Pentacam Based Quantification of the Changes in Anterior Chamber Morphology Following Laser Peripheral Iridotomy in Primary Angle Closure Suspects – A Novel Approach

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Abstract

Aim: To study and compare the clinical parameters pre and post Nd: YAG Laser Peripheral Iridotomy (LPI) in Primary Angle Closure Suspect (PACS) patients

Study design: Hospital based prospective observational study

Methods: Our study included 60 eyes of 30 PACS patients who underwent Nd: YAG LPI. Parameters like anterior chamber depth and angle using Pentacam, Intraocular pressure using Goldmann Applanation tonometer and Gonioscopy using Sussman 4-mirror goniolens were compared before and after LPI.

Results: The mean ACD significantly improved from 1.91 ± 0.2 mm before LPI to 2.01 ± 0.23 mm, 30 minutes post LPI and 2.06 ± 0.22 mm, one week after LPI. The mean ACA significantly improved from 24.4 ± 4.02° before LPI to 27.55 ± 3.74°, 30 minutes after LPI and 28.77 ± 4.09°, one week after LPI. There was a statistically significant decrease in mean IOP at 30 minutes and one week after LPI as compared to before LPI. Twenty-two (36.67%) eyes had IOP spike at five minutes after LPI (Mean IOP spike was 2.64 ± 0.95 mm Hg). The mean Shaffer grade, based on gonioscopy findings, also increased significantly after LPI.

Conclusions: We conclude that Pentacam is a useful tool for quantifying the anterior segment changes occurring after LPI. The ACD and ACA increase significantly after LPI. Also, the IOP decreases significantly one week after LPI in PACS patients.

Keywords: Primary Angle Closure Suspects, Laser Peripheral Iridotomy, Nd: YAG, Intraocular pressure, Pentacam, Anterior chamber depth, Anterior chamber angle

Introduction

Glaucoma is a chronic progressive multifactorial optic neuropathy resulting in loss of visual function. It is the leading cause of irreversible blindness worldwide. It has been predicted that by 2020, around 21 million people worldwide will have Angle Closure Glaucoma, of which 87.6% will be Asians.1 The spectrum of Primary Angle Closure ranges from Primary Angle Closure Suspect (PACS), Primary Angle Closure (PAC) and Primary Angle Closure Glaucoma (PACG).2 Primary Angle Closure Suspect is defined as greater than or equal to 180 degrees irido-trabecular contact (ITC), normal intraocular pressure [IOP], no optic nerve damage and no peripheral anterior synechiae.3 Studies revealed that 22% of subjects with PACS may progress to PAC and that 28.5% of PAC subjects may develop PACG within five years if no treatment is prescribed.4 Laser Peripheral Iridotomy (LPI) is the preferred approach of prophylactic management of angle closure.[5] Nd:YAG lasers are more commonly used for LPI with pulsed delivery and cause photodisruption. The basic principle of Nd: YAG LPI is the creation of a hole in the peripheral iris, which allows equalization of the pressure between the posterior and the anterior chamber, deepening of the anterior chamber, and opening of the anterior chamber angle. The purpose of this study is to evaluate and quantify the changes in anterior segment morphology and IOP after Nd: YAG LPI. We implemented a novel approach by using Pentacam anterior segment analyser to quantify the anterior segment changes.

Methods

This was a hospital based prospective observational study. Specified outcome parameters were compared before and after the procedure in patients undergoing Nd:YAG LPI as part of their routine care. Institutional review board approval was obtained and the study adhered to the tenets of the Declaration of Helsinki. Sample size was calculated assuming the mean IOP before procedure as 14.4 and after procedure as 11, with a common standard deviation of 5 (As per the study by He et al.). The other parameters considered for sample size calculation were 90% power of study and 5% alpha error. As per the above mentioned parameters, the required sample size was 54 eyes. To account for 10% loss to follow up, a total of 60 eyes were included in the study. The following formula was used for sample size calculation.

\[ N = \frac{(u + v)^2(\sigma_1^2 + \sigma_0^2)}{(\mu_1 - \mu_0)^2} \]

