Evaluation of corneal endothelial cell changes in diabetic patients before and after phacoemulsification surgery: A comparative study

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Abstract

Aim: The study was conducted to evaluate and compare the changes in corneal endothelial cell count density (ECD) and Central corneal thickness (CCT) between diabetic and non diabetic population before and after phacoemulsification surgery.

Settings and Design: This prospective, comparative, interventional study was carried out at government medical college and attached group of hospitals, a tertiary eye care centre in Rajasthan, India.

Materials and Methods: A total of 50 patients with type II diabetes mellitus (age group 30-80 years) and 50 age matched healthy patients of senile cataract with clear cornea without any other ocular pathology were non-randomly selected for Phacoemulsification surgery (phaco) after detailed preoperative assessment. All patients were operated by the same surgeon with phaco chop technique to exclude any surgeon's related bias. Endothelial cell count, CCT and Coefficient of Variance (CV) was measured with specular microscope pre-operatively and postoperatively at day 1st, 7th, 15th, 1 month, and 3 months serially.

Result: Postoperatively, the mean ECD was decreased in both the groups but loss of endothelial cell count was significantly more in diabetic population as compare to non diabetic groups at day 1, day 7, day 15, 1 month and 3 months. CCT was increased on first post-operative day in both the groups, subsequently decreased and then returned back to about same as pre-operative state after 1 month. But postoperatively, the change in mean CCT was not significant between both groups. The difference in % CV was significantly higher in diabetic group as compared to non diabetic group postoperatively.

Conclusion: The corneal endothelial cell changes were significantly high in diabetic population as compared to nondiabetic patients. The ECD loss, increase in mean CCT and % CV were more in diabetic population as compared to non diabetic. And patients with diabetes showed slower recovery in endothelial healing as compared to non diabetic group.

Keywords: Cataract, Cornea, Central corneal thickness, Diabetes, Endothelial cell density, Phacoemulsification.

Introduction

Cataract surgery is the most commonly performed ocular surgery, which has always been associated with damage to the corneal endothelium, especially during cataract extraction with phacoemulsification surgery.[1] Corneal endothelium plays an important role in maintaining the dehydrated state and the transparency of the cornea. Endothelial cells maintain corneal deturgescence (dehydrated state) throughout life by pumping excess fluid out of stroma through an active transport mechanism and barrier function.[2] Any compromise in these factors leads to direct effect on corneal transparency. Deturgescence of corneal endothelial stroma can be measurement by corneal endothelial cells count.[3] The endothelial cell loss (ECL) invariably occurs in all types of cataract surgery but the cell loss varies with surgical technique.[4,5] Loss or damage of endothelial cells leads to an increase in corneal thickness (edema) which may ultimately induce corneal decompensation and loss of vision.[4] In order to evaluate the degree of surgical trauma and endothelial status, morphological criteria are more precise. Corneal endothelium morphology status is usually described by endothelial cell density, percentage of hexagonal cells and coefficient of variation. The endothelial cells are also known to decline with age.[6-10] And diabetes mellitus also known to causes deleterious effect on corneal endothelium. Patients with diabetes have morphologically abnormal cells such as polymegathism and pleomorphism in their cornea.[11] Elderly diabetic population more prone to surgical trauma to corneal endothelium during phacoemulsification surgery.[11-14] This study was conducted to analyze the corneal endothelial cell changes (ECD loss, CCT and % CV) in patients with type II diabetes before and after phacoemulsification surgery and to compare them with age matched non diabetic population.

Materials and Methods

The present study was a prospective, comparative, non-randomized study conducted on 50 patients with type II diabetes mellitus and 50 age matched non-diabetic controls with senile cataract admitted under department of Ophthalmology, J.L.N. Medical College and associated group of hospitals Ajmer, Rajasthan from march 2013 to march 2014. Hundred patients fulfilling the inclusion criteria were selected from the outpatient department. All patients were informed about the procedure and a written informed consent was taken. The patients were divided into two groups: group 1 included patients with type 2 diabetes mellitus and group 2 without diabetes mellitus. The diagnosis of type 2 diabetes was made according to their medical history, blood glucose levels (fasting and 2 h postprandial), and HbA1c levels. The duration of diabetes mellitus in these patients ranged from 6 month to 20 years. Inclusion criteria were age between 30 to 80 years, both gender, visually significant senile

cataract (upto NS grade III, PSC) and require unilateral cataract extraction followed by implantation of foldable posterior chamber intraocular lens (PCIOL), Pupil dilation ≧7 mm after mydrisis, and patients with good clear cornea.

