PerFluoroCarbon Liquids in Vitreo-Retinal Surgery – Personal Experience

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Abstract— **The combination of the physical and chemical properties of the PerFluoroCarbon Liquids (PFCL) has propeled their clinical use not only for the repair of the complex retinal detachments, but also for a range of intraocular surgical maneuvres. The purpose of this study is to outline the status of the use of PFCL in vitreo-retinal surgery, as it emerges from our personal clinical experience. We have used the PFCL in 82 vitrectomies over a one-year time period (October 2009 – October 2010). The PFCL were injected into the vitreous cavity in patients with the following conditions: rhegmatogenous retinal detachment (RRD), tractional retinal detachment (TRD), combined retinal detachment (rhegmatogenous and tractional) and severe proliferative diabetic retinopathy (PDR). In the RRD group (65 cases), success has been achieved in 55 cases (84.61%), simple recurrence has been identified in 6 cases (9.23%), Proliferative VitreoRetinopathy – in 3 cases (4.61%) and Cystoid Macular Edema – in 1 case (1.53%). The remaining 17 cases in which PFCL have been used (20.71%) were all caused by diabetes. In the severe PDR subgroup, the disease has been stabilized in all the 3 cases. In the TRD subgroup, success has been obtained in all the 4 cases (retinal reattachment), whereas in the combined retinal detachment subgroup (RRD+TRD) the retina has reattached in 8 cases (80%) and maintained detached in 2 cases (20%) after surgery. PFCL have proved their efficacy in vitreo-retinal surgery.**

Keywords— **vitreo-retinal surgery, PFCL.**

I. Introduction

The PerFluoroCarbon Liquids (PFCL) have initially been developed as blood substitutes, given to their high ability to transport oxygen and their biological inaction [1]. The first experimental studies with PFCL in ophthalmology investigated their value as vitreous substitutes in healing the inferior retinal breaks induced in rabbits [2,3]. Chang et al. have studied, for the first time, the PFCL in humans [1]. The combination of the physical and chemical properties (transparency, high specific gravity, imiscibility with water) has propeled the clinical use of these liquids not only for the repair of the complex retinal detachments, but also for a range of intraocular surgical maneuvres [4].

II. Purpose

The purpose of this study is to outline the status of the PFCL in vitreo-retinal surgery, as it emerges from our personal clinical experience.

III. Method

We have retrospectively included in this study all the cases in which PFCL have been used during the posterior vitrectomy: Rhegmatogenous Retinal Detachment (RRD), Tractional Retinal Detachment (TRD), combined rhegmatogenous and tractional retinal detachment (RRG+TRD) and Proliferative Diabetic Retinopathy (PDR).

The following parameters are analyzed: the clinical condition that required the PFCL use, the technical peculiarities imposed by each type of disease, the intra- and postoperative complications related to PFCL.

In the retinal detachment groups (rhegmatogenous, tractional or combined), the 3 months results are defined as: success, simple recurrence, Proliferative Vitreo-Retinopathy (PVR) and Cystoid Macular Edema (CME).

In the PDR group, the 3 months results are defined as the stabilization or progression of the disease.

The significant progress related to the PFCL use is emphasized.

IV. Results

We have used the PFCL in 82 vitrectomies for a one-year period of time (October 2009 – October 2010). The PFCL have been injected in the vitreous cavity in the following conditions: rhegmatogenous retinal detachment (RRD), tractional retinal detachment (TRD), combined retinal detachment (rhegmatogenous and tractional) and severe proliferative diabetic retinopathy (PDR).

Case distribution according to the clinical condition that required the PFCL use is illustrated in table 1.

All the posterior vitrectomies have been performed with the Accurus machine (Alcon), we used the 20 gauge system and a high speed vitrectomy probe (2500 cuts/minute).

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Table 1 Clinical conditions that required PFCL use

The clinical condition	Number of the cases	%
RRD	65	79.26
TRD	4	4.87
RRD + TRD	10	12.19
Severe PDR	3	3.65

The *rhegmatogenous retinal detachment* has been caused by a single tear in 50 cases (76.92%), while multiple retinal tears have been identified in 15 cases (23.07%). The data regarding the size of the worse retinal tear are presented in table 2.

