Case Report

Case Series and Review Article: Perfluorocarbon Heavy Liquid as a Short-Term Tamponade after Vitrectomy for Inferior Rhegmatogenous Retinal Detachment

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Abstract

This is to report outcomes of three cases with inferior rhegmatogenous retinal detachment (RRD) which were treated with vitrectomy and perfluorocarbon heavy liquid (PFCHL) insertion as short-term tamponade. We also aim to summarise the surgical outcomes and complications from the recent studies in PFCHL usage in vitrectomy surgeries. The mean tamponade period for our case series was 11 days. Two patients developed ocular hypertension, while another developed hypotony with subsequent retinal redetachment. Migration to the anterior chamber causing pupillary block glaucoma also occurred in one patient, requiring laser peripheral iridotomy. Previous studies reported that PFCHL is particularly useful for more complex cases of retinal detachment including giant retinal tears, inferior retinal tears, chronic rhegmatogenous retinal detachment (RRD), inferior RRD and proliferative vitreoretinopathy (PVR) due to its unique physical properties. However, it is not recommended as tamponade for long duration due to possible retinal toxicity. Otherwise, most of the complications due to PFCHL can be managed either medically or surgically. PFCHL can be a useful post-operative tamponade agent in vitreoretinal surgeries. Close post-operative monitoring is crucial for the potential complications from PFCHL.

Keywords: Intraocular tamponade; perfluorocarbon; retinal detachment; rhegmatogenous retinal detachment; toxicity; vitrectomy

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Introduction

Pars plana vitrectomy (PPV) is a frequently performed procedure for repair of rhegmatogenous retinal detachment (RRD). Primary reattachment rate has increased with the advent of retinal endotamponades, especially postoperative gases or oils as temporary vitreous substitute (1). Nevertheless, vitreoretinal surgeons still face difficulties in fixing pathology located at posterior pole and inferior retina due to posturing difficulty with buoyant agents. For instance, standard gases and silicone oil endotamponades are unable to provide satisfactory surface tension to the retina break when in supine and upright posture (2). Besides that, incidence of proliferative vitreoretinopathy (PVR) is higher especially in cases of inferior retinal detachment (3).

Perfluorocarbon heavy liquid (PFCHL) is a 'heavier than water' intraocular tamponade that comes in handy in these conditions, among other intraoperative uses. Intraoperative use of PFCHL helps to drain the subretinal fluid, unfold and reappose the retina in complicated retinal detachments. It may also be used to float a dislocated nucleus or cortical matter prior to removal (4). While PFCHL has several advantages

when used intraoperatively, its function as short term vitreous substitute has remained contentious due to its composition, such as in the forms of chemical or mechanical toxicity (3,5).

Case Report

Case 1

Mr R, a 53-year-old Malay man with underlying diabetes, hypertension, dyslipidaemia and bronchial asthma presented with sudden onset of left eye reduced vision after an uneventful phacoemulsification and intraocular lens implantation 10 years previously. He reported ocular trauma during his childhood and development of left anterior subcapsular cataract, although no phacodonesis was noted. On examination, his vision was noted to drop from 6/9 to 2/60. Single piece post chamber intraocular lens (IOL) with its capsular bag were noted to have dislocated into the vitreous. There was no retinal break at that time and the intraocular pressure was 27 mmHg. He was then started on 2 anti-glaucoma eye drops and underwent left eye pars plana vitrectomy, IOL explanation with scleral fixated IOL implantation under local anaesthesia. Two weeks later, unfortunately, Mr. R developed inferior RRD with macula off (Fig. 1).

