CORNEAL ENDOTHELIAL CELL CHANGES IN THE EYES OF PRIMARY ANGLE CLOSURE SUSPECTS TREATED USING LASER PERIPHERAL IRIDOTOMY COMPARED WITH UNTREATED FELLOW EYES AT PHRAMONGKUTKLAO HOSPITAL

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Abstract

Objectives: The study's primary outcome was to compare corneal endothelial cell changes in the eyes of Primary Angle Closure Suspects (PACS) treated by laser peripheral iridotomy (LPI) and in untreated fellow eyes. The secondary outcome was to assess short-term effects of LPI on the corneal endothelium among PACS.

Study design: The study employed a prospective design.

Methods: PACS visiting Phramongkutklao Hospital were enrolled in the study. Data were collected regarding type and setting of laser parameters, endothelial cell counts and morphology, gonioscopy and underlying diseases. Randomized eyes were treated using LPI while the other eye was treated by LPI 3 months later. Rate of corneal endothelium loss in the treated eyes were assessed and compared with untreated fellow eyes. Primary outcome was interpreted by pair *t*-test while secondary outcome was interpreted using the ANOVA test.

Results: A total of 31 PACS (62 eyes)were included in the study. The median age was 67 years (range 43-90). PACS totaled 21 females (67.7%) and 10 males (32.3%). The mean total power of double frequency Nd:YAG (532 nm) laser and Nd:YAG laser, were 855.6±53.9 mW and 2.3±0.5 mJ, respectively. Concerning primary outcomes, the mean corneal endothelial cell density before LPI and postLPI 3 month was 2608.5±399.8 and 2605.6±397, respectively, 1 cell/mm^2. In untreated fellow eyes, the mean corneal endothelial cell density at 1 and 3 months was 2607.1±419.6 and 2605.0±403.2 cell/mm^2, respectively. No significance was found in rate of endothelial cell change between treated and untreated fellow eyes using LPI (p=0.981). Regarding secondary outcomes, corneal endothelial cell density did not decrease significantly in 3 months (p=0.126).

Conclusion: No difference was observed in corneal endothelial cell changes between treated and untreated fellow eyes using LPI over 3 months. LPI did not affect corneal endothelial cell loss in a short term period.

Keywords : Corneal endothelial cell, Primary angle closure, Laser peripheral iridotomy

J Southeast Asian Med Res 2018; 2(2): 98-102.
http://www.jseamed.org

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Introduction

Angle closure glaucoma is more common in Asia than in Europe and Africa.[1] The results of glaucoma research in the Romklao Community in Bangkok showed that one-seventh of 701 subjects, older than 50 years, could have angle closure glaucoma and this risk runs to women three times more than men.[2] Laser peripheral iridotomy (LPI) is the first line of treatment for this disease.[3] LPI can be performed using a neodymium (Nd):YAG laser leading to photodisruption against target tissue and the argon laser, which causes a photothermal effect against the target tissue.[3,4]

The sequential laser technique combines these two types of lasers for treatment and is more popular because they produce good results and low complication rate. Complications of LPI include corneal decompensation, bullous keratopathy.[5,11] Other complications include transient intraocular pressure rising, anterior uveitis, closure by iridotomy, hyphema, cataract formation, retinal injuries, malignant glaucoma and monocular blurring.[3]

The purpose of this study was to compare corneal endothelial cell changes in the eyes of primary angle closure suspects (PACS) treated using LPI and in untreated fellow eyes in Phramongkutklao Hospital. The secondary outcome was to assess short term effects of LPI on corneal endothelium among PACS.

Methods

The study employed a prospective design regarding PACS at Phramongkutklao Hospital. All subjects met the inclusion criteria and were listed for elective primary LPI. The inclusion criteria were patients aged more than 18 years having a diagnosis of PACS. Appositional closure was more than 180o by gonioscopy (Modified Shaffer grading), intraocular pressure (IOP) ≤21 mmHg and no peripheral anterior synechiae (PAS). Subjects were excluded when a history was reported of corneal dystrophy/ degeneration, uveitis, iritis, endopthalmitis, intraocular laser, surgery or trauma, poor compliance or loss follow up, pregnancy or allergy to anesthetic drug. Subjects were evaluated for eligibility and baseline data at the Ophthalmology Department, Phramongkutklao Hospital.

