

“Diagnosis and management of primary angle closure glaucoma in a rural medical college” A prospective study

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Abstract

Diagnosis of primary angle closure disease (PACD) involves detailed and meticulous clinical evaluation coupled with prompt and balanced decision making. Primary angle closure type is more common amongst Asians. The magnitude of glaucoma blindness in the world is more, a considerably major part of which occurs in Asians with primary angle-closure disease. The alarming prevalence of PACD in Asians calls for clinical studies to be undertaken in Asian population to screen, diagnose, treat and document this preventable blinding condition. This prospective study has been undertaken to detect, diagnose and manage this disease with different modalities, when presented at different stages in a rural medical college in Malabar region of northern Kerala to diagnose and treat early to prevent ocular morbidity.

Keywords: Gonioscopy, Vanherics grading, Primary angleclosure glaucoma.

Aims and Objectives

1. To diagnose Primary Angle Closure Disease in patients ≥ 40 years of age attending hospital OPD in a rural medical college.
2. To manage the different presentation, categories of Primary Angle Closure Disease (PACD) with appropriate modalities and to evaluate the outcome

Materials and Methods

In the present study, 4017 patients of age ≥ 40 years attending the outpatient department of ophthalmology in a rural medical college of Malabar region of northern Kerala were assessed for the peripheral anterior chamber depth with the Van Herick's technique on slit-lamp examination. Eyes with peripheral anterior chamber depth of Van Herick's grade 0, I and II were included.

402 eyes of 215 patients were enrolled in the study.

Study Design: Hospital based prospective interventional study.

Study Period: The study spanned over a period of 16 months from November 2014 to February 2016.

Source of Data: Patients attending the Outpatient ophthalmology department (OPD)

Inclusion Criteria:

1. Narrow peripheral anterior chamber angles (Van Herick grades 0, I and II)
2. Age ≥ 40 years of age
3. Patients satisfying above criteria with/without coincidental immature cataract.
4. Patients satisfying above criteria who are already under medical treatment for primary angle closure glaucoma or who have undergone LPI (Laser Peripheral Iridotomy), but in whom IOP is not under control.

Exclusion Criteria:

1. Patients with intumescent/ mature/ hypermature cataract.
2. Leucomatous peripheral corneal opacities hindering proper Van Herick's grading.
3. Any condition leading to secondary angle closure glaucoma like neovascular glaucoma, uveitis, anteriorly displaced lens, pseudo exfoliation syndrome, etc.

Sample size (estimated minimum):

≥ 50 patients with Primary Angle Closure Disease
Minimum sample size was calculated from the formula:

1. Z^2Pq / d^2
2. Where;
3. $Z = 1.96$
4. $P =$ Frequency of prevalence
5. $q = 1-P$
6. $d = 0.05$ (margin of error)

Sampling Method:

Purposive sampling

The study adhered to the Declaration of Helsinki and approval was obtained from the ethical committee. Written informed consent for inclusion in the study and to undergo different modalities of treatment was obtained from all participants.

All patients attending the ophthalmic OPD during the study period were screened on slit lamp microscope with Van Herick's technique by experienced examiners. All further examination was carried out by the same examiners. All the patients selected based on the above mentioned criteria were further evaluated by taking detailed history and thorough ocular examination. Their demographic data was documented. Best corrected

visual acuity (BCVA) for all selected patients was recorded with Snellen's distance visual acuity chart.

Patients were examined on slit lamp microscope and the anterior segment findings documented in the prescribed proforma. Pupillary reaction was observed for both direct and consensual light reflexes.

Intra ocular pressure (IOP) was recorded with Goldmann applanation tonometer. For those who needed any treatment, IOP was checked at one week, one month and six months as well.

Gonioscopy was carried out in a semi-dark room with a Sussman four mirror handheld gonioscopes. IOP and gonioscopy on subsequent visits were performed by the same examiner as on the first visit. Anterior chamber angle width on dynamic gonioscopy i.e. indentation gonioscopy was estimated in four quadrants and recorded on a scheme described by Shaffer.

Following indentation gonioscopy, eyes were classified as either open angles or narrow angles. Eyes classified as open angles were not subjected to further examination or treatment. Eyes detected with narrow angles were classified further as Primary Angle Closure Suspects (PACS), Primary Angle Closure (PAC) or Primary Angle Closure Glaucoma (PACG) as per ISGEO classification.¹

The ISGEO classification:

1. Primary Angle Closure Suspect (PACS): An eye in which appositional contact between the peripheral iris and posterior trabecular meshwork is present or considered possible, in the absence of elevated IOP, peripheral anterior synechia (PAS), disc or visual field changes.
2. Primary Angle Closure (PAC): PACS with statistically raised IOP and/or primary PAS, without disc or Visual Field changes.
3. Primary Angle Closure Glaucoma (PACG): PAC with glaucomatous optic neuropathy and corresponding Visual Field damage.

