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PREDISPOSING FACTORS FOR ENDOTHELIAL CELL INJURY IN DIABETIC PATIENTS FOLLOWING PHACOEMULSIFICATION

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Abstract:

Aim:- *To determine the risk factors contributing to the Endothelial Cell Loss (ECL) in diabetics following Phacoemulsification as compared to age and sex matched Non-diabetics.*

Results:- *It was found that Diabetics in the age group 60-69 have 4.1 times more risk of ECL than control group (OR:4.1, C.I: 1.218-2.976, p=0.03). The other major risk factors such as Effective Phaco Time (EPT) (OR: 3.1, C.I: 1.721-9.332, p=0.04), Ultrasound time (UST) (OR: 2.8, C.I: 1.416-5.727, p=0.02) and Inflammation score (OR: 4.3, C.I: 2.529-14.762, p=0.01) were significantly associated with higher risk of ECL in diabetics more than Non-diabetics. We found reduced Endothelial Cell Density (ECD), Increased Central Corneal Thickness (CCT) with statistical significance (p= 0.04, 0.03 respectively). Coefficient of variation (CV) and Hexagonality did not show any statistically significance in ECL during follow-up of 3 months post-operatively.*

Materials and Methods: *- This is a case-control study employed at Parsian Eye Clinic, Islamic Azad University, Iran with 60 patients in each Diabetic and Control group. The pre-operative baseline characteristics were obtained, Intra-operative Ultrasound time (UST), Effective Phaco Time (EPT) and post-operative Endothelial Cell Density (ECD), Central corneal thickness (CCT), Coefficient of variation (CV) and Hexagonality at 1-week, 1-month and 3-months following phacoemulsification were measured using Keelar-Konan specular microscope (Model- CSP 580).*

Conclusion: *- Our study suggests that diabetics has profound ECL, increased CCT and reduced Hexagonality following phacoemulsification. It was found that EPT, UST and Inflammation score are associated with higher risk of ECL and more so in Diabetics as compared to control group. Future studies with larger sample size and longer follow-up with alternative surgical techniques are warranted taking in account other possible factors determining the Endothelial injury.*

Keywords: *Phacoemulsification, Cataract, Endothelial Cell Loss, Diabetes.*

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INTRODUCTION:

In diabetics, long standing hyperglycemia leading to overproduction of Reactive Oxygen Species (ROS) overwhelming the antioxidant defense mechanism by polyol pathway is thought to be the primary mechanism behind the formation of Cataract [1]. The corneal endothelial cell function in diabetics is reduced significantly and any forms of deleterious stress might take longer recovery period due to oedematous cornea [2]. Corneal oedema is attributed to reduced Na+ - K+ ATPase pump [3]. The endothelial cell density and Central corneal thickness was also found to be decreased in diabetic patients [4].

An umbrella term "Diabetic Keratopathy" is used to define the complications seen in diabetic cornea, which include recurrent corneal erosions, impaired wound healing, and oedema [5]. The parameters such as Phacoemulsification technique employed, Intraocular Inflammation, lens nucleus density, axial length and anterior chamber depth play a consequential role in the endothelial cell loss [6]. The intent of this study is to underscore the factors influencing the endothelial cell damage following phacoemulsification procedure for cataract in diabetic patients.

Parameters	**Mean ± SD**		***p*-value**
	Controls (n=60)	**Diabetics (n=60)**	
Age	58.2 ± 4.3	52.7 ± 5.1	0.07
Sex (%)			
a. male	72.5	66.8	0.42
b. female	27.5	33.2	0.78
ECD	2397 ± 322	2331 ± 374	0.31
CV	42.4 ± 5.7	43.9 ± 6.1	0.28
Hexagonality (%)	37.5 ± 8.1	39.2 ±7.2	0.09
CCT (µm)	559 ± 42	564 ± 37	0.41
Inflammatory score	1	1	0.18

MATERIALS AND METHODS:

Our study is a prospective case-control study involving two study groups- nondiabetics and diabetics who underwent phacoemulsification surgery at our institute Parsian eye clinic, Islamic Azad University, Iran from June-2018 to March-2019. We included study subjects with Non-insulin dependent diabetes mellitus (Type-2) above 42 years of age and nuclear sub-type cataract and excluded other sub-types of cataract, previous ocular surgery, recent trauma and those with severe myopia (≥ 6D) and present cornea inflammation and opacities.

A preoperative extensive ocular examination, Endothelial cell density [ECD], Endothelial cell count, Coefficient of variation of cell size [CV], hexagonality, along with corneal cell count and Central corneal thickness [CCT] was obtained using Keelar-Konan specular microscope (Model- CSP 580).

