

The Influence of Phacoemulsification on Corneal Endothelial Cells at Varying Blood Glucose Levels

RuiMing Yang, Xiangyin Sha, Mingbing Zeng, Yingqian Tan, Yu Zheng, Feihong Fan
Department of Ophthalmology, the Second Affiliated Hospital of Guangzhou Medical University,
Guangzhou 510260, China

Abstract

Purpose: To investigate the influence of phacoemulsification on corneal endothelial cells in diabetes patients and normal controls.

Methods: Phacoemulsification and intraocular lens implantation were performed on 75 patients with diabetic cataract (126 eyes) who were divided into two groups; Trial group 1 (Glu ≤ 6 mmol/L); Trial group 2 (Glu 6–10 mmol/L) and 65 non-diabetic controls (112 eyes). The density and percentage of hexagonal cells and coefficient of variation of the corneal endothelia were measured before surgery and 1 day, 1 month and 3 months postoperatively.

Results: There was no statistical difference in the density and percentage of hexagonal cells and coefficient of variation of the corneal endothelia prior to phacoemulsification ($P > 0.05$) between the three groups. The density and percentage of hexagonal cells of the corneal endothelia decreased significantly after surgery in all three groups ($P < 0.05$), while the Coefficient of variation increased in all groups ($P < 0.05$). The rate of loss of corneal endothelial cells in the diabetic groups was significantly higher than for the control group ($P < 0.05$), the percentage of hexagonal cells in the diabetic groups was significantly lower than for the control group ($P < 0.05$), and the coefficient of variation in the diabetic groups was significantly higher than for the control group ($P < 0.05$) at 1 day, 1 month and 3 months post-operatively. There was no statistical difference between the two diabetic groups in terms of these post-operative measurements.

Conclusion: The corneal endothelium of diabetic patients is more prone to damage from phacoemulsification. It is advisable to evaluate the corneal endothelium routinely prior to phacoemulsification, particularly in diabetic persons. (*Eye Science* 2011;26:92–96)

Keywords: cataract; phacoemulsification; diabetic cataract; corneal endothelial cell

A growing proportion of cataract patients in China have concurrent diabetes, while diabetic patients have a significantly higher incidence of cataract than the general population. Although phacoemulsification has become the procedure of choice for cataract, due to smaller wound size and more rapid visual recovery, it may injure the corneal endothelium, particularly in diabetic patients¹. If patients' corneal endothelium is not routinely evaluated pre-operatively, this may lead to higher risk of visually-significant corneal edema among patients with hypofunctioning or even quasi-decompensated corneal endothelium.

In the current study, the corneal endothelial cell count, percentage of hexagonal cells, and coefficient of variation of endothelial cell size were evaluated pre and post-operatively among cataract patients with and without diabetes, respectively.

Materials and methods

Clinical methods

Among all cataract patients who underwent phacoemulsification and intraocular lens implantation in the Department of Ophthalmology, Affiliated Second Hospital of Guangzhou Medical University, between March 2008 and August 2010, 75 patients (126 eyes) with concurrent diabetes were selected for operation by the same experienced surgeon. These patients were recruited for the study and assigned to one of two groups. Trial group 1 included 36 patients (61 eyes) whose pre-operative fasting blood glucose was ≤ 6 mmol/L; while group 2 included 39 patients (65 eyes) whose fasting blood glucose was 6–10 mmol/L before the procedure. Another group of patients without a history of diabetes, who also underwent phacoemulsification for uncomplicated age-related cataract by the same sur-

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Corresponding author: Ruiming Yang, female, born in Mar. 1968, vice-consultant; Tel: 13556010106, E-mail: ycy602@163.com

geon at the same institution during the same period, were selected as normal controls.

