Original Article

Pars Plana Vitrectomy and Silicone Oil Injection in Phakic and Pseudophakic Eyes; Corneal Endothelial Changes

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Abstract

Purpose: To evaluate the effect of silicone oil (SO) on the corneal endothelium in SO filled phakic and pseudophakic vitrectomizied eyes.

Methods: This prospective comparative consecutive case-control study evaluated the corneal endothelial characteristics of 64 SO filled vitrectomizied eyes (case group) as compared to 46 vitrectomizied eyes without SO injection (control group). Endothelial cell densities (ECD), coefficient of variation (CV), and percentage of hexagonal cells (hexagonality) at the corneal center were evaluated preoperatively, 1 month and 6 months after surgery using noncontact specular microscopy and were compared between the two groups. Exclusion criteria were previous vitreoretinal surgery, aphakia, any degree of anterior chamber inflammation, SO bubbles in the anterior chamber and increased intraocular pressure in the postoperative period.

Results: Six months after SO injection, mean ECD was 2,438.2±327.6 cell/mm^2 in the case group and 2,462.6±361.7 cell/mm^2 in the control group (P = 0.714) and mean hexagonality was 49.6 ± 6.8 and 54.6 ± 8.9, in the case and control groups, respectively (P = 0.004). Six months after operation, CV in the case group was 39.3 ± 5.6 and that in the control group was 35.7 ± 6.4 (P = 0.003).

Conclusion: Although the presence of SO in the vitreous cavity of phakic and pseudophakic eyes causes slight reduction in the number of endothelial cells, however it leads to significant changes in endothelial cell morphology. Thus, removal of SO after reaching the desired tamponade effect is recommended.

Keywords: Corneal Endothelial Cells; Pars Plana Vitrectomy; Phakic Eyes; Pseudophakic Eyes; Silicone Oil; Specular Microscopy

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INTRODUCTION

Silicone oil (SO) has been widely used as an internal tamponade for complicated retinal detachment surgery since it was first introduced in 1962.[1] It is common practice to remove SO after a period of time to reduce its well-known complications.[2-4] Although the tolerance for intraocular SO is generally good, a number of side effects have been reported, including keratopathy, elevated intraocular pressure, ocular hypotony, SO emulsification, cataract formation, iritis and endophthalmitis.[5] Numerous reports proposed some adverse effects of SO on the cornea.[6-8] It was hypothesized that the adverse effects of SO on the cornea are related to forward migration of SO to the anterior chamber and corneal touch.[6-8] Furthermore, SO in the eye has been linked to endothelial cell toxicity.[9] Endothelial cell exposure to SO induces physiological and morphological alterations of the cornea.[10] The changes that derive from SO-associated keratopathy, include band

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keratopathy, corneal thinning, retro-corneal membrane formation, and irreversible corneal endothelial cell loss.[11,12] SO might act as a barrier that deprives human corneal endothelial cells from the nutrition normally supplied by the aqueous humor.[6] Nevertheless, the possible indirect cytotoxic effect of SO on corneal endothelial cells has not been fully evaluated because SO has been assumed to be inert in ocular tissues.[13]

Early detection of endothelial pathology is crucial to prevent further corneal damage, and early removal of SO should be considered if the retinal condition allows.[14]

The structural integrity of the cornea seems unchanged after intravitreal SO injection in phakic or pseudophakic vitrectomized eyes. However, no study has focused on the corneal endothelial cells damage in the presence of SO in the vitreous cavity without direct touch with the cornea.

The present study has evaluated the effect of intravitreal SO injection in phakic or pseudophakic vitrectomized eyes on endothelial cell density (ECD), coefficient of variation (CV), and the percentage of hexagonal cells (hexagonality) until 6 months after surgery.

METHODS

The current survey is a prospective, comparative case-control study on phakic or pseudophakic patients who underwent pars plana vitrectomy from May 2011 to June 2012 at Imam Khomeini Hospital, Jundishapur University of Medical Sciences, a referral center in the southwest of Iran, Ahvaz. All procedures were performed by two vitreoretinal surgeons (FF & MF). According to injection of SO in the vitreous cavity, the patients were divided into two groups. The eyes underwent vitrectomy with SO injection were considered as the case group and vitrectomized eyes without SO injection served as the control group. Standard examinations were performed on day 1, at 1 week, 1 month, 3 months, 6 months, and when clinically indicated after operation.

Patients with a minimum age of 18 years who were scheduled for pars plana deep vitrectomy due to vitreous hemorrhage, tractional or rhegmatogenous retinal detachment, or a combination of these situations were included.

