Zagazig University Medical Journal
www.zumj.journals.ekb.eg

Volume 28, Issue 2, March 2022, Page 239-244

Manuscript ID ZUMJ-1909-1507 (R4)
DOI **10.21608/zumj.2019.16301.1507**

ORIGINAL ARTICLE

Corneal Endothelial Cell Changes after Pars Plana Vitrectomy: Silicone vs Non-Silicone Filled Eyes

Sara Fawzy Ibrahim[1], Hassan Ali Zaki[1], Sherif Abbas Dabour[1], Ashraf Mahrous Eid [1]*
[1]Ophthalmology department, faculty of medicine, zagazig university, zagazig, Egypt

***Corresponding Author:**
Ashraf Mahrous Eid
Ophthalmology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
E-mail: ashraf.mahrous77@gmail.com

Submit Date	2019-11-13
Revise Date	2019-12-09
Accept Date	2019-12-12

ABSTRAT

Background: The corneal complications of a successful vitreoretinal surgery are not the main interest of the surgeon operating on a difficult retinal detachment. However, the surgeon should pay attention to avoid corneal decompensation. The current study was aimed to evaluate corneal endothelial cell changes in patients undergoing pars plana vitrectomy with and without silicone oil (SO) injection.

Methods: This prospective observational study includes 54 eyes divided into two equal groups: silicone-filled group (group one) and saline-filled group (group two). Endothelial cell densities (ECD), coefficient of variation (CV), central corneal thickness (CCT), and percentage of hexagonal cells at the corneal center were measured preoperatively and at the first week, the first month, and the third month postoperatively and compared between the two groups. All data were collected and statistically analyzed using the SPSS program.

Results: Three months after PPV, mean ECD in group one and in group two was highly significant ($p<0.001$) with the main decrease in cell count occurring in the first week postoperatively. However, the difference in the endothelial cell loss between the two groups was clinically insignificant ($p=0.18$) but more affected in group 1.

Conclusions: Pars plana vitrectomy (PPV) was associated with corneal endothelial cell changes which were higher in patients with SO injection than those left saline-filled; however they were statistically insignificant. Silicone oil could be a risk factor for increasing endothelial cell loss after PPV.

Keywords: Corneal Endothelial Cells; Pars Plana Vitrectomy; Silicone Oil; Specular Microscopy.

INTRODUCTION

Pars plana vitrectomy (PPV) is the surgical procedure involving the removal of the vitreous gel from the eye. [1] It is mainly indicated in rhegmatogenous retinal detachment, vitreomacular traction, vitreous hemorrhage, retained lens fragments after cataract surgery, endophthalmitis, epiretinal membrane, macular hole, and intraocular foreign bodies. [2] PPV may be contraindicated if the eye has no perception of light. [3]

Following vitrectomy, a vitreous substitute is injected into the eye to keep the retina in place. Vitreous substitutes commonly used include air, saline, sulfur hexafluoride gas (SF_6), n-perfluoropropane gas (C_3F_8), and silicone oil (SO) which is mainly used in complex retinal affections. [4]

The cornea's refracting surface is responsible for about 70% of the eye refractive power. This function is defined in terms of corneal shape, regularity, clarity, and refractive index, all of which could be susceptible to intraoperative compromise after PPV. [5]

PPV is thought to be associated with EC changes. Factors such as intraocular irrigation fluids, cumulative operative time, and IOP fluctuations may affect the corneal endothelium. Also, furthermore, damage may be related to the used tamponade such as silicone. [6]

The aim of this study is to evaluate corneal endothelial cell changes in patients undergoing pars plana vitrectomy with and without silicone oil injection.

METHODS

This is a prospective nonrandomized

comparative interventional study that included 54 eyes of 54 patients collected from the outpatient clinics of the Ophthalmology Department of Zagazig University Hospitals. All eyes were scheduled for PPV at the Ophthalmology Department, Zagazig University Hospitals, in the period between March and November 2017. Patients were divided into two groups (27 eyes) each; group 1 with SO injection and group 2 with saline injection. The patients were included if they were above 40 years old, phakic prepared for PPV or pseudophakic patients in whom cataract surgery was done at least 6 months before and have intact posterior lens capsules, prepared for PPV, with a preoperative endothelial cell count of more than 2000 cells/mm2. Exclusion Criteria were, pre-existing corneal abnormalities, previous ocular inflammations or trauma, glaucoma, patients with zonular dehiscence or subluxation. Patients scheduled for phacovitrectomy were also excluded, and patients performing any anterior segment procedures during the follow-up period were excluded.