All subjects were examined using a slit lamp and gonioscope. IOP was measured by Goldmann applanation tonometer. Central corneal endothelial cells were measured using a noncontact specular microscope. PACS were randomized to be treated using sequential LPI in one eye. Data were collected including type and setting of laser parameters, post LPI IOP, central corneal endothelial cells, central corneal thickness, coefficient variation and hexagonality of corneal endothelial cells at one, two and three months after LPI. The other eye was treated using LPI three months later. The primary outcome was assessing the short term rate of corneal endothelial cell loss in the treated eye compared with that of untreated fellow eyes. The secondary outcome was assessing the short term effects of LPI on corneal endothelial cell loss. The study was approved by the Institutional Review Board of the Royal Thai Army Medical Department. Informed consent was obtained from all subjects.

Sample size and power

The formula for calculating sample size in the present study is shown below.

$$n = \frac{(Z_{\alpha} + Z_{\beta})^2 S^2}{d^2}$$

$$\frac{(1.96 + 1.28)^2 17161}{86.51^2}$$

$$= 24.07 \sim 25 \text{ subjects}$$

- Confidence interval 95%, $\alpha = 0.05$ $Z_{\alpha} = 1.96$
- Power 90%, $Z_{\beta} = 1.28$
- $S^2 = 17161$
- d = μ_1-μ_2= 86.51

Statistical Analysis

General demographic data were described using mean, median and percentage. Corneal endothelial cell loss between eyes treated using LPI and untreated fellow eyes were compared by the paired *t*-test. Secondary outcome was interpreted using the ANOVA test. Statistical analysis was performed using Stata 11, and *p*-values of <0.05 were considered statistically significant.

Results

Thirty-five subjects (70 eyes) met the eligibility criteria,

and 4 subjects were lost to follow-up after LPI. The remaining 31 PACS (62 eyes) completed the study. The mean follow-up period totaled 3.3 months. The mean age was 67 years (range 43-90). Subjects comprised 21 females (67.7%), and 10 males (32.3%) including 11 subjects with diabetic mellitus (35.5%), 16 subjects with hypertension (51.6%) and 10 subjects with dyslipidemia (32.3%).

Table 1. Patients' demographic data

Age Mean±SD (Min-Max)	67.2±11.3(43-90)
Gender	**Number (%)**
Male	10 (32.3)
Female	21 (67.7)
Underling disease	
Diabetic mellitus	11 (35.5)
Hypertension	16 (51.6)
Dyslipidemia	10(32.3)
Type of angle closure	
PACS	31 (100)

Laser energy use in LPI is shown in **Table 2**. Mean total energy of double-frequency Nd:YAG (532) laser, and Nd:YAG laser in first treated eye were 855.6±53.9 mW, and 2.3±0.5 Joules (J), respectively. Mean total energy of double-frequency Nd:YAG (532) lasers, and Nd:YAG laser in the other treated eye were 857.3±56 mW, and 2.3±0.4 J, respectively.

Table 2. Laser energy use in laser peripheral iridotomy

	Total energy (mean±SD)	**Range of energy** (min - max)
Treatment I		
Double-frequency	855.6±53.9 mW	800-950 mW
Nd:YAG	(0.86±0.05 J/sec)	(0.8-0.95 J/sec)
Nd:YAG laser	2.3±0.5 mJ	1.2-3 mJ
Treatment II		
Double-frequency	857.3±56 mW	800-950 mW
Nd:YAG	(0.86±0.06 J/sec)	(0.8-0.95 J/sec)
Nd:YAG laser	2.3±0.4 mJ	1.5-2.9 mJ

Ocular parameters with LPI treated and untreated eyes are shown in **Table 3**. The mean rate of corneal endothelial cell change between treated and untreated eyes at three months revealed no statistical significance (p=0.981).

