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Original Research Article

Effects of ophthalmic laser procedures on corneal endothelium: A prospective study

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Abstract

Background: The endothelium of cornea is most essential for maintaining corneal transparency and deturgescence. Although laser procedures are relatively safe, there is potential for long-term risk of corneal decompensation. Hence, assessing the effect of various laser procedures and parameters on the corneal endothelium may help us reduce such corneal complications in future procedures

Materials and Methods: The present study was a prospective observational study carried out among adult patients attending a tertiary care hospital in Bangalore. All patients undergoing ophthalmic laser procedures such as Pan-retinal photocoagulation and Nd-YAG capsulotomy in our institute were considered for the study. Pre laser procedure assessment of corneal endothelial cell density was measured. The post procedural follow up was done on 1st day, 1st week, 1st month and at 6th months to assess the effect of laser procedure on corneal endothelium.

Results: A total of 63 patients were enrolled in the study of which 34 patients (54%) were less than 65 years of age and men constituted almost two-third of the subjects (40 cases, 63.5%) with a mean age of 62.3 years. 55 cases were treated with Nd:YAG capsulotomy for posterior capsular opacity. In the present study we observed statistically significant variation in corneal endothelium changes namely the coefficient of variation in both procedures (Nd:YAG and PRP) with p values of <0.001. The endothelial cell hexagonality which was significantly reduced only in Nd:YAG procedure with p value of <0.001.

Conclusion: The present study further reinforces previous studies regarding safety profile of laser procedures on corneal endothelium. There is a need to counsel the patients regarding safety and side effects of these procedures.

Keywords: Ophthalmic laser procedures, Corneal endothelium, Corneal cell density, Nd:YAG, Panretinal photocoagulation.

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1. Introduction

The corneal endothelium is most essential for maintaining corneal transparency and hydration. Endothelial cells serve a dual function in maintaining corneal hydration and transparency, acting as both a passive barrier and an active pump.[1-4] Although laser procedures are considered as a relatively safe procedures, but still there is potential long-term risk of corneal decompensation. The main mechanisms proposed for endothelial damage are direct focal injury, thermal damage, iris pigment dispersion, inflammation, turbulent aqueous flow, chronic breakdown of blood–aqueous barrier and also damage caused by bubbles that settle onto the endothelium.[3,4]

We use Nd:YAG Laser for management of posterior capsular opacification which is based on the principle of photo-disruption.[5] It can cause tissue damage and also leads to changes in corneal endothelium. Pan-retinal photocoagulation[6] procedure is typically delivered by either a slit lamp system or laser indirect ophthalmoscope. Pan-retinal photocoagulation is an effective means for curtailing the progression of proliferative diabetic retinopathy and preventing vision loss. Laser peripheral iridotomy[4] is the standard treatment modality for Primary angle closure suspects (PACS). This procedure is used to terminate the pupillary block and to alter the anterior chamber angle by balancing the pressure between the anterior and posterior chamber. However, there has been a controversy regarding the safety of the laser peripheral iridotomy procedure to endothelial cells in aspects of cell density and morphology.

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Corneal endothelial loss if severe, the cell density may fall below the threshold level, a minimum level required to maintain corneal deturgescence. It may lead to corneal oedema. Hence, knowing the degree of corneal endothelial loss may help reduce occurrence of corneal complications significantly. There is no comprehensive study in literature which has studied effects of all types of lasers on corneal endothelium. Hence, there is a need to study about effects of all types of lasers on corneal endothelium.

2. Materials and Methods

The present study was a prospective observational study carried out among adult patients attending a tertiary care hospital (Command Hospital Airforce Bangalore, India) for ophthalmic laser procedures. All patients undergoing ophthalmic laser procedures such as Pan-retinal photocoagulation and Nd-YAG Capsulotomy in our institute were considered for the study. The patients with acute ocular infections, previous laser procedures on eye, acquired diseases of cornea, gross abnormality on specular microscopy and any history of ocular trauma were excluded from the study.