Exclusion criterias were patients with senile cataract (NS IV and above), having history of other systemic diseases (Hypertension and other cardiovascular illnesses) and ocular diseases like glaucoma & anterior segment pathology specially uveitis, patients with traumatic and subluxated lens, patient with floppy iris, patients with corneal opacity, patient with past history or evidence of posterior segment pathology and patient with postoperative complications like striate keratopathy, hyphemia, raised IOP and severe anterior chamber reaction. Other exclusion criteria included longer surgical time (>15 minutes), total phaco time (>90 seconds), effective phaco time (>10 seconds), and any other intraoperative complications such as PC rent, descemet's detachment. The history was recorded using a semi-structured proforma which included sociodemographic details, duration of diminished visual acuity, duration of diabetes mellitus, and their present treatment. Patients were assessed preoperatively for uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA), anterior segment examination under slit lamp biomicroscope (including grading of nuclear sclerosis 0 to +3), posterior segment examination through a dilated pupil by indirect ophthalmoscope and all endothelial cell changes (ECD, CCT and % CV) were obtained by specular microscopy (Tomey EM 3000). Intraocular pressure was measured preoperatively with Goldman applanation tonometer. NS grade IV or higher excluded from study as higher energy was required for phacoemulsification of that kind cataract. Keratometry and biometry was performed by using same keratometer (nidek ARK- 1) and A scan machine (Biomedix). CCT, ECD and % CV were determined by non-contact specular microscope (Tomey EM3000). Three readings were recorded in every patient on each examination. And the mean of the measurement was noted. All the patients of both groups were evaluated preoperatively, 1st day, 7th day, 15th day, 1month and 3 month postoperatively, and all patients were operated by the same surgeon to exclude any surgeon's related bias.

All patients preoperatively received antibiotic eye drops (Moxifloxacin 0.3%) 2 hourly one day before the surgery and oral antibiotic (Tab ofloxacin 200 mg) twice daily for 5days starting one day prior to the surgery. And all the surgeries were performed under Peribulbar anesthesia. And postoperatively all patients were prescribed with antibiotic –steroid eye drops (Moxifloxacin+Prednisolon acetate) 6 times a day for a week after that frequency reduced to 4 times, 3 times and 2 times a day subsequently alone with nepafenac 0.1% eye drop twice a day. Patients presented with mild to moderate keratitis were advised to put antibiotic – steroid eye drops 2 hourly with sodium chloride eye drop and sodium chloride eye ointment.

Surgical Steps of Phacoemulsification Surgery: Under local anaesthesia two biplane corneal side ports were made with 15° keratome. Tryphan blue dye was injected from one side port and washed with Ringers lactate solution after 30 seconds for staining of anterior capsule. A viscoelastic substance hydroxy propyl methyl cellulose (HPMC2%) was injected in to the anterior chamber to maintain anterior chamber and protect corneal endothelium. After staining of anterior capsule, continuous curvilinear capsulorrheaxis was carried out with bent 26 gauge needle. There was a clear corneal triplaner self-sealing incision was made with 2.8 mm keratome. Hydrodissection and hydrodelineation was performed to separate the cortex from anterior capsule and nucleus from epinucleus respectively. These procedures facilitated free rotation of nucleus by using dialer. Nucleus fragmentation was done by phaco chop (direct) technique and residual cortical matter was removed by irrigation and aspiration by help of bimanual irrigation-aspiration cannula. A foldable hydrophilic acrylic PCIOL implanted in capsular bag. Residual viscoelastic was removed. All the parameters like vacuum (220-260), power (40-60%), irrigating fluid (compound Sodium Ringer Lactate solution, Inven) and phaco technique (direct chop) were kept constant. Post-operative treatment was kept same in all patients. All patients were examined on day 1, 7, 15 or 2 week, 1month and 3 months serially. At each follow up visit specular microscopy was performed to measure endothelial cell count, CCT and % CV.

Statistical Analysis

All obtained data were mentioned as mean and standard deviation (SD). Complete statistical analysis was performed using commercially available software SPSS (version 17.0). Data were analyzed by using unpaired t-test. The data were considered statistically significant with p- value ≤ 0.05.

