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RETINAL DISORDERS

Vision loss under silicone oil tamponade

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Abstract
Purpose We aimed to investigate frequency, time course and pathophysiology of vision loss in eyes with macula-on rhegmatogenous retinal detachment operated with vitrectomy and silicone oil tamponade.
Patients and methods Fifteen eyes of 15 patients who had been operated with 5,000 centistoke silicone oil between 2006 and 2014 were included in a retrospective case series. Examinations included logMAR best corrected visual acuity (BCVA), visual field testing (VF), spectral domain optical coherence tomography (OCT), electrophysiology, and fluorescein angiography.
Results Vision loss was seen in eight (53 %) eyes of 15 patients with symptomatic central scotoma, which was confirmed by VF (5/6). Preoperative median BCVA of these patients was 0.15 (0.5 to 0), prior to oil removal 0.7 (1.0 to 0.5), and 6 weeks post oil removal 1.0 (1.5 to 0.2). BCVA recovered in five patients to a median of 0.15 (0.5 to 0.1), and it remained 1.0 in three (20 %) out of 15 eyes. OCT revealed significant thinning of the foveal and parafoveal combined nerve fiber, ganglion cell and inner plexiform layers in affected eyes (mean 58.3 μm +/−13, horizontal scan through fovea, 500 μm radius) compared to their healthy fellow eyes (mean 84.5 μm +/−12.3; $p < 0.01$, n = 6 patients, 12 eyes) and compared to eyes with no vision loss under silicone oil.
Conclusions We find persisting vision loss in three out of 15 patients treated for macula-on rhegmatogenous retinal detachment with silicone oil tamponade. Thinning of inner retinal layers possibly evoked by silicone oil tamponade might be a pathophysiological explanation for vision loss in these patients.

Keywords Vision loss · Silicone oil tamponade · Inner retinal layers · OCT · Retinal detachment

Introduction

Vitrectomy is standard of care in a variety of vitreoretinal diseases. Most of the time, a tamponade is needed. The most common types are gas or air tamponades [1]. In more severe cases like retinal detachment with proliferative vitreoretinopathy [2] or proliferative diabetic retinopathy with complex retinal pathology [3], silicone oil is used. However, some surgeons promote the primary use of silicone oil even in uncomplicated macular hole surgery [4, 5]. The safety and efficacy of silicone oil in ophthalmic surgery has been demonstrated in many studies during the last decades [6, 7]. A potential toxicity of silicone oil to the human retina has been denied [8, 9]. Only a few authors have discussed a harmful effect of silicone oil to animal and human retinal structures, especially in long-term use [10–12]. Recently, unexpected and unexplained central vision loss has been described in patients who underwent vitrectomy with silicone oil tamponade [13–16]. This phenomenon can occur either during tamponade or after silicone oil removal, and it is known to many surgeons, though little is published. The underlying pathology of this idiopathic vision loss is unclear. Thinning of inner retinal layers in affected eyes and intraretinal microcysts have been discussed as a possible pathomechanism theories [13, 17].

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An explanation for this phenomenon is difficult to find, since many variables can contribute to vision loss, e.g. involvement of the macula, extend of the retinal detachment, intra- and postoperative intraocular pressure, the number of reoperations, and the experience level of the surgeon. Therefore we tried to minimize the variables by examining a homogenous group. We provide retrospective data of 15 patients with macula-on retinal detachment, who underwent vitrectomy with the use of silicone oil tamponade at our clinic. The macula remained attached during the entire follow-up period. We analyzed the frequency, time course and underlying pathology of vision loss under silicone oil tamponade.