Approval has been obtained for the current study from the ethical committee of hospital. All patients enrolled in the study were explained in detail about the procedure and the study in their vernacular language and an informed written consent was taken. A detailed sociodemographic and medical history was obtained from the study participants followed by complete ocular examination, general physical examination and systemic examination pertaining to ophthalmic laser procedure.

Pre laser procedure assessment of corneal endothelial cell density was done. Patients with posterior capsular opacification underwent Nd-YAG capsulotomy using (Nd-YAG, 1064nm, Appa YAG laser, model: 307) and they were subjected to 3-4 laser precise shots with energy of 1-2 mJ. Patients diagnosed to have proliferative diabetic retinopathy underwent pan-retinal photocoagulation (frequency doubled Nd -YAG solid green laser, Supra-532) and they were subjected to laser shots in three sessions with energy ranging between 70 and 210 mW, pulse duration 50 ms and spot size of 75um. Follow up was done on 1st day, 1st week, 1st month and at 6th month to describe effect of laser procedure on corneal endothelium.

Patients' cornea was observed through Specular Microscope (EM-4000, Tomey GmbH,). The routine clinical findings on slit lamp examination pre and post ophthalmic laser procedures were noted down. Corneal endothelium changes were measured in four parameters i.e., number of cells, cell density, hexagonality of cells and coefficient of variation (**Figure 1** a&1b).

The sample size was calculated based on the findings of the Bansal et al,[5] sample required for our study was calculated to be 63 eyes. The data was compiled in MS excel masterchart and were analysed using software Statistical package for social sciences (SPSS) version 22. Categorical study-based data have been depicted as numbers and percentages (%) and quantitative data in terms of mean and standard deviation. Quantitative variables were checked for normality of distribution and have been analysed using Student T test and Mann Whitney U test accordingly. The serial follow ups were analysed using repeated measures ANOVA. A 'p' value of <0.05 were considered as statistically significant.

3. Results

A total of 63 patients in which we have enrolled only one eye of each patient including the proliferative diabetic retinopathy patients and followed up in the study among which 34 patients (54%) were less than 65 years of age and men constituted almost two-third of the subjects (40 cases, 63.5%) with a mean age of 62.3 years. Majority of the study subjects were diagnosed with posterior capsular opacification (PCO) (55 cases, 87.3%), followed by six cases of diabetic retinopathy (9.5%) and two cases of Central retinal vein occlusion (CRVO) (3.2%). Patients diagnosed with PCO underwent ND YAG capsulotomy (55 eyes, 87.3%) and the remaining underwent pan-retinal photocoagulation (PRP) (08 eyes, 12.7%). No patients who underwent laser peripheral iridotomy were included in this study as sample size was achieved with PCO and PRP patients.

On comparison of cell density, it was observed that before the start of treatment mean cell density of the study population was observed to be 2200 ± 437 and immediate post lasered corneal endothelium (LCE) the mean density reduced to 2105 ± 414. Subsequently, there was further reduction in cell density at 1 month and 6 months of follow up with final density being noted at 2019 ± 430. This reduction in cell density post LCE was found as statistically significant (p value – 0.044). The mean cell count of the study population before procedure was 202 ± 55 and the same post LCE came down to 181 ± 49. There was slight increase in the mean cell count at one week (188 ± 49) and one month (182 ± 49) on follow up but was overall lower than the pre-surgery levels. The mean cell count at six months follow-up was found to be 176 ± 49. The overall reduction in cell count was found as statistically significant (p value – 0.017). Similar were the findings with mean coefficient of variance which reduced from 41.2 ± 4.6 (pre-LCE) to 36.3 ± 5.0 (6 months post-LCE) and cell hexagonality which reduced from 40.8 ± 7.2 (pre-LCE) to 36.9 ± 6.3 (6 months post-LCE). The above findings were to be statistically significant with p value of less than 0.001 (**Table 1**).