Where,

- \( N \) = Sample size
- \( \mu_1 - \mu_0 \) = Difference between the means (206.03-201.63= 4.4)
- \( \sigma_1, \sigma_0 \) = Standard deviations = 6

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Primary Angle Closure suspect patients who underwent Nd:YAG LPI who were willing to participate in the study were included. After obtaining an informed consent from the patient/attendant, detailed history was taken. Any family history of glaucoma was noted. Ocular examination included Visual acuity using Snellen’s charts, detailed anterior segment and undilated posterior segment examination, Intraocular pressure (IOP) using Goldmann Applanation Tonometer, anterior chamber depth (ACD) and angle (ACA) using Pentacam and Gonioscopy using Sussman four mirror Goniolens and graded using Shaffer grading. Pilocarpine 2% drops were instilled four times at intervals of 10 minutes, till the pupil constricted. Nd:YAG LPI was performed using Abraham Laser Iridotomy lens. Supertemporal quadrant was usually preferred for LPI. An area of thin iris or a large crypt was chosen and laser delivered with energy levels starting at 3 mJ, based on iris parameters. Intraocular pressure was measured within five minutes of procedure. Then patient was given 0.15% Brimonidine, 0.5% Loteprednol and antibiotic eye drops. Intraocular pressure was measured again at 30 minutes after LPI. Patient was asked to continue 0.5% Loteprednol drops four times a day till one week and come for follow up. Patient was asked to continue 0.5% Loteprednol drops two times a day for the next week.

The parameters measured and assessed for the study were: a) IOP: before LPI and at five minutes, 30 minutes and one week post LPI; b) ACD: before LPI, at 30 minutes, one week post LPI; c) ACA: before LPI, at 30 minutes post LPI and one week post LPI; d) Gonioscopy before LPI and one week post LPI; e) Anterior chamber reaction at five minutes and one week post LPI; f) Any complications that occurred during procedure; g) total energy used.

Statistical Methods
Intraocular pressure, anterior chamber depth and angle and gonioscopy findings in different quadrants were the main outcome variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots. All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-Wilk test was also conducted to assess normal distribution. Shapiro-Wilk test p value of >0.05 was considered as normal distribution. The change in the quantitative parameters, before and after the intervention was assessed by paired t-test (in case of two time periods) or one way repeated measures ANOVA (in case of comparison across more than 2 time periods). IBM SPSS version 22 was used for statistical analysis. The calculated sample size is met and the power of the study is 90%.

Results
A total 60 eyes of 30 patients who met the inclusion criteria were included in the analysis. The mean age was 59.13 ± 9.05 years. Minimum age was 36 years and maximum age was 80 years. (95% CI 56.80 to 61.47). Among the study population, 30 (50%) were right eyes and 30(50%) were left eyes. Fifty-four (90%) participants were female and remaining six (10%) participants were males. Only four (6.67%) participants had a family history of glaucoma and 56 (93.33%) participants did not have a family history of glaucoma.

The mean IOP was 17.93 ± 2.75 mm Hg before LPI, 17.67 ± 3.3 mm Hg at five minutes after LPI, 16.67 ± 3.35 mm Hg at 30 minutes and 15.1 ± 2.48 mm Hg at one week after LPI. There was no significant decrease in mean IOP at five minutes after LPI compared to mean IOP before LPI. However, there was a statistically significant decrease in mean IOP at 30 minutes and one week after LPI as compared to mean IOP before LPI (Table 1). Among the study population, 22 (36.67%) eyes had IOP spike at five minutes after LPI and 38 (63.33%) did not have an IOP spike. Among the eyes that had an IOP spike (22 eyes) after LPI, the mean spike in IOP was 2.64 ± 0.95. The maximum IOP spike was 4 mm Hg.

The mean ACD significantly improved from 1.91 ± 0.2 mm before LPI to 2.01 ± 0.23 mm, 30 minutes post LPI and 2.06 ± 0.22 mm, one week after LPI (Table 2). The mean ACA significantly improved from 3.74°, 30 minutes after LPI and 28.77 ± 4.09°, one week after LPI (Table 3).