Patients and methods

We analyzed data of all patients, who were vitrectomized between 2006 and 2014 at our center. During this time period, about 5,400 vitrectomies were performed. Approximately 900 of these cases received a silicone oil tamponade with 5,000 centistoke silicone oil. Vitrectomy was carried out in a standardized way. After vitrectomy and following reattachment of the retina by means of perfluorocarbon liquid (PFCL) and laser or cryo coagulation of retinal holes, PFCL was directly exchanged with silicone oil. Intraocular pressure was documented to be within normal limits during the operation procedure. Indications for vitrectomy with silicone oil tamponade were: recurrent retinal detachment 47 %, retinal detachment with macular involvement partly with proliferative vitreoretinopathy 28 %, retinal detachment in high myopia 6 %, high-risk proliferative diabetic retinopathy with vitreal bleeding and/or tractional retinal detachment 5 %, traumatic eye rupture 5 %, acute retinal necrosis 2 %, macula-on retinal detachment 2 %, other 5 %. Out of 900 patients who received vitrectomy with silicone oil tamponade for various indications, only 18 patients (2 %) had rhegmatogenous retinal detachment without macular involvement, three of which had to be excluded due to recurrent retinal detachment (n = 1) or macular edema (n = 1) and epiretinal gliosis (n = 1) during follow-up. Fifteen patients fulfilled the inclusion criteria of rhegmatogenous retinal detachment with an attached intact macula before, during and after vitrectomy. Only these 15 were included into the study.

Best corrected logarithmic minimum angle of resolution (logMAR) visual acuity (BCVA) and a full ophthalmological examination were carried out in all patients preoperatively at the date of diagnosis, postoperatively, 6 weeks after operation, before oil removal, after oil removal, 6 weeks after oil removal and at latest follow-up (median 36 months, range 4 to 82).

Additionally, nine out of 15 patients were reexamined at a median follow-up of 48 months (range 14 to 70 months). In these nine patients, 10° and 30° central visual field (VF) analysis (Humphrey Filed Analyzer Model 750, Carl Zeiss, USA), macular and peripapillary retinal layer measurements by spectral domain optical coherence tomography (OCT) (Spectralis®, Heidelberg Engineering, Heidelberg, Germany), single retinal layer discrimination in horizontal macular scans (Heidelberg Eye Explorer® Segmentation Editor™, Heidelberg Engineering) and the thickness of the retinal nerve fiber layer in peripapillary scans using Axonal Single Exam Report OU with FoDi™ (Heidelberg Engineering) were carried out. Further, multifocal electro retinogramme (ERG) and visually evoked potentials (VEP) were done in these nine patients (RETI-port/scan21, Roland Consult, Brandenburg a. d. Havel, Germany). In two of 15 patients, ERG could be carried out before oil removal. Fluorescein angiography (FLA) was done in three of 15 patients (Heidelberg Engineering). The treated eyes were compared intra-individually to the fellow control eye.

Statistical analysis was carried out with the programme "R" (www.r-project.org).

Written consent was obtained from all reexamined patients. For retrospective data, formal consent is not required. All measurements followed the recommendations of the university ethics committee (D453/14) in accordance to the declaration of Helsinki and German federal law.

Results

Demographics

Fifteen eyes of 15 patients were included. Median age was 61 years (range 45 to 75 years), and three women and 12 men were examined.

Vision

Figure 1 shows the time course of visual acuity before, during and after silicone oil tamponade. Vision loss was noted in eight (53 %) out of 15 eyes of 15 patients, all complaining about a central scotoma, confirmed by central visual field analysis in five out of six patients examined. Before silicone oil instillation, median logMAR BCVA of the eight patients with vision loss under silicone oil was 0.15 [20/28 Snellen equivalent] (range 0.5 [20/63] to 0.0 [20/20]). Before oil removal, BCVA of these eight patients was 0.7 [20/100] (1.0 [20/200] to 0.5 [20/63]), and 6 weeks after oil removal it was 1.0 [20/200] (1.5 [20/600] to 0.2 [20/32]). BCVA recovered in five patients to a median of 0.15 [20/28] (0.5 [20/63] to 0.1 [20/25]) at latest follow-up (>1 year), but remained 1.0 [20/200] in three patients. In four patients, vision loss happened