According to the ISGEO recommendations, the suggested definition for PACS is non-visualization of the posterior trabecular meshwork for 270° or greater. However, 180° was taken as the cutoff in our study. This was in accordance with other epidemiological studies in India^{2,3} and recent recommendations by Foster et al⁴ Also, not advising treatment for the eyes with occludable angles between 180° and 270° appeared risky.

Central fundus examination and optic nerve head analysis was carried out by direct ophthalmoscope with undilated pupils. Cup Disc ratio and neuro-retinal rim characteristics were noted and recorded. On subsequent follow-ups, the optic nerve head was assessed by the same examiner who had recorded it on the first visit to avoid inter-observer variation. In patients who were found to have occludable angles, dilated fundus examination was carried out one month following the laser procedure after ensuring that the angles have opened.

In all the patients, A-scan biometry was performed with the biomedix A-scan machine, noting axial length of eye, anterior chamber depth and lens thickness. In the first 60 eyes who underwent LPI, post-LPI anterior chamber depth was also recorded at one month post laser.

Humphrey field analysis for the central 30° visual field was performed in eyes with cup disc ratio ≥ 0.6 , IOP ≥ 21 mm of Hg, CDR asymmetry of ≥ 0.2 or in presence of disc characteristics suggestive of glaucoma like NRR notching, RNFL wedge defects on red free filter, etc. A reliable visual field test was taken into account and the initial diagnoses were revisited and revised if necessary.

Patients with open angles on gonioscopy were not followed up further in the study.

All patients with PACS were advised prophylactic Laser Peripheral Iridotomy (LPI). Patients with PAC were advised therapeutic LPI. Few patients with higher IOP were started on topical anti-glaucoma medications as well. They were frequently followed up to monitor IOP.

Patients with PACS and PAC associated with visually significant cataract were advised cataract surgery with intraocular lens implantation. Surgery was performed and IOP was monitored in the post op period at one week, one month, two months and six months.

Patients with PACG were advised therapeutic LPI. Target IOP was determined for each patient and anti-glaucoma medication started to achieve the same. Frequent IOP monitoring was carried out. Repeat gonioscopy was performed after one month of LPI. If the synechial closure was found to be more than 180°, the necessity of performing modulated trabeculectomy was explained to the patients. In advanced cases of PACG having extensive PAS, the IOP control remained suboptimal with LPI and hence trabeculectomy with releasable sutures and use of anti-metabolites was advised and performed. Patients who were not willing to undergo trabeculectomy were continued on topical medications and reviewed frequently.

PACG patients with total glaucomatous optic atrophy were also included in the study. In painful eyes with no light perception, cyclocryodestructive procedure was advised. In painless eyes with no light perception, no active intervention was carried out, but the seeing fellow eye was evaluated, categorized into one of the PACD categories and treated accordingly. The severity of the condition was stressed upon particularly in such patients.

Patients who presented with symptoms of acute angle closure attack were treated medically. After treatment, if the corneal edema resolved enough for visualization of iris, a peripheral iridotomy was performed. In patients with hazy view of the iris, the procedure was postponed by a day or two and the patients started on oral acetazolamide (250 mg) twice daily with topical medications. After the acute attack

was resolved, the patient was evaluated with applanation tonometry, indentation gonioscopy, funduscopy, visual field analysis and biometry. The eyes were classified in the appropriate PACD category and managed accordingly. All these patients were advised to undergo prophylactic LPI in the fellow eye immediately.

LPI was performed with Nd:YAG laser (1064 nm). Patients were advised topical dexamethasone sodium phosphate (0.1%) four times a day and tapered over next 7 days to decrease the inflammation induced by the laser. Steroid drops were substituted with non steroidal anti-inflammatory eye drops like bromfenac sodium (0.09%) or nepafenac (0.1%) twice a day for four weeks along with topical antiglaucoma medication which was continued till 1-2 months following the procedure to avoid inadvertent raise in the IOP. Patients with high IOP were also given oral acetazolamide 250 mg/day in divided doses for a period of 5-7 days following LPI.