A hole is a round defect in all the retinal layers, with a diameter of no more than 1- 2 mm. A normal retinal tear is larger than a hole, but smaller than 90 degrees. The dimension of a large retinal tear is comprised between 90 – 180 degrees and a giant retinal tear is defined by a more than 180 degrees size.

Table 2 Size of the worse retinal tear

Size of the worse retinal tear	Number of the cases	%
Hole	10	15.38
Normal	42	64.61
Large	10	15.38
Giant	3	4.61

The vitrectomy has been as complete as possible in all situations and we did not associate the Internal Limiting Membrane (ILM) peeling.

The retinopexy has been performed externally (with a cryoprobe) in 45 cases (69.23%) and internally (with the endolaser fiber) in 20 cases (30.76%). The endolaser cerclage has been associated in 26 cases (40%) and we used the silicone oil for the internal tamponade in all the situations.

In one case the PFCL has migrated under the retina, but it has been extracted easily. We recorded no postoperative complication related to PFCL.

The anatomical 3 months results are illustrated in table 3.

Table 3 The 3 months results in the RRD cases

The 3 months result	Number of cases	%
Success	55	84.61
Simple recurrence	6	9.23
PVR	3	4.61
CME	1	1.53

The remaining 17 cases in which PFCL have been used (20.71%) were all caused by diabetes. In the severe PDR subgroup, the disease has been stabilized in all the 3 cases. In the TRD subgroup, success has been obtained in all the 4 cases (retinal reattachment), in the combined retinal detachment subgroup (RRD+TRD) the retina has reattached in 8 cases (80%) and maintained detached in 2 cases (20%) after surgery.

V. Discussion

PFCL are completely fluorinated synthetic analogs of the carbohydrates, containing carbon-fluor bonds. In the saturated PFCL, the stability of the carbon-fluor bond makes the liquid biologically inactive and stable at temperatures of 400 – 500 °C. They are colourless, odorless, have high density (specific gravity 1.6 – 2.1) and low viscosity (2 – 3 cs at 25°C) [1].

The most common indication for the use of the PFCL on our series has been represented by the rhegmatogenous retinal detachment (RRD) without proliferative vitreoretinopathy (PVR): 65 cases (79.26%). The purpose was to drain the subretinal fluid, allowing the further retinopexy and internal tamponade.The high specific gravity as compared to water allows the hydrokinetic manipulation of the detached retina, by displacing the subretinal fluid anteriorly, through the periferal retinal breaks. Thus, the posterior retinotomies for drainage become useless.This property also permits them to flatten the detached retina delicately and uniformly. The PFCL have been injected in the vitreous cavity after the complete vitrectomy in 58 cases (89.23%). In the remaining 7 cases (10.76%), the injection of PFCL has been performed earlier during surgery, in order to stabilize a very mobile and bullous retina. In this latter situation, the vitrectomy has been continued toward the perifery and then the PFCL injection has been completed. The rationale of PFCL injection in RRD is to push the subretinal fluid toward the periferal break, thus eliminating it through it and flattening the retina. Besides this effect, the PFCL helps in identifying occult breaks: the flattening posterior force displaces the subretinal fluid through the periferal break and a line appears at the mixture of two different liquids [1].

In the RRD provoqued by big tears, located in the middle part of the retina, we used the so called „sandwich" technique: the PFCL is injected up to the posterior margin of the tear, then the fluid/air exchange is performed, concomitently with the subretinal fluid drainage through the tear, until the retina is flattened and then the exchange is continued [1]. We"ve used this technique in 5 cases, with a very good intra- and postoperative outcome. This method decreases the risk for subretinal migration of the heavier than water fluid and the volume of PFCL needed.