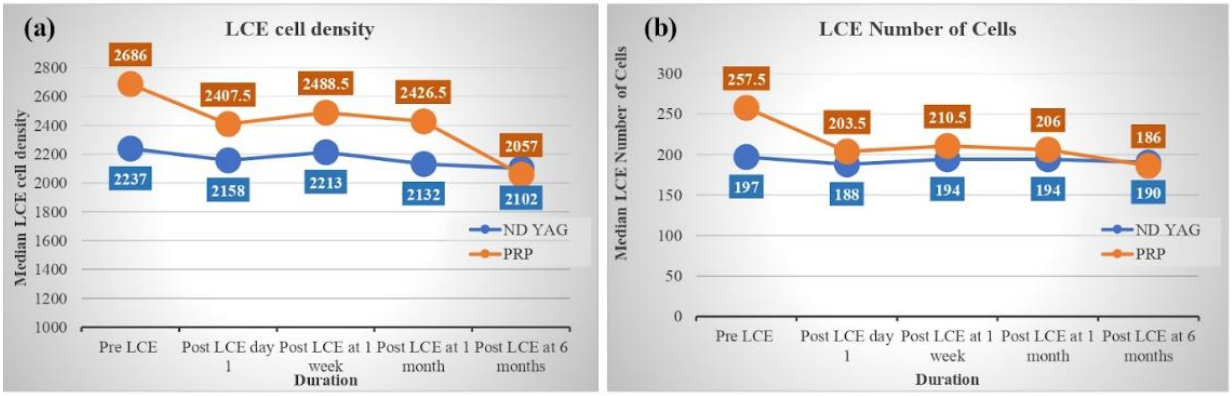

Figure 1:

Table 1: Corneal endothelium changes (mean ± SD) among study subjects

Parameter	Cell density	Cell count	Coefficient of variance	Hexagonality
Pre-LCE	2200 ± 437	202 ± 55	41.2 ± 4.6	40.8 ± 7.2
Post-LCE day 1	2105 ± 414	181 ±49	40.5 ± 5.5	41.0 ± 7.9
Post-LCE 1 week	2129 ± 431	188 ± 53	38.9 ± 5.6	41.2 ± 8.0
Post-LCE 1 month	2081 ± 412	182 ± 49	38.0 ± 4.9	38.6 ± 6.6
Post-LCE 6 months	2019 ± 430	176 ± 49	36.3 ± 5.0	36.9 ± 6.3
p-value	0.044	0.017	<0.001	<0.001

On further comparison of corneal endothelium changes with age and sex, there was statistically no significant difference in either of the four parameters (number of cells, cell density, coefficient of variation and hexagonality of cells) from pre-LCE stage to six months of follow-up. On procedure wise comparison of cell density, it was observed that there was significant lower cell density on post laser surgery (ND YAG as well as PRP) compared to pre laser cell density with a p value of less than 0.05 (**Figure 2**). Similar were the findings of cell count wherein there was a drop of median cell count from 197 (pre-surgery) to 190 (6 months follow-up) for ND YAG procedure and from median count of 257.5 (pre-surgery) to 186 for PRP procedure (**Figure 2**).

Figure 2:

The association of coefficient of variation with type of surgery was assessed in the present study and observed that there is statistically significant reduction (p value < 0.05) in hexagonality of cells from a median of 43 (pre-surgery) to 37 (6month post-surgery) for ND YAG and from 43 (pre-surgery) to 40 (6 month post-surgery) for PRP surgery. However, except for day 1 follow-up there was statistically no significant difference between these two procedures (**Table 2**). Further comparison of hexagonality of cells in the present study revealed that there was significant reduction in hexagonality post Nd:YAG procedures from a median of 41.5 to 37.0, whereas reduction post PRP was relatively on lower side from a median of 39 to 36 but the difference was statistically not significant. Significant difference between the two laser techniques were not noticed. (**Table 3**).

