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Oxidative Stress and Inflammatory Cytokines in Vitreous and Subsilicone Fluids in Patients with Rhegmatogenous Retinal Detachment

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ABSTRACT

Purpose: To investigate the oxidative stress (OS) and inflammatory cytokine (IC) levels in vitreous and subsilicone fluid (SSF) in cases with rhegmatogenous retinal detachment (RRD)

Methods: This prospective study included 21 cases of uncomplicated RRD. Total antioxidant status (TAS) and total oxidant status (TOS) in the samples were determined by automatic measurement method and IC levels were determined by ELISA method. In addition to routine ophthalmological examinations, flare, optic coherence tomography (OCT) and enhanced depth imaging-OCT measurements were performed during follow-up.

Results: There was a significant difference in the TOS and oxidative stress index (OSI) in SSF compared to vitreous ($p < 0.05$). IL-1β level was detected significantly higher in vitreous fluid ($p = 0.004$). When the correlation between TAS, TOS, OSI and cytokine levels in SSF and the difference in central macular thickness (CMT), choroidal thickness and flare changes measured in the 1st and 3rd month follow up of the cases after vitrectomy were evaluated, only negative correlation was observed between TOS, OSI, and CMT.

Conclusion: OS, which has not been previously investigated in SSF, was significantly higher in this study, and our findings suggest that OS may have an initiating role in retinal damage thought to be caused by silicone oil.

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KEYWORDS
Oxidative stress; silicone oil; subsilicone fluid; Total antioxidant status (TAS); total oxidant status (TOS)

Introduction

Rhegmatogenous retinal detachment (RRD) is a common ophthalmologic emergency, occurring at a rate of 10 to 18 per 100,000 people per year.[1] Since the description of silicone oil (SO) in vitrectomy in the early 1980s, a major step forward has been made in the treatment of challenging retinal detachments (RDs) such as inferior RD, recurrent detachments, RD with proliferative vitreoretinopathy (PVR), and giant retinal breaks.[2]

Additional pathologies such as secondary glaucoma, cataract formation, corneal degeneration, and silicone emulsification may develop in eyes exposed to SO tamponade for a long time.[3] Moreover, unexplained vision loss due to SO tamponade has also been described in a previous research.[4] The inflammatory effect caused by SO is thought to occur through four different mechanisms; immunogenicity and direct toxicity, instability of the substance, emulsification of oil, and mechanical damage due to gravity.[5] Thus, many studies have been conducted on the aqueous humor, vitreous fluid, and sub-silicone fluid (SSF) to investigate the pathophysiological effects of SO on the eye.[6,7]

The levels of some important inflammatory cytokines (ICs), such as IL-6, IL-8, IP-10 and monocyte chemoattractant protein-1 (MCP-1) in RRD have been investigated in vitreous fluid[8] and SSF.[7] In addition, research measuring retinal thickness has shown different thickness changes in various groups.[7] ICs have also been investigated in the aqueous humor of siliconized RRD cases,[9] while another study examined oxidative stress levels.[6] Another important method that shows inflammation in cases of RD is flare measurement, which is an objective indicator of anterior chamber inflammation. Some studies also support the importance of flare measurement in determining the risk of PVR.[10]

In this report, oxidative stress and ICs were investigated in the vitreous fluid in cases with RRD, as well as in SSF accumulated in the space between the posterior retinal surface and SO. To the best of our knowledge, the current study is the first in the literature that designed to investigate oxidative stress in SSF. In addition, changes in retinal and choroidal thickness and aqueous flare intensity were also assessed to determine inflammatory status after surgery.

Material and methods

This prospectively designed study included 21 patients diagnosed with uncomplicated RRD for the first time who

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were planned for 23- gauge pars plana vitrectomy with SO endotamponade at University of Health Sciences, Beyoglu Eye Training and Research Hospital Retina Clinic between February 2023 and June 2023. Informed consent was obtained in accordance with the Helsinki Declaration before all procedures, and the study was approved by the University of Health Sciences Turkey Ethics Committee (decision number 2/23).

