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Effect of Phacoemulsification on Corneal Endothelium in Type 2 Diabetic Patients Versus Normal Patients

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Abstract

Objective: This study aims to assess how phacoemulsification affects individuals with type 2 diabetes and normal corneal endothelium.

Patients and methods: This work involved 80 eyes of 80 individuals having surgery of cataract, classified into two equal groups, each of 40 eyes; group (1) with (T2DM) and group (2) without DM. After a full ophthalmic examination, the specular microscopic examination was performed for the determination of endothelial cell density.

Results: One month after surgery, a comparison between the two study groups revealed statistically insignificant differences in either group's central corneal thickness (CCT), coefficient of variation (CV%), or corneal endothelial cell density (ECD). However, their hexagonality (Hex) showed a significant difference ($P = 0.021$) in comparison between group (1 and 2). There is a significant decrease in ECD in both groups after one month of phaco surgery with a highly significant decrease in diabetic than non-diabetic groups ($P < 0.001$). The same was observed in Hex and CV%. Also, CCT was increased in both groups, more in the diabetic group (1) with highly statistically significance at ($P < 0.001$).

Conclusion: From this study, phacoemulsification decreases the corneal endothelial cell count, and type 2 DM facilitate this process and leads to more decrease in their density. Especially in diabetic individuals, phacoemulsification procedures might cause damage to corneal endothelial cells. Since diabetes individuals have impaired endothelial wound healing, maintaining endothelial cell health is crucial.

Keywords: Cataract surgery, Corneal endothelial cells, Type 2 diabetes mellites

1. Introduction

The rear of the cornea is lined by a single layer of cells called the corneal endothelium and originates in the neural crest. Endothelial cells often take on a uniformly hexagonal shape. The density of central endothelial cells diminishes from around 3400 cells/mm² at age 15 to about 2300 cells/mm² at age 85, a drop of about 0.6% each year.¹

Multiple illnesses, including diabetes² and others,³ may lead to corneal endothelial dysfunction. People suffering from DM is expected to triple in the next 20 years, from 285 million in 2015 to 693 million in 2045.⁴

Surgeons' primary focus during phacoemulsification has traditionally been on protecting the corneal

endothelium.⁵ Mechanical forces, like the jackhammer impact of longitudinal phaco cutting or the implosion of microcavitation air bubbles, are the root source of heat and increased high pressure in the anterior chamber.⁶ Both of these effects might be seen simultaneously. In a similar vein, the endothelium is subjected to a considerable amount of stress because of changes in ultrasonic power, fragment bouncing, fluid turbulence, and an increase in the formation of free radical oxygen species.⁷

There is a correlation between diabetes and an increase in the malfunction and death of endothelial cells in the clinic.² In addition, acute insults to the endothelium, such as acute glaucoma⁸ and phacoemulsification cataract surgery,⁹ may often accelerate

the death of endothelial cells, diminish the density of endothelial cells, and produce endothelial dysfunction, as well as corneal edema. However, further study is required to understand the exact causes of corneal endothelial dysfunction in diabetic people, as well as feasible treatment options for the condition.¹⁰

There is a lack of quantitative data to indicate that diabetes has a detrimental effect on the health of the corneal endothelium, despite several research indicating this affect. We thus expect this thesis to demonstrate that diabetes may compromise the health of ocular endothelial cells. Endothelium cells were lost at a higher rate after cataract surgery compared to healthy individuals. Therefore, during cataract surgery, care must be taken to prevent damage to the corneal endothelium. This study aims to assess the impact of phacoemulsification on the corneal endothelium of healthy individuals and those with type 2 diabetes.

2. Patients and methods

Between the months of January and December of 2022, this prospective clinical investigation was carried out in Egypt at the Al-Azhar University Hospital in the Ophthalmology Department. Before any participant participated in the study, written informed consent was obtained from that individual, and the technique used in the research was both approved by an institutional review board and adhered to the principles outlined in the Declaration of Helsinki.

