Vitreon, a short-term vitreoretinal tamponade

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Abstract

This investigation of the liquid perfluorocarbon, perfluorophenanthrene (Vitreon), establishes its safety and efficacy as a short-term vitreoretinal tamponade. We utilised Vitreon as an intraoperative tool and postoperative vitreoretinal tamponade in 16 patients. Proliferative vitreoretinopathy (PVR) (six), giant retinal tear (four), rhegmatogenous retinal detachment (three), retinal detachment with keratoprosthesis (two), and submacular and vitreous haemorrhage (one) were successfully repaired. Vitreon was left in the eye and removed 5 days to 4 weeks postoperatively. Complications encountered included proliferative PVR (five), limited peripheral retinal detachment (three), macular pucker (two) cataract (three), hypotony (two), excessive fibrin reaction (one), and elevated intraocular pressure (one). At the latest evaluation, all retinas are attached with a follow-up of 1.25 to 12 months (mean 6.8 months).

(Br J Ophthalmol 1992; 76: 525-528)

The denser-than-water vitreous substitutes, first introduced in 1962 by Cibis,¹ are presently experiencing renewed interest. Fluorosilicone oil, with a specific gravity of 1.35, has been shown to be an effective intraoperative tool with a continued tamponading effect postoperatively.²⁻⁴ However impurities present in this substance have made it a less than desirable high specific gravity vitreoretinal tamponade.⁵ The liquid fluorocarbons introduced into medicine in 1966⁶ were first injected into the vitreous cavity by Haidt *et al* in 1982.⁷ Other investigators soon followed, with toxic effects on the retina noted within a short period of exposure.⁸⁻¹⁰

Vitreon, the liquid perfluorocarbon, perfluorophenanthrene, was first evaluated experimentally in 1989.¹¹ We recently reported the utilisation of Vitreon for intraoperative hydrokinetic retinal manipulation in 15 patients.¹² In this paper we describe our experience with Vitreon as a denser-than-water short term vitreoretinal tamponade under a Food and Drug Administration (FDA) phase I and phase II investigation.

Patients and methods

Vitreon was used in 16 patients to treat various vitreoretinal disorders between December 1989 and December 1990. Informed consent was obtained from all patients. Of the 16 patients, six presented with proliferative vitreoretinopathy (PVR) stages C₃-D₂, four with giant retinal tears, three with rhegmatogenous retinal detachment and peripheral tear, two with retinal detachment with keratoprosthesis, and one with concurrent

submacular and vitreous haemorrhage secondary to age-related macular degeneration (ARMD) (Table 1). The ages of our patients ranged from 13 to 81 with a mean of 49.3 years (Table 2). Seven patients were female and nine were male. Preoperative visual acuity ranged from 20/100 to light perception. Six patients had a history of at least one previous vitreoretinal procedure. The lens status preoperatively was divided into six aphakic, five pseudophakic, and five phakic patients.

The surgical technique utilised was very similar to that described for our recent intraoperative series.¹³ After the partial air-fluid exchange step, the injection of Vitreon was continued to a suitable level of slightly below the crystalline or intraocular lens, or just posterior to the iris plane in aphakic patients. Subsequent steps, such as membranectomy, relaxing retinotomy, endolaser photocoagulation, and retinal cryopexy were then performed as indicated. In two patients a portion of the Vitreon was removed and replaced with silicone oil (12 500 cSt). The sclerotomies were then closed, and a No 20 band was placed around the eye slightly posterior to the muscle insertions if no previous encircling element was present. In the case of a giant retinal tear, the encircling element was placed more posteriorly. The infusion cannula was removed last, in order to make any adjustments to the intraocular pressure (IOP) and/or the Vitreon level prior to closing.

