THE EFFECTS OF CATARACT SURGERY ON ENDOTHELIAL CELLS IN DIABETIC PATIENTS

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Cataract develops at an earlier age and more frequently in patients with diabetes. Corneal endothelium is a delicate tissue that is damaged during cataract surgery and appears that diabetic patients have an additional metabolic stress induced by hyperglycemia. Our purpose is to find the particularity of corneal endothelial cells in patients with diabetes mellitus before and after cataract surgery. We performed a study on a group of 32 cataract patients divided into cataract and diabetes mellitus group and cataract group. A preoperative specular microscopy was done. After phacoemulsification was performed, the effective phacoemulsification time (EPT) was recorded for each patient. Postoperatively, at one week and one month we made another specular microscopy. We studied the morphology and function of corneal endothelium before and after cataract surgery in diabetic patients compared to control group. Cataract surgery causes statistically significant damage in diabetic patients (101.57 cell/mm²/1sec EPT) compared with control group (20.91 cell/mm²/1sec EPT) after one month postoperatively. Corneal endothelium has a greater vulnerability in diabetic patients, so cataract surgery is recommended from the initial stages of evolution as the endothelial stress is lower.

Keywords: endothelial cells, cataract surgery, diabetes mellitus type 2, specular microscopy, effective phacoemulsification time

INTRODUCTION

World-wide 366 million people are estimated to have diabetes with an increasing trend towards younger people to develop diabetes. This number is expected to increase to 552 million by 2030 according to the International Diabetes Federation1. Diabetes mellitus is a systemic disease that can determine, due to chronic hyperglycemia, alteration in all the structures of the eye. As we know, patients can develop impaired corneal sensitivity, superficial punctuate keratitis, pupil abnormalities, cataract, retinopathy, hemorrhagicus, retinal detachment and vascular occlusions2. According to World Health Organization which the cataract remains the leading cause of blindness in developed and developing countries that occurs at an earlier age, affecting the working population, and and 2–5 times more frequently in patients with diabetes3. In a study from Iran, Janghorbani and Amini evaluated 3,888 type 2 diabetic patients and reported a rate of cataract formation of 33.1 per 1000 persons after a mean follow-up of 3.6 years. Studies related to the pathogenesis of cataract in diabetic patients have shown that the polyol pathway is involved in reducing the glucose to sorbitol by aldose reductase which accumulates intracellular creating a hyperosmotic shift with infusion of fluid into the lens and osmotic stress leading to cataract formation by inducing lens epithelial cells apoptosis4. It appears that hyperglycaemia is associated with loss of lens transparency in a cumulative manner due to osmotic overhydration leading to lens fibres swelling and rupture. Increased glucose levels in the aqueous humor may also induce glycation of lens proteins with generation of superoxide radicals and the formation of advanced glycation endproducts5. In mild degrees, the refractive index of the lens is affected with fluctuation of refraction with the plasma glucose level. First develop the fluid vacuoles witch later evolve into opacities. Rapid decline of serum glucose levels in patients with marked hyperglycaemia may induce temporary lens opacification and swelling as well as transient hyperopia6.

It is estimated that 20% of cataract surgeries are performed in diabetic patients and they have higher complication rates from cataract surgery than nondiabetics thus, an earlier cataract extraction is recommended6. Corneal endothelium is a delicate tissue that is damaged during cataract surgery and appears that diabetic patients have an additional metabolic stress induced by hyperglycemia. Our purpose is to find the particularity of corneal endothelial cells in patients with diabetes mellitus before and after cataract surgery.
MATERIAL AND METHODS