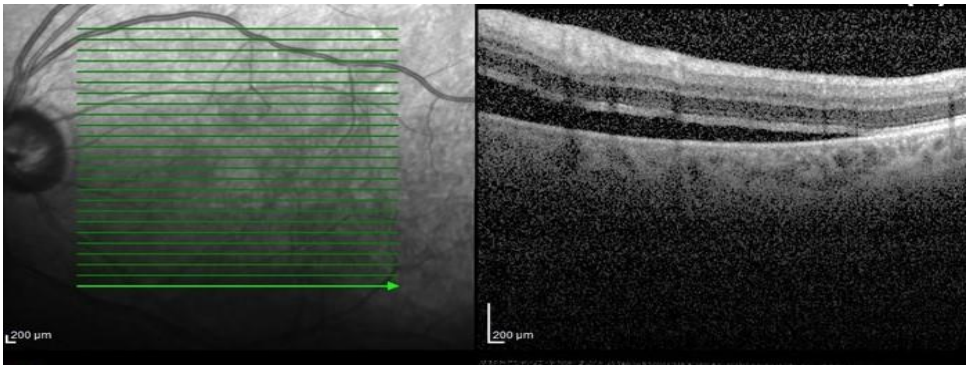

FIGURE 1: Ocular coherence tomography of left eye macula. An inferior retinal detachment was observed

He underwent emergency PPV, endolaser and cryotherapy. Intraoperatively, he was noted to have a small retinal break at 6 o'clock near the ora serrata. PFCHL (Decalin, Ophthafutur, Deutshchland) was used as intra-and post-operative tamponade, with 80% fill, after subretinal fluid drainage, to allow the patient posturing sit up post-operatively. Unfortunately, he developed pupillary block with secondary ocular hypertension day 1 post-operatively. Multiple heavy liquid globules were noted to have migrated into the AC in the form of "fish-egging" (Fig. 2).

Due to the PFCHL globules in anterior chamber (AC), his intraocular pressure (IOP) rose to 44 mmHg. He was started on oral acetazolamide and 2 topical antiglaucoma eyedrops. A peripheral laser iridotomy (PI) was performed at 12 o'clock to relieve the pupillary block. The intraocular pressure came down to 24 mmHg within the same day. The PFCHL was subsequently removed after 1 week. Intraoperatively the break had sealed, however, there was fibrosis and thickening involving the nasal retina, which nevertheless was attached at the end of surgery. He later divulged that sleep on his right side was his habit. His intraocular pressure normalised after the surgery, and he was discharged the next day, with good vision on day 1. Unfortunately, two days later he again complained of visual field defect due to total retinal re-detachment. He underwent left eye vitrectomy, endolaser, broad retinectomy, surgical ando peripheral iridotomy (PI) and silicone oil post-operative tamponade. Intraoperatively, there was shortening of the nasal retina with intraretinal fibrosis, in the absence of a tear. Intravitreal triamcinolone staining of the remaining vitreous found no appreciable vitreous involving the retina in this area. His vision remained 1/60 under oil tamponade with another surgery planned.

Case 2

Madam C, 75-year-old Chinese woman with no known medical illness, presented with left eye generalised blurring of vision with superior visual field defect for 1-year duration associated with floaters. On examination, her left vision was 6/36, 6/24, N24. Her left eye was noted to have nuclear sclerosis grade 2 to 3, chronic inferior RRD from 5 to 7 o'clock with macula on and a retinal break at 5 o'clock, with PVR Grade B. Madam C underwent left eye

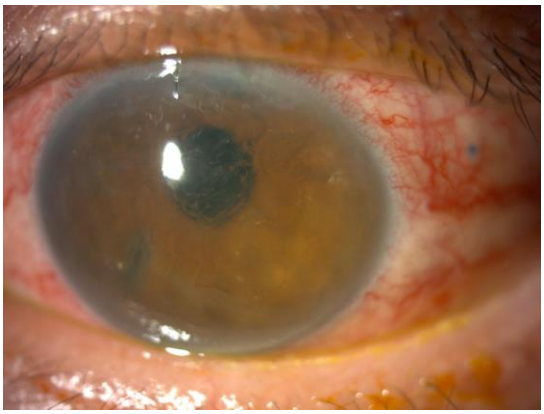

FIGURE 2: Anterior segment photograph. Fish-egging appearance of heavy liquid was seen in anterior chamber of left eye with superior and inferior peripheral iridotomies

phacoemulsification, pars plana vitrectomy, retinotomy and subretinal drainage and post-operative tamponade using PFCHL (Decalin, Ophthafutur, Deutshchland), endolaser and intraocular lens implantation. No PI was performed. Post-operatively, patient was well except for ocular hypertension in which her IOP rose to 28 mmHg, and responded well to low dose oral acetazolamide and one topical anti-glaucoma medication. She also developed a small posterior synaechiae (PS) and multiple large, round, speculated retro-lenticular precipitates over the posterior capsule at 2 weeks after surgery (Fig. 3).