Table 3. Ocular parameters with pre- and postlaser peripheral iridotomy at 3 months

	Pre – LPI (mean±SD)	**Post – LPI 3 months** (mean±SD)	***p*-value**
IOP(mmHg)			
Treated eye	15.5±3.1	14.6±2.5	0.198
Untreaed eye	15.5±2.9	15.1±2.8	
ECD(cell/mm2)			
Treated eye	2608.5±399.8	2605.6±397.1	0.981
Untreaed eye	2607.1±419.6	2605.0±403.2	
CCT(μm)			
Treated eye	537.5±40.2	535.1±40.2	0.072
Untreaed eye	533.8±40.1	530±41.8	
C.V.(%)			
Treated eye	40.5±7.1	40.6±7.2	0.094
Untreaed eye	38.4±6.6	38.7±6.5	
Hexagonality(%)			
Treated eye	51.7±8.9	51.7±8.5	0.886
Untreaed eye	52.3±8.3	52±7.9	

a Paired t-test

LPI = laser peripheral iridotomy, IOP = intraocular pressure, A/C depth = anterior chamber depth, ECD = Corneal endothelial cell density, CCT = Central corneal thickness, C.V. = coefficient variation in size of corneal endothelial cell

Mean corneal endothelial cell density after LPI is shown in **Table 4** and indicating that corneal endothelial cell density did not decrease significantly over three months (p=0.126)

Table 4. Ocular parameters with pre- and post-laser peripheral iridotomy

	Pre - LPI (mean±SD)	Post – LPI 3 months (mean±SD)	Parameter Change (mean±SD)	p-value
IOP(mmHg)	15.5±3.1	14.6±2.5	3.3±2.1	0.544
ECD(cell/mm^2)	2608.5±399.8	2605.6±397.1	13.6±15	0.126
CCT(μm)	537.5±40.2	535.1±40.2	13.2±10	0.178
C.V.(%)	40.5±7.1	40.6±7.2	4.7±4.2	0.556
Hexagonality(%)	51.7±8.9	51.7±8.5	8.9±7.2	0.206

Discussion

This study compared corneal endothelial cell changes in the eyes of PACS treated by LPI and in untreated fellow eyes showing the short term effects of LPI. The mean rate of corneal endothelial cell change between treated and untreated eyes at three months revealed no significance (p=0.981). Regarding the secondary objective, corneal endothelial cell density did not decrease significantly over three months (p=0.126). The results were similar to related studies. Jess Smith's study[5] showed corneal endothelial loss of 125 cell/mm^2 after argon LPI (p=0.09) while Shiu-Chen Wu's[7] study showed significant corneal endothelial cell loss within one year after LPI but without significance at three months (p=0.467). However, William C. Panek's study [8] demonstrated significant corneal endothelial cell loss of 95 cells/mm^2 among subjects with occludable angles at the treated site after Nd:YAG LPI (p=0.04). many studies have shown the effect of laser treatment concerning the corneal endothelium depending on pre-existing corneal disease [5], total energy use[6] and type of laser.[6, 9, 11]

Jess Smith and Peter Whitted [5] showed corneal endothelial loss if 812 cells/mm^2 after argon LPI among patients who had pre-existing Fuchs' dystrophy and corneal edema. However, pre-existing corneal diseases were excluded in the present study and no corneal edema was found among all subjects.

The mean total energy of LPI in the present study was lower than related studies [6, 11] (**Table 2**). Tony Ho and Richard Fan[11] showed the long term effects of sequential argon-YAG LPI in dark irides and reported the total amount of energy in argon and Nd:YAG lasers was 3.6 J and 9.4 mJ, respectively. The procedures were safer involving fewer complications than argon or YAG laser alone. In addition, Wilhelmus RK[6] reviewed five case reports of corneal edema after high energy of argon laser LPI reporting 63, 48.5, 7, 25, and 25 J.

The advantage of the present study was the aged-match control group of LPI concerning corneal endothelial cell loss. The present study was limited by the small sample size, reproducibility of ocular parameter measurements and

short term follow-up period. Research in a larger population including long term effects on corneal endothelial cell change are necessary for further investigation.

Conclusion

No difference was observed regarding corneal endothelial cell changes between treated and untreated fellow eyes using LPI at three months. LPI did not affect corneal endothelial cell loss over a short term period.

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