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Prolonged gas tamponade as a method of treatment for persistent macular holes

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Key words:

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Purpose. *To assess the efficacy of prolonged gas tamponade in patients with persistent idiopathic macular holes (IMHs) who had received a vitrectomy with classical internal limiting membrane (ILM) peeling.*

Material and Methods: *Nine eyes (8 patients, including 7 women and 1 man; mean age [SD], 67.9 (7.5) years) with persistent IMHs were followed. In two eyes, a revision procedure without extended ILM peeling and with C3F8 15% tamponade was performed. In seven eyes, not a revision procedure, but a replacement tamponade with C3F8 15% was performed for prolonging the duration of C3F8 15% tamponade.*

Results: *At 1-1.5 months after primary MH surgery, IMHs failed to close in all study eyes. Mean minimum MH size (SD) significantly improved in all eyes from 404.4 (131.4) μm to 282.1 (160.0) μm ($p = 0.017$). Mean best-corrected visual acuity (BCVA) (SD) improved from 0.11 (0.056) to 0.24 (0.13), $p = 0.008$. In all study eyes, with the prolonged duration of gas tamponade and two weeks of facedown positioning, IMHs closed and mean BCVA (SD) improved significantly ($p = 0.003$) to 0.43 (0.22).*

Conclusion: *Prolonged C3F8 15% tamponade is an effective method of treatment for persistent IMHs after vitrectomy with classical ILM peeling.*

Introduction

Idiopathic macular hole (IMH) is caused by anteroposterior and/or tangen-tial vitreomacular traction [1, 2, 3]. Vitrectomy with internal limiting membrane (ILM) peeling and gas tamponade is the standard of surgery for IMH, provides a high macular hole (MH) closure rate and reduces the risk of MH recurrence [4]. Removal of the ILM relieves tangential vitreomacular traction, increases the elasticity of the retina at the site of the MH, promotes glial cell proliferation, and prevents epimacular membrane formation and MH recurrence [5]. Once the gas bubble contacts the IMH, its surface forms a closed space between bubble mar-gins and basis, preventing the contact of the vitreous fluid with the retina at the site of the hole. Other contributors to MH closure include the buoyant force of a gas bubble on a MH in the facedown position, the pump action of the retinal pigment epithelium (RPE) to create vacuum in the hole, and glial cell migration to the MH aperture [6, 7]. There is an evolving discussion around ILM peeling size, tamponade selection, the time required for IMH closure and, consequently, the duration of postoperative facedown positioning. Two disc-diameter (DD) ILM peeling, short-term gas tamponade (SF6 20% or air) and less than one day of facedown positioning are effective in MHs with a minimum diameter less than 250 μm, with optical coherence tomography (OCT) confirmation of MH closure in 93% of these eyes. Larger than two disc-diameter (DD) ILM peeling, C2F6 15% or C3F8 15% tamponade and more than one week of facedown positioning are believed to be most effective in 400-600 μm IMHs [8, 9].

Persistent IMH is defined as an IMH that failed to close one month after primary MH surgery. Such IMHs usually require a revision procedure with an increase in the diameter of ILM peeling and use of air/gas tamponade. Refractory full-thickness macular hole (FTMH) is a definition that includes both a “reopened FTMH” and a FTMH that failed to close within three months. The surgical tech-niques used for treating FTMH refractory to pars plana vitrectomy (PPV) and ILM peeling include autologous platelet concentrate (APC); lens capsular flap transplantation; free ILM flap; enlargement of ILM peeling; macular hole hydro-dissection (MHH); silicon oil (SO); human amniotic membrane (hAM); perifoveal relaxing retinotomy; and arcuate temporal retinotomy [10, 11]. If the role of gas tamponade in IMH closure is not less than that of ILM peeling, prolonged gas tamponade with prolonged facedown positioning would be beneficial in the treatment of early IMH non-closure.

The purpose of the study was to assess the efficacy of prolonged gas tam-ponade in patients with persistent IMH who had received a vitrectomy with clas-sical ILM peeling.