Inclusion criteria: ① No history of intraocular incisional or laser surgery, high myopia, or ocular trauma; ② Normal pre-operative slit lamp examination (specifically, with no evidence of keratopathy, glaucoma, or uveitis); ③ Normal pre-operative ocular mode-B ultrasound (specifically without evidence of severe vitreous opacity or retinal detachment); ④ Intraocular pressure < 21 mm Hg pre-operatively; ⑤ No known history of hypertension or renal diseases; ⑥ No significant complications during or after the procedure. Hardness of the lens nucleus was rated as grade 3 to 4, according to the Emery-Little classification system.

All patients mentioned above underwent non-contact corneal endothelial microscopy (Topcon SP-2000P, Japan) by the same proficient technician. Images presented on the monitor were analyzed and processed by software on the device, which automatically calculated endothelial cell density, percentage of hexagonal cells and coefficient of variation. Each picture was analyzed three times and the mean value recorded. Preoperative evaluation was performed, and at 1 day, 1 month and 3 months post-operative evaluation was conducted.

Surgical approach

Before the procedure, tropicamide topical eye drops were administered to achieve adequate mydriasis, and surface anesthesia was induced with three drops of topical Alcaine. A self-sealing 3.2 mm clear corneal incision was made at 10:30–12:00, supplemented by a 1 mm limbal incision at 14:00. Sodium hyaluronate gel (Qisheng Biology Ltd., Shanghai) was injected into the anterior chamber; and a 5–5.5 mm continuous curvilinear capsulorhexis was created. A stop-and-chop technique was used for phacoemulsification inside the capsular bag; cortex was removed by I/A suction. A SA60AT foldable artificial lens (Alcon Laboratories, Inc, Ft. Worth, TX) was implanted into the capsular bag. After the procedure, corticosteroid and antibiotic eye drops were administered topically. The identical phacoemulsification system was used for all procedures (Infiniti, Alcon Laboratories, Ft. Worth TX). Mean negative pressure was 300–400 mm Hg throughout the pro-

cedure, with a mean ultrasonic energy of 19% and a mean ultrasound duration of 1–3 min.

Statistical analysis

SPSS 10.0 (IBM Corp., Armonk NY) statistical software was used for all statistical analysis and data processing. Comparisons among three groups and between either two of the groups were made with the t-test, with $P < 0.05$ indicating statistical significance.

Results

Demographic and clinical information

Trial group 1, with blood glucose ≤ 6 mmol/L included 61 eyes of 36 subjects (16 males (28 eyes) and 20 females (33 eyes) aged 50 to 81 years, with a mean of 67.5 years. Trial group 2, with blood glucose 6–10 mmol/L, included 65 eyes of 39 subjects (18 males (30 eyes) and 21 females (35 eyes)) aged 53 to 84 years, with a mean age of 68.6 years. Finally, the control group of non-diabetics consisted of 65 patients (112 eyes), including 33 males (61 eyes) and 32 females (51 eyes), aged 51 to 83 years, with a mean of 67.8 years. For all patients, visual acuity ranged from hand movement to 6/30. The duration of diabetes was 1 to 17 years.

No statistically significant differences were found among the three groups in terms of age, gender, or pre-operative visual acuity ($P > 0.05$ for all). Hardness of the lens nucleus was rated according to the classification system of Emery-Little, and no significant differences were detected between the three groups ($P > 0.05$). Best-corrected visual acuity was 6/12 to 6/5 at 3 months post-operatively for all three groups, with no significant differences.