She was then scheduled for heavy liquid removal within 2 weeks. Intraoperatively, there were no new breaks and the original break was well sealed. No tamponade agent was injected after removal of the PFCHL. She recovered well with best corrected visual acuity 6/12 and a flat retina in the left eye, up to 12 months postoperatively. IOP was controlled with one topical antiglaucoma and the retro-lenticular precipitates resolved after heavy liquid removal.

Case 3

Madam T, 73-year-old Chinese lady with underlying bilateral keratoconus and history of right eye penetrating keratoplasty done 10 years ago, presented with sudden onset of eye redness, pain and blurring of vision. On examination, her right vision was perception of light and she was noted to have right eye cornea ulcer with endothelial plaque. There was also evidence of severe anterior chamber reaction and fibrin, hypopyon level and locution in vitreous on B-scan ultrasound, suggestive of exogenous endophthalmitis. She received multiple intravitreal, intracameral, intrastromal and systemic antifungal and antimicrobial injections. In view of her poor response to the treatment, she underwent combined vitrectomy and penetrating keratoplasty.

During the combined surgery, the original cornea graft was explanted and a temporary keratoprosthesis (Boston KPro, Woburn, Massachusetts, USA) was sutured to the limbus to allow a clear view for PPV (Fig. 4). The intraocular lens was explanted and dense vitritis was noted intraoperatively, with adherent membranes and pus. During core and peripheral vitrectomy, an iatrogenic tear over inferotemporal retina near the scleral port incision, complicated by bullous RRD was noted. PFCHL (Decalin, Ophthafutur, Deutshchland) insertion was carried out to flatten the retina and retained. Endolaser was performed 360° to barricade the peripheral retina.

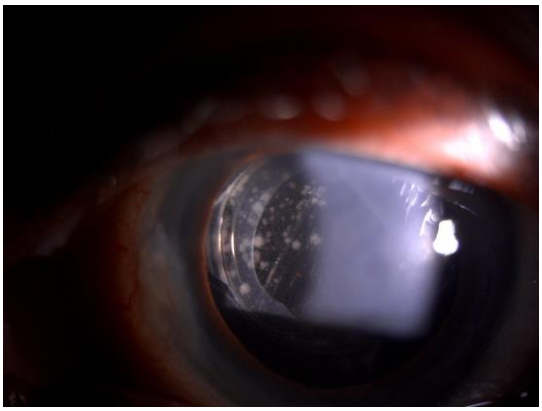

FIGURE 3: Anterior segment photograph of left eye. Multiple, round, speculated white precipitates were seen in the retrolenticular posterior capsule

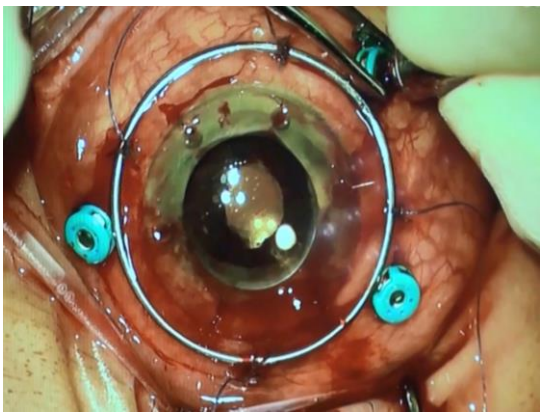

FIGURE 4: Intraoperative photograph. Temporary keratoprosthesis (k-Pro) and three scleral ports during combined pars plana vitrectomy and penetrating keratoplasty are seen in which the k-Pro was aimed to create a clear view for vitrectomy procedure

Within one-week post-surgery, patient's vision improved to hand movement. There were few heavy liquid globules noted in the anterior chamber. Her intraocular pressure was at the low side (ranging 4 to 6 mmHg) and choroidal detachment was noticed over the superior temporal quadrant as a complication of ocular hypotony. There was suspicion of re-RRD.