Trabeculectomy was performed in superonasal quadrant with a limbus based flap with the use of antimetabolite mitomycin C.

Follow-ups were scheduled after 1 week, 1 month and 6 months in PACS; after 1 week, 1 month, 3 months and 6 months in PAC and more frequently in PACG. During these visits and also at the end of 6 months, IOP, best corrected visual acuity and gonioscopic evaluation was done and participants were managed accordingly. In patients whom trabeculectomy was performed, findings at 6 month follow-up were considered for the study.

The data collected with respect to demographic factors like age and sex of the patients, the biometric measurements including axial length, anterior chamber depth and lens thickness were analyzed and compared amongst open angle group and PACD group, amongst PACS, PAC and PACG groups themselves and also between pre-LPI and post-LPI groups. The visual outcome and IOP response to LPI and/or medical line of management was statistically analyzed and compared with other studies.

Statistical Methods: All data were analyzed by a descriptive analysis. The Chi-Square Test procedure tabulates a variable into categories and computes a chi-square statistic. Chi-Square value was determined for all variables. Results for the different groups, i.e. open angles on gonioscopy and PACD, and PACS, PAC and PACG were analyzed by using crosstabs (contingency tab analysis). Its mean values were analyzed by Independent Sample T test. One way ANOVA procedure was used to analyze amount of hypermetropia, pre and post treatment IOP and biometry values. p value less than 0.05 were considered to be statistically significant. All the statistical

calculations were done through SPSS for windows (version 16.0)

Results and Analysis

In the present study, 4017 patients in the age group ≥ 40 years, attending the hospital OPD were screened.

Slit lamp examination was carried out and 402 eyes of 215 patients who had Van Herick's grade of 0, I and II were enrolled. The before mentioned inclusion and exclusion criteria were abided by.

On indentation gonioscopy, 149 eyes out of 402 eyes were diagnosed with primary angle closure disease (PACD) and 253 eyes were found to have open angles on gonioscopy. The 253 eyes with open angles were not followed up further in the study.

Eyes with PACD were further classified on the basis of gonioscopy, fundus evaluation and visual field assessment in selected cases into PACS (68 eyes), PAC (43 eyes) AND PACG (38 eyes) according to the ISGEO definition, but with non-visualization of 180° of trabecular meshwork as a cutoff.

Observations were compared between the 253 eyes with open angles on gonioscopy and 149 eyes with PACD. Also, data between the three subgroups, PACS, PAC and PACG was compared and analyzed.

All the eyes with PACD were advised treatment and monitored regularly.

A p-value < 0.05 was considered statistically significant.

Statistical Methods

All the data was compiled and analyzed statistically with the help of following methods and software:

1. Descriptive
2. Contingency table analysis (Cross tabs)
3. Independent samples t test
4. One-Way ANOVA
5. Repeated measure ANOVA.

All the statistical methods were carried through the SPSS for windows (version 16.0).

Age

The age distribution in the study population was analyzed. It was found that numbers of patients with PACD were more in the age group of 60-69 years, and this was statistically significant. ($p = 0.007$). A statistically significant female preponderance was found in the total study group size, i.e. 293 eyes in females and 109 eyes in males (72.9 %). ($p=0.000$).

Majority of the eyes in the study group were hypermetropes (358 eyes out of 402 eyes, 89.1 %),

This is highly significant as patients with hypermetropia were found to have shallow peripheral anterior chamber by van herick's test ($p=0.000$).

Table 1: Refractive error distribution in PACS, PAC and PACG groups

	PACS		PAC		PACG		Total	
	No. of Eyes	%	No. of Eyes	%	No. of Eyes	%	No. of Eyes	%
Hypermetropia	63	92.6	40	93	32	84.2	135	90.6
Myopia	5	7.4	3	7	6	15.8	14	9.4
Total	68	100	43	100	38	100	149	100

The predominance of hypermetropia was found in all the three groups. Eyes with hypermetropia were 92.6 %, 93 % and 84.2 % in PACS, PAC and PACG groups respectively ($p = 0.000$).

However, there was no significant difference in the PACS, PAC and PACG groups with respect to the distribution of hypermetropes and myopes. ($p=0.732$)

Sixty one out of sixty eight eyes (89.7 %) with PACS were found to have vision $\geq 6/12$. But only twenty seven out of thirty eight eyes (71.1 %) with PACG had vision $\geq 6/12$. ($p = 0.029$)

Four eyes in the PACG group were found to have no light perception at presentation (10.5 %) ($p=0.029$).

