathy and VF changes are termed as pigmentary ocular hypertension (POH) or PDS with ocular hypertension. Hence, these both terms, i.e., PDS with ocular hypertension and POH are synonymously used

Conclusion

Our study demonstrates that LI could be a beneficial adjunct in the treatment of patients with PG in terms of the reduction of IOP and number of medications required for disease stabilization. Larger and long-term prospective studies are required to give the final answer on the effectiveness of this safe and cost-effective procedure in patients with PDS and PG.

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