A clinical prospective study was performed on a group of 32 Caucasians patients scheduled to undergo cataract surgery. Patients were investigated, surgically treated and followed in the Ophthalmology Clinic of the Emergency University Hospital, Bucharest. The dates were collected between July 2015 and September 2015. The study respects the ethical criteria of the medical community, provided in the WHO Helsinki Declaration and the patients signed a written consent before inclusion into the study. In the study were included patients with cataract diagnosis confirmed at slit-lamp examination that signed the informed consent for cataract surgery. From the study were excluded patients with type 1 diabetes mellitus, patients incapable of understanding the procedure, with mental illness or those who refused the postoperatively treatment or the tests necessary for follow-up, patients with a history of previous ocular disease, contact lens wear, trauma or intraocular surgery, those with co-existing ocular disorders (conjunctivitis, keratitis, uveitis, glaucoma, pseudoexfoliative syndrome, corneal dystrophies, scars, corneal leukomas), endothelial cell density under 1500 cells/mm², intraoperatively complications such as posterior capsule rupture, an phacoemulsification time (called also effective phacoemulsification time- EPT) under one second or higher than 10 seconds, postoperative ocular hypertony, patients with complications post cataract surgery and those that missed the post-surgical mandatory follow-ups. After we performed a blood glucose level à jeun to disclose undetected diabetes and serum glycosylated haemoglobin, HbA1c, in all type 2 diabetic patients to evaluate their glycaemic status, we formed one group of 16 patients with cataract and a group of 16 patients with cataract and diabetes mellitus type 2 with similar age and sex. Preoperative, at one week and one month all patients were investigated, by the same technician, in the eye scheduled to undergo cataract surgery using a non-contact Topcon SP-3000P specular microscope. The recorded parameters were central corneal thickness (CCT), standard deviation of cell area (SD), cell density (CD), coefficient of variation (CV) and percentage of hexagonal cells (HEX). An automated cell analysis was done and center to center method was used to determine cell area from adjacent polygon centers with about 100 cells counted per frame. One day before surgery were recorded for each patient: visual acuity for both eyes, corneal keratometry and biometry, visual field, IOP (intraocular pressure using Goldmann aplano-tonometry), slit-lamp and posterior fundus examination. At 1 week and 1 month after cataract surgery VA, slit-lamp examination, non-contact specular microscopy and IOP were performed. All the enrolled patients were examined and surgically treated by the same ophthalmmo-logist using the same phaco-machine (Stellars) and surgical technique (stop and chop with posterior chamber foldable artificial intraocular lens implantation). After phaco-emulsification was performed, the effective phaco-time (EPT) was recorded for each patient. Postoperatively, at one week and one month we made another specular microscopy. We studied the morphology and function of corneal endothelium before and after cataract surgery in diabetic patients compared to control group.

Statistical analysis was performed. Were considered statistically significant p values <0.05. The results were presented as a mean ± standard deviation.

RESULTS AND DISCUSSION

We can observe an initial higher standard deviation (SD) of the mean cell area in the diabetic group of 164.9 ±85.26 versus 134.61±45.12 in the control group, statistically significant. The coefficient of variation (CV) was statistically significant different between both groups, the diabetic group and the non-diabetic group, initial as well at one week and at one month postoperatively. (Figure 1) An initial higher CV was observed in the diabetic group (37.81±15.52 μm²) compared to non-diabetic group (28.93±6.21 μm²). At one week after cataract surgery CV presents an increase until 31.78±6.33 μm² in non diabetic group versus 39.79 ± 13.80 μm² in diabetic group. A decrease in the variability of cells size (CV) was observed at one month toward the initial values for both groups (29.83±5.74 μm² in non-diabetic group and 36.69±13.65 μm² in diabetic group). The variability of cells size, taking into account the effective phacotime, was greater in diabetic group related to non diabetic group but the difference wasn’t statistically significant.

![Figure 1](image_url)

**Figure 1** Coefficient of variation initial, at one week and at one month in group 1 (non-diabetic group) and in group 2 (diabetic group)

The initial central corneal thickness (CCT) in control group (514.38±23.6μm) is similar to diabetic group (520.76±23.90 μm) with no statistical significance. (Figure 2) Compared to the initial values, at one week postoperatively there is an increase in mean CCT in the control group of 19.27±19.34 μm and in the diabetic group of 16.92±21.18 μm with a slightly decrease at one
month (−8.33 ± 23.61 14.27 versus −4.84±14.27) but with no statistical significance.

Figure 2 Initial central corneal thickness, at one week and one month in group 1 (non-diabetic group) and in group 2 (diabetic group)

Watching the changes in endothelial cell density in diabetic group at one week postoperatively we observe a greater and statistically significant loss of endothelial cells in the centre of the cornea of 320.15±245.03 cells/mm² compared to control group of 132.94±111.19 cells/mm ² (p<0.05). The loss of endothelial cells at one month compared to the initial values was statistically significant, 111.44±131.55 cells/mm² in control group and 290.84±215.51 cells/mm² in the diabetic group, p<0.01. (Figure 3, Figure 4)

Figure 3 Endothelial cell density in group 1= non-diabetic group and in group 2, diabetic group initially, at one week and at one month

Figure 4 Endothelial cells loss at one week and one month in group 1= non-diabetic group and in group 2= diabetic group

At one week after cataract surgery related to EPT (effective phacoemulsification time) in the diabetic group are lost 111.90±132.94 cells per one second during cataract surgery compared to control group where is a lost of 30.41±24.36 cells per one second of EPT. The difference in CD at one month is of 20.91±22.56 cells per second of EPT in the control group compared to diabetic group 101.57±112.53 cells per second of EPT. (p<0.001) (Figure 5)

Figure 5 The differences in endothelial cell density related to 1 second of EPT in group 1 (non-diabetic group) and in group 2 (diabetic group)
Increased variability in the size of corneal endothelial cells is termed polymegathism. Yee et al reported a CV range of approximately 0.22 to 0.31 for young adults with an average of 0.27. It appears that polymegathism is often seen in diabetics when no other ocular disease is apparent. The mechanism it’s not fully understood but it appears that polyol pathway is responsible not only for cataract formation but also for the accumulation of sorbitol into the endothelial cells. This process is being possible due to the presence of aldose reductase also at this level leading to a rise in endothelial cell osmolality and secondary fluid accumulation causing alterations in cells size and shape (pleomorphism). This possible mechanism leads to the idea that inhibitors of aldose reductase reverse endothelial poly-megathism. The clinical significance of endothelial polymegathism remains uncertain. As a general anecdotal consent it appears that polymegathism occurs in diseased corneas with a reduced functional reserve capacity and that they are more prone to develop corneal oedema after cataract surgery.