Another surgery was performed at about 2 weeks after to remove the heavy liquid and fix the RRD, including pre-placing a 360° 40 band using partial thickness scleral tunnels. However, intraoperatively the retina was noted to be flat and the breaks had sealed. The remaining peripheral vitreous was trimmed and the PFCHL was removed. Scleral buckle tightening was done before resuturing the cornea graft. Post-operatively, patient's retina remained flat on B scan ultrasound and the infection was controlled. However, the hypotony persisted and cornea graft subsequently failed. Her vision remained hand movement with good light projection up to 10 months after surgery. She was not keen for any further surgical intervention. These three cases were summarised in Table 1.

Discussion

PFCHL was first introduced by Chang et al. as a surgical tool in vitrectomy surgeries (3). It was used to treat complicated retinal pathologies such as giant retinal tears and PVR (6,7). Nowadays, short term intraocular tamponade with PFCHL has slowly become a more popular choice compared to scleral buckling in treating inferior retinal detachment with or without PVR and bullous detachment. Scleral buckling is associated with risk of intraoperative suprachroidal haemorrhage, infection, intrusion or extrusion of buckle, change of refractive error, globe ischaemia and potentially inadequate coverage of the retina breaks especially the posterior ones (8). These complications can be avoided by choosing PCFHL as a short term post-operative endotamponade in cases of inferior retinal detachments. Since it was introduced, a number of series have reported the anatomical and visual outcomes of PFCL as post-operative tamponade agent. Comparison of these studies is summarised in Table 2.

There are series that also describe insertion of gas after PFCL removal. However, two of our patients did not need this after PCFL was removed. With adjunct of PFCHL as post-operative tamponade, rate of retinal redetachment was found to be significantly lower. This is because retinopexy with PFCHL as tamponade induces a better apposition of the retinal tear to its underlying RPE, resulting a more effective chorioretinal adhesion and lower risk of posterior slippage or reopening of retinal tears (9). Given a greater surface tension compared to silicone oil and specific gravity twice that of water, PFCHL is a perfect substance to exert relatively large pressure against the retina layer. This allows the surgeon to fold out the retina in a more controlled manner, at the same time displacing the subretinal fluid anteriorly away from macula (5). Due to the specific gravity causing the total surface contact area to increase up to 262 mm^2 for each milliliter of bubble, PFCHL becomes a perfect tamponade for inferior retinal breaks (5). Bhurayanontachai et al. did an outcome analysis on PFCHL as tamponade in complex retinal detachments

TABLE 1: Preoperative, operative, and post-operative outcome parameters in 3 patients with inferior retinal detachment treated with vitrectomy and perfluorocarbon heavy liquid as a short-term tamponade

Case	Macula	History	PFCHL time (day)	PFCHL substitute	Pre-operative BCVA	Post-operative BCVA	Final retinal attachment	Complications
1	On	2 weeks post PPV/ IOL explant and scleral fixated IOL	8	Silicone oil	6/9	1/60	No[#]	Ocular hypertension, Retinal redetachment after silicone oil insertion, PVR
2	On	Chronic inferior RRD for a year	12	BSS	6/24	6/12	Yes	Ocular hypertension, Posterior synechiae
3	On	Iatrogenic inferior bullous RRD during PPV for endophthalmitis in a post PK eye	13	BSS	PL	HM	Yes	Hypotony, failed cornea graft

PFCHL=perfluorocarbon heavy liquid; BCVA=best corrected visual acuity; PPV=pars plana vitrectomy; IOL=intraocular lens; PVR=proliferative vitreoretinopathy; RRD=rhegmatogenous retinal detachment; BSS=balanced salt solution; PK=penetrating keratoplasty; PL=perception of light; HM=hand movement; [#]planned for further surgical intervention to reattach retina.