Table 1: Comparison of mean Intraocular Pressure at different follow-up periods (N= 60)

| Follow-up periods | Intraocular Pressure before PI (Means STD) (in mm of Hg) | Mean Differe | 95% CI of mean difference | P-value |
|------------------|----------------------------------------------------------|--------------|---------------------------|---------|
| Before PI        | 17.93 ± 2.75                                             |              |                           |         |
| After 5 min      | 17.67 ± 3.3                                              | 0.27         | 0.40 0.94                 | 0.428   |
| After 30 min     | 16.67 ± 3.35                                             | 1.27         | 0.72 1.81                 | <0.001  |
| After 1 week     | 15.1 ± 2.48                                              | 2.83         | 2.38 3.28                 | <0.001  |

STD: Standard Deviation; CI: Confidence Interval; mm of Hg: Millimeters of mercury

Table 2: Comparison of mean Anterior chamber depth at different follow-up periods (N= 60)

| Follow-up periods | Anterior chamber depth (Mean± STD) (in mm) | Mean Difference | 95% CI of mean difference | P-value |
|------------------|-------------------------------------------|----------------|---------------------------|---------|
| Before PI        | 1.91 ± 0.2                                 | 0.10           | 0.07 0.13                 | <0.001  |
| After 30 min     | 2.01 ± 0.23                                | 0.15           | 0.12 0.18                 | <0.001  |
| After 1 week     | 2.06 ± 0.22                                | 0.15           | 0.12 0.18                 | <0.001  |

STD: Standard deviation; CI: Confidence Interval; mm: millimeters
The mean Shaffer grade, based on gonioscopy findings, significantly increased in all angles (Table 4). The correlation of the Shaffer grades before LPI to one week after LPI is elaborated in Table 5, 6. In terms of complications, two (3.33%) eyes had Corneal burn after LPI and 11 (18.33%) had iris bleeding with no to minimal hyphaema. At five minutes after LPI, seven (11.67%) eyes had grade 1 flare in anterior chamber, 42 (70%) had grade 2 flare and remaining 11 (18.33%) had grade 3 flare. At one week after LPI, the anterior chamber was quiet in all eyes. The mean total energy used for LPI was 13.85 ± 6.05 mJ. Minimum energy used was 6 mJ and maximum energy was 40 mJ. (95% CI 12.29 to 15.41).

| Follow-up periods | Anterior chamber angle (Mean± STD) (in degrees) | Mean Difference | 95% CI of mean difference | P-value |
|-------------------|-----------------------------------------------|-----------------|--------------------------|---------|
|                   | Mean | Difference | Lower | Upper |                       |        |
| Before PI         | 24.4 ± 4.02 |          |       |       |                       | <0.001 |
| After 30 min      | 27.55 ± 3.74 | 3.15 | 2.47 | 3.82 | <0.001 |
| After 1 week      | 28.77 ± 4.09 | 4.37 | 3.56 | 5.18 | <0.001 |

STD: Standard deviation; CI: Confidence interval

| Shaffer grade in superior angle before PI | Shaffer grade in superior angle 1 week after PI |
|------------------------------------------|-----------------------------------------------|
| 0(N=44)                                  | 1 (2.3%) 18 (40.9%) 25 (56.8%)                |
| 1(N=10)                                  | 0 (0%) 2 (20%) 8 (80%)                        |
| 2(N=6)                                   | 0 (0%) 1 (16.7%) 5 (83.3%)                    |

| Shaffer grade in inferior angle before PI | Shaffer grade in inferior angle 1 week after PI |
|------------------------------------------|-----------------------------------------------|
| 0(N=32)                                  | 4 (12.5%) 28 (87.5%)                          |
| 1(N=10)                                  | 2 (20%) 8 (80%)                               |
| 2(N=18)                                  | 2 (11.1%) 16 (88.9%)                          |