Material and Methods

Nine eyes (8 patients) in which a MH failed to close 1-1.5 months after primary MH surgery were followed at the Vitreoretinal Pathology Department, SI “The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine”, in 2021-2025. Of those nine eyes, eight had been primarily operated on at the department and one eye, at another eye

clinic. Seven of the eight patients were women and one was a man. The mean age (standard deviation [SD]) was 69.7 (7.5) years.

Written informed consent for surgery (vitrectomy and replacement tamponade) was obtained from all subjects. Study procedures followed the Declaration of Helsinki regarding ethical standards for studies involving human participants. The study was a part of the research program "To determine the features of vitreoretinal surgery in the time of war" (registered number, № 0125U002074).

An eye examination was performed before primary and repeat surgery and included visual acuity assessment; refractometry; tonometry; slit-lamp biomicroscopy; dilated fundus examination using a slit lamp with a 90-D lens and binocular ophthalmoscope with a 20-D lens; and OCT (OPTOPOL Technology S.A., Zawiercie, Poland) with the determination of the apical and basal diameters of the MH. The exclusion criterion was myopia exceeding 6.0D.

A 25-G PPV was performed using the Alcon Constellation vitrectomy machine (Alcon Laboratories, Inc., Fort Worth, TX) and a wide-angle viewing system (BIOM; Oculus, Wetzlar, Germany). After the posterior hyaloid was removed, the ILM was stained with TWIN (trypan blue 0.18% and blulife 0.03%, Alchimia srl, Padova, Italy), and ILM peeling was performed either classically (a 2 DD ILM peeling) or using a proprietary fovea-sparing technique [12]. Subsequently, either SF6 20% tamponade (7 eyes) or 15% C3F8 tamponade (2 eyes) was performed. Patients were instructed to maintain face down positioning for a week after surgery. Surgeries were performed by three surgeons of the Vitreoretinal Pathology Department of the institute. MH non-closure was diagnosed 1-1.5 months after surgery.

In two eyes, a vitreous cavity revision procedure with ILM staining was performed to assess the peeling diameter. Because the ILM peeling diameter was sufficient (≥ 2 DD), surgery was completed by gas tamponade (C3F8 15%), and these patients were instructed to maintain face down positioning for two weeks after surgery.

In seven eyes, not a vitreous cavity revision procedure, but a replacement tamponade with C3F8 15% was performed, and these patients were also instructed to maintain face down positioning for two weeks after surgery.

The procedure of replacement tamponade was as follows. The patient was placed in the sitting position with the head positioned vertically, and received topical anesthesia with oxibuprocaine 0.4%. After the lid speculum was placed and betadine 5% was applied into the conjunctival sac, a 23-G needle connected to a 5.0 cm3 syringe filled with C3F8 15% was used to puncture the pars plana 4 mm from the limbus at the 6 o'clock position. Some vitreous fluid was aspirated by alternate-reciprocated movements of the syringe plunger, the same volume of the air-gas mixture was injected into the vitreous cavity, and this was repeated until the fluid was completely replaced by the gas. Throughout the procedure of replacement tamponade, the position of the needle was monitored using a binocular indirect ophthalmoscope (Omega 500, Heine Optotechnik, Herrshing, Germany), and a near-to-normal intraocular pressure (IOP) was maintained. After complete replacement of the endovitreal fluid with the gas-air mixture, the injection needle was retracted from the eye, and the spatula was used to smooth over the site of injection and pressurize the vitreous cavity.

Visual acuity, minimum MH diameter, basal MH diameter, presence of cystic changes involving the MH margin before and after vitrectomy, and macular hole closure pattern were assessed 1 month after additional gas tamponade.

Data were entered into the spreadsheet and analyzed using IBM SPSS Statistics software (IBM Corp., Armonk, NY). Mean and SD were calculated for normally distributed data, and median and interquartile range (IQR) were calculated for non-normally distributed data. Student t-test was used to assess the difference.

Results

At baseline (before the first operation) MH duration ranged from 2 weeks to 7 months, with a median (IQR) value of 3.0 (1.0-6.0) months. Additionally, best-corrected visual acuity (BCVA) ranged from 0.04 to 0.2, with a mean (SD) value of 0.11(0.056). Of the 9 eyes, 4 were emmetropic, 3 were myopic (-1.0D) and 2 were hypermetropic (+2.5D and +3.5D). Moreover, minimum MH diameter ranged from 225 to 528 μm, with a mean (SD) value of 404.4 (131.4), and basal MH diameter ranged from 714 to 1063 μm, with a mean (SD) value of 897.4 (128.1) μm. All nine eyes showed cystic edema of MH margin (Table 1).