Results

The present study sample included 50 patients with type II diabetes (Group I), of which 16 (32%) were male and 34 (68%) female. The mean age of the patients was 57.78 $\pm$ 9.54 (age range 35 to 72).Whereas control group (non-diabetic) included 21(42%) male and 29 (58%) female. Their mean age was 61.04 $\pm$ 7.45 (age range 41 to 77). The difference in age between both the groups was statistically not significant (P = 0.669). In group I, preoperative mean endothelial cell density (ECD) was 2484$\pm$277.44 cells/mm^2 (range 2024-2720 cells/mm^2), whereas in group II, the preoperative mean ECD was 2393$\pm$251.92 cells/mm^2 (range 1951-2907 cells/mm^2). This difference was statistically not significant (p=0.09). The preoperative

mean CCT was 504.20 ±67.54µm (range 428-560µm) in group I, while in group II mean preoperative CCT was 502.31±37.61µm (range 426-601µm).The difference between two groups was not statistically significant (p=0.86). Preoperative mean CV in group I was 34.99±4.73% (range 31.66-38%) whereas in group II Mean CV was found 36.17±3.99% (range 32.64-40.66%) the difference was statistically not significant (p=0.18).

Postoperatively, the mean endothelial cell count in group 1 was 2105.4±615.91 cells/mm^2 on day 1, 2067.6±590.20 cells/mm^2 on 7day, 2049.4 ± 579.21 cells/mm^2 on day 15, 2042 ± 576.95cells/mm^2 on 1 month and 2025.4± 566.33 cells/mm^2 on 3 months. Similarly, in group II the mean ECD was 2213.52±278.00 cells/mm^2, 2189.22±277.88 cells/mm^2, 2169.80±274.69 cells/mm^2, 2145.08± 279.69 cells/mm^2, 2138.48±269.03 cells/mm^2 on day1, day 7, day 15, 1 month and on 3 month respectively [Table 1].

The postoperative mean CCT in group I was 556.6±78.88 µm on day 1, 521.00±62.42 µm on 7day, 514.00±68.08 µm on day 15, 507.40±68.78 µm on 1 month and 505.02±70.72 µm on 3 months. Whereas in Group II, the Mean CCT was 543.46±47.64 µm, 516.93±40.96 µm, 510.66±38.43 µm, 504.99±38.20 µm, 502.97±38.63 µm on day 1, day 7, day 15, 1 month and on 3 months [Table 2].

In group I, postoperative mean endothelial cell loss (ECL) was found 378.60±347.44 cells/mm^2 (15.24%) on day 1, 416.40±324.97 cells/mm^2 (16.76%) on day 7, 434.60±313.71 cells/mm^2 (17.19%) on day 15 442.00±311.16 cells/mm^2 (17.51%) on 1 month and 458.60±302.75 cells/mm^2 (18.46%) on 3 months. while in group II, the mean ECL was 180.82±140.29 cells/mm^2 (7.55%), 204.71±151.77 cells/mm^2 (8.55%), 224.13±151.11 cells/mm^2 (9.36%), 248.85±156.63 cells/mm^2 (10.39%), 255.53±155.03 cells/mm^2 (10.67%) on day 1, day 7, day 15, 1 month and on 3 months. The difference between both groups was statistically significant (p value<0.05) [Table 1]. This fashion of ECD loss shows that there was a steep loss in endothelial cell count just after phaco surgery in both the groups.

In group I preoperative mean CV was 34.99±4.73% and 37.93±2.26% at 3 month postoperatively while in group II preoperative mean CV was 36.17±3S.99% and 38.93±1.67 at 3 months postoperatively [Table 3]. Postoperatively, the % CV was increased at 3 month it was statistically significant from preoperative values. The increase in CV was higher in group I than group II and it was statistically significant at 1 month (p value-0.0008).

Table 1: Distribution of mean endothelial cell count changes between diabetic and non – diabetic population

	Mean ECD (cell/mm^2) ± S.D/ ECD Loss (%)		**Unpaired t test**	
	Diabetes Population (N=50)	**Non-Diabetic Population (N=50)**	**t score**	**p value**
Pre-operative	2484±277.44	2393.93±251.92	1.6995	0.092
PO day 1 ECD Loss	2105.4±615.91 378.60±347.44 (15.24%)	2213.31±278.00 180.82±140.29 (7.55%)	3.7324	0.0003
PO day 7 ECD Loss	2067.6±590.20 416.40±324.97 (16.76%)	2189.22±277.88 204.71±151.77 (8.55%)	4.1735	0.0001
PO day 15 ECD Loss	2049.4±579.21 434.60±313.71 (17.19%)	2169.8±274.69 224.13±151.11 (9.36%)	4.2740	0.0001
PO 1month ECD Loss	2042±576.95 442.00±311.16 (17.51%)	2145.08±279.76 248.85±156.63 (10.39%)	3.9206	0.0002
PO 3 month ECD Loss	2025.4±566.33 458.60±302.75 (18.46%)	2138.4±269.03 255.53±155.03 (10.67%)	4.2216	0.0001