All the involved study subjects were detailed with regards to the study and written informed consent was obtained.

Tropicamide, Phenylephrine was used for pupillary dilation, ketorolac-tromethamine 0.4% for pain, Ofloxacin-prednisolone for antibiotic coverage. The "Divide and Conquer" phacoemulsification technique was employed in all the cases. Aspiration flow rate with ringer's lactate was set at 30 mL/min. After making a clear corneal incision at with a 2.5 mm (double- bevel) incision knife. Next, ophthalmic viscosurgical device (OVD) was introduced in the anterior chamber. Aurolab hydrophobic foldable acrylic intraocular lenses were preferred Intra ocular lenses in all the subjects. The clear corneal wound was sutured with nylon 10-0. Intra-operatively we noted phacoemulsification time and mydriasis, Post-operatively visual acuity, ocular inflammation scores, coefficient of variation, corneal thickness and hexagonality were calculated at 1-week, 1-month and 3-months later. We used chi-square test for categorical variables, Independent student's *t*-test for continuous variables to compare the difference among the groups. Multiple logistic regression was employed to establish the independent risk factor associated with the outcome measured. An alpha criterion of 0.05 was set and p-value ≤ 0.05 was considered statistically significant. All the obtained data was analysed using

SPSS (version 20.0, SPSS Inc. IBM, Armonk, NY, USA).

DISCUSSION:

In this study, we make an attempt to delineate the determinants leading to endothelial cell loss and injury following phacoemulsification. As a person ages, there is linear physiological decline of corneal keratocytes and endothelial cells [7,8]. In the past, there were studies that estimated the Endothelial cell reduction with each passing year. A study conducted by Moller-Pedersen et al. showed an estimated 0.3% loss every year whereas Niederer et al. reported it to be 0.5% every year [9,10]. In addition, diabetics have decreased baseline Endothelial Cell Density (ECD) and Central Corneal Thickness (CCT) in comparison to healthy individuals as demonstrated by Beata Urban et al [11]. In a recent study done by Sahu PK et al. there was proportionately higher decline in ECD following phacoemulsification as compared to healthy non-diabetic control group, another similar study by He X et al. shows higher Endothelial Cell Loss (ECL) in diabetics (p=0.03) supports the findings of our study [12,13]. Although the diabetics have a more preponderance for ECL, there are many factors such as Phacoemulsification technique, time, viscoelastic substance used and nuclear density which are shown to contribute in the ECL postoperatively [14,15]. In contrast, Misra et al. in his prospective study distinctively concluded that diabetes is not a risk factor for ECL but rather sub-basal nerve plexus density determines the ECL and sub-basal nerve density is reduced after cataract surgery in both diabetics and non-diabetics [16]. Hudod M et al. study reveals greater ECL (p= 0.04) and decreased hexagonality (p= 0.01) in diabetic group under glycemic control as compared to control groups without diabetes three months after Phacoemulsification, it supports the outcome of our present study [17].

Moreover, Storr-Paulsen suggested that phaco-chop technique had less deleterious effects on ECL than divide and conquer technique as it involves less phaco power usage [18]. In this study the coefficient of variation (CV) in cell size was found to be increased following phacoemulsification in both diabetics and non-diabetics as compared to pre-operative state after 3 months. Sunil Ganekal et al. (p >0.05) study demonstrated no statistical significance in CV post-operatively, whereas Lee JS et al. established findings akin to our present study with a statistical significance (p<0.05)[19,20].

RESULTS:

We recorded the initial baseline parameter of all the included study population as shown in Table-*1*. The mean age of control group is 58.2 ± 4.3 and Diabetics is 52.7 ± 5.1 (p= 0.07). There was no statistically significant difference in the mean values of ECD, CV, Hexagonality and CCT (p= 0.31,0.28,0.09 and 0.41 respectively). The median Inflammatory scores were noted to be 1 in both groups with no statistical significance (p= 0.18). (Table-*1*)

Demographic attributes and baseline parameters in Non-Diabetics vs Diabetics

Parameters	**Mean ± SD**		***p*-value**
	Controls (n=60)	**Diabetics (n=60)**	
Age	58.2 ± 4.3	52.7 ± 5.1	0.07
Sex (%)			
a. male	72.5	66.8	0.42
b. female	27.5	33.2	0.78
ECD	2397 ± 322	2331 ± 374	0.31
CV	42.4 ± 5.7	43.9 ± 6.1	0.28
Hexagonality (%)	37.5 ± 8.1	39.2 ±7.2	0.09
CCT (µm)	559 ± 42	564 ± 37	0.41
Inflammatory score	1	1	0.18

