Complications Associated with the Use of Silicone Oil in 150 Eyes after Retina–vitreous Surgery

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Abstract: Complicated retinal detachments (RDs) were successfully managed in 150 eyes of 170 consecutive patients by one surgeon (JLF) using silicone oil in conjunction with modern pars plana vitrectomy. Long-term postoperative complications were observed between 6 months and 5 years of follow-up. Cataracts developed in all phakic eyes and all corneas with oil-endothelial touch showed band keratopathy within 6 months. Recurrent detachments were noted in 22% of eyes during silicone oil tamponade and occurred in 13% of eyes after the oil had been removed. Other complications associated with the use of oil for vitreous surgery included pupillary block glaucoma (3%), closure of the inferior iridectomy (14%), fibrous epiretinal and subretinal proliferations (15%), pain (5%), and subconjunctival deposits of oil (3%). Without exception, within a period of 1 year the intraocular silicone oil showed some degree of emulsification, suggesting that the physicochemical characteristics of the oil injected may be an important variable in long-term complications. [Key words: complications, silicone oil, vitrectomy.] Ophthalmology 95:870–876, 1988

Complications and difficulties associated with the mere injection of silicone oil to repair complicated retinal detachments (RDs) led to its disuse in the 1960s.^{1,2} Despite these discouraging early reports, the combination of silicone oil with microsurgical vitrectomy techniques improved the rate of anatomic reattachment of the retina where other procedures had failed.^{3,4} In conjunction with sophisticated vitrectomy, the use of sili-

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cone oil tamponade has found increasing acceptance over the past few years, and its role and limitations have been the subject of many publications.⁵⁻³⁰ In this report, we describe the postoperative complications observed in 150 eyes with complicated vitreoretinal problems. Most of these difficulties are due to the proliferative nature of the underlying disease, some to technique and altered intraocular physiology, and last, but not least, some may be due to the characteristics and purity of the specific oil used.³¹

MATERIALS AND METHODS

We reviewed the patient records of 150 eyes of 170 consecutive cases with complicated RDs which were successfully anatomically reattached combining silicone oil tamponade with modern pars plana vitrectomy techniques. All surgery was performed by one surgeon (JLF)

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Table 1.	Frequency of	of Preoperative	Diagnoses	in 150 Cases
	of Comp	licated Retinal	Detachmen	t

No. of Patients	
103	PVR C3 or worse
32	PDR with traction RD
8	Giant retinal tear
3	Expulsive choroidal hemorrhage
2	Uveitis and ocular hypotension
2	Foreign body with RD and PVR

PVR = proliferative vitreoretinopathy; PDR = proliferative diabetic retinopathy; RD = retinal detachment.

using the techniques and principles described by Zivojnović et al.^{13,14} The preoperative diagnosis was proliferative vitreoretinopathy (PVR) C3 or worse on 103 eyes and proliferative diabetic retinopathy (PDR) with traction RD and PVR in 32 eyes. The remaining complicated RDs were due to giant retinal tears in eight eyes, expulsive choroidal hemorrhages in three, uveitis with ocular hypotension in two, and intraocular foreign body in two (Table 1). The mean age of the diabetic patients was within the fourth decade, whereas the mean age of the remaining patients was within the sixth decade. The patients were followed from 6 months to 5 years (mean follow-up, 31.6 months).

All eyes had complete preoperative examinations, including visual acuity, applanation tonometry, biomicroscopic examination, and binocular indirect ophthalmoscopy. Postoperative follow-up evaluations took place at 2 weeks and 1, 2, 3, and 6 months, and then every 6 months thereafter. At each follow-up visit, a complete ocular evaluation was performed, including visual acuity testing, measurement of intraocular pressure, slit-lamp examination with and without contact lens, and binocular indirect ophthalmoscopy.

VISUAL FUNCTION

In general, optimal visual acuity was reached at 3 months and, in agreement with other authors, usually

remained stable or decreased thereafter.^{5,7,29} In order to relate visual function to the presence or absence of silicone oil, the visual acuities of 77 eyes with greater than 30 months of follow-up were evaluated at 30 months. Two groups were formed: 42 eyes in which intraocular silicone oil was present (Table 2), and 35 eyes in which the oil had been removed between 3 and 6 months after the initial surgery (Table 3). In more than half of the eves of each group, there was an obvious explanation why the visual function had not improved. Cataracts, pupillary block glaucoma, recurrent RDs, macular pathology, and band keratopathy were the reasons for the lack of visual improvement after the 3-month visit in 22 of the eyes with intraocular oil (Table 2). Cataracts, recurrent detachments, macular pathology, and chronic uveitis with macular edema were the reasons for lack of visual improvement in 21 eyes in the group where the oil was removed (Table 3).