Inclusion criteria for the current study were determined as ≥18 years of age, absence of additional systemic or ocular disease other than RRD, presence of multiple and giant retinal tears, and planning for 23-gauge pars plana vitrectomy with SO endotamponade (*SO is specifically preferred in cases with giant retinal tears and/or when the breaks are located in the inferior quadrants*).[2] Patients with concomitant ocular pathology, high degenerative myopia, acute or chronic inflammatory diseases, or RRDs developing after ocular trauma were excluded from the current study, as were those who had smoked for more than 10 years, those with a body mass index ≥30, those with a history of glaucoma or increased intraocular pressure after surgery, those with a history of long-term medication use and those having had ocular surgery other than cataract surgery.

Patients' age, sex, lens status, duration of symptoms before RRD diagnosis, axial length, number of tears, location of tears, size and location of the detachment and macular involvement were noted. Routine biomicroscopic ophthalmological dilated fundus examinations using a 90D lens were conducted preoperatively; at 1 week, 1 month and 3 months after vitrectomy; and at 1 month after silicone removal. In addition, best corrected visual acuity (BCVA) was assessed using the Snellen chart, and BCVA measurements were converted to logMAR for statistical analysis. In cases of retinal detachment, axial length measurements were obtained using optical biometry prior to surgery and before the progression of macular involvement whenever possible. In macula-off cases where optical biometry was not feasible, ultrasound biometry was used. In cases where refractive data could not be measured, values were retrieved from pre-detachment medical records whenever available. Intraocular pressures were preoperatively and postoperatively measured using the Goldmann applanation tonometer. The flare measurements were performed with Kowa FM-600 Laser Flare Meter (Kowa Company, Japan), with flare meter values expressed in photon counts per millisecond (pc/ms). At each visit, central retinal thickness (CRT) and central choroidal thickness (CCT) were measured using a Spectralis OCT device (Heidelberg Engineering, Germany) with a 6 mm × 6 mm volume scan and a single horizontal enhanced depth imaging OCT (EDI-OCT) line scan passing through the foveal center, respectively. CRT was automatically calculated within the standard Early Treatment Diabetic Retinopathy Study (ETDRS) macular grid using the device's built-in auto-segmentation algorithm. All scans were carefully reviewed to ensure accurate segmentation, and manual corrections were performed when necessary. CCT was manually measured by two independent observers (SÖ, TOD) as the vertical distance from the outer border of the hyperreflective retinal pigment epithelium (RPE) line to the choroidal-scleral junction at the subfoveal region. The values obtained by both observers were compared and averaged for statistical analysis.

All surgeries were performed using 23-gauge pars plana vitrectomy. Perfluorocarbon liquid was used intraoperatively to stabilize the retina. Endolaser photocoagulation was applied as a 360-degree treatment to the peripheral retina in all cases. None of the patients underwent combined phacoemulsification and vitrectomy. In all cases, 5000 centistoke (cSt) SO (Silicone oil; Teknomek, Istanbul, Türkiye) was used as the endotamponade, and the tamponade was removed at 12 weeks (3 months) postoperatively.

Sample collection and analysis

Vitreous fluid and SSF samples were collected as follows. We obtained the vitreous fluid samples by dry vitrectomy at the time of vitrectomy surgery using a 23-gauge vitreous cutter before the opening the infusion. To obtain SSF samples, the standard three port cannulas were placed, and a 2.5-mm syringe with a 23-gauge blunt needle and endoillumination were used, along with a closed infusion line in the SO-filled eye. The edge of the needle was positioned at the SO-SSF interface above the surface of the optic disc. Next, the surgeon (ŞÖ) aspirated the SSF with the help of the other physician (EE) while monitoring the fundus using a 60D lens and a RESIGHT surgical microscope (Zeiss, Oberkochen, Germany). All samples were taken into microcentrifuge tubes (Eppendorf®) and transferred to a -80^{0}C freezer, where they were kept until analysis.