Eighty individuals with cataracts were randomly assigned to participate in the trial after providing informed permission, for a total of eighty eyes. Group 1 had type 2 DM, whereas group 2 did not, and both groups had 40 eyes in total.

All included patients were eligible for cataract surgery with age more than 50 years. Patients had intact clear cornea and intact anterior chamber with CCT between 500 and 600 μm . However, patients with elevated intraocular pressure (IOP), corneal diseases (e.g., pterygium, ulcer, opacity, dystrophy, ... etc), symblepharon or conjunctival scar, previous trauma or surgery, posterior segment diseases were excluded.

2.1. Methodology

History and clinical ophthalmic examination, including visual acuity, refraction, anterior chamber (AC) slit-lamp biomicroscopy, IOP measurement, and specular microscopy (SM), were done.

Different results can be obtained from modern specular microscopy (NIDEK CEM-530, Japan), such

as central corneal pachymetry with endothelial cell analysis (ECD; cells/square millimeter; an average value for adults is 2400 cells/ mm^2 ; ranged from 1500 to 3500), cell morphology providing the polymegathism or CV% (>0.40 might not tolerate intraocular surgery), and/or the pleomorphism (the number of six- Now that SM is available, alterations in endothelial cells may be tracked over time. In addition, because it does not involve physical touch, it may be used to get information from individuals of all ages. The number of endothelial cells in the central cornea was counted using a 640×480 -pixel resolution (ROBO; Konan Storage System KSS 300; Konan Medical, Hyogo, Japan) noncontact specular microscope. Each patient had three endothelium readings recorded. Mean was calculated from these three readings. At a single clinical location, a single person took all the measures.

2.2. Statistical analysis

SPSS v23 (SPSS Inc., Chicago, Illinois) was used for the statistical analyses. For quantitative variables, descriptive statistics (means, correlations, and standard deviations) were computed. Parametric data were analyzed using two-tailed Chi-square, student's, and analysis of variance tests; non-parametric variables were analyzed with Mann–Whitney U and Kruskal–Wallis tests. *P* values below 0.05 were judged statistically significant, whereas those over 0.05 were deemed inconclusive.

3. Results

In this study, there were a total of 40 cataractous eyes, and they were split evenly between two groups: group (1) included people with type 2 diabetes, while group (2) excluded those with diabetes. In group 1, there were 24 males, which is 60% of the total, and 16 women, which is 40%. In group 2, there were 22 men, which is 55% of the total, and 18 women, which is 45%. The members of Group 1 ranged in age from 42 to 72 years old. With a mean and SD of 62.1 ± 5.36 years, while Group 2's age ranged from 45 to 74 years, with a mean and SD of 63.3 ± 6.42 years, respectively. Age and sex distributions of the two groups were comparable ($P > 0.05$) (Table 1).

Between the two study groups, the blood glucose level measurements revealed a statistically significant difference ($P < 0.001$). In contrast to the two study groups, the ocular metrics (IOP, K-reading, spherical equivalent, and axial length) were statistically insignificant ($P > 0.05$). The effective phaco

Table 1. Patients' characteristics of the two studied groups.

Sex	Group (1)		Group (2)		Significance	
	Number (%)		Number (%)		χ^2	P
Males	22 (55.0)		24 (60.0)		0.162	0.789
Females	18 (45.0)		16 (40.0)		0.154	0.872
Total	40 (100)		40 (100)			
Age (years)	Min	Max	Min	Max	t	P
Range	42	72	45	74		
Mean \pm SD	62.1 \pm 6.00		63.3 \pm 7.33		0.058	0.924

SD, standard deviation; t, unpaired t-test; χ^2 , Chi square.

time was 79.4 ± 15.7 and 78.6 ± 13.6 s in diabetic and non-diabetic groups, respectively. Moreover, the mean operation time was 12.13 ± 2.46 and 11.92 ± 1.93 min in diabetic and non-diabetic groups, respectively. In contrast to the other two groups, none of them showed a difference that was not statistically significant ($P > 0.05$) (Table 2).