Patients with a history of previous vitreoretinal intervention or subjects who underwent combined vitrectomy and cataract extraction were excluded. Exclusion criteria also included aphakic eyes, clinically significant coexisting ocular pathology, including glaucoma, inflammatory eye disease, any anterior segment and corneal disorders such as pseudoexfoliation syndrome, Fuchs endothelial dystrophy, and evidence of previous traumatic corneal injuries. Postoperative conditions that might cause corneal endothelial cell damage such as evidence of SO in anterior chamber, high intraocular pressure and anterior chamber inflammation and also patients who did not complete the follow-up period were excluded. Eyes requiring additional surgery, e.g. cataract extraction, glaucoma surgery, penetrating keratoplasty, intravitreal gas injection, and SO removal within 6 postoperative months were also excluded.

Demographic information, past medical and ocular history, initial best corrected visual acuity (BCVA), cornea and lens status, intraocular pressure, fundus details, and indication of surgery were recorded. When the diagnosis required to be confirmed, ancillary tests such as echography and fluorescein angiography were performed. Preoperatively, 1 month and 6 months postoperatively the non-contact specular microscopy (Topcon SP-3000P, Topcon Ltd., Tokyo, Japan) was performed in all eyes in the center of the cornea. Of the several measurements, the one that showed maximum counted endothelial cells was chosen. The ECD (cells/mm^2), CV (standard deviation [SD]/mean cell area × 100), and percentage of hexagonality were evaluated at each examination. All photographs and cell analyses were done by a single observer.

All patients underwent pars plana vitrectomy. The procedure included a standard 20 gauge three-port pars plana vitrectomy using the Alcon Accurus system (Alcon Laboratories, Inc., Fort Worth, Texas, USA). At the end of the operation the vitreous cavity was filled with SO 5000 (Siluron 5000, Fluoron GmbH, Ulm, Germany) (case group) or with gas or balanced salt solution plus (BSS+) (control group) according to the surgeon's discretion. Finally, sclerotomies and the conjunctiva were repaired. After surgery, the patients were asked to keep a face-down position if SO or a long-acting gas had been used.

To evaluate the validity of the study, repeated measurement tests were performed. Comparing the mean age and sex differences between two groups, independent-samples *t*-test and Chi-square tests were performed, respectively. Paired *t*-test and Student's *t*-test were used to compare preoperative and postoperative means of BCVA, ECD, CV, and hexagonality between the two groups and in each group, respectively. All tests of association were considered to be statistically significant if $P \leq 0.05$. Analysis was performed using SPSS 19.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

From a total of 156 eyes, 46 eyes were excluded, in the course of study, due to need to SO removal in 26 eyes, anterior chamber inflammation in 4 eyes, progression of cataract leading to phacoemulsification surgery in 10 eyes and rise of intraocular pressure in 6 eyes. One hundred ten eyes of 99 patients completed the study after 6 months of follow-up. For 64 eyes vitrectomy with SO injection and for 46 eyes vitrectomy without SO injection were performed. Patient's demographics in the

two groups are summarized in Table 1. There were no statistically significant differences between measured parameters.

In the SO group, mean logMAR BCVA was 1.76 ± 0.60 preoperatively as compared to 1.82 ± 0.52 in the control group (P = 0.655), and after surgery, mean logMAR BCVA in the SO group was 1.68 ± 0.56 as compared to 1.55 ± 0.63 in the control group (P = 0.23).

There were no significant differences between the study and control groups in preoperative ECD, CV, and hexagonality. At 6 months, mean endothelial cell difference between the two groups was not statistically significant, but CV and hexagonality showed statistically significant difference, between the two groups [Table 2].

Mean ECD loss, CV changes, and reduction of hexagonality preoperatively and 6 months after surgery and significance of differences between these values are shown in Table 3.

Six months after the operation, phakic and pseudophakic eyes in case and control groups were separately compared. From this perspective, CV and hexagonality difference between the two groups were statistically significant in both phakic and pseudophakic eyes [Table 4].

DISCUSSION

Silicone oil has been widely used as an internal tamponade for complicated retinal detachment surgery.[1] Although the tolerance for intraocular SO is generally good, a number of side effects have been reported, such as keratopathy.[5] It has been hypothesized that the adverse effects of SO on cornea are related to forward migration of SO to the anterior chamber and corneal touch.[6-8] However, possible indirect cytotoxic effect of SO on corneal endothelial cells has not been fully evaluated since SO has been assumed to be inert in ocular tissues.[13]

The effect of SO in direct touch to cornea on endothelium have been studied before,[5-8] but no study has focused on the effect of SO in the vitreous cavity of phakic and pseudophakic eyes on endothelium. The structural integrity of the cornea seems unchanged after SO injection in the vitreous cavity of phakic and pseudophakic vitrectomized eyes. However, no study has focused on the corneal endothelial cells damage in the presence of SO in the vitreous cavity without direct touch with the cornea.