Total antioxidant status (TAS) and total oxidant status (TOS) levels were measured with commercially available kits (Rel Assay Diagnostics®, Mega Tıp, Turkey). TAS levels are based on the bleaching of characteristic color of a more stable ABTS (2,2′ - Azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)) radical cation by antioxidants. In our study, the results were expressed as μmol Trolox equivalent/L.[11] Measurement of TOS levels may be done spectrophotometrically and is based on measuring the color intensity resulting from the ferric ion formed in the medium producing a colored complex with xylenol orange in an acidic medium, and is related to the total amount of oxidant molecules. The assay was calibrated with hydrogen peroxide, and the results were expressed in terms of micromolar hydrogen peroxide equivalent per liter (μmol H_2O_2 equivalent/L).[12] The ratio of TOS to TAS was used to represent the oxidative stress index (OSI), calculated using the following formula: OSI (arbitrary unit) = TOS (μmol H_2O_2 equivalent/L)/TAS (μmol Trolox equivalent/L).

Enzyme-linked immunosorbent assay (ELISA) was used to measure IL-1β, IL-6, IL-8, IL-10, MCP-1 and IP-10 expression levels in vitreous fluid and SSF samples. All ELISA kits were purchased from R&D Systems (Minneapolis, MN, USA). All operations strictly followed the manufacturer's instructions. Optical density (OD) values at 450 nm were determined.

Statistical analysis

Statistical analyses were done with R software (version 4.2.0) (R Foundation for Statistical Computing, Vienna, Austria,

https://www.r-project.org/). For general statistical analyses, gtsummary v1.6.0, rstatix v0.7.0 and ggplot2 v3.4.2 packages were used. The normality of the variables was determined by Shapiro-Wilk test and Q-Q plot and histogram graphs. Continuous variables were expressed as median (minimum-maximum) and mean ± standard deviation. Categorical variables were expressed as frequency (percentage). The Mann-Whitney U test was used to analyze continuous data in independent groups because the data were not normally distributed, and Wilcoxon and Friedman tests were used in dependent groups because the data were not normally distributed. Holm-Bonferroni correction was performed in post-hoc pairwise analyses. The correlation between continuous data was evaluated by Spearman correlation test. For all analyses, $p < 0.05$ was accepted as significant.

Results

This prospectively designed study started with 32 cases of RRD. However, eight patients were excluded due to the necessity of anti-glaucomatous use because of high postoperative intraocular pressure; one patient was excluded due to PVR development during silicone removal; and two patients were excluded due to inadequate sampling during SSF removal. Finally, 21 eyes of 21 patients were included and analyzed. The mean age of the patients was 58.2 ± 9.3 years. The patients were 52% pseudophakic and 48% phakic, and no combined cataract operation was required during vitrectomy and SO removal. Macular involvement was observed in 71% of patients, while 29% had no macular involvement. Compared to the mean preoperative BCVA of 1.99 ± 1.25 LogMAR, the mean postoperative BCVA showed a statistically significant improvement, with 0.57 ± 0.44 LogMAR ($p < 0.001$). The duration between the first symptom development and the time of operation was considered the duration of symptoms and was recorded as 8.0 ± 4.3 days on average. Ocular and demographic characteristics of the patients are detailed in Table 1.

Table 1. Demographic and Ocular Characteristics of The Patients.