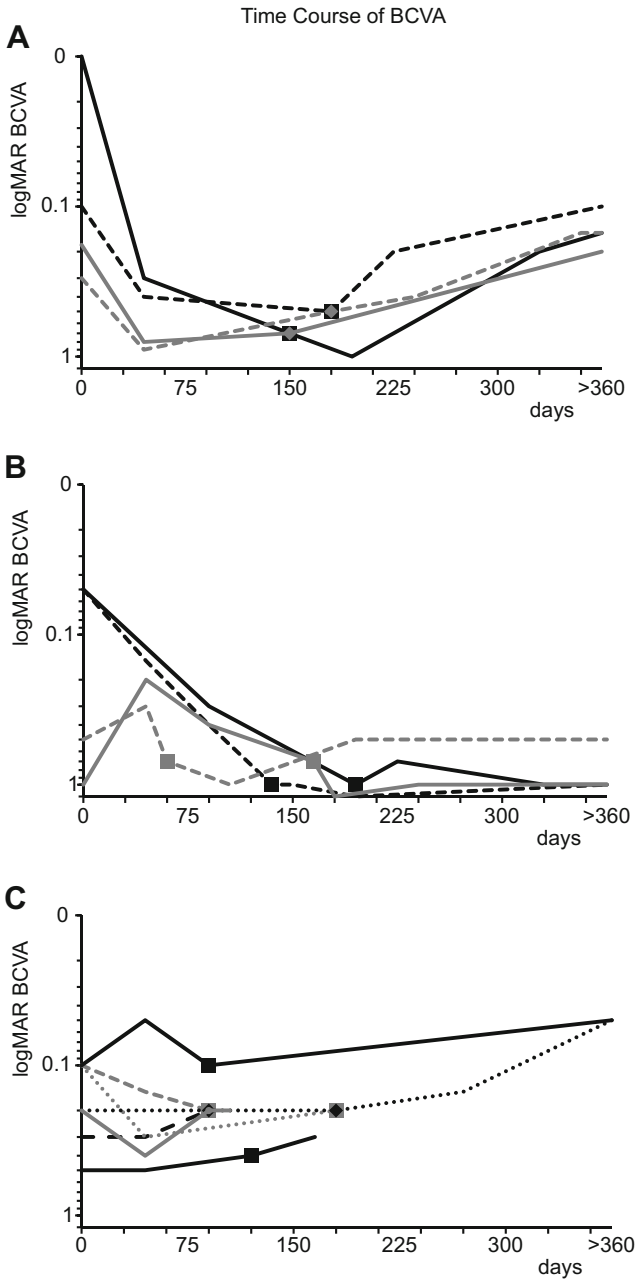

Fig. 1 Time course of logMAR best corrected visual acuity (BCVA) of all patients. Quadrants indicate the time of silicone oil removal. Note that all patients with early vision loss recovered. **a** patients with vision loss under silicone oil tamponade with early vision loss (within the first 6 weeks) **b** patients with vision loss under silicone oil tamponade with late vision loss (later than 6 weeks). Two patients had vitreal bleeding upon first presentation; therefore, vision was low. Intraoperatively, the macula was noted to be attached. **c** patients without vision loss under silicone oil

within the first 6 postoperative weeks; all of these recovered. The other four patients complained about vision loss within the first 3 months; three of these did not recover. Vision loss always occurred before oil removal. The time point of oil removal did not affect the vision outcome.

Clinical examinations

All patients presented with macula-on retinal detachment. Eleven of 15 patients had rhegmatogenous retinal detachment with multiple peripheral holes at initial presentation. Four of 15 patients had giant tear retinal detachment. The time of retinal detachment was less than 6 h in all cases. Vitreal bleeding was present in two cases, resulting in a reduced preoperative visual acuity. The macula stayed attached at all times before, during and after operations.

In all patients, slit lamp examination did not show any pathological finding at initial presentation or at follow-up visits. The postoperative healing process was uneventful in all cases. Intraocular pressure was normal at all times in all patients. Optic media were clear at all times. Five out of eight patients with vision loss under silicone oil were initially pseudophacic, and three patients (BCVA recovered in two of these) received phacoemulsification with intraocular lens implantation in a combined operation with the oil explanation. Funduscopy showed no macular abnormalities. Optic disc was generally vital in all patients; temporal paleness was noticed in two, both with vision loss under silicone oil. A myopic cone was seen in 12 of 15 patients.