Symptoms in the Eyes with PACD

Symptoms of angle closure like headache, ocular pain, diminution of vision, redness of eyes, colored halos and nausea or vomiting were enquired and documented.

A statistically significant occurrence of headache ($p=0.000$) and redness of eyes ($p=0.010$) was found in patients with PACG.

Six patients, who presented with acute angle closure attack in one eye, complained of severe ocular pain, headache, redness in eyes, severe drop in vision and history of episodes of pain in the same eye earlier. Four eyes with acute attack gave positive history of seeing coloured halos.

Seventy five out of one hundred and forty nine eyes (50.3 %) with PACD came with complaint of diminution of vision. But as projected earlier, these patients had a good best corrected visual acuity. This can be attributed to the hypermetropia and presbyopia in these patients.

Signs in Eyes with PACD

Clinical signs were assessed and documented in all the eyes with PACD.

Eyes with PACS and PAC were not found to have any obvious signs of any acute attack in the past.

Eyes with PACG also did not show any specific signs except the six eyes in acute angle closure attack.

Eyes with acute angle closure attack (6 eyes) revealed signs like conjunctival congestion and corneal edema. None of the patients were found to have AC cells and flare or iris atrophy patches.

Van Herick's Test

Van Herick's test was conducted in this study to screen all 4017 patients in order to detect eyes with shallow anterior chamber.

Totally, 402 eyes were grouped under Van Herick's grade 0, I and II (as shown in Table 16).

The distribution of different Van Herick's grades amongst the eyes with open angles on gonioscopy and those with PACD was analyzed.

It was found that 95.83 % eyes with Van Herick's grade '0' were in the PACD group. ($p = 0.000$)

Also, 98.66 % eyes with a Van Herick's grade 'II' were in the open angles group. ($p = 0.000$)

Though 2 eyes (1.34 %) were screened to have Van Herick's grade 'II', they were found to have occludable angles.

So it was observed that most of the patients graded under Van Herick's grade '0' have PACD in one stage or another, whereas in those with Van Herick's grade 'I', about 50 % eyes had PACD.

Data for PACS, PAC and PACG was also analyzed with respect to the Van Herick's grades.

VAN HERICK test in PACS, PAC and PACG. It was observed that 60.5 % (23 out of 38 eyes) eyes with advanced stage (PACG) had Van Herick's grade '0', and 82.4 % (56 out of 68 eyes) of those with earlier stage (PACS) had Van Herick's grade 'I'. ($p = 0.000$) (TABLE 17)

Out of 46 eyes with PACD in the Van Herick's grade '0' group, 23 had already developed PACG, indicating that there are 50 % chances of finding eyes with PACG in eyes found to have Van Herick's grade '0'.

Gonioscopy

After the enrollment of 402 eyes in the study by Van Herick's test, indentation gonioscopy was performed for all eyes.

The eyes were classified in three groups – Primary Angle Closure Suspects (PACS), Primary Angle Closure (PAC) and Primary Angle Closure Glaucoma (PACG) on the basis of gonioscopy findings, fundus examination and visual field analysis where required.

Eyes with PACS revealed appositional angle closure of $\geq 180^\circ$.

Eyes with PAC revealed appositional as well as synechial closure. Thirty eight out of forty three eyes (88.37 %) with PAC had presence of peripheral anterior

synechiae of $\leq 180^\circ$. Remaining five eyes (11.63 %) had peripheral anterior synechiae of $\geq 180^\circ$.

Eyes with PACG too had both appositional and synechial closure. Twenty seven out of thirty eight eyes (71.05 %) with PACG had presence of peripheral anterior synechiae of $\leq 180^\circ$. Remaining eleven eyes (28.94 %) had peripheral anterior synechiae of $\geq 180^\circ$.

Intraocular Pressure (IOP)

IOP at presentation was analyzed statistically. Mean IOP in PACS and PAC groups was 15.89 ± 2.87 and 16.62 ± 3.99 mm of Hg respectively; whereas it was 28 ± 13.45 mm of Hg in PACG group. ($p=0.000$)

IOP in PACG group ranged from 16 to 60 mm of Hg as this group had 6 eyes that presented with an acute angle closure attack, and the IOPs of these six eyes ranged from 43 to 60 mm of Hg.

It was observed that the mean axial length (AXL) of eyes with PACD was 22.16 ± 0.78 mm, which was significantly less than the eyes with open angles on gonioscopy which was 22.56 ± 0.75 mm ($p=0.000$).