TABLE 2: Surgical outcomes in case series of heavy liquid usage in vitreoretinal surgeries

Study	Title	Number of subjects	Indications	Duration of PFCHL retention	Pre-operative BCVA (LogMAR)	Post-operative BCVA (LogMAR)	Final retinal attachment	Complications
Chang et al. 1988	Intraoperative perfluorocarbon liquids in the management of proliferative vitreoretinopathy	23	Intraoperative use for internal drainage of subretinal fluid in retinal detachments with PVR	Nil	N/A	N/A	16 (65.2%)	No significant complications noted.
Rofail & Lee 2005	Perfluoro-n-octane as a postoperative vitreoretinal tamponade in the management of giant retinal tears	16	GRT without significant PVR	16 days	1.67	1.06	15 (93.6%)	Redetachment (6.3%), Cataract (54.5%), ERM (25%), hypotony (16%), phthsis bulbi (6.3%)
Drury & Bourke 2011	Short-term intraocular tamponade with perfluorocarbon heavy liquid.	17	Complex inferior retinal pathology (inferior RD and PVR)	7 days	1.32	0.97	13 (76%)	Cataract (60%), macula atrophy (5.8%), PVR (11.6%), elevated IOP (100%), mild iritis (5.8%)
Rush et al. 2012	Postoperative perfluoro-n-octane tamponade for primary retinal detachment repair	39	RRD with inferior/ multiple tear or GRT	11 days	2.07 ± 0.86	0.76 ± 0.79	36 (92.4%)	Ocular inflammation (20.6%), elevated IOP (35.9%), cataract (36%)
Randolph et al. 2016	25-gauge pars plana vitrectomy with medium-term postoperative perfluoro-n-octane for the repair of giant retinal tears	23	GRT	18 days	1.01 ± 0.75	1.08 ± 0.81	21 (91.3%)	PVR (21.7%), cataract (43.5%), transient IOP elevation (30.4%)
Bhurayanon tachai et al. 2020	Outcomes of a postoperative perfluorocarbon liquid tamponade for complex retinal detachments: 12 years of experience in southern Thailand	122	Complex retinal detachments	12 days	1.8 ± 0.4	1.6 ±0.7	98 (80.3%)	Immediate postoperative IOP elevation (51.2%), hypotony (23%), optic nerve atrophy (22.1%), cataract progression (22.1%), ERM (13.1%)

PFCHL=perflurorocarbon heavy liquid; BCVA=best-corrected visual acuity; PVR=proliferative vitreoretinopathy; GRT=giant retinal tear; ERM=epiretinal membrane; RD=retinal detachment; IOP=intraocular pressure; RRD=rhegmatogenous retinal detachment

such as giant retinal tears, chronic retinal detachments and previous failed vitreoretinal surgeries. The retinal reattachment rate was 80.3%. The rate was even higher in cases of giant retinal tear (84.4%) likely due to first attempt of surgery and less PVR involved (10). Our patients had good anatomical outcomes after insertion of PFCHL except for Patient 1 (Mr R). In the case of Patient 1, we postulated that he experienced pressure necrosis of his left supero-nasal retina causing intraretinal fibrosis. While this was not commonly encountered, it could explain the brisk fibrosis was seen involving this part of the retina and explained why retinal reattachment was difficult.

It is undeniable that PFCHL has benefits towards both surgeons and patients when used as a short-term tamponade in vitrectomy. First, it reduces the need for scleral buckling because its ability to drain the subretinal fluid efficiently in the highly detached retina. It also shortens the surgical time compared to gas and silicone oil tamponade because it reduces the intraoperative fluid/fluid and fluid/gas exchanges (3,9). Moreover, the physical properties of PFCHL also allow surgeons to remove it easier and faster than silicone oils after completed tamponade period. From patients' perspective, PFCHL allows patients to be at supine or erect position rather than prone positioning which in return increases the compliance of posturing and yields better post-operative outcomes (3). PVR formation rate could be reduced with the use of PFCHL tamponade due to its haemostatic effect especially when it is used in inferior retinal breaks (11,12).