Table 2: Procedure wise comparison of median coefficient of variation among study participants

Coefficient of Variation	ND YAG	PRP	p-value
Pre LCE	43.0	43.0	0.507
Post LCE day 1	40.0	44.5	0.009
Post LCE 1 week	38.0	42.5	0.057
Post LCE 1 month	37.0	41.0	0.125
Post LCE 6 months	37.0	40.0	0.192
p-value	<0.001	0.005	-

Table 3: Procedure wise comparison of median hexagonality among study participants

Hexagonality	ND YAG	PRP	p-value
Pre LCE	41.5	39.0	0.535
Post LCE day 1	41.0	37.8	0.186
Post LCE 1 week	41.1	37.6	0.694
Post LCE 1 month	38.5	37.0	0.901
Post LCE 6 months	37.0	36.0	0.694
p-value	<0.001	0.172	-

4. Discussion

Corneal endothelial loss if sufficiently severe, leads to endothelial cell density to decline below threshold level, a minimum level required to maintain corneal deturgescence. It may lead to corneal edema. Hence, knowing corneal endothelial loss may help reduce occurrence of corneal complications significantly.[2,7] Although laser procedure has been believed to be a safe procedure, studies show that few patients undergoing Nd:YAG laser progress to corneal decompensation. Endothelial cell damage were due to various mechanisms that may include thermal damage, iris pigment dispersion, inflammation, turbulent aqueous flow, chronic breakdown of blood–aqueous barrier and also damage from bubbles that deposited onto the endothelium.[3,4]

Since there is no regeneration, existing cells spread out to replace the lost cells of the corneal endothelium and its pivotal role in visual function, it is critical to understand those conditions that could reduce ECD and improvise an appropriate strategy to conserve and preserve the endothelium to prevent progressive corneal blindness. Corneal endothelial cells have been reported to be highly sensitive and can be damaged due to variable factor which includes systemic disorders, eye diseases, and ophthalmological intervention.

Our study comprised of patients with a mean age of 62.3 years. In studies by Jamali H et al[8] and Bansal N et al[5] the mean age of subjects were 53.4 years and 51.5 respectively which were comparable to our study. 55 cases were treated with Nd:YAG capsulotomy for posterior capsular opacity. In our present study we noticed statistically significant reduction in corneal endothelium changes namely the cell count, cell density and coefficient of variation in both surgical procedures (ND YAG and PRP) except for cell hexagonality which was significantly reduced only in ND YAG surgery.

In a study conducted by Jamali H et al,[8] there was reduction in endothelial cell count post treatment by peripheral iridotomy performed at 3-month, 6-month, and 12-month regular follow-up visits, as peripheral iridotomy is performed with minimum energy and shots at iris consequently did not state statistical significance. The changes noted in the number of cells, the hexagonality of cells and the coefficient of variation (CV) in all quadrants of cornea were also not significant.

A retrospective cohort study by H C Chen et al,[9] 48 patients were divided into 2 groups in which one group received early Nd-YAG capsulotomy (<12 months of cataract surgery) and other group received late Nd-YAG capsulotomy (>12 months of cataract surgery). On follow up at 1st week and 4th week they found endothelial corneal cell density in the early group was noted to be significantly decreased one week after treatment (2221.50 ± 327.73/mm^2 vs 2441.55 ± 321.80/mm^2, $p < 0.001$), which then improved to 2369.95 ± 76.37/mm^2 four weeks after concluding the treatment but was slightly lower than the preoperative status ($p < 0.001$), whereas, the hexagonality of cells (percentage) exhibited a significant reduction at four weeks after treatment ($p = 0.028$).