Corneal endothelial cell density

Central corneal endothelial cell density, percentage of hexagonal cells, and coefficient of variation of cell size for all subjects pre-operatively and at different time points post-operatively are shown in tables 1, 2 and 3. No statistically significant differences were seen among the three groups for any of these parameters pre-operatively. Corneal endothelial cell count decreased post-operatively for all three groups. The two diabetic groups had significantly lower post-operative corneal endothelial cell density than the control group at various time points, while no significant differences were detected between the

Table 1 Comparison on density of central corneal endothelial cells before and after the procedure (mean \pm SD)/mm²

Groups	Before procedure	1 day after procedure	1 mo after procedure	3 mo after procedure
Trial group 1	2700.00 \pm 548.00	2100.00 \pm 458.00	2140.00 \pm 567.00	2200.00 \pm 447.00
Trial group 2	2690.00 \pm 492.00	2050.00 \pm 501.00	2160.00 \pm 517.00	2220.00 \pm 490.00
Control group	2700.00 \pm 487.00	2300.00 \pm 520.00	2470.00 \pm 433.00	2430.00 \pm 531.00

Table 2 Comparison on percentages of central corneal hexagonal cells before and after the procedure (mean \pm SD)/%

Groups	Before procedure	1 day after procedure	1 mo after procedure	3 mo after procedure
Trial group 1	53.20 \pm 3.11	42.30 \pm 1.31	43.00 \pm 8.52	45.50 \pm 9.17
Trial group 2	51.90 \pm 6.58	41.70 \pm 5.67	42.90 \pm 7.23	44.00 \pm 3.19
Control group	55.30 \pm 3.68	48.00 \pm 2.18	48.60 \pm 8.58	49.40 \pm 3.28

Table 3 Comparison on coefficient of variation in central corneal endothelial cell size before and after the procedure (mean \pm SD)

Groups	Before procedure	1 day after procedure	1 mo after procedure	3 mo after procedure
Trial group 1	41.60 \pm 2.12	66.40 \pm 3.98	60.20 \pm 2.78	59.60 \pm 3.66
Trial group 2	42.30 \pm 1.09	69.30 \pm 9.10	61.80 \pm 3.16	61.00 \pm 2.89
Control group	40.20 \pm 2.12	56.20 \pm 6.76	51.40 \pm 1.69	49.00 \pm 2.78

two diabetic groups regarding endothelial cell density post-operatively.

Percentage of hexagonal cells in corneal endothelium

No statistically significant difference was found between the three groups pre-operatively. For all groups, the percentage of hexagonal cells in the corneal endothelium was reduced post-operatively. The two diabetic groups had significantly lower percentages of hexagonal corneal endothelial cells than the control group measured at all time points. Between the two diabetic groups, no significant differences were found at any time point.

Coefficient of variation in corneal endothelial cell size

Preoperatively, no significant differences were detected among the three groups. For all three groups, the coefficient of variation of corneal endothelial cell size was increased post-operatively. The two diabetic groups had significantly post-operative greater coefficient of variation of corneal endothelial cell size than the control group at various time points, while no statistically significant differences were seen between the two diabetic groups at any time point.

Discussion

Corneal endothelial cells possess particular properties when compared to other types of endothe-

lial cells: (1) A stable hexagonal structure. (2) Inter-cellular tight junctions that act as a passive barrier. (3) A requirement of Na⁺-K⁺-ATPase enzyme as a biological sodium pump². These specific structures and functions in endothelial cells play a vital role in the maintenance of constant stromal water content and corneal transparency.

The density of corneal endothelial cells and percentage of corneal hexagonal cells directly reflect the health of the corneal endothelium. The coefficient of variation of cell size has also been recognized as a sensitive marker for endothelial damage.

Inoue k et al suggested age as a major factor influencing the morphology of the corneal endothelium before surgery, while axial length and the presence or absence of diabetes were not correlated with any endothelial morphologic parameters³. In the results of the current study, no statistically significant differences were noted among the two diabetic groups and the control group in density of corneal endothelial cells, percentage of hexagonal cells, and coefficient of variation pre-operatively, demonstrating that corneal endothelial morphology was not related to diabetes, consistent with Inoue's findings.