A subtype of retinal detachment that has benefited substantially from the PFCL use is the one provoqed by a giant retinal tear (180 degrees or more). Before the PFCL era, the repair of giant retinal tears with vitrectomy required turning the patient in the prone position during surgery, allowing to a gas bubble, as it was progressively injected into the eye, to unfold the inverted retinal flap of the giant tear. The PFCL bring a major improvement, permitting the retinal flap to be inverted with the patient in the normal supine position. The significant advantages of this approach include the gentle manipulaiton of the tear and the possibility to treat it (retinopexy) with the retina in the proper position, reducing the risk of retinal pigment epithelial dispersion. After the PFCL have been introduced in the clinical practice, the success rate in retinal detachment with giant retinal tear has improved considerably (more than 90% reattachments) [1]. On our series, we had only three cases of retinal detachment with superior giant retinal tear (180 degrees) and they all had a favorable outcome after posterior vitrectomy with PFCL use. It was no need for lens removal and scleral buckle.

Before the PFCL/air exchange, care must be taken in order to remove all the anterior subretinal fluid, as it may result in the slippage of the tear. If this occurs, the PFCL is reinjected after the air is replaced with saline. Then the PFCL/silicone oil exchange is performed directly via an automated infusion system. Slippage of the retina is prevented by the mechanical advantage of oil over gas. As a relatively incompressible liquid, the incoming oil meniscus engages the edge of the tear as the PFCL is removed. None of the two giant retinal tear cases on our series have complicated with retinal slippage.

The significant tamponade force of PFCL is approximately 6 times higher than that of the fluorosilicon oil and therefore, it has been attributed the role of a „third hand" stabilizing the retina during peeling and membrane delamination [1,5]. This property has been validated on our cases that implied membrane dissection: TRD, tractional and rhegmatogenous retinal detachment and PDR (20.74%). All these situations were the consequence of advanced diabetes, which explains the less number of cases as compared to the RRD category, given the fact that the diabetic retinopathy screening has improved substantially over the last years.

The most severe situation has been represented by the combined retinal detachment (rhegmatogenous and tractional). The complexity of the surgical act in these circumstances is given by the necessity to dissect very thick and adherent membranes from the surface of a mobile retina, with the risk of enlarging the already present retinal tear (s) and producing additional ones. This is the circumstance where without the use of the PFCL, the accomplishment of the surgical goals had not been possible. The PFCL injection has maintained the retina attached during the delicate maneuvers of epiretinal tissue dissection.

The optical clarity of these liquids and their very similar to water refractive index guarantee the optimal visualization during surgery and allow the intraoperative delivery of the laser energy on the attached retina. The properties of PFCL create ideal conditions for laser delivery during surgery: their boiling point being higher than the one of water, there is no risk of intraocular vaporization; they do not absorb the laser radiations (wavelengths between 488 – 810 nm), allowing the complete penetration of the laser energy through the liquid bubble [6]. Endolaser photocoagulation has been necessary in all the cases: for the treatment of the retinal tear (retinopexy – in the rhegmatogenous and combined retinal detachments), cerclage (in the RRD cases) or panretinal photocoagulation (in the diabetes cases).

Their imiscibility prevents the penetration of blood or of the silicone oil in the PFCL bubble, thus maintaining a very good level of visualization during surgery [1,5]. This has been particularly important in the diabetes cases that bleed frequently, even if we have administered preoperatively anti-VEGF (Vascular Endothelial Growth Factor).

The low superficial tension of PFCL (and subsequently, the high interfacial tension) decreases the risk of their subretinal migration. These substances are cohesive: they stay in a one, big bubble (fig.1). We have had only one case of subretinal PFCL migration, but we,ve extracted it easily, thanks to its cohesiveness and low viscosity.

The low viscosity is another desirable quality of these liquids (0.8-8.03 cs at 25°), permitting their easy injection and aspiration, through very thin instruments (fig.1).

Figure 1 shows the intravitreal injection of a PFCL bubble, through a very thin and long cannula. The retina is attached under the bubble and still detached in the periphery. As the PFCL is injected, the subretinal fluid is pushed through the tear and the retina is progressively attaching.

This is also very useful in two circumstances: as a diagnostic tool (to evaluate the areas of residual retinal traction) and during the fluid/air exchanges [1,4].