A prospective observational study by A H Pathak et al,[10] in which 40 patients were evaluated for corneal endothelial changes after Nd YAG capsulotomy, mean endothelial corneal cell density pre-laser was 2356.76 cells/mm^2, which decreased to 2231.8 cells/mm^2 at 1 week and 2199.2 cells/mm^2 at 1 month follow up after laser procedure, the decrease in cell density was statistically significant at 1 month (p<0.0001). The pre laser assessment of coefficient of variation was 33.74, at 1week 35.58 and at 1month it was 37.12. The difference in coefficient of variation was statistically significant (p<0.0001). The mean hexagonality also decreased from a pre-laser baseline value of 65.34% to 62.02% and 60.42% at 1week, 1 month respectively with statistical significance (p<0.0001).

In a study by Makitie J et al.[12] to assess the corneal endothelium after photocoagulation. About 20 successive diabetics outpatient receiving laser therapy for proliferative diabetic retinopathy were observed. The morphology of hundred individual endothelial cell from each central cornea were analysed using a digitizer. Statistically no significant correlations observed between mean cell areas or standard deviations of mean and the amount of previous laser energy received. Laser therapy received or the type of diabetes did not lead to statistically significant changes in the endothelial cell areas examined.

In a prospective comparative cohort study by Abell RG et al.[13] to assess the varied effect of photo disruptive femtosecond laser assisted cataract surgery on the corneal endothelium. The research group included 405 eyes whereas control group had 215 eyes. The study group had considerably decreased postoperative ocular edema at 1 day and 3 weeks. At 6 months, the change was insignificant. At 3 weeks, the study group showed significantly lower ECD loss than the control group, but not at 6 months (6-month mean 150 cells/mm^2 ±244 [SD] versus 149 cells/mm^2 ±233). At 6 months, patients in the study group who underwent laser-automated corneal incisions had lost more endothelial cells

than eyes in the study group with manual corneal incisions or eyes in the control group (P<.0001).

A retrospective cohort study was done by Aran Kanagarathnam et al.[14] Patients undergoing laser procedures such as retinal photocoagulation and selective laser trabeculoplasty were evaluated for corneal endothelium changes by using specular microscopy. They concluded that retinal photocoagulation seemed to transiently increase polymegathism suggesting stress on corneal endothelium. Selective laser trabeculoplasty causes transient decrease in endothelial cell density and increase in central corneal thickness.

In a study demonstrating acute transient corneal endothelial changes after laser therapy by Andrew JR White et al,[15] concluded that transient change in endothelial cell count was evident but did not have impact on cell count or visual acuity on long term follow up.

The findings of our study are consistent with the findings of the above studies and the current literature.[5,11] Other research has found that laser iridotomy can affect the lasered corneal endothelium, resulting in a variety of outcomes. Although the procedure has been considered to be relatively safe, there is a long-standing risk of corneal decompensation in patients. It has been reported that the time span between laser iridotomy and corneal decompensation may be up to eight years. Laser type, delivery, and amount are all intervention-related risk considerations. The relevance of these risk factors and their direct relationship with the development of corneal decompensation are yet unknown. Understanding these risk factors would help the doctors properly counsel their patients. The use of sequential laser iridotomy in all cases may help to reduce the amount of laser energy used and perhaps amount of endothelial damage.[6] The current trend of doing prophylactic LPI in fellow eyes may need to be reassessed in view of this sight threatening risk.

5. Limitations of Study

This study does not follow up for more than 6 months and thus long term changes cannot be commented. It does not include the changes of corneal endothelium due to systemic diseases such as diabetes mellitus and ocular disease such as glaucoma.

6. Conclusion

The present study documented a considerable effect of ophthalmic laser procedure on the corneal endothelium cell density, number of cells and coefficient of variation on follow up using the non-contact specular microscopy. Specular microscopy should be included as investigative modality in all patients undergoing ophthalmic laser procedures, if feasible. Laser procedures are safe, but extra care may be taken in cases with pre-existing low corneal endothelial cell counts in order to reduce the risk of further endothelial cell loss and subsequent decompensation.

7. Source of Funding

None.

8. Conflict of Interest

None.

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