Another interesting observation with usage of PFCL comes from the advantage of not having to remove the PFCL at the end of surgery. This is especially so when poor view during air-fluid exchange is anticipated. For instance, Patient 3 was rendered aphakic during the initial PPV and it was anticipated that view through a cornea graft in contact with air, during PFCL-air exchange, would not permit safe removal of all the PFCL. An alternative would be to perform direct PFCL-silicone oil exchange with good view through the temporary K-Pro. In these cases, the decision is influenced by whether there is a barrier between the cornea and the filtered air infused. The presence of a barrier in the form of capsule, lens or intraocular lens, permits either gas, PFCL or oil to be selected. However, when there is no barrier, PFCL can be another option. Furthermore, the presence of inferior breaks made the PFCL be a more patient-friendly option for postoperative posture to be successful. Indeed Patient 2 selected the PFCL option because it allowed a more comfortable sit up posture during post-operative recovery, despite the earlier removal date and need for another operation. In the case of aphakia or scleral fixated lens where PFCL is injected as postoperative tamponade, a PI should be created superiorly near 12 o'clock to avoid the pupil block as observed in Patient 1.

Further on the issue of complications, two of our patients developed ocular hypertension after the insertion of PCFHL. The incidence of elevated IOP in patients who underwent PPV with post-operative PCFHL as tamponade, was reported to range between 4.8% to 36%. (3,13-15). Pathogenesis of secondary glaucoma in a vitrectomised eye with PCFHL insertion is most commonly due to pupillary block especially in aphakic or pseudophakic eyes or when there is closure or blockage of the peripheral iridotomy (PI) by fibrin, blood or residual capsule (16). This condition can be prevented if a large superior PI is created to prevent pupillary block. It will be covered by the upper eyelid.

PCFHL can also migrate into AC and angle causing inflammation, synechiae formation, trabeculitis and direct mechanical obstruction of aqueous outflow at the angle (16). Most studies show that this condition can be treated medically with antiglaucoma medication, as well as controlling the inflammation (9,10,17). However, early removal might be indicated in persistent ocular hypertension or in the event of pupillary block glaucoma. In addition, complete removal of PFCHL after the short-term tamponade is crucial to prevent secondary IOP elevation. This can be achieved by repeating the air-fluid exchange several times after the initial PFCL bubble is removed. Nevertheless, it is possible that small amounts are retained and these are usually not harmful. Alster et al. (1996) reported a case of pupillary block caused by residual small PFCL bubble after incomplete removal which blocked an Ando PI at 6 o'clock but the IOP returned to normal after surgical removal (18).

Other than ocular hypertension, PFCHL can induce several complications involving the anterior segment if it migrates to the anterior chamber especially when there is no capsule to separate anterior segment from posterior segment. It was also reported small droplets of PFCHL can enter the AC by passing through the zonules of the phakic and pseudophakic eyes (5). Sigler et al. (2013) reported 22% of patients with phakic and pseudophakic eyes had migration of PFCHL to the AC in the absence of zonular dehiscence (19). Prolonged contact of PFCHL and the cornea endothelium may lead to cornea oedema, deep cornea vascularisation or even cornea decompensation. In case 1, our patient did not develop any cornea problems despite retention of heavy liquid in AC for more than a week. This could be due to the "fish-

egging" form of the heavy liquid globules, which might allow aqueous humour to seep through between globules to supply adequate nutrients to the cornea endothelium for survival (20). Wilbanks et al. (1996) concluded that the response of cornea endothelium towards PFCHL was dose and time dependant, in which cornea decompensation occurred 4 to 13 weeks after PFCHL-endothelial contact (21). This means that it is potentially reversible if the retained PFCHL can be removed in a timely fashion.

However, surgeons should be cautious not to let the PFCHL become trapped in the subconjunctival space during removal. This is because it can cause limbal inflammation and toxicity. It has been previously reported a central corneal epithelial defect 3 months after PFCHL removal due to subconjunctival retention (22). This has become rare with small gauge PPV, in which there are trocars, even valved trocars at the ports.

Even without cornea endothelial touch; PFCHLs can also induce severe inflammatory reaction in the AC especially in young patients (23). One of our patients developed posterior synaechiae as a consequence of AC reaction although it was previously reported that the inflammation is usually without evidence of synechiae regardless of the severity (24). Figueroa el al. (2014) hypothesised that granulomatous inflammation occurs when PFCHL induces local foreign body type, macrophage stimulating molecular pathway (25). Most of the patients will develop keratic precipitates and white flaky materials over intraocular structures including posterior lens capsule. Residual posterior capsule deposits may persist after PFCHL removal but usually disappear by 1 month. Furthermore, delayed type hypersensitivity does not happen after the surgical removal (25). On the other hand, cataract progression rate was noted to range from 70 to 87%, either when used as a short-term tamponade or an intraoperative tool (9,26,27).