Characteristics	*N* = 21
Age (years)	
Median (25%-75%)	57.0 (54.0-66.0)
Mean ± SD	58.2 ± 9.3
Sex, n (%)	
Male	11 (52%)
Female	10 (48%)
Laterality, n (%)	
Right	7 (33%)
Left	14 (67%)
Lens status, n (%)	
Phakic	10 (48%)
Pseudophakic	11 (52%)
Aphakic	0 (0%)
Macular involvement, n (%)	
On	15 (71%)
Off	6 (29%)
Number of tears, n (%)	
One	13 (62%)
Two	2 (10%)
Three	3 (14%)
More than three	3 (14%)
Location of tears, n (%)	
Superior	6 (29%)
Inferior	8 (38%)
Mixed (superior and inferior)	7 (33%)
Size of tears, n (%)	
<30°	9 (43%)
30°-90°	5 (24%)
Giant tear	7 (33%)
Duration of symptoms (day)	
Median (25%-75%)	7.0 (5.0-11.0)
Mean ± SD	8.0 ± 4.3
Axial length (mm)	
Median (25%-75%)	24.04 (23.36-24.51)
Mean ± SD	23.82 ± 0.97
Pre-op IOP (mmHg)	
Median (25%-75%)	16.0 (13.0-18.0)
Mean ± SD	15.9 ± 4.3
Pre-op SE (diopter)	
Median (25%-75%)	0.00 (-1.00-0.50)
Mean ± SD	−0.25 ± 1.34
Pre-op BCVA (LogMAR)	
Median (25%-75%)	3.10 (0.52-3.10)
Mean ± SD	1.99 ± 1.25
Pre-op flare unhealthy eye (pc/ms)	
Median (25%-75%)	27 (14-40)
Mean ± SD	33 ± 28
Pre-op flare healthy eye (pc/ms)	
Median (25%-75%)	7.1 (4.7-8.7)
Mean ± SD	7.4 ± 3.8

BCVA: Best Corrected Visual Acuity, IOP: Intraocular pressure, Pre-op: preoperative, SD: Standard Deviation, SE: spherical equivalent.

TAS, TOS, and IC levels in vitreous fluid and in SSF of the same patients are reported and statistically compared in Table 2. A significant difference was observed in the TOS level in SSF compared to vitreous fluid. In addition, there was a significant difference in OSI due to the alterations in TOS level. Furthermore, no significant difference was observed in cytokine levels except IL-1β, whose level was significant in favor of vitreous fluid.

The mean central macular thickness and choroidal thickness measurements of the patients at 1 week, 1 month and 3 months after vitrectomy and at 1 month after SO removal are shown in Figure 1 and Figure 2, respectively. Analyzing the correlation between TAS, TOS, and cytokine levels in patients' SSF and the changes in CMT and choroidal thickness measurements between the 1st month and 3rd months after vitrectomy, a significant negative correlation was found only between TOS levels, OSI and CMT changes, while no significant correlation was found with other cytokines (r=-0.56, r=-0.63 and $p = 0.008$, $p = 0.002$, respectively) (Table 3).

Figure 3 shows the changes in flare measurements in pathological and healthy control eyes in the preoperative period, at 1 day postoperatively, 1 week postoperatively, 1 month postoperatively, 3 months postoperatively and 1 month after silicone removal. There was no statistically significant difference between the 1st and 3rd month flare measurements after vitrectomy ($p = 0.281$, Wilcoxon test). In addition, no significant correlation was found between the change in flare measurements between the 1st and 3rd months after vitrectomy and TAS, TOS, and cytokine levels in SSF.

Discussion

SO, which is frequently used in the surgery of complicated retinal detachments such as giant and multiple retinal detachments, has been shown to be a biocompatible,

Table 2. Comparison of TAS, TOS, OSI and cytokine levels in vitreous and SSF.