Postoperative follow-up of the patients consisted of daily examinations until stable, then weekly evaluations until the Vitreon was removed. Observation of postoperative complications, possibly secondary to the presence of Vitreon, resulted in an early removal date. The goal was to maintain Vitreon's tamponading effect long enough for the formation of firm chorioretinal adhesion by laser or cryotherapy, but to remove it prior to the development of potential complications as determined by earlier animal studies.¹¹ Positioning restrictions were minimal, with the sitting or supine position easily maintained by all patients. Mandatory supine positioning was recommended in only one aphakic patient, without an intact anterior capsule, to decrease Vitreon contact time with the cornea. Vitreon was removed earlier in this aphakic patient and in one patient with a post-

Table 1 Preoperative profile

Proliferative vitreoretinopathy		6
C ₃	2	
D ₁	3	
D ₂	1	
Giant retinal tear		4
Rhegmatogenous retinal detachment		3
Retinal detachment with keratoprosthesis		2
Submacular and vitreous haemorrhage		1
Total		16

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Accepted for publication
28 February 1992

Table 2 Patient series

Case	Age/sex	Preoperative diagnosis	Pre-operative visual acuity	Intra-operative compli-cations	Postoperative complications	Vitreon removal	Follow-up (months)	Post-operative visual acuity
1	58 F	PVR D1	LP	0	0	3 weeks	8	CF
2	21 M	Giant retinal tear	CF	0	Localised RD upon removal	3-5 weeks	8-5	20/70
3	15 F	PVR C3	20/100	0	PVR with redetachment, reoperation Hypotony Cataract	3 weeks - 1st operation 5 days - 2nd operation 3 weeks	9	CF
4	73 M	Vitreous haemorrhage with submacular haemorrhage secondary to ARMD	HM	0	PVR	3 weeks	6-5	20/300
5	55 M	Giant retinal tear	CF	0	Cataract scheduled for ECCE	3 weeks	12	CF
6	74 M	PVR D1	LP	0	0	11 days	10	CF
7	42 F	Giant retinal tear	CF	0	Cataract	7 days	11	20/100
8	18 F	Prosthokeratoplasty with RD	20/300	0	0	2-5 weeks	9	20/100
9	13 M	PVR D1	HM	0	PVR with redetach reoperation	2 weeks	1-5	HM
10	57 M	Rhegmatogenous RD	CF	0	1. Elevated IOP 2. Limited peripheral RD 3. Macular pucker; peeled postop	8 days	8	20/80
11	52 F	Prosthokeratoplasty with RD and endophthalmitis	HM	0	PVR with redetach reoperated	4 weeks, 1st operated; presently in eye 8 weeks, 2nd operation 3-5 weeks	7	20/400
12	81 M	PVR C3	CF	0	1. Macular pucker 2. PVR with redetachment, reoperation	3-5 weeks	7-5	HM
13	70 M	PVR D2	HM	0	0	3 weeks	5	CF
14	70 F	Rhegmatogenous RD with vitreous haemorrhage	HM	0	Hypotony localised RD	4 weeks	2-5	20/300
15	13 M	Giant retinal tear	CF	Silicone oil mix		4 weeks	2	20/80
16	76 F	Rhegmatogenous RD	HM	Silicone oil mix	Excessive fibrin reaction necessitating tPA injection	3-5 weeks	1-25	20/100

ARMD, age-related macular degeneration; F, female; M, male; RD, retinal detachment; Reop, reoperation; CF, counting fingers; HM, hand motion; IOP, intraocular pressure; PVR, proliferative vitreoretinopathy; Redetach, redetachment; LP, light perception.

operative IOP rise (patient 10). Removal of Vitreon in all patients was performed using a three-port system to accommodate the infusion cannula, light pipe, and a 20-gauge flute needle. A Vitreon-air exchange was initially performed, followed by multiple fluid washings to ensure complete removal of the Vitreon. At this time, the decision was made whether to leave balanced salt solution (BSS), sulphur hexafluoride (SF₆) (15–20%), or silicone oil (12 500 cSt) in the eye, depending on what type of postoperative tamponading effect was desired.

Postoperative follow-up upon removal of Vitreon consisted of daily examinations until stable, then weekly, bimonthly, and monthly evaluations for the first 6 months. Those eyes with silicone oil were similarly followed with immediate oil removal for any silicone-related complications. Recurrent retinal detachment, PVR, and significant macular pucker were repaired with further surgery.