PO= Post-operative, ECD= Endothelial cell density or count, SD= Standard deviation

Table 2: Distribution of mean CCT changes between diabetic and non – diabetic population

	CCT (Mean±SD)/Changes in CCT		t-test	p-value
	Diabetic Population (N=50)	Non Diabetic Population (N=50)		
Pre-operative	504.20±67.54	502.31±37.61	0.1729	0.8631
PO day 1 Changes in CCT	556.60±78.88 52.40±35.82	543.46±47.64 41.15±31.67	1.6638	0.0994
PO day 7 Changes in CCT	521.00±62.42 16.80±24.31	516.93±40.96 14.62.±21.12	0.4787	0.6332
PO day 15 Changes in CCT	514.00±68.08 9.80±4.91	510.66±38.43 8.35±12.20	0.7796	0.4375
PO 1month Changes in CCT	507.40±68.78 3.20±4.76	504.99±38.20 2.68±7.59	0.4104	0.6824
PO 3 month Changes in CCT	505.02±70.72 0.82±7.96	502.97±38.63 0.66±3.71	0.1288	0.8979

PO= Post-operative, CCT= Central corneal thickness, SD= Standard deviation

Table 3: Distribution of mean %CV changes between diabetic and non-diabetic population

	CV% (Mean±SD)/Difference in CV		t-test	p-value
	Diabetic Population (N=50)	Non Diabetic Population (N=50)		
Pre-operative	34.99±4.73	36.17±3.99	1.3484	0.1806
PO day 1 Difference in CV%	40.93±6.04 5.94±4.72	40.02±3.1 3.85±3.10	2.6171	0.0103
PO day 7 Difference in CV%	39.66±3.49 4.67±1.51	39.65±2.16 3.48±1.81	3.5698	0.0006
PO day 15 Difference in CV%	38.86±1.55 3.93±1.46	38.95±1.95 2.78±1.50	3.8848	0.0002
PO 1month Difference in CV%	38.80±1.70 3.81±1.61	38.94±1.87 2.77±1.37	3.4787	0.0008
PO 3 month Difference in CV%	37.93±2.26 2.94±2.24	38.93±1.67 2.76±1.57	0.4653	0.6472

PO= Post-operative, CV= Coefficient of variance, SD= Standard deviation

Discussion

The results of our study show that the corneal endothelial cell density was changed after phacoemulsification surgery in both the groups. The preoperative mean endothelial cell count difference was statistically not significantly in both the groups while postoperatively the difference was significantly higher in diabetic population than non diabetic population. Diabetes mellitus causes structural and functional changes in corneal endothelial cells and their integrity,[11] there are several studies which reported that diabetic patients have various corneal abnormalities such as increased CCT, reduced ECD, lower corneal sensitivity and increased permeability, low hexagonality and increased percentage of CV.[15] The mean ECD loss was statistically significant between both groups in our study. Previous studies reported endothelial cell loss after cataract surgery.[1,20,28] Hugod et al[20] reported a mean loss in ECD was 6.2% in patients with diabetes but only 1.4% in the non diabetic controls at the end of 3 months after surgery. Morikubo et al[1] reported 3.2% loss in mean ECD in non diabetes patients and 7.2% in patients with diabetes at postoperative 1 month follow up visit. Dick et al[28] had shown that endothelial cell loss was maximum at early postoperative period (7.9%) and 6.7% after 6 months. Our study also reported maximum endothelial cell loss was found on day 1 post operatively which was 15.24% in diabetic and 7.55% in non-diabetic group. This higher loss in ECD might be explained by fragility of corneal endothelium caused by several metabolic mechanisms in patients with diabetes. The fragility of diabetic corneal endothelial cells increases due to enhanced polyol pathway and accumulated sugar alcohol in cells. The suppression of Na^+-K^+ ATPase of the corneal endothelium cells in diabetic patients causes morphological and functional changes of the endothelial cells.[16] Furthermore, accumulation of advanced glycation end products (AGEs) in diabetic cornea causes oxidative DNA damage which suggests apoptotic damage of corneal endothelial cell in diabetic patient.[30] The duration of diabetes mellitus and blood glucose level have proven to be associated with the severity of corneal damage caused by phacoemulsification.[39,40] Dhasmana et al[31] reported a severe increase in endothelial cell loss in diabetic group

compared to the control after surgery. Our study reported decrease in ECD in both the groups which was higher in group I and there was a steep decline in mean ECD on day 1 post operatively. Wright et al,[25] Thakur SKD et al[17] and Amon et al[26] also reported similar finding.