One month after vitrectomy with ILM peeling, the MH failed to close, but BCVA improved compared to baseline in eight of nine eyes to a mean (SD) value of 0.24 (0.13), and the difference was significant ($p = 0.008$). Mean minimum MH size (SD) significantly improved in all eyes from 404.4 (131.4) μm to 282.1 (160.0) μm ($p = 0.017$). Basal MH diameter decreased in eight eyes and increased from 979 1042 μm in one eye (MH margin became somewhat higher, although the apical MH diameter decreased from 568 to 492 μm in this eye). In nine eyes, mean basal MH diameter (SD) decreased to 660.2 (269.5) μm compared to baseline values, and this decrease was significant ($p = 0.03$). It is noteworthy that the cystic edema of MH margin was still observed at follow-up.

Therefore, although the IMH did not close completely, it had a trend to close. Moreover, because the configuration of MH margin and the presence of edema indicated the potential for MH closure, prolonged gas tamponade was justified under these circumstances.

At 1 month after additional gas tamponade, the MH was closed, with all nine eyes having a U-shaped closure pattern [13]. Visual acuity improved in all eyes, with a mean BCVA (SD) of 0.43 (0.22) ($p = 0.003$).

Figures 1 to 3 show OCT data at baseline and before and after additional gas tamponade.

Table 1. Morphometric characteristics of idiopathic macular hole (IMH) and visual acuity at baseline and before additional gas tamponade

	Baseline			Before additional gas tamponade			After IMH closure
	Minimum IMH diameter (μm)	Basal IMH diameter (μm)	Best-corrected visual acuity	Minimum IMH diameter (μm)	Basal IMH diameter (μm)	Best-corrected visual acuity	Best-corrected visual acuity
1.	250	715	0.17	176	700	0.4	0.8
2.	400	880	0.12	290	598	0.35	0.6
3.	350	960	0.1	276	900	0.25	0.65
4.	407	970	0.17	311	700	0.4	0.5
5.	520	1000	0.1	80	204	0.08	0.25
6.	568	979	0.04	492	1042	0.08	0.12
7.	332	796	0.2	238	511	0.25	0.35
8.	225	714	0.04	115	254	0.25	0.4
9.	588	1063	0.1	561	1033	0.1	0.2
Mean (SD)	404 (131.4)	897.4 (128.1)	0.11 (0.056)	282.1 (160.0) p = 0.017	660.2 (269.5) p = 0.03	0.24 (0.12) p = 0.04	0.43 (0.22) p_1 = 0.001 P_2 = 0.003

Note: p_1, P-value for statistical difference between the final visual acuity and the visual acuity at 1 month after primary surgery; p_2, P-value for statistical difference between the final visual acuity and baseline visual acuity; IMH, idiopathic macular hole.

Discussion

Most vitreoretinal surgeons use air endotamponade or SF6 endotamponade after vitrectomy because (1) a 93% rate of OCT evidence of MH closure on the next day after surgery has been reported for IMH eyes having vitrectomy and gas tamponade, and (2) they strive to minimize the duration of facedown positioning in MH patients who are mostly elderly. It was argued that the use of prolonged gas tamponade after vitrectomy for MH is not reasonable. If, however, the IMH did not close after vitrectomy, a revision procedure is required with the use of additional techniques for MH closure, such as extended ILM peeling, free ILM flap, APC, MHH, human amniotic membrane, and peripheral neurosensory retinal graft [8, 10]. A systematic review [14] included 12 studies that represented 940 eyes. The authors [14] showed that using long-acting gas was associated with improved post-operative BCVA.

Additionally, prolonged gas tamponade (namely, replacement tamponade) does not cause significant anatomical changes, very rarely has complications, and is supposed to be beneficial for reducing the rate of re-surgery after failure of primary vitrectomy for persistent IMH. A recent study by Baumann and colleagues [15] evaluated the efficacy of repeat PPV and gas tamponade for persistent MHs. A total of 27 patients with a persistent MH after primary MH surgery were identified, all of whom underwent a second operation with PPV and gas tamponade with an ILM peel extension in 20 cases. The authors concluded that, for a persistent IMH, simple repeat PPV with gas tamponade has a good anatomical and functional success rate in selected cases. The minimum linear diameter and MH index can be useful OCT markers for prognostic guidance [15].