The aspiration of the PFCL from the eye at the end of surgery is mandatory, because of their toxicity and dispertion. The dispertion (fragmentation of the large bubble in smaller ones) occurs at 2-3 days after surgery, at the interface PFCL-vitreous fluid. The consequences are: the loss of the optical clarity (interfering with the visualisation of the retina), the passage of the bubbles through the retinal breaks (impending the reattachment of

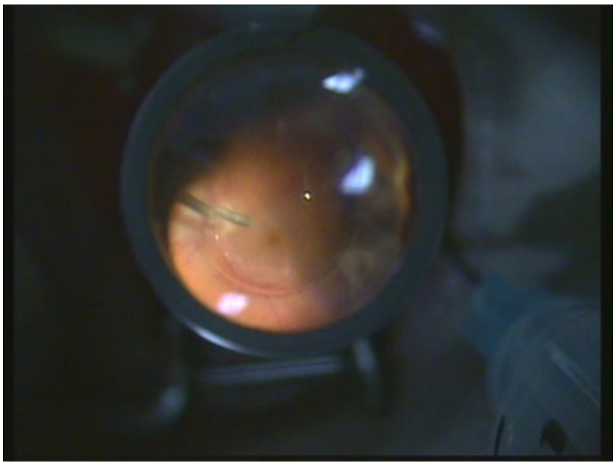

Fig. 1 Injection of PFCL liquid

the retina) and the blockage of the trabeculum by macrophages that have ingested the small bubbles (generating the secondary glaucoma) [1,7]. We,ve never left deliberately PFCL in the eye, but in one case we,ve discovered a few bubbles under the retina in the next day (they reached that space through inferior retinal breaks). We removed them, because they did not allow the retina to flatten inferiorly. Some authors report the good tolerability of very small volumes of PFCL, but in this particular case, the location of the substance under the retina forced us to re-opeate.

The toxicity of the PFCLs is generated by several facts: due to the high specific gravity, they compress the retina, leading to the loss of the external plexiform layer; later, the displacement of the photoreceptors nuclei in the external segment, the distortion of the external segment and the pigment epithelium atrophy have been identified; their concentration in polar impurities (H2) allows the absorbtion of lipoproteins and proteins, inducing a fibroblastic reaction and the formation of the preretinal membranes [1,7].

The litterature reports situations of PFCL identification in an eye after removing the silicon oil. When placed together in water, between the two liquids (PFCL and silicon oil) there is a natural attraction, because the interfacial energy between them is low. Therefore, when the silicon oil is infused in the eye, any drops of PFCL will adhere to the surface of the oil. When the PFCL volume increases and mixes with the silicon oil, the combination will have a specific gravity higher than the one of water [1].

The possible complications related to the PFCLs use in vitreo-retinal surgery are: the subretinal migration (0.9%), if the fish egg phenomenon occurs or if there are tractions at the margins of the retinal tear; the small rezidual bubbles (1 - 11%), which are well tolerated; if large amounts of PFCL remain in the eye, they induce a macrophagic response, translated by cell deposits on the lens, the cilliary body and the peripheral retina; in the aphakic eyes, the contact of the PFCL with the cornea generates the loss of the endothelial cells with its subsequent opacification [8].

VI. Conclusions

1. The PFCL have proven their physical and chemical qualities as adjuvant tools in vitreo-retinal surgery according to our experience.

2. The most common indication for the use of the PFCL on our series has been represented by the rhegmatogenous retinal detachment (RRD): 65 cases (79.26%).

3. The PFCL have brought a major improvement in the management of the RRD with giant retinal tear: all the 3 cases with superior giant retinal tears had a good outcome.

4. The combined rhegmatogenous and tractional retinal detachment represents a circumstance where without the use of the PFCL, the accomplishment of the surgical goals had been impossible. The PFCL injection has maintained the retina attached during the delicate maneuvers of epiretinal tissue dissection in all the situations.

5. We recorded no postoperative complication related to the PFCL use on our series.

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