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A pilot study on the use of silicone oil–RMN3 as heavier-than-water endotamponade agent

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Abstract *Aims:* This work was conducted to report an interventional non-comparative pilot study using Oxane HD, a mixture of ultra-purified silicone oil and RMN3, a partially fluorinated olefin, as heavier-than-water internal tamponade. *Methods:* Twenty-eight consecutive patients were recruited for this study. Indications included recurrent retinal detachment (RD) with proliferative vitreoretinopathy (PVR) (stage ≥C2) arising from inferior or posterior tears, recurrences after vitreoretinal surgery, penetrating trauma and combined rhegmatogenous and choroidal detachment. The patients underwent a pars plana vitrectomy, membrane peeling, and Oxane HD was used as long-term internal tamponade. *Results:* Oxane was removed after 88 days (range 45–96 days) and exchanged with BSS in five eyes, long-acting gas in 14 eyes and with silicone oil in nine eyes. Retinal reattachment was achieved in 15 eyes. The overall anatomical success rate obtained using Oxane HD was 53.5%. In 15 patients with previous marked scleral buckling, the success rate was 26%: in nine patients recurrent RD occurred in the inferior sector, in five patients new tears were detected in the lower sectors; membrane formation was observed in 15 eyes. In 13 patients without marked scleral indent, the success rate was 84.6%. There was no evidence of dispersion and excessive inflammation. *Conclusion:* Oxane HD may be a useful tool in complicated RD with large inferior breaks, inferior PVR or combined rhegmatogenous, and choroidal detachment without marked scleral buckling, which put the eye profile out of shape, led to a higher failure rate and reduced the tamponading effectiveness of Oxane HD.

Keywords Long-term internal tamponade · Oxane HD · Proliferative vitreoretinopathy · Retinal detachment

Introduction

Retinal detachment (RD) complicated by inferior retinal breaks and proliferative vitreoretinopathy (PVR) remains difficult to treat. The most frequently used long-term endotamponade agent is silicone oil, which is lighter than water and floats with a positive buoyancy. It is ineffective at supporting the inferior retina, especially if there is a slight under-fill [3]. Moreover, it always leaves a space in the inferior sector filled by fluid where reproliferation may occur. Therefore, a tamponade that sinks would be useful in many situations. Several heavier-than-water endotamponades have been suggested, such as perfluorocarbons [7, 14], double filling [1] and semi-fluorinated alkanes [5]. Recently we proposed the combined use of 70% F6H8 and 30% silicone oil and achieved encouraging results in a pilot study [9] and in a multicentric non-comparative study [8]. The double filling F6H8–silicone oil was mixed inside the eye, resulting in an effective but unstable biphasic mixture. Further attempts were performed to develop a vitreous

substitute that is transparent, stable and homogeneous. Oxane HD (Bausch & Lomb) is a new "heavy silicone oil" that was recently proposed in the treatment of complicated retinal detachment [4, 13]. The aim of this study was to evaluate the efficacy and safety of Oxane HD as heavier-than-water endotamponade in the treatment of complicated retinal detachment involving the lower quadrants of the retina.

Materials and methods

Study design

We performed a prospective interventional non-comparative study on 28 eyes of 28 consecutive patients who were recruited from our clinic between May 2003 and June 2004. The study was approved by the local ethics committee.

Main outcome measures

The primary study end-point was the anatomical reattachment of the retina. Cases were judged successful when there was reattachment of the retina in the absence of any tamponade agent.

Our secondary study goal was to record the functional outcome and the complications, which might or might not be related to the use of Oxane HD.

Baseline examination consisted of a detailed ophthalmic history, slit-lamp biomicroscopy, Goldman applanation tonometry, and direct and indirect ophthalmoscopy. Best-corrected visual acuity (BCVA) was reported during examination upon the subject's entry into the study and at the last follow-up visit; best-corrected Snellen visual acuity was obtained and converted into a logarithm of the minimum angle of resolution (logMAR). The grade of PVR was defined according to the classification of the Retinal Society [6]. Follow-up examinations were scheduled 1 day, 1 week, 1 month, 3 months after the initial surgery and 1 week, 1 and 6 months after Oxane HD endotamponade removal.