In our study we found an initial coefficient of variation statistically significant higher in diabetic group (37.81±15.52 μm²) versus control group (28.93±6.21 μm²). Also an initially statistically significant higher standard deviation of the mean cell area in the diabetic group of 164.92±85.26 versus 134.61±45.12 correlates well with the polymegathism observed in diabetic patients according to the formula used (CV= standard deviation cell area/ mean cell area, μm²)

It is also known in the specialty literature that after cataract surgery because of surgically induced trauma there is an additional variability in cells size, this idea is also supported by the results encountered in our study showing an increase in CV at one week and one month after cataract surgery in all patients from the both groups. Therefore, at one week after cataract surgery CV presents an increase to the value of 31.78± 6.33 μm² in non diabetic and to 39.79 ± 13.80 μm² in diabetic group with a return in the variability of endothelial cells size at one month toward the initial values for both groups (29.83±5.74 μm² in non diabetic group and 36.69±13.65 μm² in diabetic group).

In our study, the initial central corneal thickness, which is an indirect indicator of the corneal endothelial Na⁺ /K⁺ pump function, is slightly higher in diabetic group (520.76±23.90 μm) than in control group (514.38±23.6 μm) with no statistical significance. There are studies that reported a statistically significant increase in CCT in diabetic patients but still with no clinical relevance as there wasn’t corneal oedema observed in the studied patients. There are studies on corneal endothelium in diabetic patients that reported a decrease in the percentage of hexagonal cells (HEX), so a higher pleomorphism (increased cell shape variation) but in our study we did not find any statistically significant differences between the groups. As regarding the corneal endothelial cell density in type 2 diabetic patients we did not find any statistically significant differences compared to non-diabetic patients with similar age. These results are consistent with the results found in different studies. It appears that an endothelial cells lost is more likely to be found in patients with type 1 diabetes. The mean endothelial cell density is approximately 6000 cells/mm² during the first month of life, 3400 cells/mm² at the age 16 and 2300 cells/mm² at age 85 years with an average rate of natural decrease throughout life of about 0.6%/year. These facts together with an abnormal morphology of the corneal endothelium in diabetic patients, caused by chronic metabolic changes at the cellular level affecting the endothelial cells, makes it less stable and more vulnerable to surgical trauma and has a delay in the healing process leading to cataract surgery recommendation from the initial stages of evolution as the endothelial stress is lower. The response of corneal endothelium in surgically induced trauma, such as cataract surgery, is an acute accelerated loss of endothelial cells and a minimum of approximately 500 normal cells are required to prevent corneal decompensation that can lead to pseudophakic bullous keratopathy according to specialty literature. Thus, the corneal endothelial cell density is a parameter used in quantifying corneal function postoperatively.

At one month postoperatively it seems to be a partial recovery of endothelial cell density measured in the centre of cornea (probably due to a redistribution process) in both groups. Despite this redistribution the endothelial density remained under the initial values at one month. After cataract surgery a natural healing process takes place and the remaining endothelial cells enlarge trying to occupy any remaining free spaces between the cells in order to obtain a contiguous monolayer of cells, inducing short time polymegathism and pleomorphism. After the healing process ends, the endothelium becomes stable and CV and HEX regain the initial values, before phacoemulsification. This healing process appears to start later and to take longer in diabetic patients compared with non-diabetics. We have been studied also the endothelial cells loss related to the effective phaco time used during cataract surgery for each patient. By approximation, at one month there was a 5 times bigger loss of endothelial cells per second of EPT in the diabetic group.

CONCLUSIONS

A diabetic patient loses approximately five times more endothelial cells per 1 second EPT than non-diabetics therefore they are more vulnerable and more prone to develop complications post cataract surgery such as corneal decompensation and pseudophakic bullous keratopathy. Cataract surgery is recommended from the initial stages of evolution as the endothelial stress is lower and additional intraoperative measures for preserving endothelial cells should be taken into account. We found an initial polymegathism in diabetic patients compared to non-diabetic patients. Corneal endothelium’s morphology in diabetic patients was
analyzed by different authors but the results are inconsistent and further studies needs to be done.

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