OCT and macula

Figure 2a shows the mean thickness of the nerve fiber, ganglion cell and inner plexiform layers (NFL, GCL, IPL) in a horizontal OCT scan through the macula of eyes with vision loss under silicone oil in comparison to their fellow eyes. It reveals significant ($p < 0.01$, n = 6 patients) thinning of the NFL, GCL and IPL 500 μm temporal and nasal from the fovea (mean 58.3 μm +/−13), when compared to the healthy fellow eyes (mean 84.5 μm +/−12.3). An example of such a scan is given in Fig. 3. This thinning was not seen ($p = 0.08$, n = 3 patients) in horizontal OCT scans through the macula of eyes without vision loss under silicone oil (mean 93.5 μm +/−7.2, 500 μm temporal and nasal from the fovea, Fig. 2b). There was even a trend towards thickened inner retinal layers when compared to the healthy fellow eyes (mean 77.8 +/−15.1, 500 μm temporal and nasal from the fovea). A comparison between eyes with continuing vision loss and those with vision recovery was not possible due to limited case numbers. All other retinal layers did not show any significant difference ($p > 0.05$) between operated eyes with or without vision loss and their fellow eyes.

Significant thinning of the combined NFL, GCL and IPL was mainly obvious in the macular region, especially in a parafoveal ring of 500 μm radius (see Fig. 3). Microcysts were seen in five of six eyes with vision loss under silicone oil, usually in the inner plexiform and inner nuclear layers. These cysts appear to be hypo reflective,

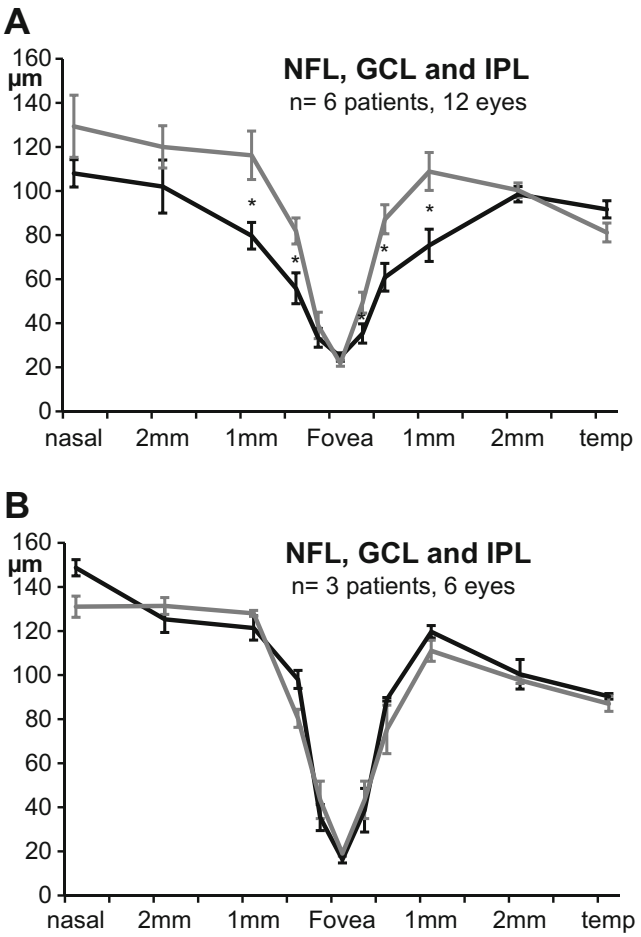

Fig. 2 Thickness of the combined Nerve Fiber (NFL), Ganglion Cell (GCL) and Inner Plexiform Layers (IPL) measured in horizontal fovea centered OCT scans of the macula. Reduction of inner retinal layer thickness is only seen in eyes with vision loss under silicone oil. **a** Mean thickness and standard deviation of eyes with vision loss under silicone oil (*black*) compared with their healthy fellow eyes (*grey*); asterisks indicate statistically significant differences between values. **b** Mean thickness and standard deviation of eyes without vision loss under silicone oil (*black*) compared to their fellow eyes (*grey*)

as shown in Fig. 3. No microcysts were seen in eyes without vision loss under silicone oil.