Central anterior chamber depth (CACD) was assessed for 398 eyes. Four eyes which had already undergone Laser Peripheral Iridotomy elsewhere were not considered for the mean central anterior chamber depth calculation. CACD in eyes with PACD was found to be 2.53 ± 0.25 mm, which was significantly less than in eyes with open angles on gonioscopy which was 2.80 ± 0.24 mm. ($p=0.0001$)

Considering central anterior chamber depth in normal population being about 3.13 mm⁵, it is observed that all the 402 eyes in present study had shallower central anterior chamber depths.

The axial length was short in all the three groups as compared to eyes with open angles on gonioscopy. But it did not correlate with the severity of the disease.

The mean central anterior chamber depth in eyes with PACG was found to be 2.43 ± 0.33 mm, and was shallower than that of PACS and PAC. ($p = 0.012$)

The lens thickness in all the three groups was found to be similar to the lens thickness in general population⁶ and not associated with the disease occurrence.

Post Treatment Results

In the present study, one hundred and forty nine eyes were diagnosed with primary angle closure disease.

Of the 149 eyes with PACD, one was painless blind eye and was not advised any further management. Its fellow eye was diagnosed with PAC and managed accordingly.

The remaining 148 eyes were advised treatment in accordance with the line of management as mentioned in the materials and methods.

PACS:

1. Of the 68 eyes with PACS, 66 eyes were advised to undergo prophylactic Laser Peripheral Iridotomy (LPI).
2. Two eyes had visually significant cataract and were advised cataract surgery at the earliest.

PAC:

1. Of the 43 eyes with PAC, 39 eyes were advised therapeutic LPI. Those eyes which had elevated IOP after LPI were further managed with topical anti-glaucoma medications.
2. Four eyes had visually significant cataract. They were advised cataract surgery urgently.

PACG:

1. Of the 38 eyes with PACG, all eyes were started on topical medications.
2. 29 eyes were advised therapeutic LPI.
3. Five eyes were advised trabeculectomy with mitomycin C.
4. Four eyes had lost perception of light owing to total glaucomatous optic atrophy, 3 of whom were painful. They were advised cryo-cyclodestructive procedure.
5. Of the eyes which underwent LPI in PACG group, three eyes did not have control of IOP and were further advised to undergo filtering surgery.

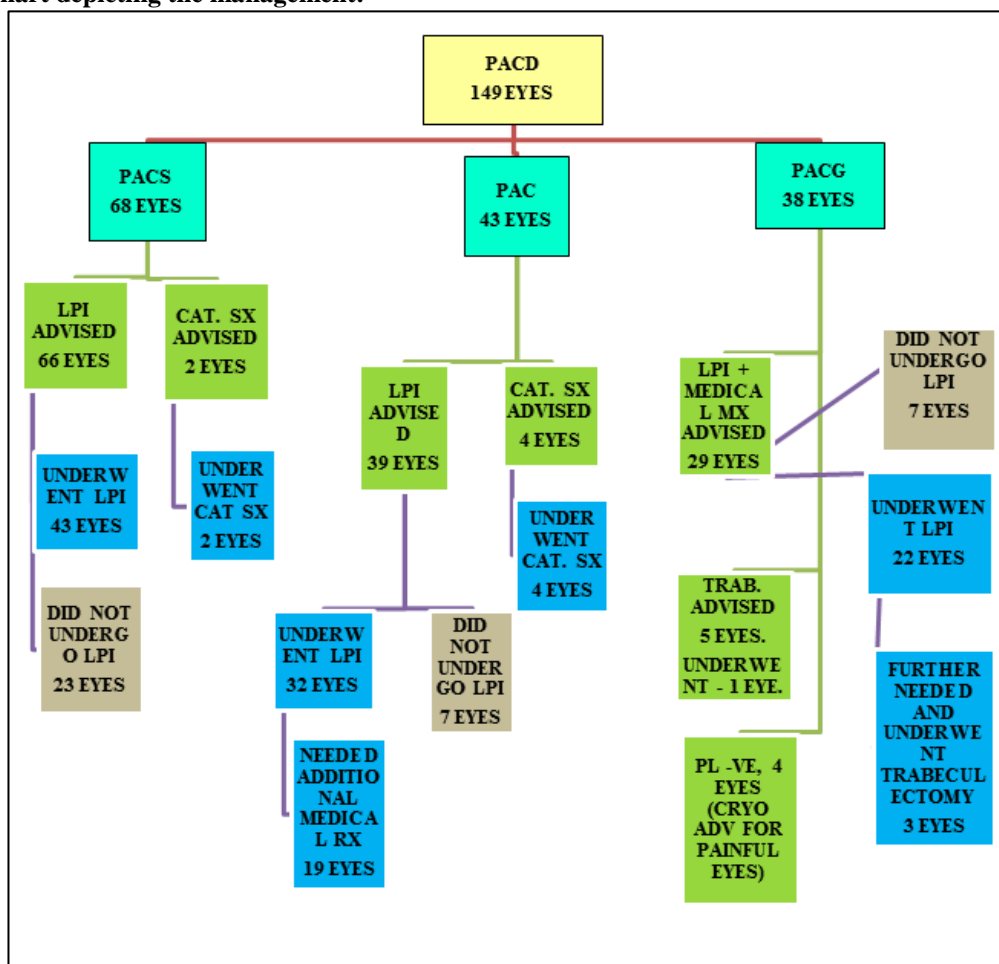
Amongst the 148 eyes which were advised treatment as mentioned above, 104 (70.3 %) eyes followed treatment as advised and the course and clinical findings of these eyes is discussed ahead.