In the 20 eyes with oil present, where there was no apparent reason for the visual acuity not to improve, the visual function decreased slightly during the period of follow-up (Table 2). In the 14 eyes of the 35 where the oil had been removed and where there was no obvious pathology to explain a decrease in vision, the visual acuity either stabilized or showed a slight trend toward improvement (Table 3).

In comparing these two groups of no apparent pathology, the slight difference in favor of removal of silicone oil could be due to the refractive qualities of the silicone or to actual oil-tissue interactions leading to progressive dysfunction as a result of prolonged retinal exposure to oil. It is also possible that the 14 eyes in which the oil was removed had the potential for better visual function initially. We cannot make a conclusion from our somewhat arbitrary samples.

Visual function variability was described by some of the aphakic patients. Those with a visual acuity of 6/60 or better complained of subjective changing of vision several times during the day. We attributed this phenomenon to the constantly changing shape of the oilaqueous interface at the pupillary opening in those aphakic eyes that did not have a total fill.

	Obvious Reason for Decrease in Visual Acuity (n = 22)			No Apparent Reason for Decrease in Visual Acuity (n = 20) $$				
		Postoperative			Postoperative			
Visual Acuity	Preoperative	3 Mos	12 Mos	30 Mos	Preoperative	3 Mos	12 Mos	30 Mos
NLP	10	4%	4%	18%		1998 V.S	5%	5%
LP	46%	23%	46%	46%	60%	15%	20%	20%
HM	36%	36%	27%	23%	25%	40%	30%	30%
CF	9%	10%	23%	13%	15%	20%	25%	20%
6/120	9%	23%				10%	10%	15%
6/60+		4%				15%	10%	10%

Table 2. Visual Acuity in Eyes with Intraocular Oil Present to the 30-month Follow-up

n = number of patients; NLP = no light perception; LP = light perception; HM = hand motions; CF = counting fingers,

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	Obvious Reason for D	ecrease in Visu	al Acuity (n = 21)	No Apparent Re	ason for Decrea	se in Visual Acui	ty (n = 14)
			Postoperative				Postoperative	
Visual Acuity	Preoperative	3 Mos	12 Mos	30 Mos	Preoperative	3 Mos	12 Mos	30 Mos
NLP				14%				
LP	38%	14%	24%	19%	36%			
HM	43%	19%	28.5%	28.5%	36%	14%	14%	14%
CF	14%	24%	28.5%	28.5%	21%	36%	29%	29%
6/120	5%	24%		5%	7%	14%	14%	14%
6/60+		19%	19%	5%		36%	43%	43%

Table 3. Visual Acuity in Eyes without Oil to the 30-month Follow-up

n = number of patients; NLP = no light perception; LP = light perception; HM = hand motions; CF = counting fingers.

EMULSIFICATION

Like other authors, we use the term emulsification to describe tiny intraocular droplets of silicone. The frequency with which these have previously been noted varies from 5 to 25%.^{3,5,7,12,16,18,25,26} In our cases, they were seen floating freely in the anterior chamber, on the corneal endothelium, infiltrating the iris stroma, in the superior angle, in the posterior chamber, on the posterior surface of the iris and on the anterior lens capsule, on the zonules, on and between the ciliary processes, on the posterior capsular surface, on the posterior surface of the oil bubble, on the epiretinal surface, and in some cases with detached retina, on the retroretinal surface. At 1 month, 1% of eyes showed emulsification, at 2 months 6%, at 3 months 11%, and by 6 months 85% of the eyes showed tiny intraocular droplets. The mean time for the development of emulsification in this group was 5 months and at the 1-year follow-up examination 100% of the eyes with an oil fill showed some degree of emulsification. In most of the eyes in which the oil was permanently removed, oil droplets were found moving (like cells) throughout the aqueous and vitreous compartment.

CATARACT

Thirty-three of the 150 eyes were phakic after successful reattachment of the retina. Cataracts developed in all of the phakic eyes. The rate of formation of the cataract was directly proportional to the duration of lenticular contact with the oil, an observation shared by other authors.^{5,7,25} Posterior subcapsular changes were most common and were seen to occur earlier in the diabetic as compared with the nondiabetic patients. The mean time for cataract development was 3 months in the diabetic group as opposed to 6 months in the remaining patients.

In two eyes, the silicone oil was removed while the lens was clear. Cortical and nuclear changes developed within 6 months in one patient who had a giant retinal tear. Blood staining of the cornea secondary to neovascular glaucoma developed 6 weeks after oil removal in the other patient who was a diabetic.