Results

All 16 cases were successfully repaired at the conclusion of surgery. Postoperative follow-up revealed recurrent retinal detachment secondary to PVR formation in one case (6%), with the Vitreon still in the eye. This detachment was repaired upon removal of Vitreon at 3 weeks.

Four other eyes (25%) developed PVR after removal of Vitreon, with three of these (19%) necessitating further surgery. Three patients (19%) were noted to have limited peripheral retinal detachments, one during Vitreon removal, and two after Vitreon removal. All three retinal detachments were repaired with air-fluid exchange and subsequent photocoagulation. Macular pucker occurred in two patients (12.5%), one necessitating further surgery due to macular distortion, and the other due to concurrent PVR. Cataract formation occurred in three patients (19%); one patient was treated by pars plana lensectomy during Vitreon removal, one is scheduled for an extracapsular cataract extraction, and the third is presently being observed.

Only one patient (6%) was noted to have an elevation of IOP postoperatively with the Vitreon still in the eye. This was possibly an overfill phenomenon, with the Vitreon pushing the iris diaphragm forward, causing an angle-closure component. Postoperatively we removed 0.75 ml of Vitreon at the slit-lamp, with the rest being removed at 8 days in this patient. The timing of removal of Vitreon varied from as early as 5 days to as long as 4 weeks postoperatively. Vitreon was replaced with BSS in 10 eyes, silicone oil in five eyes, and SF₆ in one eye. Of the four reoperations for PVR, three required silicone oil, and one eye still has intraocular Vitreon present after 8

weeks. This last case was a recurrent retinal detachment with PVR complicating a Cardona keratoprosthesis. This patient is being closely followed for the first signs of emulsification, where upon prompt removal will be performed.

Only one patient (6%) was observed to have an excessive fibrinous reaction postoperatively, which was treated by tissue plasminogen activator (tPA) injection. This patient was one of two patients in our series who also had approximately 1–2 ml of silicone oil injected over the Vitreon bubble to provide a tamponading effect for the superior retina. Hypotony (IOP <5 mm Hg) was noted to occur in two patients (12.5%) postoperatively. No cases of corneal decompensation or residual intraocular Vitreon were observed.

Upon latest evaluation all retinas are presently attached (retina flat posterior to buckle), with a follow-up of 1.25 months to 12 months (mean 6.8 months). Postoperative visual acuities range from 20/70 to hand motion vision with improvement noted in 12 (75%), no change in two (12.5%), and a decrease in two (12.5%). An ERG was performed postoperatively on one patient with no significant difference between the operated and the normal fellow eye noted.

Discussion

We recently reported the first human investigation of Vitreon in a limited Phase I FDA-approved evaluation.¹² Fifteen patients with a variety of retinal detachments (six PVR, five rhegmatogenous retinal detachments, two giant retinal tears, one retinal dialysis, one tractional retinal detachment) were successfully treated by intraoperative hydrokinetic retinal manipulation utilising Vitreon. The Vitreon was removed intraoperatively in all cases. Two patients developed PVR necessitating further surgery, and one patient developed hypotony. Residual Vitreon was noted in five patients postoperatively, with the future recommendation of multiple fluid washings to ensure complete removal. One patient developed a postoperative IOP rise, most probably secondary to the use of intraocular gas. No patients demonstrated any unusual inflammatory or toxic reaction secondary to the use of Vitreon. All the retinas were reattached upon follow-up, with a mean duration of 6.3 months.