In the remaining 44 (29.7 %) eyes, LPI was performed in 12 eyes but were later lost for follow up and 32 eyes did not undergo prescribed treatment during the study period.

The mean energy used for LPI in the study was $4.88 \text{ m J} \pm 0.22 \text{ m J}$ and the average numbers of shots used were 7.47 shots per eye.

The following flowchart depicts the management as described above:

Flowchart depicting the management:



Best Corrected Visual Acuity Post – Treatment: It was observed that the BCVA in PACS group pre and post treatment was stable.

BCVA in two eyes with PAC showed improvement following treatment with LPI and anti-glaucoma medications.

None of the treated eyes showed a fall in vision.

Intraocular Pressure Post – Treatment: The mean IOP was recorded at 6 months follow up for the 104 eyes which were compliant with the treatment and compared with the IOP at presentation.

A statistically significant fall was seen in the mean IOP of eyes with PACG following treatment. ($p=0.000$)

The mean IOP in eyes with PAC and PACS also showed a decrease following treatment, which was not statistically significant. ($p = 0.82$)

In the six eyes which presented with acute angle closure attack, IOP at presentation were in the range of 43 – 60 mm of Hg. After control of IOP with medical management and further followed by LPI and filtering surgery (which was required in three eyes), the IOP was stabilized to < 20 mm of Hg at the end of six months.

Chamber Depth Pre and Post LPI: The mean central anterior chamber depth (CACD) was recorded with A –

scan ultrasound 1 month post- LPI, in a random subgroup of 64 eyes that underwent LPI.

It was observed that 48 eyes (75 %) showed deepening of the central anterior chamber following LPI whereas 16 eyes (25%) remained same. Mean CACD showed a higher value post LPI suggesting an overall deepening of ACD after LPI and was found to be statistically significant. ($p=0.000$)

Six eyes underwent cataract surgery with IOL implantation in the present study. All the six surgeries were uneventful with good post operative vision.

Four eyes underwent trabeculectomy with mitomycin C in the present study. All the four surgeries were uneventful. Diffuse filtering blebs were formed after the surgery with control of IOP in the range of 10 to 16 mm of Hg.

At Six Months: All the eyes which were compliant with the prescribed treatment showed a control of IOP and no further optic nerve head damage was found, as observed during the study period.

Conclusions

1. Primary Angle Closure Disease (PACD) is a progressive blinding disease, which if detected on

- time, can be controlled and the blindness can be prevented.
2. PACD tends to be asymptomatic but is detectable in early stages on detailed slit-lamp examination and indentation gonioscopy.
 3. Van Herick test is a simple, quick, effective and essential tool to screen for primary angle closure disease, and it correlates well with the severity of the disease.
 4. Female gender and Hypermetropia are strongly associated with PACD. Shorter axial length and shallow central anterior chamber depth are associated with the eyes diagnosed with PACD.
 5. Laser Peripheral Iridotomy (LPI) is a safe and effective prophylactic measure in Primary Angle Closure Suspects.
 6. LPI with or without topical anti-glaucoma medications is safe and effective in management of eyes with Primary Angle Closure.
 7. LPI with topical anti-glaucoma medications is enough for few eyes with Primary Angle Closure Glaucoma (PACG).
 8. Filtering surgery causes remarkable reduction in IOP in eyes with PACG with extensive PAS, high IOP and advanced glaucomatous optic nerve head damage.

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