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Preliminary Observation of Short-Term Intraocular Filling with Perfluorocarbon Liquid in the Treatment of Giant Retinal Detachment

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Abstract

Objective: To observe the clinical manifestations of patients with Giant Retinal Tear (GRT) after short-term filling with Perfluorocarbon Liquid (PFCLs), and to explore the role and safety of PFCLs, to provide a new clinical basis for complex vitreoretinal surgery.

Methods: 23 eyes diagnosed with GRT and filled with PFCLs in our hospital from 2018 to 2021 were collected retrospectively. Visual acuity, cornea, lens, optic nerve, and retinal reattachment and proliferation were recorded before and after the operation.

Results: At the last follow-up showed that the visual acuity of 78.3% (18/23) was better than that before the operation, and 82.6% of the retina remained anatomic reduced. The corneal endothelium count, the incidence of cataracts, the average thickness of optic nerve fibers, the incidence of pre-retinal proliferative membrane, and the results of visual electrophysiology all changed with the extension of PFCLs placement time. There was no significant difference in these changes when PFCLs were placed within 2 weeks (P>0.05). When PFCLs were placed for more than 2 weeks, the difference was significant (P<0.05).

Conclusion: This study confirmed that filling PFCLs within 2 weeks can increase the omental reduction rate and protect visual function in GRT patients. This study provides new clinical evidence for short-term PFCLs filling after the operation. It provides a new method and idea for complex retinal surgery.

Keywords: Giant retinal tear; Perfluorocarbon liquid; Vitreous cavity filler; Retinal vitreous surgery; Drug toxicity

Introduction

Since Chang et al. [1] used Perfluorocarbon Liquids (PFCLs) as fillers in vitreous surgery in 1987; PFCLs have become an indispensable tool in complex vitreoretinal surgery. PFCLs are primarily used as intraoperative temporary fillers, which can flatten the retina in Retinal Detachment (RD), strip proliferative membranes in Proliferative Vitreoretinopathy (PVR), assist in the removal of the basilar vitreous, and reposition Giant Retinal Tears (GRT), protect the macula or lift the fallen lens, drain suprachoroidal hemorrhage, stop bleeding intraoperatively, separate the proliferative membrane in proliferative diabetic retinopathy, or strip the inner limiting membrane [2-5].

However, when PFCLs remain in the eyeball for more than 48 h, toxicity has been reported in both animals and humans due to the prolonged use of PFCLs [6-12]. This toxicity is mainly manifested as an inflammatory reaction, and in severe cases, it can lead to complications, such as corneal decompensation, optic atrophy, and intractable glaucoma in humans and animals. The current status quo is that it is generally accepted that PFCLs should be removed at the end of surgery. Experts at home and abroad recognize that PFCLs cannot be retained in the eyeball for more than 48 h [13,14]. In recent years, the situation has changed. Okonkwo et al. [15,16] individual operators used PFCLs to fill the vitreous cavity for a short time, and no serious toxic damage was observed, and the patients achieved retinal reattachment and improved vision.

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This study selected patients with postoperative vitreous cavities filled with PFCLs, retrospectively observed the conditions of the patients, analyzed the therapeutic effect and safety of PFCLs, and provided new clinical evidence and diagnostic ideas for vitreoretinal surgery.

Materials and Methods

Research objects

This study retrospectively analyzed 23 eyes (21 people) of patients who were diagnosed with GRT and underwent postoperative PFCLs (RTEDCALIN, 7 ml, Germany, ZEISS) from June 2018 to June 2021 at Xi'an Purui Eye Hospital. The average age was 30 ± 15.9 years, and 71.4% (15/21) were male. All patients underwent a slit-lamp examination in both eyes to rule out keratopathy, cataract, glaucoma, and previous surgery. Fundus, intraocular pressure, and visual acuity examinations were performed on all patients. All patients were informed of surgical risks and signed informed consent forms. This study passed the ethical review of the Ethics Committee of Xi'an Purui Eye Hospital.