In the present investigation, we used Vitreon as both an intraoperative and postoperative tool in the repair of various types of retinal detachments in 16 patients. The surgical technique was very similar to that described in our initial series, with the exception of leaving the Vitreon in the eye at the conclusion of surgery. Past animal studies have shown lack of toxicity when left in rabbit eyes for up to 6 weeks,¹¹ and in primate eyes for up to 5.5 months.¹³

In cases of Cardona prosthokeratoplasty, the occurrence of retinal detachment postoperatively is not uncommon.^{14–16} Due to inadequate visualisation and limiting mechanical restriction, retinal detachment repair is very difficult.^{15,17} Endophthalmitis also occurs at a higher frequency post-prosthokeratoplasty, complicating one of the two patients in our series. Both patients were treated with pars plana vitrectomy

by indirect ophthalmoscopy with Vitreon injection, endolaser photocoagulation, retinal cryopexy, and scleral buckling procedure. The patient with concurrent endophthalmitis was also treated with infusion fluid augmented by gentamicin and clindamycin during vitrectomy. After Vitreon removal, this patient developed PVR and underwent a second procedure with limited membranectomy and Vitreon reinjection. The Vitreon has been present intraocularly for 8 weeks with the retina attached. The other patient underwent only one Vitreon procedure with the retina attached at 9 months follow-up.¹⁸

PVR was the most common preoperative diagnosis in our series. Past investigations have already shown the efficacy of the liquid perfluorocarbons as an intraoperative tool in the treatment of PVR.^{12,19} In the present series Vitreon was utilised to assist in reattachment of the retina intraoperatively and to provide a further tamponading effect postoperatively. This latter effect is most important with inferiorly located retinal pathology. Conventional vitreous replacement with intraocular gas or silicone oil has led to an increased incidence of recurrent PVR in the inferior retina.^{20,21} PVR in the inferior retina did not occur in our series, possibly as a result of a lack of pooling of RPE cells or membrane-promoting factors in the inferior gravity-dependent region.

Four patients in our series had a diagnosis of giant retinal tear. Past treatment recommendations have been exceedingly complex.^{22,23} The efficacy and ease of the liquid perfluorocarbons as an intraoperative tool in the treatment of giant retinal tears have already been established.^{12,24} In the series by Chang and associates, using various perfluorocarbons, posterior slippage of the retinal tear occurred in a few patients intraoperatively during air-fluid exchange, and in one patient postoperatively, leading to a permanent retinal fold.²⁴ In the present series, the advantage of allowing the Vitreon to remain in the eye postoperatively was demonstrated by the lack of posterior slippage of the retinal tears. One patient was noted to have a localised detachment superiorly upon removal of the Vitreon at 3.5 weeks, which was successfully treated by air-fluid exchange and postoperative laser photocoagulation.

Two patients in our series received a combination of Vitreon and silicone oil in order to provide a postoperative tamponading effect to all quadrants of the retina. One day postoperatively, one patient experienced an excessive fibrinous reaction, necessitating tPA injection into the anterior chamber. In both patients two separate meniscus lines were evident throughout the first 3 weeks, indicating the immiscibility of the two substances. After 3 weeks, however, mixing and

Table 3 Complications

Proliferative vitreoretinopathy		5
Recurrent	3	
New onset	2	
Limited peripheral retinal detachment		3
Macular pucker		2
Cataract		3
Hypotony		2
Excessive fibrin reaction		1
Elevated IOP		1

possible breakdown of the two separate substances were noted. Removal was performed by aspiration via a three-port pars plana system. Thus the dual tamponading effect seemed to last as long as the Vitreon and silicone oil remained apart. Further investigation along these lines seems warranted.

Postoperative positioning restrictions were easy to follow in our series. A supine or sitting position led to the desired tamponading effect. When dealing with lighter-than-water vitreous substitutes such as silicone oil or gas, the mandatory prone positioning can be very uncomfortable, thus leading to lower patient compliance levels. The postoperative complications encountered in our series are similar to those encountered with silicone oil vitreous substitution in the past (Table 3).^{21,24}

The FDA-approved investigation of Vitreon has proceeded in a logical stepwise fashion. This report establishes the safety and efficacy of Vitreon as a short-term vitreous substitute. Future investigation will further delineate the indications for the use of Vitreon as an intraoperative tool and short-term postoperative vitreous substitute.

This work was supported in part by US Public Health Service grants EY07541 and EY02377 from the National Eye Institute, the National Institutes of Health Services, Bethesda, MD.

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