Patients

Inclusion criteria consisted of retinal detachment with PVR stage ≥C2 (according to the classification of the Retina Society), PVR of the inferior quadrants of the retina, retinal detachment (RD) caused by inferior giant retinal tears, penetrating trauma and combined rhegmatogenous and choroidal detachment.

Exclusion criteria were: age under 18 years, severe systemic disease, pregnancy, any uncontrolled ocular disease other than RD, participation in another study, missing informed consent.

A total of 28 eyes of 28 patients were included in our study (18 male, 10 female). The mean age was 59 years (range 23–83 years). Twenty-five patients had previous RD repair: 20 had undergone one surgery for RD repair, 3 had undergone two surgeries and 2 had more than two previous surgeries.

Out of this set of 25 eyes, recurrence of RD occurred in 12 eyes after scleral buckling, in 6 after pars plana vitrectomy, in 7 after combined scleral buckling and vitrectomy. Three patients had not been previously operated on. In 11 of the previously vitrectomized eyes conventional silicone oil had been used: in 6 eyes a recurrent RD occurred with oil still in situ, while in 5 the recurrences occurred after the removal. In 2 previously vitrectomized eyes gas tamponade had been used, and the retina redetached after the gas reabsorption. At baseline 9 patients were aphakic, 8 phakic and 11 pseudophakic.

On baseline examination the macula was detached in all eyes and 15 eyes showed marked previous scleral buckling. We defined as marked scleral buckling a large radial or circumferential episcleral explant causing high buckle effect putting the eye profile out of shape.

Materials

Oxane HD (Bausch & Lomb) is a new "heavy silicone oil" with a high specific gravity. It is a mixture of ultra-purified silicone oil (Oxane 5700; Bausch & Lomb) and RMN3, a partially fluorinated and hydrocarbonated olefin. The solution is homogeneous and stable in the presence of water, air or perfluorocarbons. It has a density of 1.02 g/cm^3 and a viscosity of 3300 mPas. Its interfacial tension is higher than 40 mN/m.

Surgical technique

Surgery was performed in regional anesthesia. A standard three-port pars plana vitrectomy was performed in all patients. In six eyes silicone oil was in situ and was removed. Vitrectomy was combined with cataract surgery in five eyes. The intraocular lenses (IOLs) were left in situ. Epiretinal membranes were peeled in 14 eyes. Peeling was trypan blue or triamcinolone acetonide-assisted. A relaxing retinotomy was applied in nine eyes. The retina was flattened using perfluoro-*n*-octane, which was removed via fluid–air exchange. Endolaser photocoagulation was carried out. The vitreous cavity was then filled with Oxane HD.

Oxane HD was removed 45–96 days after the initial surgery in regional anesthesia, through a pars plana approach. Under endoillumination and microscopic visualization, a 19-gauge Teflon tip cannula was held over the optic disc and the Oxane HD was aspirated using the active

aspiration of the vitrectomy system. Finally, several BSS–air exchanges were performed.

Patients who failed to improve with Oxane HD were given further procedures using conventional silicone oil.

Results

Anatomical results

Retinal reattachment was achieved in all eyes at the end of vitrectomy and Oxane HD filling the vitreous cavity.

At the time of the tamponade removal with Oxane HD still in the vitreous cavity, 19 eyes showed retinal reattachment and nine eyes showed recurrent RD of the inferior retina (Fig. 1). New tears were detected in the lower sectors in five patients. Intraoperatively, epiretinal membranes were observed and peeled in 14 eyes. The membranes were diffuse or localized in the inferior sector, posterior and on top of the scleral buckling. The level of difficulty in their removal was similar to that of the membranes usually found with conventional silicone oil. Membranes and inferior recurrences developed in 15 eyes where a previous broad and marked indent was evident (height of scleral buckle >3 mm with a steep slope and deep recesses, or very tight encircling elements with "hourglass" distortion of the globe).