When the preoperative corneal endothelial cell parameters of the two groups were compared with one another, there was not a statistically significant difference ($P > 0.05$) in the preoperative corneal endothelial cell parameters of either group (Table 3).

Comparison between the two studied groups one month postoperatively showed that a non-significant

difference in ECD, CV% and CCT in both groups. However, their hexagonality showed significant difference ($P = 0.021$) in comparison between group 1 and 2 (Table 4).

After one month following phaco surgery, there is a considerable drop in ECD in both groups, with a statistically highly significant decrease in diabetes than in nondiabetic groups ($P < 0.001$). The same was observed in hexagonality and coefficient of variance. Additionally, both groups' postoperative central corneal thickness rose, with the diabetic group (1) showing a statistically significantly greater rise ($P < 0.001$) (Table 5).

4. Discussion

There have been several studies showing how cataract surgery affects people with and without diabetes' morphological alterations, endothelial cell density, and central corneal thickness. However, between diabetes and nondiabetic individuals, morphological, endothelial cell loss, and central corneal thickness alterations differed greatly.^{11–13}

This study aims to assess how phacoemulsification affects individuals with type 2 diabetes and

Table 2. Comparison of preoperative and operative findings of the two studied groups.

Groups Item	Group (1)	Group (2)	Significance	
	With T2DM	Without DM	t	P
FBG (mg/dl)			1.216	0.001 ^a
Mean \pm SD	189.43 \pm 40.18	124.16 \pm 16.55		
Range	126–250	92.5–145		
PPBG (mg/dl)			2.167	0.000 ^a
Mean \pm SD	270.4 \pm 41.3	136.2 \pm 33.2		
Range	158–412	119–185		
HbA1c (%)			1.928	0.000 ^a
Mean \pm SD	9.43 \pm 2.82	4.16 \pm 1.22		
Range	6–12	3.5–5.65		
IOP (mmHg)			0.128	0.232
Mean \pm SD	16.4 \pm 1.49	17.6 \pm 3.24		
Range	13–19	13–20		
K-reading (D)			0.161	0.132
Mean \pm SD	41.3 \pm 1.38	42.2 \pm 1.41		
Range	38.1–43.2	38.9–44.5		
SE (D)			0.257	0.059
Mean \pm SD	−4.45 \pm 2.37	−3.50 \pm 2.71		
Range	−1.5 to −12.0	−1.25 to −10.0		
Axial length (mm)			0.127	0.192
Mean \pm SD	25.2 \pm 1.22	24.5 \pm 1.06		
Range	22.8–28.2	22.6–27.9		
EPT (sec)			0.043	0.624
Mean \pm SD	79.4 \pm 15.7	78.6 \pm 9.67		
Range	67–110	66.5–105		
Operation (min)			0.036	0.762
Mean \pm SD	12.13 \pm 2.46	11.92 \pm 0.83		
Range	9.35–13.4	9.25–12.9		

EPT, Effective phaco time; FBG, Fasting blood glucose; HbA1c, glycosylated hemoglobin concentration; IOP, intraocular pressure; PPBG, Post-prandial blood glucose; SE, spherical equivalent.

^a $P < 0.001$ = statistically significant difference.

Table 3. Comparison of preoperative endothelial cell and corneal thickness in the two studied groups.

Groups ECD	Group (1) Mean ± SD	Group (2) Mean ± SD	Significance	
			t	P
Mean ± SD	2618.2 ± 331.4	2543.6 ± 287.7	0.014	0.921
Range (cells/mm ²)	1864.5–3299	1716–3274		
Hexagonality (%)	51.9 ± 9.11	52.2 ± 7.49	0.036	0.762
CV (%)	38.2 ± 6.35	37.9 ± 6.32	0.048	0.596
CCT (µm)	523.6 ± 13.78	526.4 ± 14.93	0.016	0.912

$P > 0.05$ = insignificant.

CCT, Central Corneal Thickness; CV, Coefficient of Variance; ECD, Endothelial cell density; SD, Standard Deviation; t, unpaired t-test.

Table 4. Comparison of endothelial cell and corneal thickness one month post-operatively in the two studied groups.