Characteristics	Vitreous fluid	Subsilicone fluid	p value[a]
TAS (µmol Trolox Eqv./L)			0.633
Median (25%-75%)	2.19 (1.69-2.63)	2.64 (1.73-3.22)	
Mean ± SD	2.29 ± 0.91	2.52 ± 1.04	
TOS (µmol H2O2 Eqv./L)			0.003
Median (25%-75%)	6.5 (4.2-9.0)	13.7 (10.7-16.1)	
Mean ± SD	8.1 ± 6.6	14.0 ± 5.1	
OSI (µmol H2O2 Eqv./L) / (µmol Trolox Eqv./L)			0.006
Median (25%-75%)	3.2 (1.7-4.2)	5.0 (3.9-9.0)	
Mean ± SD	3.8 ± 3.1	6.8 ± 4.3	
IL-6 (pg/mL)			0.473
Median (25%-75%)	63 (50-84)	56 (51-79)	
Mean ± SD	69 ± 26	67 ± 28	
IL-10 (pg/mL)			0.081
Median (25%-75%)	201 (189-226)	185 (163-207)	
Mean ± SD	205 ± 32	190 ± 41	
IL-8 (pg/mL)			0.130
Median (25%-75%)	207 (187-233)	184 (162-208)	
Mean ± SD	206 ± 46	185 ± 65	
IP-10 (pg/mL)			0.109
Median (25%-75%)	1000 (880-1063)	837 (757-951)	
Mean ± SD	962 ± 136	1130 ± 1,349	
IL-1β (pg/mL)			0.004
Median (25%-75%)	1293 (1158-1494)	1117 (1049-1169)	
Mean ± SD	1306 ± 256	1090 ± 122	
MCP-1 (pg/mL)			0.296
Median (25%-75%)	390 (352-439)	350 (334-374)	
Mean ± SD	403 ± 106	390 ± 164	

[a]Wilcoxon signed rank exact test.
IL: Interleukin, IP-10: Interferon gamma-induced protein 10, MCP-1: Monocyte chemoattractant protein-1, OSI: Oxidative stress index, TAS: Total antioxidant status, TOS: Total oxidant status.

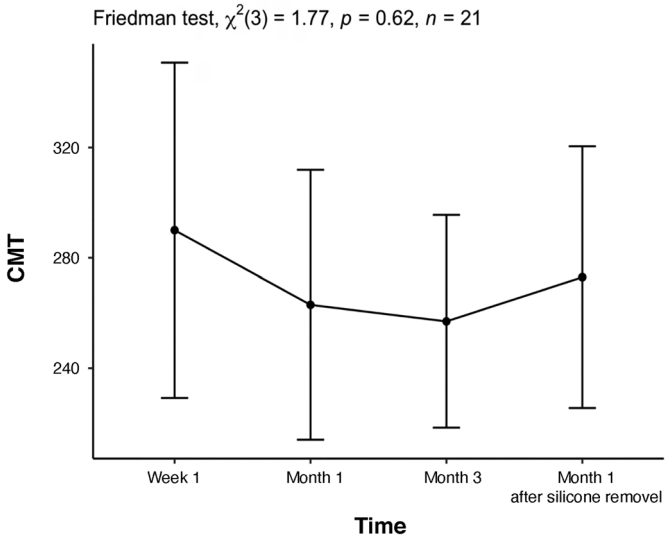

Figure 1. Time-dependent changes in central macular thickness measurements.

immunologically tolerant material that remains in the vitreous cavity for months without causing any significant intraocular damage. However, early silicone removal is recommended against potential pathologies such as keratopathy, cataract and glaucoma.[13,14] Also, in the light of the data obtained from enucleated glaucomatous eyes regarding the effect on the posterior segment, it is known that SO droplets are penetrable into the trabecular meshwork, optic nerve, neuroretina, and pigment epithelium,[15,16] with some studies suggesting that this is caused by the low molecular weight of SO.[17] In addition, some cases of sudden vision loss

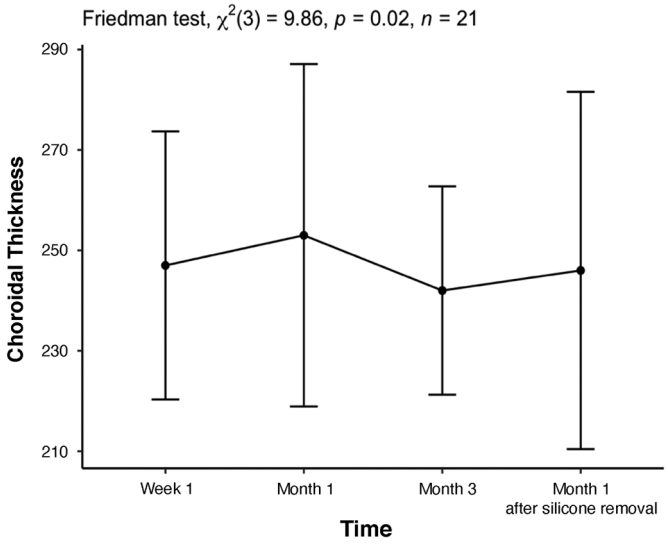

Figure 2. Time dependent changes of choroidal thickness measurements.