Table 4: Comparison of mean Shaffer grade before LPI and 1 week after LPI in all angle (N=60)

| Angle            | Parameter | Mean ± STD (Shaffer grade in superior angle) | Mean Difference | 95% CI of mean difference | P-value |
|------------------|-----------|---------------------------------------------|-----------------|--------------------------|---------|
| Superior angle   | Before PI | 0.37 ± 0.66                                 | -2.23           | -2.44                    | -2.03   | <0.001 |
|                   | After 1 week | 2.6 ± 0.59                                    |                 |                          |         |       |
| Inferior angle   | Before PI | 0.77 ± 0.89                                  | -2.10           | -2.35                    | -1.85   | <0.001 |
|                   | After 1 week | 2.87 ± 0.34                                   |                 |                          |         |       |
| Nasal angle      | Before PI | 0.3 ± 0.59                                   | -2.35           | -2.55                    | -2.15   | <0.001 |
|                   | After 1 week | 2.65 ± 0.48                                   |                 |                          |         |       |
| Temporal angle   | Before PI | 0.28 ± 0.58                                  | -2.47           | -2.63                    | 2.30    | <0.001 |
|                   | After 1 week | 2.75 ± 0.44                                   |                 |                          |         |       |

STD: Standard deviation; CI: Confidence interval

Discussion

Laser Peripheral Iridotomy results in a reduction of IOP in PACS due to widening of angle and reduced resistance to the flow of aqueous humour. A possible mechanism for this lower IOP in wider angles may be the result of greater tension on the trabecular beams, resulting in wider pores and increasing outflow. This hypothesis is supported by evidence of a fall in IOP after cataract surgery and pilocarpine treatment. In our study we found a statistically significant decrease in IOP of 2.83 mm Hg at one week post LPI. Our findings are similar to Mingguang He et al, who reported that IOP decreased significantly by an average of 3 mm Hg in treated eyes at two weeks. In another study, IOP was found to decrease by 2.3 mm Hg six months after LPI. Caballero et al reported that mean IOP decreased by 2.5 mm Hg one month after LPI in Primary angle closure spectrum. In addition, Fleck et al, Krupin et al, Lewis et al and Li et al reported a decrease in mean IOP after LPI similar to our findings.