Written informed consent was obtained from every patient after an explanation of the procedure. IRB committee at the faculty of medicine, Zagazig University approved the study according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Preoperatively, complete ophthalmic examinations were performed on all patients including history, visual acuity, slit-lamp examination, IOP measurement, fundus examination, and imaging of the corneal endothelium by noncontact specular microscope (NIDEK CEM-530, Ltd., gamagori, Japan) to assess corneal endothelial cell density (ECD), central corneal thickness (CCT), coefficient of Variation (CV) and Hexagonal cells.

In group I; 18 eyes had a macular hole, 6 eyes had combined rhegmatogenous and tractional retinal detachment, 2 eyes had tractional retinal detachment, and 1 eye had a rhegmatogenous retinal detachment. In group II; 23 eyes had a non-resolving vitreous hemorrhage and 5 eyes had epimacular membrane.

20-gauge PPV was done depending on the reason for the vitrectomy with tamponade; SO (silicone 5000 Cs) in group 1 and saline in group 2. Intraoperative events were recorded during surgery including total irrigation volume used, cumulative operation time, and intraoperative complications. Regular postoperative follow-up was conducted on day 7, 1st month, 3rd month with special attention to slit-lamp examination (corneal state), IOP, visual acuity, and imaging of corneal endothelium.

Statistical analysis

All data were analyzed using IBM SPSS Statistics Version 22 (IBM, NY, USA). Quantitative data were presented as a mean and standard deviation. Qualitative data were presented as frequency and percentage. Numeric data were explored for normality using the Kolmogorov-Smirnov test and Shapiro-Wilk test. The repeated measure analysis of variance was used to compare preoperative and postoperative values. Categorical variables were compared with the chi-square test. Multivariate regression analysis was done to assess risk factors associated with ECD loss at the third month postoperatively.

P-value < 0.05 was considered statistically significant, p-value < 0.001 was considered highly statistically significant, and p-value > 0.05 was considered not statistically significant. All tests were two-tailed

RESULTS

The demographic data of the patients is summarized in Table 1. The corneal ECD, hexagonality, CV, and CCT are summarized in Table 2.

Table 3 shows mean EC changes preoperatively, 1week, 1month, and 3month postoperatively. IOP was measured throughout the study and values are shown in table (4).

Table 4 shows the IOP assessment during the study. Corneal ECD changes were further analyzed in diabetic and non-diabetic patients (Table 5). To show the effect of previous cataract surgery on corneal endothelium; corneal ECD changes over the 3-months follow-up period according to lens status were estimated and compared between both phakic and pseudophakic eyes as shown in Table 6. When all significant variables that affect endothelial cell density (ECD) in the level of univariate analysis entered into multiple linear regression, it was found that silicone oil tamponade was the only independent prognostic factor to affect endothelial cell density (p<0.001). And this is shown in table 7.

Table 1: Demographic data of the studied groups, postoperative silicone-filled eyes (27 eyes) vs postoperative fluid-filled eyes (27 eyes).

	Silicone-filled eyes	Fluid-filled eyes	P-value
Age; mean±SD	54.6±8.7	55.8±8.9	0.62*
Sex; *n* (%)			1.0**
male	13 (48.1)	13 (48.1)	
female	14 (51.9)	14 (51.9)	
Diabetes Mellitus			
Yes	11	16	
No	16	11	
Laterality			
OD	17	14	
OS	10	13	
Phakic eyes	20	13	
pseudophakic eyes	7	14	

* Student t-test

** Qui square test

Table 2: Preoperative corneal data (mean±SD) of the studied eyes in silicone-filled eyes (27 eyes) vs preoperative fluid-filled eyes (27 eyes).