In the current study, the minimal size of the IMH decreased after primary MH surgery. Moreover, we believe that persistent cystic edema of MH margin is a sign that this MH has every change to close after prolonged gas tamponade. Chen and Yang [16] used repeat intravitreal injections (IVI) of pure C3F8 as a method of prolonged gas tamponade in MHs that failed to close after primary surgery. Twelve of 19 eyes (63%) achieved MH closure after 1 to 3 times IVI C3F8. The other 7 eyes (37%) indicated persistent MHs after IVI C3F8. They had repeat vitrectomy with extension of ILM peeling or ILM flap technique. Chen and Yang [16] concluded that early IVI of C3F8 can be a cost-effective first-line treatment for early persistent MHs after primary surgery [16].

In brief, their method was as follows. When the gas bubble was gradually absorbed to less than 50% of vitreous cavity and allowed OCT detection of a persistent macular hole, additional gas injection was arranged. An anterior chamber paracentesis was performed, and 0.2–0.3 ml pure C3F8 gas was injected into the vitreous cavity. The gas volume was increased in the eyes with longer axial length. After the outpatient injection, the patient was instructed to take a prone position for 7 days until the next follow-up clinic. Two IVIs were performed in three eyes and three IVIs, in one eye of 19 eyes. One case developed acute angle closure attack. Another case had rhegmatog-

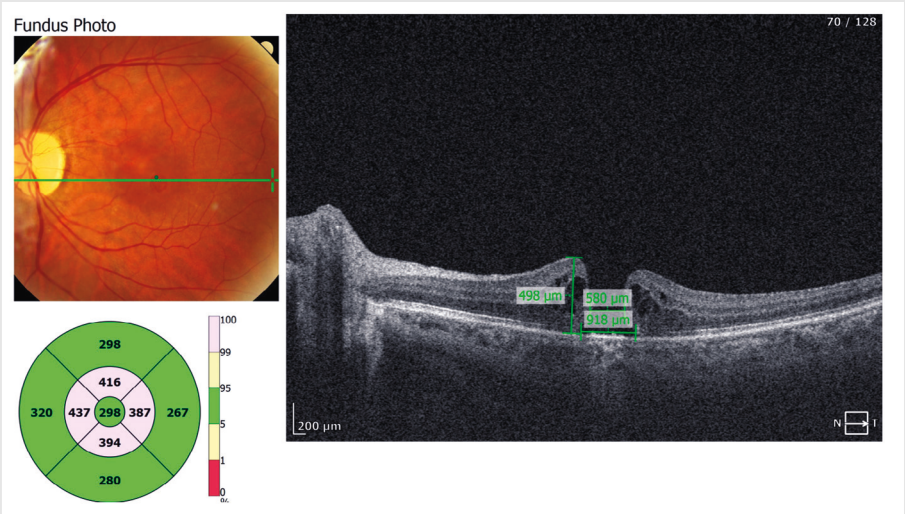

Fig. 1. Parameters of idiopathic macular hole (IMH) before vitrectomy in a 62-year-old female patient who experienced a reduction in best-corrected visual acuity to 0.17 over a month, had a vitrectomy with internal limiting membrane peeling and SF6 20% tamponade, and maintained face down positioning for two weeks after surgery.