OCT and optic disc

Optic disc OCT measurements were carried out in six out of eight patients with vision loss under silicone oil. Two of these six patients had no vision recovery, while the other four patients experienced vision recovery during the follow-up period. Optic disc OCT revealed thinning of the NFL in the papillo-macular bundle in those two patients (33 µm and 35 µm, respectively [normal thickness 56 µm]) who had no vision recovery, as shown in Fig. 4. Thinning of the NFL in the papilla-macular bundle was also seen in one patient (33 µm), with vision loss under silicone oil and following vision recovery. This patient, however, had the worst vision in the vision recovery group (BCVA 0.5 logMAR [20/63 Snellen equivalent]). The other three patients with vision loss under silicone oil and vision recovery had no thinning of the NFL in the papillo-macular bundle. Patients without vision loss under silicone oil had normal OCT findings.

Multifocal ERG

Nine patients were examined by multifocal ERG after silicone oil removal. Six of those nine patients had vision loss under silicone oil, three did not experience vision loss. All nine patients had normal multifocal ERG findings at the median follow-up of 48 months (range 14 to 70 months) after oil removal. In two patients, both with vision loss under silicone oil, multifocal ERG was additionally done before oil removal. It showed a reduction in electrophysiological activity of all stimulation areas before oil removal, most likely due to the insulation effect of the silicone oil. Six weeks after oil removal, the electrophysiological activity of central stimulation areas was still reduced, although the insulation effect of silicone oil was absent, as depicted in Fig. 5. The amplitudes improved over time (follow-up 7 to 12 months after oil removal), but vision remained 0.1 logMAR [20/200]. VEP was physiological in all examined eyes (9/9).

Fluorescein angiography

FLA was carried out in three out of eight eyes with vision loss under silicone oil. One patient was examined 1 month after oil removal. No perfusion abnormalities were seen. The second patient had a normal FLA 4 days after oil removal. The third patient had an FLA 1 day before oil removal. Retinal perfusion was intact and there were no pathological findings.

Discussion

Vision

During a time period of 9 years, about 900 vitrectomized patients received a silicone oil tamponade at our center. Only 15 of these had macula-on rhegmatogenous retinal detachment with an attached intact macula before, during and after operations. All of these patients were included. Eight patients out of this group of 15 experienced vision loss with central scotoma, three of whom have never recovered even years after oil removal. This means that 20 % of these patients suffer from vision loss with permanent poor vision. In a similar, though smaller, consecutive case series with nine eyes of nine patients, Christensen describes vision loss in one-third of the patients after silicone oil removal [13]. Moya et al. report a similar high incidence of vision loss in ten of 20 fovea-sparing

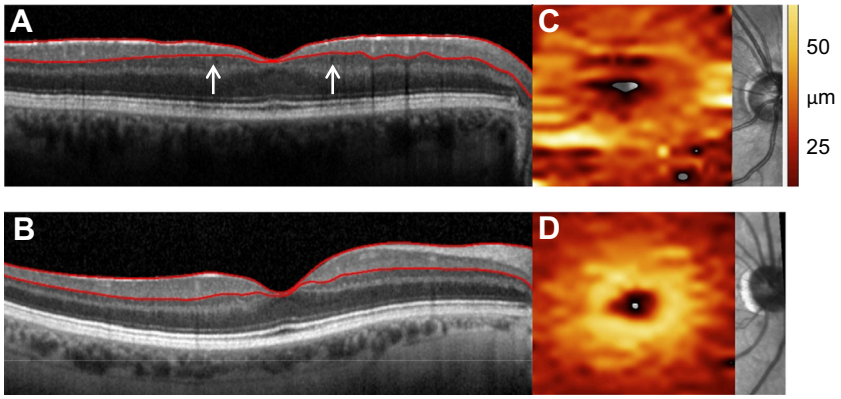

Fig. 3 OCT example of retinal layer thickness in horizontal scan and in macula thickness map. Reduction of inner retinal layer thickness surrounds the fovea in eyes with vision loss under silicone oil. **a** Right eye affected by vision loss under silicone oil; *red lines* indicate the margin the internal limiting membrane (*above*) and the border between inner plexiform and inner nuclear layer (*below*); *arrows* indicate intraretinal cysts in the inner nuclear layer. **b** Mirrored left fellow eye; *red lines* margin the same borders as in A. **c** Macular retinal thickness map of the ganglion cell layer of an eye with vision loss (same as in A) showing a thin central ring. **d** Mirrored macular retinal thickness map of the fellow eye (same as in B) showing a normal central ring thickness

giant tear retinal detachment patients, who underwent vitrectomy with silicone oil tamponade and following oil removal. Five (5/14) of these cases had vision recovery [16].