For all three groups, the decrease in corneal endothelial density, percentage of hexagonal cells, and the increase in coefficient of variation of cell size were more prominent at 1 day post-operatively than at 1 or 3 months, when these changes tended to be

mild, suggesting a certain reparative capacity for corneal endothelial cells. At various time points within 3 months after the procedure, all patients in the three groups presented with lower corneal endothelial density, a lower percentage of hexagonal cells, and higher coefficients of variation as compared to those before the procedure. At various time points after the procedure, the decrease in corneal endothelial density and percentage of hexagonal cells and the increase in coefficient of variation for the two groups of diabetic patients were significantly greater than those in the control group. This indicates that diabetic patients are more susceptible to corneal endothelial damage during phacoemulsification, which might be explained by the fact that the activity in polyol pathway is increased in diabetic patients, so that additional glucose is transformed into sugar alcohols, and then accumulates in cells. Aldose reductase in the polyol pathway is distributed over the corneal epithelial and endothelial cells, while accumulation of sugar alcohols leads to increased osmotic pressure, rendering corneal endothelial cells more vulnerable. It has been suggested that high levels of glucose reduce the cornea's ability to control hydration/dehydration, and impairs the activity of the $\text{Na}^+ - \text{K}^+ - \text{ATPase}$ enzyme in corneal endothelial cells and interferes with the functions of this fluid "pump"⁴.

Such metabolic stress evidently impairs the ability of corneal endothelial cells to resist mechanical stress, such as phacoemulsification. Moreover, since glucose concentration in the aqueous humor is frequently increased in diabetic patients on a long-term basis, normal glucose metabolism in the cornea is affected, possibly resulting in metabolic acidosis in the corneal matrix and subsequent changes in corneal endothelial morphology and function. Capacity for repair and compensation are decreased, reducing the ability to cope with ocular disease, injury and surgical trauma.

Phacoemulsification has become the treatment of age-related cataract due to the small incision, which results in better control of post-operative astigmatism and more rapid recovery of visual acuity when compared to larger-incision techniques. Still, endothelial cell damage is a potential concern. A critical require-

ment in obtaining good visual acuity after phacoemulsification is to maintain corneal transparency, which depends on intact corneal structure, normal endothelial cell density and good endothelial pump function. Since corneal endothelial cells are terminal cells, incapable of division, damaged areas will not be repaired by mitosis and proliferation when cells are injured. Such areas can only be covered by enlargement, expansion and migration of adjacent cells. As a result, significant changes in cell size and morphology are inevitable after such repair. Among patients undergoing phacoemulsification, loss of corneal endothelial cells is unavoidable due to the mechanical injury caused by repeated insertion and withdrawal of surgical instruments and the heat injury induced by ultrasonic energy. It has been suggested that the rate of loss of corneal endothelial cells is highly and positively correlated with the levels of ultrasonic energy used intra-operatively¹. Hence, proper pre-operative treatment regimens should be established for diabetic patients. This, combined with careful pre-operative assessment of the condition and compensating capacity of the corneal endothelium, proper selection of surgical approach, and minimal duration of phacoemulsification during the procedure, may help to reduce the risk of corneal decompensation. In addition to limiting ultrasonic energy to the extent possible, phacoemulsification should also be performed within the capsular bag, and a stable anterior chamber should be maintained. Mechanical injury caused by repeated insertion and withdrawal of surgical instruments from the eye should be limited, and high-quality perfusate⁵ and viscoelastic agents^{5,6} administered. These measures are critically important to reduce the loss of corneal endothelial cells and maximize recovery of visual acuity after the procedure in patients with cataract and concurrent diabetes.

Since corneal endothelial cells have significant reserve capacity, severe complications, such as bullous keratopathy, will generally only be seen when insults exceed the cornea's ability to compensate. Therefore, although the phacoemulsification in the current study caused a decrease in density of endothelial cells and the percentage of hexagonal cells, no significant complications, such as severe corneal

edema, were observed.

In summary, maintaining adequate corneal endothelial health poses a particular challenge after phacoemulsification and intraocular lens implantation in diabetic patients.

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