ECD: Endothelial Cell Density
CV: Coefficient of Variation
CCT: Central Corneal Thickness

In our study, it was found that Diabetics in the age group 60-69 have 4.1 times more risk of Endothelial Cell Loss (ECL) than control group (p=0.03). Sex of the patients have no impact on the ECL but Ultrasound time (UST), Effective Phaco time (EPT) and Inflammatory score were proven to be a significant risk factor in both Non-diabetics and Diabetics with statistical significance (p<0.05). (Table-*2*)

Risk factors for endothelial cell loss (ECL)

Parameters	**Non-Diabetics**		**Diabetics**	
	OR (C.I)	***p*-value**	**OR (C.I)**	***p*-value**
Age				
a. 45- 59				
b. 60-69	2.1 (1.339-4.196)	0.06	4.1 (1.218-2.976)	0.03
c. ≥70	3.6 (0.744-3.976)	0.47	2.7 (1.891-3.844)	0.22
Sex				
a. male	2.3 (0.588-3.918)	0.26	0.8 (0.414-2.954)	0.17
b. female	1.9 (0.889-4.755)	0.41	1.4 (0.979-2.319)	0.32
UST	1.8 (1.332-4.191)	0.02	2.8 (1.416-5.727)	0.02
EPT	2.4 (0.489-3.882)	0.05	3.1 (1.721- 9.332)	0.04
Inflammation score				
a. 0.5-1				
b. 1-2	1.3 (0.822- 4.293)	0.03	4.3 (2.529-14.762)	0.01
c. 2+				

UST: Ultrasound time
EPT: Effective phaco time

Endothelial Cell Density Pre-operatively (baseline) and Post-operatively (1-week, 4-weeks, 1-month)

ECD (n=120) (cells/mm2)	**Mean (SD)**				***p*-value**			
	Baseline	**1-week**	**4-weeks**	**3-months**	**Baseline**	**1-week**	**4-weeks**	**3-months**
Control (n=60)	2397 (322)	2284 (286)	2318 (265)	2941(284)				
Diabetics (n=60)	2331 (374)	2421 (275)	2387 (312)	2316 (309)	0.31	0.04	0.91	0.52

ECD: Endothelial Cell Density

Central Corneal Thickness Pre-operatively (baseline) and Post-operatively (1-week, 4-weeks, 1-month)

CCT (n=120) (µm)	**Mean (SD)**				***p*-value**			
	Baseline	**1-week**	**4-weeks**	**3-months**	**Baseline**	**1-week**	**4-weeks**	**3-months**
Control (n=60)	559 (42)	568 (32)	563 (39)	552 (42)				
Diabetics (n=60)	564 (37)	574 (43)	570 (48)	563 (39)	0.41	0.032*	0.071	0.812

CCT: Central Corneal Thickness

Coefficient of Variation Pre-operatively (baseline) and Post-operatively (1-week,4-weeks, 1-month)

CV (n=120)	Mean (SD)				*p*-value			
	Baseline	1-week	4-weeks	3-months	Baseline	1-week	4-weeks	3-months
Control (n=60)	42.4 (5.7)	46.3 (5.3)	47.7 (7.2)	48.2 (6.1)				
Diabetics (n=60)	43.9 (6.1)	51.2 (5.9)	49.4 (7.8)	48.1 (7.9)	0.28	0.018	0.024	0.038

CV: Coefficient of Variation

Hexagonality Pre-operatively (baseline) and Post-operatively (1-week, 4-weeks, 1-month)

Hexagonality (n=120) (%)	Mean (SD)				*p*-value			
	Baseline	1-week	4-weeks	3-months	Baseline	1-week	4-weeks	3-months
Control (n=60)	37.5 (8.1)	36.5 (8.6)	37.6 (7.8)	37.1 (8.0)				
Diabetics (n=60)	39.2 (7.2)	38.6 (6.9)	39.4 (8.1)	38.4 (7.4)	0.04	0.08	0.09	0.08

In our study, the ECD in diabetics were elevated 1-week post-operatively with p=0.04 as shown in Table-3, similarly it was found that diabetics have higher CCT, CV and Hexagonality 1-week following phacoemulsification (p= 0.032,0.018,0.08 respectively) [Table- *4,5,6*].

CONCLUSIONS:

Our study suggests that diabetics has profound ECL, increased CCT and reduced Hexagonality following phacoemulsification. It was found that EPT, UST and Inflammation score are associated with higher risk of ECL and more so in Diabetics as compared to control group. Future studies with larger sample size and longer follow-up with alternative surgical techniques are warranted taking in account other possible factors determining the Endothelial injury.

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