Inspection method

The conjunctiva, cornea, anterior chamber, pupil, and lens of all eyes were examined by the deputy chief physician of the ophthalmology general clinic using a German Zeiss SL30 slit microscope. Use Midorie Eye Liquid to dilate your pupils, 1 time/5 min, 3 times in total. The pupils were dilated to 8 mm in diameter, and the same senior special examination professional attending physician performed corneal endothelioscopy, Zeiss Clarus 500 fundus photography, OCT, ocular ultrasound, and visual electrophysiological examinations on both eyes of the patients. The reading and diagnosis of the examination results were completed by the same deputy chief physician of the fundus specialty. The visual acuity examination was performed using the Early Treatment of Diabetic Retinopathy Study (ETDRS) vision chart with a distance of 2.5 meters, and the Best-Corrected Visual Acuity (BCVA) was recorded.

Surgery and experimental design

All eyes were operated on by three-channel 23G or 25G vitrectomy by the same deputy chief physician of ophthalmology. The patient underwent at least two surgeries: PFCL placement and PFCL removal. The 1 day before the surgery to implant the PFCL was defined as the start date of the study. Data were recorded 1 day before surgery, 1 week, 1 month, 3 months, and 6 months after surgery and at the last visit. Recordings included BCVA, postoperative retinal status, and postoperative complications. Postoperative complications mainly include concurrent cataracts, decreased corneal endothelial cells, and increased intraocular pressure, thinning of the epiretinal membrane, optic nerve fiber layer, and abnormal electrophysiology.

Statistical methods

Statistical analysis was performed using SPSS 13.0 software. First, the data were tested for normality. The data that met the normal distribution was tested by t-test and Student's t-test. Multiple groups of data were analyzed by LSD Duncan's multiple variance analysis. Reattachment status was assessed using Kaplan–Meier survival estimates. Use nonparametric tests on data that do not meet the criteria All statistics use P<0.05 as the significance test standard.

Results

The general condition of the patient

Table 1 summarizes the general characteristics of the patients.

Table 1: General characteristics of patients.

Features	23 eyes (21 people)
Age	
Average	30 (± 15.9)
Median	32 (12-69)
Gender	
Male	15
Female	6
Right eye	14
Left eye	9
Preoperative BCVA	
>20/200	1
20/200—20/400	5
<20/400	17
Preoperative ETDRS BCVA	
Mean (± standard deviation)	2.1 (± 2.0)
Median (range)	2 (0-7)
Meantime from mesh removal to surgery (days)	168.4 (± 122)
PFCL placement time (days)	
<7 day	13
7-14 day	6
>14 day	4
Mean (± standard deviation)	6.2 (± 3.3)
Median (range)	7 (4-30)
Net off again	
Yes	4
No	19
Follow-up time	
Mean (± standard deviation)	156 (± 103.3)
Median (range)	128 (30-365)
Final vision ETDRSBCVA	
Mean (± standard deviation)	3.9 9 ± 3.1)
Median (range)	3 (0-12)

The study included 23 eyes of 21 patients. BCVA ranged from 20/150 to light perception. 34.8% (8/23) of eyes had lower visual acuity than manual/anterior vision. The mean time from symptom onset of retinal detachment to surgical placement of the PFCL was 168.4 ± 122 days, while postoperative PFCL placement time was 6.2 (± 3.3) days (Table 1). Twenty-three eyes were all GRT, of which 17 eyes were in the inferior hiatus, 4 eyes were in the temporal side, 2 eyes were on the nasal side, and 0 eyes were in the upper part. Among them, 11 eyes had high myopia, 7 eyes had eyeball contusions, and 1 eye had congenital iris and choroid defects.