Many authors argue that vision loss appears after the removal of silicone oil [13, 18–22]. Others present cases of vision loss during silicone oil tamponade [14, 17]. In our case series, all patients had vision loss during the time of silicone oil tamponade. Vision loss occurred within the first 6 postoperative weeks in four out of eight eyes affected. The other four patients suffered from vision loss later, within the first two to three postoperative months. Therefore, the length of the tamponade does not seem to affect vision loss. However, an early vision loss under silicone oil seems to be of better prognosis. A long-term follow-up of more than 1 year can be recommended, since vision may recover over such a time period after oil removal.

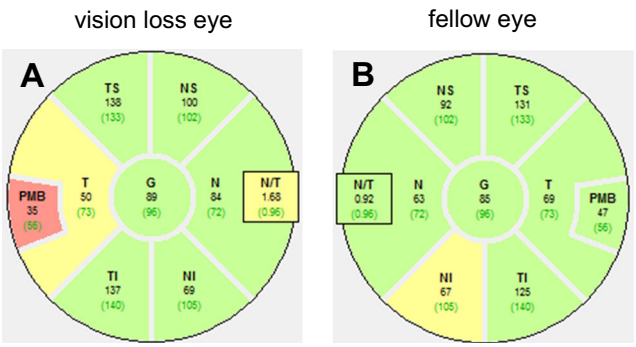

Fig. 4 Optic disc OCT of NFL. The NFL thickness is reduced in the papillo-macular bundle in eyes with permanent vision loss. **a** Right eye with vision loss under silicone oil; numbers show the NFL thickness in µm, normal values in brackets; TS = temporal superior, NS = nasal superior, N = nasal, NI = nasal inferior, TI = temporal inferior, T = temporal, TS = temporal superior, G = mean NFL thickness, PMB = papillo-macular bundle, N/T = nasal/temporal thickness quotient; note the reduced thickness of the NFL in the PMB. **b** Left fellow eye of the same patient as in A

A time dependency of silicone oil removal concerning visual outcome remains unclear. Early oil removal is discussed to be of better prognosis [13, 23]. In our case series, the time of silicone oil removal does not affect visual outcome.

OCT

High resolution time domain or spectral domain OCT have revealed thinning of inner retinal layers and intraretinal microcysts [13, 17, 24]. We utilized OCT based retinal layer thickness analysis and compared the treated eyes intra-individually to the untreated control fellow eyes. We show a significant reduction in thickness of the combined NFL, GCL, IPL of the inner parafoveal ring in vision loss eyes compared to their fellow eyes. This is not seen in eyes without vision loss under silicone oil. All other retinal layers are anatomically normal in affected and unaffected eyes. We assume that the

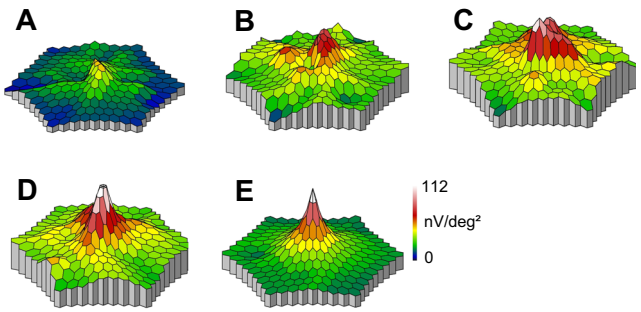

Fig. 5 Multifocal ERG of a patient with vision loss under silicone oil. Initially logMAR BCVA was 0.05 [20/22 Snellen equivalent]. It fell to 1.0 [20/200] before oil removal and remained sub-reading vision, even though mfERG recovered. **a** Right eye under silicone oil tamponade before removal (logMAR BCVA 1.0). **b**) Same eye 6 weeks after oil removal (logMAR BCVA 1.0). **c** Same eye 7 months after oil removal (logMAR BCVA 1.0). **d** Left eye without vision loss under silicone oil (logMAR BCVA 0.1 [20/25]). **e** Reference

reduction of the retinal ganglion cell associated layers (NFL, GCL and IPL) is a consequence of ganglion cell death, possibly due to silicone oil tamponade.