Table 3. Correlation between the change in the difference between 1st and 3rd months in CMT, flare and choroidal thickness measurements with the parameters analyzed in SSF.

Parameters	Choroidal thickness	CMT	Flare
TAS	r = 0.32	r = 0.39	r=-0.11
	p = 0.153	p = 0.08	p = 0.65
TOS	r=-0.095	**r=-0.56**	r=-0.053
	p = 0.682	**p = 0.008**	p = 0.821
OSI	r=-0.24	**r=-0.63**	r = 0.12
	p = 0.294	**p = 0.002**	p = 0.614
IL-6	r = 0.092	r=-0.015	r = 0.082
	p = 0.691	p = 0.949	p = 0.724
IL-10	r=-0.12	r = 0.27	r = 0.28
	p = 0.649	p = 0.283	p = 0.255
IL-8	r = 0.097	r=-0.15	r = 0.16
	p = 0.701	p = 0.547	p = 0.537
IP-10	r=-0.38	r = 0.046	r = 0.2
	p = 0.119	p = 0.856	p = 0.438
IL-1β	r=-0.26	r = 0.086	r=-0.24
	p = 0.357	p = 0.763	p = 0.397
MCP-1	r=-0.07	r=-0.093	r=-0.15
	p = 0.805	p = 0.743	p = 0.584

Spearman Correlation (<0.25 very weak correlation; 0.26-0.49 weak correlation; 0.50-0.69 moderate correlation; 0.70-0.89 high correlation; 0.90-1.0 very high correlation).

associated with SO have been reported in the literature.[18,19] Unfortunately, there is still no study that conclusively reports how SO causes these conditions. In the current study, we investigated whether the toxic effects of SO, which are thought to cause sudden visual losses, are due to inflammatory mechanisms or oxidative stress, a relationship which has not been previously studied.

Several sources have stated that SO can cause sudden vision loss. The most controversial of these is potassium sink theory. In normal eyes, the vitreous is considered to serve as a sink for potassium released from Müller cells. Retinal capillaries are also involved in this K^+ buffering. In this theory, replacement of the vitreous with SO blocks this effective K^+ buffering mechanism, causes an increase in K^+ ions in the retina, leading to excitotoxicity and apoptosis pathways that are triggered by these sudden alterations in potassium concentration.[18,20] However, previous studies have