	Silicone-filled eyes	Fluid-filled eyes	P-value
Corneal endothelial cell count; (cells/mm^2)	2751.25±442-75	2690.25±358.49	0.18
Coefficient of variation (%)	29.48%±5.08%	30.96%±5.86%	0.42
Hexagonality (%)	69.48±4.89	68.04±7.67	0.25
Central corneal thickness; (µm)	555.40±47.60	556.74±42.12	0.46

Table 3:Corneal parameters preoperative and 3 months postoperative in silicon filled eyes (*n*= 27) (group 1), and in saline-filled eyes (*n*= 27) (group 2).

	Group 1			Group 2			p-value**
	Preoperative	3 months postoperative	p-value*	Preoperative	3 months postoperative	p-value*	
Corneal ECD	2751.25±442.75	2032.92±434.41	<0.001	2690.25 ±358.49	2320.37± 331.88	<0.001	0.18
Corneal endothelial pleomorphism (%)	69.48±4.89	65.66±8.05	0.04	68.04±7.67	65.59±7.25	0.23	0.25
Coefficient of variation (%)	29.48±5.08	31.03±5.97	0.31	30.96±5.86	32.29±8.23	0.50	0.42
Central corneal thickness	555.40±47.60	552.51±32.01	0.79	556.74± 42.12	560.67±40.64	0.73	0.46

* Student t-test between the same group.

** student t-test between both groups.

Table 4: Intraocular pressure (mmHg) preoperative and 3 months postoperative in silicon-filled eyes (group 1), and in saline-filled eyes (n= 27) (group 2).

Group 1 (n= 27)			Group 2 (n= 27)			P-value**
Preoperative	3 months postoperative	p-value*	Preoperative	3 months postoperative	p-value*	
13.55±2.39	16.00±1.66	<0.001	14.63±1.86	14.44±1.72	<0.001	0.018

* Student t-test between the same group.

** student t-test between both groups.

Table 5: Corneal endothelial cell density (cells/mm^2) preoperative and 3 months postoperative in eyes of diabetic patients in both groups, and in eyes of nondiabetic patients in both groups.

Diabetic patients (*n*= 27)			Nondiabetic patients (*n*= 27)			p-value**
Preoperative	3 months postoperative	p-value*	Preoperative	3 months postoperative	p-value*	
2671.26±408.45	2138.74±420.48	<0.001	2770.26±368.68	2214.56±425.12	<0.001	0.51

* Student t-test between the same group.

** student t-test between both groups.

Table 6: Corneal endothelial cell density (cells/mm^2) preoperative and 3 months postoperative in phakic eyes in both groups' vs pseudophakic eyes in both groups.

Phakic eyes (*n*= 33)			Pseudophakic eyes (*n*= 21)			p value**
Preoperative	3 months postoperative	p-value*	Preoperative	3 months postoperative	p-value*	
2640.81±327.57	2192.86±460.80	<0.001	2771.63±419.75	2166.33±460.70	<0.001	0.598

* Student t-test between the same group.

** student t-test between both groups.

Table 7: Multiple linear regression analysis to assess variables that affect ECD.

ECD	B	t	p-value	95.0% Confidence Interval for B	
				Lower Bound	Upper Bound
Tamponade (SO)	0.123	5.410	<0.001**	0.077	0.168
Lens (Pseudophakic)	0.180	1.65	0.11	-0.99	0.20
Irrigation volume	0.106	0.90	0.37	-0.97	0.15

DISCUSSION

This study included 54 eyes of 54 patients. Patients were divided into two equal groups according to the used tamponade, group one (silicone filled) and group two (salisaline-filled group one SO was retained in the vitreous cavity throughout the whole follow-up period (three months) without being removed or detected in the anterior chamber.

Corneal endothelial cell count has significantly affected after pars plana vitrectomy in both groups (p<0.001). These results were compared with the results of Cinar [6] who evaluated corneal endothelial cell (EC) damage after vitreoretinal surgery using gas (SF6) or SO. Also, the results of Friberg and Guibord [7] showed that retained SO in the vitreous body contributed significantly to EC loss. They stated a major conclusion that EC loss after vitreoretinal surgery might increase further because of the long-term SO retention.