PAIN

In seven patients, pain was a significant complaint, as also noted in other reports.^{16,29} Subconjunctival oil was found in four of these eves resulting from extravasation through the sclerotomy. The pain was relieved after repair of the sclerotomy and removal of the subconjunctival oil. Removal of subconjunctival silicone is difficult, because the oil becomes multiloculated and elicits a lipogranulomatous response in the episcleral connective tissue spaces. We used a cotton-tipped applicator, applying pressure over the infiltrated areas to mechanically express the oil. The other three patients experienced relief of pain only after complete removal of intraocular silicone oil. Topical atropine and steroids did not relieve the pain in these three cases. Five of the painful eyes had a diagnosis of PVR, one eye was in a patient with uveitis and one was in a patient with diabetes. The diabetic and uveitis patients had subconjunctival extrusion of silicone after removal of which the pain was relieved. We could not explain the reason for the pain. There was no evidence of inflammation, increased pressure, or keratopathy.

SILICONE OIL KERATOPATHY

Band keratopathy occurred in all 20 eyes that showed silicone oil-corneal endothelial touch, agreeing with other reports.^{2,3,5,7,10} In six eyes of diabetic patients with oil-endothelial touch, the mean time for the appearance of keratopathy was 3 months, whereas in the 14 remaining eyes the mean time for development of keratopathy was 5 months. All of these eyes were aphakic at the time of silicone instillation; 15 had a total fill (including the aqueous compartment) due to insufficient iris tissue, whereas the inferior iridectomy closed in the other five eyes, resulting in forward displacement of the oil.

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Table 4. Ocular	Complications	Associated	with Silicone Oil
Com	bined with Vitr	eoretinal Su	rgery

Complication	Percentage
Emulsification	100.0
Cataract	100.0
Oil keratopathy	100.0
Flare and cell	
After oil removal	48.3
With oil present	6.7
Postoperative RD	
After oil removal	13.3
With intraocular oil	22.0
Silicone oil replacement	16.7
Fibrous proliferation	15.3
Inferior iridectomy closure	14.3
Glaucoma	
Chronic glaucoma	10.0
Pupillary block	3.3
Clumped pigment inferior angle	7.3
Pain	4.7
Macular pucker	3.3
Pupillary membrane	2.7
Separate anterior chamber oil bubble	2.7
Subconjunctival oil	2.7
Subretinal hemorrhage	1.3
Rubeosis with oil	1.3
Hyphema with oil-rubeosis	1.3
Endophthalmitis	0.7

RD = retinal detachment.

CLOSURE OF THE INFERIOR IRIDECTOMY

An inferior iridectomy was performed whenever there was adequate iris tissue in aphakic and pseudophakic patients. Of the 105 eyes with inferior iridectomies, 90 remained patent and functioning, whereas 15 closed (14.3%). In 10 of the 15 that closed, the oil was removed before keratopathy developed, and in all of these there was forward displacement of oil. Closure of the iridectomy was believed to be due to inflammation, rubeosis and/or pigment cell proliferation in the inferior angle.

FLARE AND CELL-CHRONIC UVEITIS

Of the 150 eyes with a silicone oil fill, only 10 (6.7%) showed evidence of flare and cells at 1 month postoperatively. Eight of these eyes had PVR, two of which had chronic uveitis preoperatively and the additional two were eyes of diabetic patients. Iritis had also been noted by other authors.^{16,18,28}

A much larger percentage of eyes appeared with flare and cells after silicone oil removal. The oil was removed in 60 of the 150 eyes, and 29 of these eyes (48.3%) showed persistent flare and cells for more than 1 month postoperatively.

SILICONE OIL REINSTILLATION

It was necessary to replace the silicone oil in 10 of the 60 eyes (16.7%) in which the oil was removed. Nine of

these eyes had PVR and the other had PDR. The causes for oil reinstillation could be grouped into three categories: (1) six eyes with recurrent RD in which the oil was replaced within 6 months of removal, (2) two eyes in which rubeosis developed after a 360° peripheral RD necessitating replacement of oil within 2 months of removal, and (3) three eyes that required oil replacement within 3 months of removal due to the development of intense flare (4+) and cells (1+) associated with hypotension. All ten of these eyes were stable after the oil was replaced and the detachments were repaired; the rubeosis regressed and adequate pressure was maintained in otherwise quiet eyes.