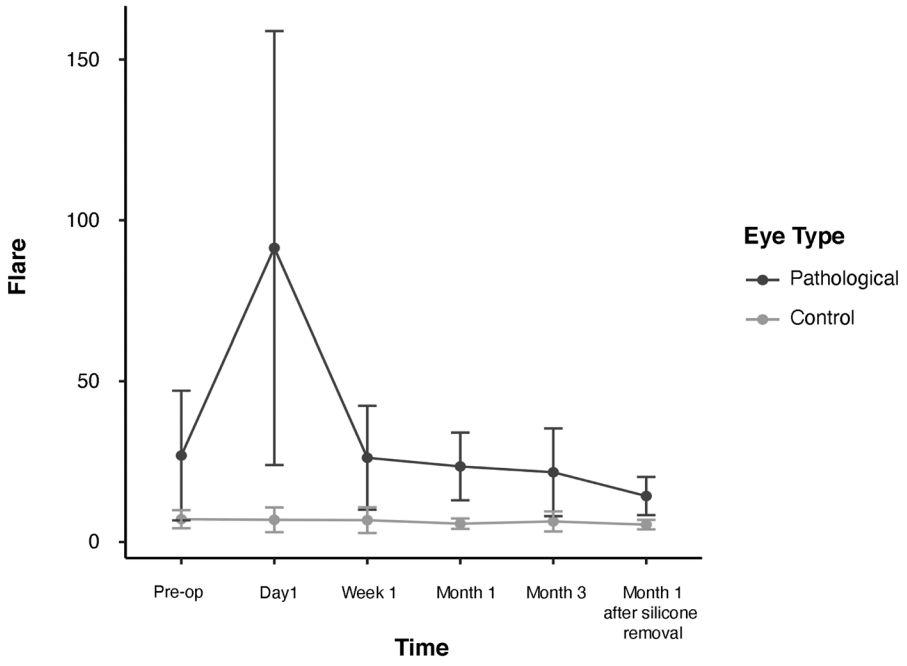

Figure 3. Time-dependent changes of flare measurements in pathological and control eyes.

not found a significant increase in K^+ ion concentration in SSF, so this theory is not a reasonable explanation for sudden vision loss due to SO.[7,21]

Another theory is that this pathogenesis may occur as a result of increased concentration of cytokines and growth factors in SSF. In this regard, Asaria et al.[22] reported that fibroblast growth factor and IL-6 levels were increased in SSF. On the contrary, when Shimizu et al.[7] compared ICs in vitreous fluid and SSF of the same RRD patients, no significant difference in cytokine levels was observed, similar to our current study. Therefore, cytokines thought to be increased in SSF do not seem to be involved in this pathogenesis.

Takahashi et al.[8] investigated IC levels in vitreous fluids of RRD cases and found that MCP-1 and IP-10 levels were significantly increased compared to macular hole cases. In addition, based on the experimental study of Nakawaza et al.[23] showing MCP-1 expression in Müller cells 6 h after RRD develops, MCP-1 appears to induce photoreceptor apoptosis and could be an important mediator in the development of PVR. Shimizu et al.[7] observed that MCP-1 levels in the vitreous were high, echoing the findings of Takahashi et al.[8] According to the present findings, an increase in MCP-1 levels was observed when compared with SSF, but this increase was not found to be statistically significant. The reason why MCP-1 and IP-10 levels were not as high as those reported by Takahashi et al.[8] could be that cases without PVR and any systemic comorbidities were included in the current study.

Another cytokine that has been shown to increase 1 h after RRD formation is IL-1β, which is thought to induce MCP-1 expression.[24] In other studies investigating IL-1β levels in SSF,[7,25] no increase in IL-1β levels was noted. Interestingly, in the current study, IL-1β levels were detected at a certain level, unlike other studies,[7,25] and a significant increase was detected in the vitreous compared to the SSF. The fact that IL-1β, a pro-inflammatory mediator, was detected at lower levels in SSF has moved us further away from the theory of sudden vision loss associated with increased IC levels. In addition, no major differences were detected in the other cytokine levels investigated compared to other studies.[7,8,25]

Another theory that has been offered on this subject is that sudden vision loss occurs as a result of phototoxicity. High exposure to blue light from the visible light spectrum is thought to damage the outer blood-retina barrier, cause oxidative stress and increase photoreceptor outer segment phagocytosis. Unfortunately, SO is known to allow more blue light to pass through and to involve more ultraviolet exposure than vitreous fluid. Based on this knowledge, it is thought that eyes with SO exposed to high amounts of visible light exposure cause phototoxic damage by triggering oxidative stress.[19,26] In addition, it is even believed that SO further increases this phototoxicity by disrupting the structure of lutein and zeaxanthin, which have excellent photoprotective properties.[19] In particular, tissues such as the retina are exposed not only to intense lipid peroxidation due to the high amount of membrane lipids, but also to intense oxidative stress due to the high oxygen concentration.[27] Therefore, in the current study was planned to investigated TAS, TOS, and OSI, which have not been investigated in SSF before in the literature.