Oxane HD was exchanged with BSS or air in five eyes. In 14 eyes, Oxane HD was exchanged with long-acting gas, and in nine eyes it was exchanged with silicone oil, due to diffuse epiretinal membranes or inferior recurrences.

At 6 months follow-up after the tamponade removal, 15 eyes showed retinal reattachment while 13 eyes showed recurrent RD. In the five eyes where Oxane HD was exchanged with BSS or air, the retina remained attached.

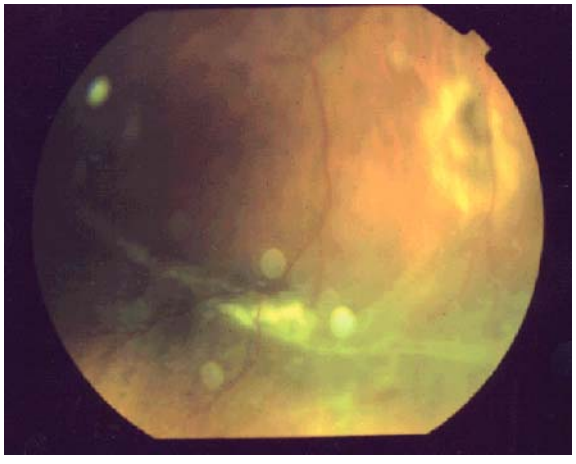

Fig. 1 Recurrent inferior retinal detachment with epiretinal membranes near marked scleral buckling with Oxane HD in the vitreous chamber

Out of the 14 eyes exchanged with long-acting gas, eight cases showed a further RD recurrence. Out of the nine eyes exchanged with conventional silicone oil, endotamponade removal was successfully carried out in four eyes, while five eyes underwent further surgeries. Retinal reattachment was achieved in four out of the 15 patients with previous marked scleral buckling (26%) and in 11 out of the 13 patients without marked scleral indent (84.6%)

Functional results

At baseline examination, the mean BCVA ranged from +2.3 logMAR units to +1.00 (mean +1.7). At 6 months follow-up it was +1.5 logMAR units (range +2.3 to +0.4).

BCVA remained unchanged in 12 eyes (42.9%), improved in ten eyes (35.7%) and decreased in six eyes (21.4%).

Complications

Eight eyes were phakic at baseline examination. One eye showed marked cataract formation during Oxane HD filling and underwent cataract extraction at the time of Oxane HD removal. During the follow-up period, two more eyes underwent cataract surgery. Raised intraocular pressure (IOP) was observed in four eyes with Oxane HD in situ. In three eyes, IOP was controlled with normal medication. In one phakic eye, part of the Oxane HD bubble was dislocated into the anterior chamber; this was immediately removed. No corneal damages were observed. Dispersion or emulsification into small bubbles of Oxane HD was not observed in the other patients. Membrane formation under Oxane HD was observed in 15 eyes. No patient showed intraocular inflammation with Oxane HD in situ.

Discussion

To the best of our knowledge, no randomized clinical trial on the efficacy of heavier-than-water endotamponades has been performed so far. Various agents have been studied with anatomic success rates varying between 50% [1], 83% [5], 86% [10], 94% [13] and 100% [11], depending on the different period of follow-up and on the definition of anatomic success. In fact, only Kirchhof [5] reported successful retinal reattachment without any endotamponade. Using a double filling of silicone oil and F6H8, we achieved complete retinal attachment without any endotamponade in 77% at 12 months follow-up [9].

The overall anatomical success rate using Oxane HD in this study was 53.5%. In the 13 patients without marked scleral indent, the anatomic result was satisfactory, with a success rate of 84.6%.