Comparison of preoperative and final visual acuity in affected eyes

At the last follow-up, 78.3% (18/23) eyes had better visual acuity, 13.0% (3/23) had the same visual acuity, and 8.7% (2/23) had worse visual acuity. The visual acuity of 3 eyes was only HM, and 2 eyes were dependent on silicone oil. At the last visit, 60.9% (14/23) of the eyes had cataracts, all of which had undergone phacoemulsification combined with intraocular lens surgery. There were no complications

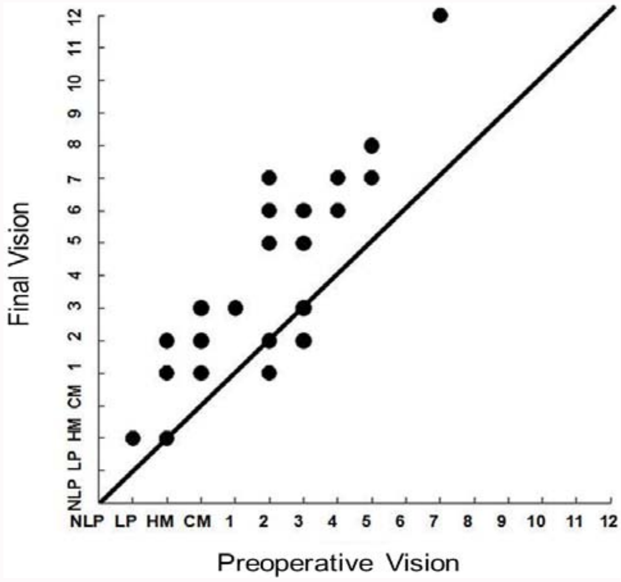

Figure 1: Comparison of preoperative VA and postoperative VA of diseased eyes.
NLP: No Light Perception; LP: Light Perception; HM: Manual; CM: Index/frontal; 1-12: ETDRS BCVA letter number

during the surgery, and the lens did not affect the final visual acuity. A comparison of preoperative visual acuity and final visual acuity is shown (Figure 1).

Retinal reattachment of the affected eye

After PFCL removal, 13.0% (3/23) eyes were replaced with balanced salt, 52.2% (12/23) eyes were replaced with sterile air, and the remaining 34.8% (8/23) eyes were replaced with silicone oil (Zeiss, Germany).

By the end of the observation, 17.4% (4/23) eyes had retinal detachment again and underwent reoperation, and 1 eye underwent retinal incision due to proliferative traction. PFCL was placed again in 1 eye after surgery, and finally, 4 eyes were filled with silicone oil, two of which became silicone oil-dependent eyes, and 1 eye refused to be filled with silicone oil again, resulting in eyeball atrophy. In all cases, retinal reattachment was achieved, while the PFCL remained in the vitreous cavity. The reattachment rate at the last follow-up was 82.6% (19/23). Figure 2 shows that recurrent RD after PFCL removal is more likely to occur at an early stage. At 10 weeks, retinal reattachment occurred with a retention rate of 80%. By week 20, the follow-up patients still retained their post-operative retinal reattachment status (Figure 2).

Injuries to the cornea, lens, macula, and optic nerve due to intraocular placement of PFCL

All eyes were divided into <7 days group, 7 to 14 days group, and >14 days group according to the duration of PFCL placement in the vitreous cavity. At the last follow-up, the corneal endothelial count, optic nerve fiber layer thickness, the time of subcapsular opacity after the occurrence of the lens, the presence of pre-retinal proliferative membrane, and the changes in optoelectronic physiology were compared among the three groups.

The results of corneal endothelium examination showed that the count of corneal endothelium in the >14 days group was significantly lower than that of the other two groups, and the <7 days group was

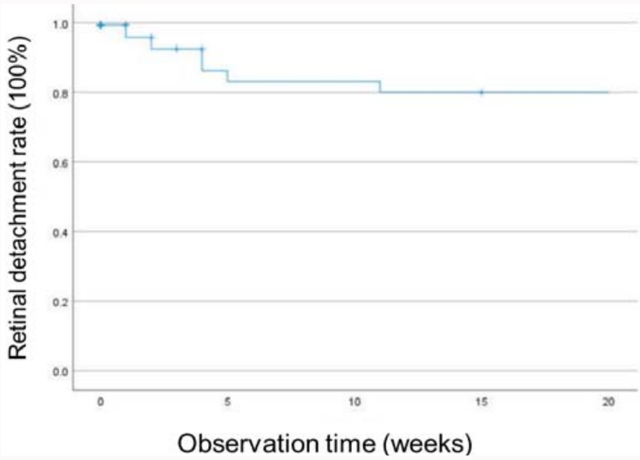

Figure 2: Kaplan-Meier estimated the relationship between retinal attachment rate and time.

better than the 7 to 14 days group. There were significant differences among the three groups. And >14 days group, the difference was statistically significant ($p<0.05$).