GLAUCOMA

There were 15 eyes (10%) with chronically elevated intraocular pressure as compared with an incidence of 2 to 40% in other reports.^{2,7,10,12,14,18,23,25,28,29} The glaucoma was controlled postoperatively with topical medications alone in 11 eyes, controlled with topical medications and oral drugs in 3, and with cryoablation of ciliary body in 1. We could not definitely attribute the glaucoma to the presence of silicone oil because all of these eyes had had multiple previous procedures resulting in anterior synechiae, pigment in the angle, rubeosis, or a combination of these findings. Only two eyes had massive emulsification; however, removal of the oil did not change the need for topical medications.

Pupillary block related to the silicone oil developed in five eyes (3.3%) after the initial instillation of silicone oil. In each case, the silicone was behind the plane of the iris at the conclusion of surgery. Postoperatively, varying between 24 hours and 3 weeks, the silicone oil bubble moved forward resulting in pupillary block. In four of these eves, this complication occurred within 72 hours of surgery. Two eyes had a large subretinal and preretinal hemorrhage which forced the silicone forward (1 in a phakic eye). The other two eyes had large choroidal detachments forcing the silicone forward (aphakic eves). The fifth case of postoperative pupillary block occurred 3 weeks after surgery and was thought to be due to closure of the inferior iridectomy. The two eyes with intraocular hemorrhage eventually became phthisical: the two eyes with choroidal detachments were successfully managed by removing the oil and using a long-acting gas. Surgical readjustment of the oil volume and reopening of the iridectomy successfully managed the last case.

POSTOPERATIVE RETINAL DETACHMENT

Recurrent RDs occurred in 33 eyes (22%) with intraocular silicone oil present. The overall redetachment rate reported ranges from 11 to 53%.^{2,3,5,6,10,11,16,18,-19,23-27,29} "Late" redetachments range from 45 to 53%.^{6,19} In our study, the majority (23 eyes) showed peripheral detachments which were most commonly present within 3 months after oil instillation. Nineteen of these eyes were inferior peripheral detachments,

Novartis Exhibit 2287.004 Regeneron v. Novartis, IPR2021-00816 whereas four were found in the superior periphery. Four of these peripheral detachments were not apparent until 12 months after silicone injection. Total detachments developed in eight eyes within 6 months of silicone instillation. The earliest total detachment was seen within 2 weeks; most were present within 3 months. In two eyes, a shallow detachment of the posterior pole was present within 3 months of oil instillation.

The silicone oil was removed in 60 eyes and recurrent RDs occurred in 8 of these eyes (13.3%) which agrees with the experience of other authors.²⁹ Five of these detachments involved the posterior pole, whereas three were peripheral only. In two of the eyes with peripheral detachments that developed after oil removal, rubeosis developed within a few weeks. Most of the recurrent detachments occurred within 6 months of oil removal. In all cases, the retina could be reattached when the oil was replaced. Rubeosis, if present, showed signs of regression.

POSTOPERATIVE FIBROUS PROLIFERATION

Epiretinal fibrous proliferation was seen in 23 eyes (15.3%) of the 150 with silicone oil fill. The reported rate of recurrent proliferation ranges from 3^{14} to 71%.²⁶ In seven of our eyes, subretinal fibrosis in the form of bands and/or sheets was also found. In almost all instances, the epiretinal fibrosis occurred at the edge of large retinotomies and appeared to conform to the posterior surface of the silicone bubble. Subretinal fibrosis was only found in those eyes with persistent subretinal fluid and typically occurred in locations where fluid was present.

PUPILLARY MEMBRANES

Inflammatory pupillary membranes occurred in four eyes (2.7%). These may have been the result of heavy photocoagulation; however, in most cases it was believed to be related to the silicone. In one case, the membrane resolved spontaneously, another was opened with the YAG laser and the other two were so dense that they were surgically excised at the time of silicone oil removal.

ENDOPHTHALMITIS

Endophthalmitis developed in one eye (0.7%) within 2 weeks of silicone oil instillation.

SEPARATE ANTERIOR CHAMBER OIL BUBBLE

A separate silicone oil bubble was found in the anterior chamber of four eyes (2.7%); two of these were aphakic, one was pseudophakic, and one was phakic. By having the aphakic patient's head placed in a prone position, the anterior chamber oil bubble connected with

MACULAR PUCKER

A macular pucker developed in five eyes (3.3%) after silicone oil removal, and occurred within 2 months in all cases as also noted by other authors.^{14,17}

CLUMPED PIGMENT IN THE INFERIOR ANGLE

Clumps of pigment were found in the inferior angle in 11 eyes (7.3%) with PVR. Pigment in the inferior angle was not found in eyes of diabetic patients. These clumps of pigment and pigmented membranes were similar in appearance to the pigment seen on the surface of the retina in advanced PVR. The amount of pigment seen in these eyes did not appear to increase over time and was believed to be debris from the surgery that settled into the inferior aqueous compartment (i.e., the inferior angle). The silicone oil tamponade of the vitreous compartment appeared to concentrate debris in the anterior chamber. Even though there must have been fluid between the silicone oil bubble and the peripheral retina in more cases than we were aware of, clumped pigment was not appreciated biomicroscopically in this area.