Groups ECD	Group (1) Mean ± SD	Group (2) Mean ± SD	Significance	
			t	P
Mean ± SD	1682.1 ± 232.8	1785.6 ± 290.4	0.023	0.754
Range (cells/mm ²)	1319–2079	990.5–2541		
Hexagonality (%)	42.1 ± 9.01	51.9 ± 7.499	0.336	0.021 ^a
CV (%)	41.2 ± 5.71	38.7 ± 6.34	0.044	0.602
CCT	532.7 ± 15.19	529.1 ± 14.97	0.013	0.923

$P > 0.05$ = insignificant.

CCT, Central Corneal Thickness; CV, Coefficient of Variance; ECD, Endothelial cell density; SD, Standard Deviation; t, unpaired t-test.

^a $P < 0.05$ = significant.

normal corneal endothelium. We conducted prospective interventional research to examine the endothelial status of individuals having phacoemulsification with posterior chamber IOL implantation who had type 2 diabetes mellitus and those who did not. Cell density, hexagonality, size of the cell variation, and CCT as a stand-in marker for functional status were all included in the endothelium status.

Table 5. Comparison of change of endothelial cells and corneal thickness pre- and one month post-operatively in the two studied groups.

Groups ECD	Group (1) Mean ± SD	Group (2) Mean ± SD	Significance	
			t	P
Mean ± SD	936.1 ± 130.8	758 ± 101.6	3.127	0.000 ^a
Range (cells/mm ²)	545.5–1220	480–992		
Hexagonality (%)	9.8 ± 4.44	0.3 ± 0.23	10.38	0.000 ^a
CV (%)	3.0 ± 0.64	0.8 ± 0.756	1.844	0.001 ^a
CCT	9.1 ± 5.28	2.7 ± 0.809	5.714	0.000 ^a

CCT, Central Corneal Thickness; CV, Coefficient of Variance; ECD, Endothelial cell density; SD, Standard Deviation; t, unpaired t-test.

^a $P < 0.001$ = highly significant.

In this study, the effective phaco time was 79.4 ± 15.7 and 78.6 ± 13.6 s in diabetic and nondiabetic groups, respectively. Moreover, the mean operation time was 12.13 ± 2.46 and 11.92 ± 1.93 min in diabetic and nondiabetic groups, respectively. Phaco time and operation time comparisons between both groups did not reveal any significant differences ($P > 0.05$).

Patients whose nuclei are exceedingly difficult to grade (Grade IV and above) were excluded from our research because of the significant energy requirements of treating such severe cases of cataracts. There was statistically insignificant difference in nuclear density distributions between the two groups. This mirrored the findings of Sahu et al.,¹⁴ the first to report the impact of nucleus grading in phacoemulsification on corneal endothelium density. The amount of ultrasonic energy dissipated, or CDE, during phacoemulsification. The linear mode was disabled and only torsion power was employed. Torsional duration was divided by 0.4 times the average torsional amplitude to get CDE.

After a month after surgery, the present research found statistically insignificant differences in ECD, CV%, or CCT between the two groups. The hexagonality, however, was significantly different between the two groups ($P = 0.021$). After one month has passed after the phaco surgery, there is a decrease in ECD that is statistically significant in the diabetic group when compared to the non-diabetic group (P less than 0.001). The pattern could be seen in both the hexagonality and the coefficient of variation measures. In addition, after surgery, the thickness of the central cornea increased in both groups, but the increase in the diabetic group (1) was statistically significant. ($P < 0.001$).

Sahu et al.¹⁴ found that the average reduction in ECD was 5.95% (SD 3.08) in the DM group and 4.52% (SD 1.97) in the control group, which is consistent with our findings. There was a significant difference here ($P = 0.010$). Similar results were reported by Hugod et al.,¹⁵ who found a 6.2% decrease in ECD in diabetics but only a 1.4% decrease in nondiabetics at the end of 3 months following surgery, and by Morikubo et al.,¹⁶ who found a 3.2% decrease in ECD in nondiabetic patients and a 7.2% decrease in diabetic patients at the postoperative 1-month follow-up.