The results of optic disc OCT showed that the average thickness of RNFL in the 14-day group was significantly lower than that of the other two groups, and the <7 days group was better than the 7 to 14 days group, but there was no significant difference between the three groups ($p>0.05$).

After the placement of PFCL in the vitreous cavity, some affected eyes developed lens nuclei opacity one after another. The earliest 9 weeks after the operation, comparing the time of lens nuclei opacity in the three groups of eyes, the >14 days group was significantly earlier than the other two groups, <7 days. The group was later than the 7 day to 14 day group, and there was a significant difference among the three groups, and there was a statistically significant difference between the <7-day group and the >14-day group respectively ($p<0.05$).

Comparing the proportion of pre-retinal proliferative membranes in the affected eyes to the end of the observation, the >14 days group was significantly higher than the other two groups, reaching 100%, and the <7 days group was lower than the 7 to 14 days group, and there was a significant difference between the three groups ($p<0.05$).

The results of the electrophysiological examination showed that the PVEP P100 peak in the >14 days group was significantly later than the other two groups, and the <7 days group was earlier than the 7 days to 14 days group. There were significant differences among the three groups. There were statistically significant differences between the day group VS>14 days group and the 7 to 14 day group VS>14 days group ($p<0.05$) (Table 2).

Discussion

In routine vitreoretinal surgery, PFCLs are an effective and safe intraoperative packing that does not cause inflammation. When used as intraoperative packing, PFCLs can achieve good anatomical reduction, with an average success rate of 97% to 100%, and the success rate remains 63% to 100% after PFCLs and PFCL removal [17-19]. When faced with GRT, severe PVR, traumatic retinal detachment, and recurrent retinal detachment, due to the high specific gravity of PFCLs, it can still exert better retinal reattachment ability than other intraoperative packing's. Even more and more ophthalmologists use

Table 2: Comparison of the corneal, lens, macular, and optic neurotoxicity under different PFCL placement times.

PFCL	<7	7-14	>14	*F* value	*P* value
Placement time (days)	(n=13)	(n=6)	(n=4)		
Corneal endothelial count	2188 ± 94.9	2128 ± 115.5	1955 ± 118	7.87	0.003*
			<7 **VS** >14**		7E-04
RNFL average thickness (microns)	93.5 ± 11.0	89.9 ± 14.3	74.0 ± 11.4	2.93	0.076
Lens opacity time (weeks)	15.5 ± 2.4	14.5 ± 3.1	11 ± 1.8*	4.9	0.018
			<7 **VS** >14**		0.005
Proliferative membrane (incidence %)	30.8	50	100		0.040*
PVEP P100 (millisecond)	122 ± 11.1	139 ± 21.7	156 ± 25.3	6.09	0.008
			<7 **VS** >14**		0.002
			7-14 **VS** >14**		0.024

Note: The LSD Duncan test was used for the comparison between the three groups, in which the incidence of the macular epidermal membrane was nonparametric data, and the Kruskal-Wallis nonparametric test was used, *represents a significant difference among the three groups, **represents a significant difference between the two groups (p<0.05)

PFCLs for short-term or even long-term tamponade after surgery to achieve a higher retinal reattachment rate and better postoperative visual function [19-22].