RUBEOSIS IN OIL-FILLED EYES

The development of rubeosis or an increase of already present rubeosis was found to occur in two eyes (1.3%) while silicone was present. These were eyes of diabetic patients, and all had rubeosis before surgery. In one of these eyes, a peripheral detachment was present and this was thought to be the cause of the increased rubeosis. An intense fibroproliferative/neovascular response developed in the second eye with increased rubeosis despite massive photocoagulation and a flat retina. In two eyes of diabetic patients in which rubeosis was present before the instillation of oil, hyphemas developed postoperatively. We were not impressed with the development and progression of a neovascular response in the fluidfilled cavities of the diabetic eyes after the injection of silicone oil. As a matter of fact, there were five eyes of diabetic patients in this series with aggressive rubeosis preoperatively which showed regression of rubeosis and stabilization after surgical reattachment of the retina with pars plana vitrectomy and instillation of silicone oil. Of the remaining 23 diabetic eyes, there was no evidence of the development of rubeosis as long as the oil was present. In two of these eyes, rubeosis became apparent within 2 weeks after oil removal.

SUBCONJUNCTIVAL SILICONE OIL

Extravasation of silicone oil through the sclerotomy into the subconjunctival space was found in four eyes (2.7%). All four patients presented symptomatically with pain, and a delle developed in one of the patients.

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DISCUSSION

Cataract formation and oil keratopathy were found much more frequently in our patients than in previous reports, reflecting the greater length of follow-up. We also noted a high incidence of emulsification (100%) and chronic uveitis in 6.7% of oil-filled eyes and 48.3% of eyes after oil removal. These complications are possibly caused by the presence of silicone oil. There is no doubt that the silicone oils used in several reports differ in origin and therefore differ in their chemical and physical properties.³¹ Since as a rule only the viscosity of the liquid silicone and not the origin of the oil is disclosed, it is difficult to determine whether such complications are related to mechanical oil-tissue interactions or differing properties of the oils. We believe that more attention needs to be given to the physicochemical properties of the various oils with regard to incidence and severity of complications.

In our series, the fibrous proliferation, closure of the inferior iridectomy, pain, and the immediate postoperative appearance of pupillary membranes in a small number of cases may all be related to low-grade inflammation. Gabel et al³¹ reported the presence of low molecular weight components capable of diffusing into surrounding tissues to incite a toxic and/or inflammatory reaction. It is possible that variations in the heat sterilization of the oils at the different clinical centers may result in undesirable low molecular weight fractions which incite an inflammatory response depending on their concentration. We used the same source of oil for all cases; however, the different incidences in which the presumed oil-related inflammation occurred may be due to variations in heat sterilization.³¹

Our incidence of recurrent RD is low compared with several previous reports. This may reflect the technique of extremely complete silicone-fluid exchange during pars plana vitrectomy via an automated oil pump, activated by a foot pedal. We believe this technique affords a more complete internal drainage of subsilicone and subretinal fluid, thus allowing a more complete oil fill. In addition, we use extensive endolaser photocoagulation in all cases under direct clear view through the silicone, ensuring closure of all holes and retinotomies. The low incidence of fibrous proliferation may be related to the extensive laser treatment, and also to the fact that in the absence of an extra silicone fluid space there may be less movement between the surface of the retina and the surface of the silicone.

Improvements in surgical techniques have lessened the incidence of complications ascribed to the mechanical effects of silicone.¹⁻³⁰ The physicochemical properties that characterize the biocompatibility of the silicone may be much more important than viscosity or mechanical intraoperative considerations.³¹

As has been observed by other authors, many of the complications reported here did not occur until after the 3-month follow-up visit. If the oil is to be removed, we suggest this be done within 3 months of the initial procedure of instillation. If oil is to be used as a permanent tamponade, then a highly biocompatible oil must be used. Clinical studies comparing tissue effects of oils from various origins would be useful in determining biocompatibility. We believe silicone oil is an important adjunct in the treatment of complicated vitreoretinal problems and because of its optical clarity and high surface tension, is often an indispensable tool in meticulous microsurgery of the retina.

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