Laser Peripheral Iridotomy can cause an acute and transient post-laser rise in IOP in some patients. The incidence of this IOP spike can vary from 5.7% to 40% after an LPI. These transient pressure elevations occur most commonly in...
the first three hours after LPI. To date, no consistent risk factors have been identified for these post-LPI IOP spikes, nor has any consistent approach been followed in their management. One of the mechanisms postulated for this IOP spike is that the use of Nd:YAG lasers results in relatively more bleeding and pigment dispersion and the deposition of debris from blood and pigment in the juxta-canalicular trabecular meshwork may impede aqueous outflow and cause IOP elevation. Another possible mechanism postulated that an IOP spike after LPI may be associated with both increased aqueous production mediated by prostaglandin release and decreased outflow facility resulting from debris, denatured proteins, or cells. Many ophthalmologists use ocular hypotensive medications as pre-treatment before LPI to reduce the incidence of IOP spikes. In our study, the mean IOP remained more or less the same and there was no overall spike in the mean IOP at five minutes post LPI compared to before LPI. However, we found a mean IOP elevation of 2.64 ± 0.95 mm Hg at five minutes after LPI in 36.67% of our patients. An IOP spike of ≥5 mm Hg was not seen in any of our patients. No other study had measured IOP immediately after LPI. In contrast to our study, Yuzhen Jiang et al reported that, of the 734 treated eyes of PACS, an IOP spike of ≥8 mmHg occurred in 72 eyes at one hour after LPI. They also reported a mean increase in IOP of 1.9 ± 4.1 mm Hg one hour after LPI in their patients. The amount of laser energy used in their study was much higher compared to our study. They also found that the total laser energy used was significantly higher in eyes with IOP spike (205.8±185.2 mJ) than those without (146.0±118.5 mJ). But, several other studies reported no correlation between amount of laser energy used and post LPI IOP elevation. We also could not find such a correlation. Shani et al reported a series of 212 eyes of Angle closure glaucoma treated by Nd:YAG laser without pre-treatment with any pressure-lowering medication. Despite the lower energy applied (26.9 ± 28 mJ) in their study, 21.2% and 2.8% of cases had an IOP elevation of more than 10 mmHg and 20 mmHg respectively. However, compared with other studies in which eyes were pre-treated with ocular hypotensive agents found no correlation between amount of laser energy used and post LPI IOP elevation. It is also possible that the incidence of IOP rise in this series was somewhat higher. Lewis et al studying the in vivo anterior segment morphology after LPI using Pentacam in 20 eyes post LPI showed similar results. In our study compared to other studies may be attributed to instillation of one drop of 0.15% Brimonidine after LPI after the five minutes IOP measurement. The Pentacam is capable of evaluating the anterior chamber, from the surface of the cornea to the posterior surface of the lens, with a rotating photographic camera which works on the Scheimpflug principle. The rotating Scheimpflug camera in Pentacam allows precise visualization of the angle structure and the scleral spur. A-scan, anterior segment ocular coherence tomography (AS-OCT) and ultrasonic biomicroscopy (UBM) all have been used to observe the morphological changes of anterior chamber of PAC patients after LPI. However, when compared to Pentacam, AS-OCT and UBM only obtain cross-sections of the anterior segment, and this cannot provide the full information of the 3-D eyeball. Cristina López-Caballero et al studied anterior segment morphology after LPI using Pentacam in 20 eyes and found that mean ACA increased significantly by 1.99° one month after LPI and central ACD increased significantly from 1.79 mm (SD 0.22) before LPI to 1.85 mm (SD 0.21) one month after LPI. Alireza Esmaeili et al studied anterior segment parameters using Pentacam in 48 eyes having PACS who underwent LPI. They found that the mean ACA increased significantly by 0.87° one month after LPI. However, the rise in the ACD was not statistically significant. Shuning Li et al studied the anterior segment morphology after LPI using Pentacam in 37 eyes having a spectrum of Primary angle closure. They found that ACA widened by 2.6° after LPI in 9 o’clock direction, and by 2.14° in 3 o’clock direction. No statistically significant change occurred in ACD. Our results were similar to previous studies as mean ACA significantly increased by 4.37°, one week after LPI. In contrast to some studies, we found that the mean ACD significantly increased by 1.5 mm one week after LPI. Several studies have also shown that angle width based on Shaffer grading increases significantly after LPI. Cristina López-Caballero et al reported that mean Shaffer grade increased significantly in all angles after LPI. Alireza Esmaeili et al reported that mean Shaffer grade increased significantly by 0.54 in superior angle, 0.65 in inferior angle, 0.50 in nasal angle and 0.44 in temporal angle. In our study also, we have found a significant increase in Shaffer grade in all angles after LPI. The common complications that can occur after Nd:YAG LPI include iris bleeding/hyphaema, rise in intraocular pressure, corneal burn, and injury to anterior lens capsule. Fleck et al reported that 58% of their patients had iris bleeding after LPI but no patient had macro-hyphaema. Yuzhen Jiang et al reported iris bleeding in 40.3% of their patients who had a post LPI IOP spike and in 30.7% of patients who did not have a post LPI IOP spike. They also reported one case of corneal burn in 734 patients. Robin et al reported that 45% eyes treated with the Nd:YAG laser had bleeding from the iridotomy site and 35% eyes had focal non-progressive corneal opacities above the iridotomy site. In our study, 18.33% eyes had iris bleeding, resulting in no hyphaema to minimal hyphaema. This lesser incidence of iris bleeding in our study compared to other studies may be attributed to lesser amount of energy used. 3.33% eyes had corneal burn during LPI in our study. With careful focusing of the laser beam on the iris and use of Abraham iridotomy lens, this complication can be avoided. A limitation of our study was that the IOP at 30 minutes after LPI was influenced by using one drop of 0.15% Brimonidine, which decreases IOP. This could be a possible confounding factor. In all cases, Pilocarpine 2% drops were used before
LPI. The IOP measured before LPI was before instillation of Pilocarpine drops. The IOP measured at five and 30 minutes after LPI was therefore influenced by the effect of Pilocarpine, which has an effect on IOP. This could be a possible confounding factor.

Conclusions
We conclude that Anterior chamber depth and angle increases significantly after LPI. To the best of our knowledge, ours is the first study on Indian population which evaluated the changes in anterior chamber after LPI using Pentacam. We found that Pentacam is a very useful tool in quantifying the anterior segment changes occurring after LPI. It gives a numerical picture on how much the angle widens after LPI. Also IOP decreases significantly one week after LPI in PACS patients.

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