When PCFHL is being used as a post-operative tamponade for more than a week, there is a potential inflammatory reaction in up to 30% of cases. White, round and spiculated precipitates have been observed on the retina, blood vessels and optic nerve head which differed from characteristic inflammation seen after the regular vitrectomies (25). Posterior lens opacities may also impair the visualisation of the posterior segments (24). Retinal toxicity secondary to PFCHL can be either due to chemical and mechanical toxicity. Chemically, the toxic impurity is caused by the unsaturated carbon bonds and hydrogen-containing compounds in PFCHL. Long term usage or subretinal retention may lead to damage of retinal pigment epithelium and photoreceptors (5). However, the retina seems to tolerate PFCHL well unless in a long-term vitreous replacement due to the significant alteration of retinal structure. Stolba et al. (2004) studied the histological changes of retina after two different concentrations of PFCHL were injected as a vitreous substitute. As early as 4 weeks, moderate changes were displayed at inferior retina in the eyes with higher concentration of PFCHL such as cell loss of outer nuclear and photoreceptors, thinning of outer plexiform and Muller cell hypertrophy. Irregularity of all retinal layers were noticed at 8 weeks post-surgery (28). Another study found that patients with longer term of PFCHL in the eye had worsened toxic effects, which resulted in poorer visual acuity and optic atrophy (29). This effect seems to demonstrate in the aggressive fibrosis and retinal shortening encountered with Patient 1, who preferred to posture on his right lateral position. However, the response is nevertheless idiosyncratic given the short duration it was retained in the eye in this case. This means PFCHL with higher concentration and specific gravity or with longer duration, has been proven to cause severe retinal intolerance. Besides that, subretinal PFCHL can be a disastrous complication if the retention is over subfoveal area, which needs removal. The risk factors identified were large peripheral retinotomies during vitrectomy, unrelieved retinal traction and lack of saline rinse during fluid-air exchange (30).

In this case series, all patients received the same PFCHL with the same specific gravity which was Decalin (Ophthafutur, Deutshchland). A review of PFCHL available in the market and those in the past has found a number of cases in which the product was withdrawn when toxic ingredients were discovered. Romano et al. (2021) found out 6 out of 8 PCFHLs which had serious adverse incidents of ocular toxicity were cytotoxic to the standard of ISO 10993-5:2009 (31). None of our patients had developed ocular toxicity to Decalin. The response in patient 1 remained idiosyncratic due to the safe utilisation in the other 2 cases as well as the favourable response when used intraoperatively.

Nevertheless, Rofail et al. (2005) reported that complication rate of PFCHL as a short-term tamponade did not differ from intraoperative use (13). Most studies have described PFCHL has a satisfactory safety profile when used as an adjunct vitrectomy surgeries (15,19,32). Another alternative to PFCHL is heavy silicone oils such as Densiron® 68 (Fluoron, Germany), Oxane 5700 (Bausch & Lomb, France). These allow a longer retention time of 6 weeks to 3 months, but should not be retained for longer. However, these heavy oils are not without their

complications including raised intraocular pressure, progression of cataract, anterior uveitis that were similar to PFCHL (2). Another challenge with them is the need for 3 ports and difficulty removing with the flute cannula or vitrectomy probe, unlike the easy removal of PFCHL using 3 ports. Removal of heavy oil also requires active extrusion pack with rotation of the extrusion port to be in contact with the oil bubble at all times.

Conclusion

In a nutshell, given their physical properties and anatomical results, PFCHL can be a useful post-operative tamponade agent in vitreoretinal surgeries, particularly for inferior retinal pathologies and aphakic patients undergoing combined PPV-keratoprosthesis with RRD. Close post-operative monitoring is crucial for the complications, which can involve the anterior segment or posterior segment

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