The mechanism by which SO leads to corneal endothelial cell changes remains controversial. Many studies reported that it has been related to emulsification causing very small SO droplets to liberate from the large bubble in the vitreous cavity and diffuse into the anterior chamber. [8] A direct destructive ''barrier'' effect with solubilization of the cell membrane or a mechanical prevention of nutrients reaching the corneal endothelial cells may be of importance. [9,10]

However, Munirul and Vazeen had focused on the corneal endothelial cells damage with the presence of SO in the vitreous cavity without direct corneal touch. [11] Cinar was believed that, even with intact iris-lens diaphragm, there was possibility of SO toxicity on corneal endothelium. [6] Damage to corneal EC may lead to corneal complications that range from striate keratopathy to deep corneal edema, clouding, and decompensation. [12]

In this study, corneal ECD changes over the 3-month follow-up period according to lens status were estimated and compared between both phakic patients and pseudophakic patients. EC loss over the three-month follow-up period was highly significant (p<0.001) in both groups However, the difference in endothelial cell loss between both groups was statistically insignificant. These results can be explained by the fact that eyes that had undergone previous phacoemulsification were weaker and hence more prone to EC loss than phakic eyes. [6] These results also were comparable with those by Cinar [6] which showed mean EC loss was less in phakic than in pseudophakic eyes. Also Rosenfeld [13] reported a reduction of ECD at 6 months postoperatively in phakic eyes less than with aphakic eyes.

In this study, the overall changes in hexagonal cells HEX (pleomorphism) were statistically significant over the 3-month follow-up period without significant difference between both groups. And this is comparable to the results of Farrahi [14] who found that the presence of SO in the vitreous cavity of phakic and pseudophakic eyes has no statistically significant effect on ECD but has a significant effect on hexagonality (P=0.004) and CV (P=0.003). The corneal endothelial cell loss was not statistically significant, but it was remarkable.

Measurement of corneal thickness is useful for assessing the extent of surgical stress following vitrectomy. [15] In our study, CCT was measured by noncontact specular microscopy, we found that there were no statistically significant changes over the three-month follow-up period. The mean CCT remained nearly the same throughout the study. Our results slightly differ from the results of Buch and Nielsen [16] who measured CCT by ultrasonic pachymetry for two groups. Abrams [17] showed similar results as Buch and Nielsen [16] in eyes treated with silicone oil and C3F8. Watanabe [18] showed similar results but they used pentacam to measure CCT for 20 eyes that had undergone PPV with SO injection.

In this study, corneal ECD changes in diabetic and nondiabetic patients were estimated showing highly significant EC loss (p < 0.001) in diabetic and nondiabetic patients without significant difference in EC loss between them. These results also stated by Chung [19] and Hiraoka [20] who found that, in diabetic patients, high incidences of corneal complications after PPV had been reported. These complications were often resistant to ordinary therapy and require long-term treatment. They assumed that corneal complications after vitrectomy in diabetic patients take place more than nondiabetic patients due to intraoperative damage combined with preexisting subclinical corneal abnormalities.

In this study; When all significant variables that affect endothelial cell density (ECD) in the level of univariate analysis was entered into multiple linear regression, it was found that silicone oil tamponade was the only independent prognostic factor to affect endothelial cell density (p<0.001).

Despite valuable results of our study, it has some limitations. The enrolled patients were only followed up for three months. Thus, a long-term study is needed with EC counts to be measured at consecutive follow-up visits. One should further keep in mind the fact that EC losses may be even higher if patients were followed up for a longer time period. Also, the relatively low number of patients in each group as a result may be more significant when more patients are included in the study, so more patients should be enrolled in future studies. In addition, the imbalance between the indications for PPV surgery between both groups may also have an indirect effect on EC loss because patients with retinal detachment in the SO group probably have required longer surgery times.

CONCLUSION

In conclusion; pars plana vitrectomy is associated with corneal endothelial cell changes in the form of EC loss and pleomorphism. Also, silicone oil could be a risk factor for increasing endothelial cell loss after pars plana vitrectomy, so use of silicon oil should be limited to severe retinal affection and complicated cases and should be removed within six months after surgery to guard against endothelial cell toxicity and permanent corneal damage. To guard against corneal decompensation after PPV, preoperative corneal assessment is mandatory especially in diabetic and pseudophakic patients.

Conflict of Interest: None.

Financial Disclosures: None.

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