In our study, there was no significant difference in preoperative mean ECD count, CCT and CV% between both the groups. These results are similar to older study,[11,18-20] where they did not find any significant differences in preoperative mean ECD in diabetic and non diabetic group. While other studies found that mean ECD was significantly lower in patients with type II diabetes compared with controls.[21-23]

We found that the preoperative mean CCT was slightly higher in group I (504.20±67.54) as compare to group II (502.31±37.61) but there was no significant difference in preoperative mean CCT between both the groups. Mean central corneal thickness (CCT) obtained in diabetic group was higher as compared to non diabetic group in early postoperative period but on comparing the changes later at 3 months, it was found to be not significant. (p -0.09). Similar results were found by earlier studies.[20,26] Few studies did not report significant difference in CCT between diabetic and non diabetic group.[32] These finding were supported by Inoue et al[29] but he found variable results with systemic and ocular factors to cause endothelial damage**.** Moriquobo S et al[1] observed the postoperative mean increase in CCT at day 1was 4.2%, at 1 week was 0.9% and on day 30, it was 0.045 in non diabetic patints after phacoemulsification. Methew et al.[15] showed an initial increase in CCT till 2 post-operative weeks followed by reduction in CCT in subsequent follow up and further reduction in the last follow up. Results of our study showed significant increase in mean CCT in immediate post-operative period that was on day 1, which returned back to pre-operative status for 1 month to 3 months. Previous studies reported similar finding that there was increase in CCT was maximum at day 1, and week 1 post operatively and then gradually decreased for at least 3 months.[1,29,31,33,34] Altintas et al[35] found that corneal thicknesses were greater in both diabetic and non diabetic patients at 1 week postoperatively than in later follow up, while there were no differences in corneal thickness according to phaco time or diabetes status**.** A population based cross sectional study revealed that diabetes is associated with greater CCT, independent of age, sex and intraocular pressure levels.[14] Lee et al[24] concluded that patients with diabetes had morphological abnormalities specially decreased ECD increased CCT and CV as compared to healthy controls. Whereas there are several studies mentioned a delayed recovery of post-operative corneal edema in diabetics compared to normal controls.[1,27, 31,33,34] The effect of diabetes mellitus on central corneal thickness is still not clear but there are several explanations which suggest detrimental effect on corneal thickness such as endothelial pump inhibition, increased osmotic pressure in cell stroma and increased endothelial permeability due to diabetic metabolic stress.[36]

Endothelial cell count is used to evaluate the status of the cornea after cataract surgery. The surgical trauma is reflected by decrease amount of corneal endothelial cells, which is higher in diabetic patients who have lower capability in the process of repair.[20] A healthy cornea is able to compensate for transient increase in corneal thickness, but when cornea is diseased recovery occurs slowly. The loss of endothelial cells is responded promptly into enlargement of remaining cells and attempts to cover-up the gap, and this shows a short-term increase in cell size and decrease in the percentage of hexagonal cells. This increase in cell size and decrease in hexagonal cells coupled with increase in % CV. In patients with polymegathism recovery of corneal thickness to preoperative values is significantly slower than control with normal endothelium.[37] In our study increase in mean CV% was 5.94±4.72 at day 1 and 2.94±2.24 at 3 month in group I whereas in group II, it was found 3.85±3.10 at day 1 and 2.76±1.57 at 3 month postoperatively. There was a significant difference in %CV between both the groups and between preoperative and postoperative periods. There are many studies which found a significant difference in CV and % HC between diabetic and non diabetic groups or postoperative and preoperative periods.[27,31,33,38] In our study maximum increase in % CV starts between day 1 and 1 week then tends to reduce slowly for 3 months. On postoperative day 1 the difference in CV% was significant between diabetic and non diabetic group (p=0.01) and became peak between 2week to 1 month and then disappeared at 3 months (p=0.64). These findings were supported by earlier studies.[1,33] Theoretically, this process of repair might be delayed or diminished in diabetes due to different durations of diabetes mellitus and blood glucose control.

Conclusion

To conclude we observed that corneal endothelium in patients with diabetes was more prone to surgical trauma than normal corneal endothelium and showed slow recovery fashion postoperatively. This might be due to metabolic stressful events occurring in corneal endothelial stroma. So it is important to choose proper timing with good glycemic status to perform cataract surgery in diabetic patient. It is suggested that diabetic corneal endothelium requires additional care and protective measures during cataract surgery to minimize surgical trauma.

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How to cite this article: Dandaliya I, Bedi D. K, Nainiwal S. K. Evaluation of corneal endothelial cell changes in diabetic patients before and after phacoemulsification surgery: A comparative study. Indian J Clin Exp Ophthalmol. 2018;4(4):458-464.