In our observation of eyes filled with PFCLs after GRT, the placement of PFCLs after surgery effectively reduced the chance of retinal detachment again. By the end of our observation, the retinal reattachment rate of eyes with GRT was still higher than 80%, and postoperative recurrence of retinal detachment occurs mainly in the early stage (within 10 weeks). At the same time, the postoperative packing of PFCLs can effectively improve the visual function of patients. Of course, the degree of improvement is restricted by the macular function of the patients before surgery. For eyes with macular detachment for more than 1 year, even if the retina is well repositioned, the postoperative vision can only reach 0.05 (1–5 ETDRS letters/1 meter). Surprisingly, with prolonged macular detachment, even more than 5 years, the eye still had a chance to recover to 0.05 postoperatively. This may indicate that the retina beyond the macula can provide patients with a visual acuity of 0.05.

Certainly, observations of retinal and visual function strongly encourage the acceptance of PFCLs as routine postoperative packing. However, in recent years, some ophthalmologists have reported the complications of PFCLs postoperative packing. When the tamponade exceeds 1-week, various inflammatory responses will be induced. When PFCLs remain in the vitreous cavity, dispersion occurs a few days after injection, and PFCL droplets may enter the anterior chamber, although there is no evidence that how much PFCL and how long PFCL remains in the vitreous cavity contributes to this complication. However, the placement of PFCLs can induce corneal endothelial damage, which has been confirmed by animal experiments. Observations of rabbit eyes showed severe inflammation when half of the anterior chamber was filled with PFCLs. Within a week, corneal stromal edema developed, and the edema affected the entire corneal area, not just the lower half of the cornea. After 2 or 4 weeks of removal of PFCLs, rabbit eyes developed irreversible corneal scarring. In addition, half of the rabbit eyes developed sub-epithelial neovascularization. In our observations, there was no significant decrease in the endothelial counts of PFCLs packed within 2 weeks, and there was a significant difference in corneal endothelial counts beyond 2 weeks. Our results were significantly better than those observed in the rabbit eye, presumably due to the lower number of PFCLs diffusing into the anterior chamber from the vitreous cavity. At the same time, a nuclear cataract appeared in the observation, which is similar to that of Kirchhof [23]. During the 4-week follow-up period in the eyes of rabbits and pigs, histological changes in the retina were seen. The degree of change and the number of PFCL droplets increased with longer follow-up. PFCLs penetrate deeper retinal layers, involving the photoreceptor nuclear and outer segment layers, and produce morphological changes [7,10,24-27]. We observed the average thickness of the RNFL in the affected eyes after surgery. In the early stage of PFCL filling (within 1 week), there was a slight increase in thickness, which was related to optic nerve fiber layer edema caused by postoperative inflammation. When the PFCL filling exceeded 2 weeks, the RNFL thickness appeared to decline, which other scholars believe is related to the long-term oppression of the RNFL [14,28-30]. An examination of PVEP also revealed abnormalities, with a significant decrease in the P100 peak with prolonged PFCL tamponade, which was similar to that observed in animals. Chang [11] believed that the abnormality of PVEP was related to the destruction of the optic nerve myelin sheath, and silicone oil-filled eyes had similar changes. In animal observations, an inflammatory response of mononuclear macrophages was observed on the inner surface of the lower retina after 1 week of PFCLs in the vitreous cavity. Fibroblasts form a thick, highly organized pseudo membrane containing abundant newly formed extracellular matrix components [9,24]. We also found localized pre-retinal proliferative membranes in eyes with PFCLs placed for more than 2 weeks, and these proliferative membranes did not cause retinal stretch. At the same time, no PVR was found in patients with the long-term placement of PFCLs. This is consistent with the observations of other scholars who believe that PFCLs have a strong compressive ability, failing RPE cells, chemoattractant, and serum components to aggregate on the lower retina and lacking the material basis for PVR [24,31-33].

In general, PFCLs are like a double-edged sword, and their excellent effects and numerous risks have become the focus of debate. In our observations, short-term PFCLs postoperative filling can increase the rate of retinal reduction in GRT-affected eyes. Protect the visual function, intraocular placement of PFCLs in less than 2 weeks, although there are some risks, does not cause irreversible damage to the cornea, lens, retina, and other tissues. It is a surgical method worthy of promotion for GRT-affected eyes.

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