Apart from the clear thinning of the inner retinal layers, there are hyporeflective intraretinal cysts possibly of degenerative origin or filled with silicone oil. Those findings can only be detected in eyes with vision loss. Intraretinal cysts have been described before and shown to be filled with silicone oil droplets [25–30]. However, these hyporeflective intraretinal cysts are not as clearly detectable.

Latest OCT measurements of peripapillary NFL in patients who underwent vitrectomy with silicone oil tamponade reveal thickening of the NFL in operated eyes, compared to fellow eyes [31]. In our study, NFL in peripapillary OCT scans of patients without vision loss (3/3) were normal. In contrast, patients with permanent vision loss under silicone oil had thinning of the NFL in the papillo-macular bundle, likewise shown by other authors [31], underlining again ganglion cell death of the inner parafoveal ring region.

Electrophysiology

Our limited data suggests an initially pathological multifocal ERG with a reduction in central stimulation areas in patients with vision loss after silicone oil removal. However, at long-term follow-up (many months, up to years after oil removal), multifocal ERG is nearly physiological and comparable to the fellow eye. Cazabon carried out multifocal ERG in his case series shortly after oil removal, showing a reduction in central stimulation areas [18]. He did not document the long-term follow-up. ERG is a function of photoreceptor integrity. We interpret the recovery of multifocal ERG recordings as recovery of photoreceptor functionality, without ganglion cell recovery. This supports our theory of exclusive ganglion cell death in eyes with vision loss, leaving the photoreceptors untouched.

Pathophysiology

Our data clearly show a reduction of ganglion cells in the parafoveal retina of patients with vision loss, who were treated with vitrectomy and silicone oil tamponade for macula-on retinal detachment. Toxicity of silicone oil to retina bound cells is a widely discussed mechanism. In vitro and in vivo studies have proposed a harmful effect of silicone oil to retinal structures, and toxic substances in removed silicone oil have been described [8–12]. Following this theory, silicone oil has to be in close proximity to retinal structures to be harmful. Intraretinal and intra optic nerve silicone oil droplets have been described [25, 29, 32]. Epiretinal or intraretinal silicone oil might damage ganglion cells directly. Also, microglia within the retina could be activated by silicone oil, leading to inflammatory processes with consecutive cell death. All these cells are in direct proximity to the silicone oil surface. If silicone oil directly or indirectly damages ganglion cells, it remains, however, unclear why first of all, not all eyes are affected, and why second of all, thinning of the combined NFL, GCL, IPL is mainly found in the inner parafoveal ring. We have no explanation for the fact that not all eyes are affected. A further study to correlate the amount of silicone oil within the eye bulb and the number of patients with vision loss under silicone oil might be helpful to find an answer to this question. The fact that a reduction of NFL, GCL and IPL thickness is mainly seen in the inner parafoveal ring might be due to the fact that the by far largest amount of ganglion cells is found in the inner 4 to 5° parafoveal ring [33]. Changes in the number of ganglion cells would be most prominent here.

Enhanced phototoxicity, especially at the time of silicone oil removal, is a different discussed mechanism of vision loss [34]. Since all of our patients experience vision loss before oil removal, we do not support this theory.

Conclusion

Silicone oil is one of the best-known intraocular tamponades and it is widely used and considered to be safe. In many vitreoretinal surgery cases, there is no alternative to silicone oil. Our data suggests that there are unexplained cases of vision loss under silicone oil tamponade and that the number of these cases might be underestimated.

Patients with vision loss under silicone oil treated for macula-on retinal detachment show a significant thinning of the inner retinal layers compared to the untreated fellow eyes. We conclude that ganglion cell death might be a reason for vision loss in these patients. The underlying pathophysiological mechanisms remain unclear. Pathomechanism directed in vivo and in vitro studies and a comparison to patients who received a gas tamponade are needed.

We suggest to consider the possibility of vision loss if utilizing silicone oil and to limit its use to patients with a complicated vitreo-retinal situation. OCT monitoring might be helpful to detect early changes in inner retinal layer thickness and remove silicone oil early.

Compliance with ethical standards

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Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing

arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

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