Khan et al.¹¹ and Elbasiounny et al.,¹² who conducted research that demonstrated the same thing, reported data that demonstrated that in the first postoperative month following phacoemulsification, there were no statistically significant differences in corneal endothelium density between diabetic and nondiabetic patients. Hugod et al.¹⁵ and Yang et al.¹⁶ concluded that endothelial cell loss was greater in diabetes patients than in nondiabetic persons for up

to three months following surgery. These results, however, ran opposite to those of Hugod et al.¹⁵ and Yang et al.¹⁶.

Endothelial cells are severely affected by the trauma caused by the ultrasonic energy used in phacoemulsification. Because of their smaller pupils, diabetic patients may need more irrigation solution and more ultrasound energy, increasing the risk of endothelial cell loss during surgery.¹⁵

Mean percentage of hexagonality was significantly different between the diabetes and control groups at one-month post-surgery in the present investigation. Both Hugod et al.¹⁵ and Yang et al.¹⁶ found that the hexagonality of their samples decreased more in their diabetes patients than in their control samples. Measuring endothelial density alone was insufficient to assess corneal endothelial cell function after intraocular surgery. Focusing on polymegathism, as evaluated by the coefficient of variation, and polymorphism, as measured by hexagonality, is an effective way to enhance the evaluation of corneal endothelial stress.¹⁷

Approximately 0–30% of endothelial cells are lost during intraocular surgery. A reduction in hexagonality is a parameter of corneal endothelial wound healing owing to trauma,^{15,18} and The phacoemulsification therapy itself is responsible for the loss of endothelial cells as an indirect impact.

Diabetic individuals may need more than 4 weeks following surgery to achieve a full corneal endothelial healing response, as shown by our finding of a larger drop in hexagonality % in the diabetic group 1 month after surgery. Diabetic individuals undergoing phacoemulsification may need more than a 4-week follow-up period. Endothelial cells are notoriously difficult to return to their stable hexagonal configuration after undergoing structural alterations. Diabetic individuals' restoration of hexagonality may take longer than three months. The cornea's endothelial cells, which compose its framework, are arranged in regular hexagonal patterns. Instability in the layer of corneal endothelial cells may result from the shifts in hexagonality.^{15,16,18}

The normal corneal endothelium is made up of hexagonal cells. This morphology is altered (pleomorphism) after an injury, and the proportion of hexagonal cells decreases. Our research shows that both diabetes and nondiabetic individuals experience a reduction in the proportion of hexagonal cells, however this trend is not statistically significant. Lee et al.¹⁹ and Sahu et al.¹⁴ found results that were quite similar. Similar findings were reported by Morikubo et al.,²⁰ whose research was limited by a 1-month follow-up that may have introduced bias since alterations do not settle at this point.

Hugod et al.¹⁵ found, in contrast, that only in diabetic individuals did the fraction of hexagonal cells decrease significantly. This disparity between our work and Hugod et al.¹⁵ may have been caused by racial differences in the metabolic profile of diabetic patients, this may have influenced how the ocular endothelial cells responded to the invasive surgical procedure.²¹ In addition, the corneal endothelial cells that were imaged for analysis were in the middle cornea, suggesting that the approach may miss morphological alterations that are more peripheral in nature.¹⁴

After phacoemulsification, there was no change in CV% between diabetic and non-diabetic individuals. Since corneal endothelial cells cannot renew, they instead extend and cover the cornea following surgery. That's why it's common for the CV % to rise and the hexagonality to fall following surgical intervention. The CV and hexagonality percentages, however, revert to prerecovery levels after the endothelial cells have completely recovered. After surgery, a patient's CV % quickly rises, peaks at 1 week, and then gradually drops to 19 months later. This might take more time in diabetic people. The outcomes may vary depending on the duration of diabetes and how well it is controlled.²²