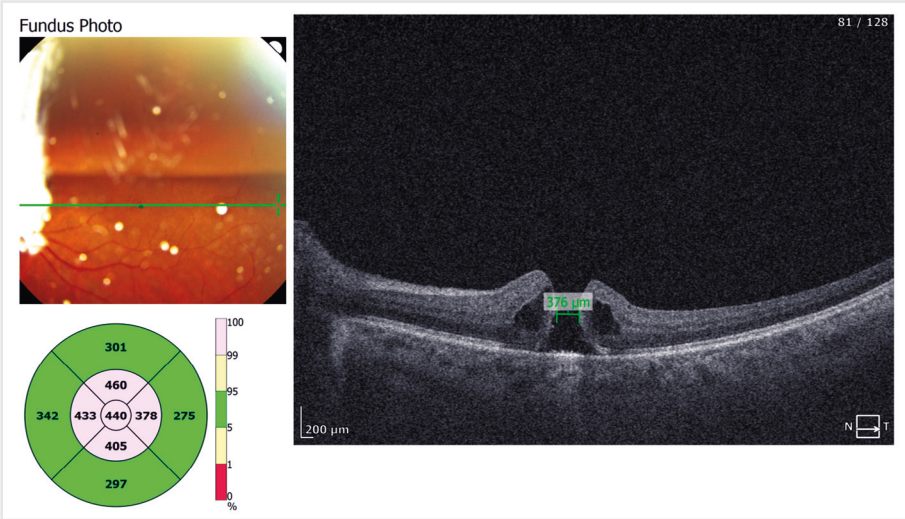

Fig. 2. Parameters of idiopathic macular hole (IMH) at 10 days after vitrectomy (the eye had a less than 50% gas fill; the IMH did not close, but minimum and basal IMH diameters decreased; the edema of MH margin was still observed; best-corrected visual acuity was 0.3).

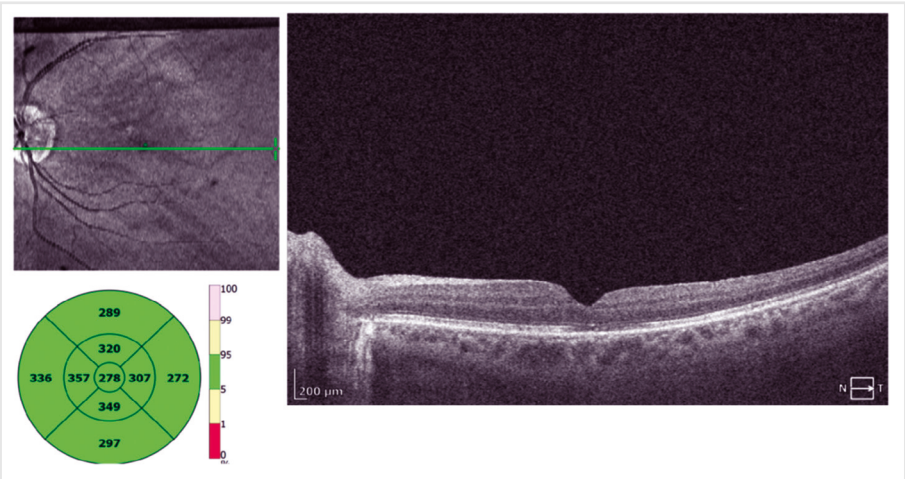

Fig. 3. Macular hole closure pattern after additional C3F8 15% tamponade and two more weeks of face-down positioning. Best-corrected visual acuity was 0.5.

enous retinal detachment 3 weeks after the second vitrectomy, necessitating a third operation.

Our technique for replacement tamponade enables almost complete vitreous cavity gas fill, IOP control during and after the procedure, and normalizing the IOP. In our department, this technique has already been used after vitrectomy with ILM peeling for large MHs [17].

Of note is another beneficial feature of the technique: an accurate concentration of the non-expansile C3F8 (15%) in the eye is achieved, and the gas bubble is long acting. This is another factor that has contributed to MH closure after replacement tamponade.

We believe that the major factors that have contributed to the anatomical success of treatment were a post-vitrec-

tomy decrease in the minimal diameter (and, in most cases, the basal diameter) of the IMH, and the presence of cystic changes involving the MH margin; that is, these persistent MHs had a trend to close.

Because this study was limited by a small sample size, a larger sample is required for a more in depth statistical analysis.

In conclusion, a prolonged C3F8 15% tamponade is an effective method of treatment for persistent IMHs after vitrectomy with classical ILM peeling. The major factors contributing to the closure of persistent IMHs in the presence of additional gas tamponade are (1) a post-vitrectomy decrease in the minimal diameter of the IMH, and (2) the presence of cystic changes in the MH margin.

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Abbreviations: *BCVA, best-corrected visual acuity; ILM, internal limiting membrane; IMH, idiopathic macular hole.*