Our study revealed 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 and CV. The difference in endothelial cell loss between the study eyes and the control eyes, even if not statistically significant, was remarkable. It might have become statistically significant if more patients had been enrolled in the study. Recently, Goezinne et al[15] reported <5% ECD loss and no statistically significant effect on hexagonality and CV 12 months after vitrectomy with SO tamponade for complex rhegmatogenous retinal detachments in phakic and pseudophakic eyes.

Silicone oil is also cytotoxic to cultivated human endothelial cell and contact with SO inhibited endothelial cell proliferation, while higher viscosity SO suppressed cell cycling significantly more than lower viscosity SO.[9]

Table 1. Patient's demographic parameters

Parameter	Group	
	Case	Control
Patients (n)	64	46
Mean age (years)	53.5±11	57.5±11
Sex (male/female)	29/35	18/28
Right/left eye	30/34	23/23
Phakic/pseudophakic	53/11	38/8
Diabetes mellitus (%)	47 (73.4)	36 (78.3)
Hypertension (%)	26 (40.6)	17 (36.9)
Hyperlipidemia (%)	13 (20.3)	12 (26)
IHD (%)	18 (28.1)	11 (23.9)

IHD, ischemic heart disease

Table 3. Endothelial parameter changes analysis preoperatively and at 6 months postoperatively

Parameter	Mean±SD		P value
	Case	Control	
ECD loss (cell/mm^2)	158.3±120.6	128.5±168.8	0.87
Reduction of hexagonality (%)	5.29±5.43	2.23±5.83	0.027
CV changes (%)	3.25±2.80	0.59±2.90	0.001

ECD, endothelial cell densities; CV, coefficient of variation; SD, standard deviation

Table 2. Endothelial morphometric analysis preoperatively, at 1 and 6 months postoperatively

Parameter	Mean preoperative Mean±SD		P value	Mean postoperative 1 month Mean±SD		P value	Mean postoperative 6 months Mean±SD		P value
	Study	Control		Study	Control		Study	Control	
EDC (cell/mm^2)	2,596.6±339.6	2,591.6±333.0	0.835	2,482.0±345.7	2,505.7±333.4	0.794	2,438.2±327.6	2,462.6±361.7	0.714
Hexagonality (%)	54.9±7.8	56.8±7.0	0.185	54.3±7.4	55.0±5.8	0.599	49.6±6.8	54.6±8.9	0.004
CV (%)	36.0±5.7	35.1±5.8	0.440	36.9±5.5	36.2±5.5	0.469	39.3±5.6	35.7±6.4	0.003

ECD, endothelial cell densities; CV, coefficient of variation; SD, standard deviation

Table 4. Analysis of parameters based on lens status at 6 months after operation

Parameter	Phakic		*P* value	Pseudophakic		*P* value
	Case	Control		Case	Control	
BCVA	1.77±0.51	1.66±0.54	0.681	1.26±0.61	1.30±0.65	0.902
Cell density (cell/mm^2)	2,501.8±293.5	2,540.5±348.4	0.568	2,131.8±351.5	2,092.3±198.8	0.743
Hexagonality (%)	50.5±6.7	55.3±7.8	0.016	45.0±5.6	51.0±3.7	0.020
CV (%)	38.6±5.5	35.0±6.5	0.007	42.4±5.5	39.3±4.7	0.024

BCVA, best corrected visual acuity; CV, coefficient of variation

Damage to endothelium, in addition to reducing cell density, increases mean cell size and disrupts the normal morphological pattern.[16] Damage to endothelial cells reflects a reduction in cell density, which may lead to corneal decompensation and opacity. A more sensitive indicator of endothelial damage after ocular surgery may be specular microscopy for cell size and shape.

Despite the prospective controlled design of our study and meticulous selection of patients as described in the exclusion criteria, there are certain limitations to our study. First, our data could have been affected by the imprecision of specular microscopy, which determines the cell count with a SD of 5.0%.[17] Second, the difference in endothelial cell loss between study eyes and control eyes was remarkable, but it wasn't statistically significant. It might have become statistically significant if more patients had been enrolled in the study.

In conclusion, the presence of SO in the vitreous cavity of phakic and pseudophakic eyes has significant effect on corneal endothelial morphometric analysis. Thus, we recommend removal of SO even in phakic and pseudophakic eyes after reaching the desired tamponade effect and before the appearance of irreversible endothelial cell morphologic changes.

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