In the present study, a significant increase in TOS and OSI values were recorded in SSF compared to vitreous fluid. This suggests that the toxic effects of SO on the retina may be more likely to be mediated by oxidative stress mechanisms. However, as it is well known, oxidative stress and inflammatory processes are closely related to each other because both processes trigger each other as a result.[28] The key point here is to understand which pathway starts the

process in the first place. The current study found no significant increase in inflammatory mediators in SSF compared to vitreous fluid, which matches the finding of a similar study.[7] Our study also found no significant increase in flare measurements, which is an indicator of inflammation in the anterior chamber.[10] This study also examined choroidal thickness measurement, as it is another parameter used to evaluate inflammation and would be expected to increase in the initiation of an inflammatory process,[29] and found no increase in choroidal thickness. All these results suggest that oxidative stress mechanisms rather than inflammation are the first pathway to initiate the damage caused by SO.

Oxidative stress resulting from excessive accumulation of reactive oxygen species initiates a series of biological processes such as apoptosis, necrosis and autophagy.[28] Through these mechanisms, photoreceptor loss and retinal damage are considered to cause sudden visual loss. The cases included in the current study did not experience any sudden visual loss. Moreover, a significant visual acuity gain was observed between preoperative and postoperative BCVA ($p < 0.001$). In another study, Christensen et al. showed a statistically significant thinning of the inner retinal layers in patients operated with SO.[30] In contrast to visual improvement, we observed a significant negative correlation between central macular thickness and TOS and OSI levels. In this respect, the present study suggests that there may be a relationship between oxidative stress and retinal damage, a possibility that needs further evaluation.

It is important to consider that certain intraoperative factors may have contributed to the observed postoperative inflammatory and oxidative stress responses. The use of perfluorocarbon liquid, which facilitates retinal stabilization and minimizes intraoperative trauma, has been associated with transient inflammatory responses due to residual droplets or surface tension effects.[31] Additionally, 360-degree endolaser photocoagulation, although effective in securing retinal attachment, may lead to increased oxidative stress by inducing thermal injury to peripheral retinal tissue and enhancing cytokine release.[32,33] The choice of SO tamponade may also influence the postoperative intraocular environment. In the present study, a single standardized SO formulation (5000 cSt) was used in all cases to ensure surgical uniformity. Although certain physicochemical properties of SO have been implicated in modulating intraocular inflammatory responses,[34] the consistent use of the same tamponade across all patients minimized procedural variability and allowed for a more reliable evaluation of postoperative biochemical alterations. While the surgical protocol was standardized across all cases, the potential cumulative effects of intraoperative factors on oxidative and inflammatory pathways should still be considered. Future studies incorporating stratified surgical subgroups may provide further insight into how these variables influence intraocular biochemical dynamics.

This study has several limitations. First, the relatively small sample size, primarily due to the challenges and risks associated with SSF collection, may reduce the ability to detect rare complications or subtle inflammatory responses related to SO. Second, the absence of comparison with different RD types and with RRD cases involving PVR may limit the broader applicability of the findings. Although PVR cases were deliberately excluded to avoid confounding effects from PVR-related oxidative stress and inflammation, this exclusion inherently reduces generalizability. Additionally, obtaining accurate axial length and refractive measurements in macula-off retinal detachment cases was difficult, which may have affected data consistency. Furthermore, since SO was routinely removed at 3 months postoperatively, any potential late-phase IC elevation could not be assessed. Lastly, the narrow age distribution of the study population may not fully represent the demographic spectrum of RRD patients.

In conclusion, there are many opinions regarding the toxic damage of SO on the retina. Our study is significant for being the first study in the literature to examine oxidative stress in SSF and to show that the toxic damage believed to be caused by SO on the retina may be initiated by oxidative stress mechanisms.

Contributors

All authors contributed to the study conception and design.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data that support the findings of this study are available from the corresponding author, [EE], upon reasonable request.

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