The dispersion of endothelial cell size may be measured by its coefficient of variation. Pleomorphism is strongly correlated with value. It's a sign that the endothelium's mending and repair mechanisms are at work. In our investigation, preoperative results were similar across diabetic and nondiabetic individuals. Both groups demonstrated a statistically significant increase in CV% at the 3-month post-operative follow-up (relative to preoperative values), although the diabetic group showed a statistically substantially smaller change.¹⁴ This shows that endothelial cell regeneration is more sluggish and less robust in diabetics. This conclusion is supported by the trend analysis, which showed a decreasing rate of change in the diabetes population. Even, while Hugod et al.¹⁵ observed a lower CV% (33.2 after 3 months as opposed to 33.7 preoperatively), they did not find this difference to be statistically significant. Other research has shown no statistically significant variations in CV% shifts, including that of Morikubo et al.²⁰ and Lee et al.¹⁹ This finding is novel and lends credence to the hypothesis that endothelium in diabetes individuals exhibits a sluggish and subpar repair response.¹⁴

This study's findings showing diabetic and non-diabetic patients did not vary in CCT after surgery were consistent with those of Hugod et al.,¹⁵ Khan et al.,¹¹ Elbassiouny et al.,¹² and Budiman.¹⁷ The findings of many investigations with follow-up

periods of up to three months have been consistent. The impact of diabetes on CCT, however, remains unclear. Endothelial pump dysfunction, decline, stromal edema, and metabolic changes associated with diabetes all have the potential to enhance permeability. Corneal endothelial cells maintain the cornea's moisture and clarity by preventing stromal edema. Endothelial cells' apical tight connections function as physical barriers. The endothelial ionic pump, meantime, keeps water circulating from the cornea into the anterior chamber. Thus, diminished endothelial ionic pump activity or anatomical barrier deficiencies account for the increased central corneal thickness seen in patients who have had corneal surgery. The severity of endothelial cell damage determines the severity of these diseases.^{15,23,24}

Due to a variety of reasons, including polyol pathway activity and sorbitol buildup in endothelial cells because of a prolonged hyperglycemia state, the corneal endothelial cells of people with diabetes are more susceptible to damage. This makes diabetic patients' corneas more susceptible to damage. An increase in osmotic pressure is an additional factor that leads to this sensitivity. The accumulation of advanced glycation end products (AGEs) in diabetic patients' ocular endothelial cells has been linked to a higher risk of ocular complications.¹⁷ Causes oxidative stress to be experienced by the DNA cores of diabetic individuals. Diabetes causes a decrease in the amount of Na⁺ K⁺-ATPase activity in endothelial cells, which are cells that are important for maintaining the endothelium's integrity.^{15,16} It was discovered that the density of corneal endothelial cells, the hexagonality of the cells, and the CV were all comparable across groups who had different amounts of fasting blood glucose before surgery.

Ganesan et al.²⁵ found that after phacoemulsification, there was not a perceptible shift in the density of endothelial cells at any point throughout the study. They hypothesized that the diabetic population would have a considerable reduction in hexagonality. These findings coincide with the ones we found. This study's findings of reduced hexagonality suggest that delayed corneal healing in diabetes individuals and inflammation may play crucial roles.

This research may be limited by its short period of follow-up (4 weeks) and the fact that it did not examine pupil size or irrigation volume, both of which potentially alter endothelial cells following phacoemulsification in diabetes individuals.

4.1. Conclusion

From this study, phacoemulsification decreases the corneal endothelial cell count and type 2 DM

facilitates this process and leads to more decrease in their density. Diabetic individuals are at risk for corneal endothelial cell damage during the phacoemulsification operation. Diabetic patients, who have impaired endothelial wound healing, benefit greatly from measures taken to keep endothelial cells healthy.

Consent for publication

Not applicable.

Availability of data & materials

Data & materials were available.

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Authorship

The study plan and experiments design were done by Ali Ahmad Ali Khalifa. Experiments were carried over by Ehab Abdel Salam Azab El sheikh. Data analyses were carried over by Naef El sayed Abdel Aziz Ali. All authors read and approved the final version of the manuscript.

Conflicts of interest

Authors claim to have no conflicts of interest.

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