In contrast, in 15 patients with previous marked scleral buckling, the success rate was 26%. In this subgroup, recurrences occurred in the inferior sector of nine patients and membranes developed in 15 eyes.

We did not expect to find recurrence in the inferior sector alone. There was a certain amount of apprehension regarding superior redetachments because tamponading efficacy with heavier-than-water endotamponades is usually insufficient in the upper sector in the orthostatic position.

In fact, Wolf et al. [13] observed 18% of residual retinal detachments in the superior quadrants with Oxane HD. For our part, we found recurrences in the upper sectors in 10% with the double filling (F6H8 30% and silicone oil 70%).

Therefore in the group with previous marked scleral buckling, the goal for the use of heavier-than-water endotamponade was not achieved. We wish to point out that the severity of retinal conditions and PVR were similar in the two groups.

The reason for this failure might be that the specific density of Oxane HD is too light, as Wetterqvist et al. demonstrated in model eye chamber measurements [12]. However, we are convinced that the main problem dealing with Oxane HD is related to its low affinity to the retinal surface.

In fact, Wetterqvist has demonstrated in an in vitro study that a solution of F6H8 and silicone oil (with a specific gravity of 1.06 g/cm^3) has similar physical properties to silicone oil in terms of the shape of the bubble, and thus its ability to act as an internal tamponade agent. More recently, Wong tested in vitro the efficiency of silicone oil, F6H8 and various tamponade solutions such as silicone oil–F6H8 (1.01, 1.02, 1.03, 1.06 g/cm^3) and silicone oil–RMN3 (1.02 g/cm^3) by using a model eye chamber modified with lateral indents (personal communication). He demonstrated that qualitatively, F6H8 made good contact with the chamber and tended to fit into recesses created by the indents. Silicone oil bubbles, in contrast, were rounded and made poor contact; moreover, they did not fill the "nooks and crannies". The point is that all homogeneous solutions of silicone oil–F6H8 and silicone oil–RMN3 tended to behave like silicone oil and displayed a rounded shape and made poor contact with the sides of the buckling.

This could explain the results obtained in our series. In fact, we achieved anatomical success when no marked scleral buckling was present. It is likely that the Oxane HD bubble, behaving like silicone oil, cannot fit the modification of the eye profile caused by the indent, and leaves the lateral recesses filled with fluid. As the exclusion of the fluid from the surface of the retina is important to prevent re-proliferation [5], the presence of a free space filled by fluid surrounding the indent may account for the high reproliferation rate (100%): epiretinal and subretinal membranes were found in this group in correspondence with the buckling.

Another explanation might be that the olefin RMN3 compound of Oxane HD might stimulate membrane formation; however, it is difficult to determine whether these proliferations were PVR membranes or a biological reac tion due to the endotamponade.

The rate of epiretinal or subretinal membrane formation due to heavier-than-water endotamponades is variable in literature. De Molfetta et al. [2] found postoperative proliferation in 90%, and Kirchhof et al. [5] reported macular pucker formation in 9%. Using a double filling of F6H8 and silicone oil, we found epiretinal membranes in 37% and subretinal membranes in 5% [9]. In his experiments, Sparrow did not find any evidence that silicone oil and perfluorocarbon liquids differ in stimulating cellular proliferation and membrane formation [8].

On the other hand, Oxane HD showed good intraocular tolerance with a few minor complications, and an encouraging success rate in the group without marked indent. Therefore, our preliminary results suggest that it may be a useful tool in complicated RD with large inferior breaks or inferior PVR, and in combined retinal and choroidal detachment without marked irregularity of the eye profile.

Functional results were less encouraging than anatomical results because BCVA improved only in 35.7%. This was attributed to the severe previous retinal conditions and to the anatomic success rate.

Our study is limited by the lack of a control group; therefore, no definite conclusions regarding the use of Oxane HD in respect to the other endotamponades are possible.

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