Combined Subthreshold Laser with Push-Pull Fluid Exchange for Treatment of Refractory Macular Hole

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Abstract
We report on a 55-year-old patient presenting with a 400 μm macular hole which failed to resolve with vitrectomy and internal limited membrane peeling. In accordance with patient wishes to avoid further surgery, subthreshold laser was applied to the macular hole followed by gas exchange with euvoletic C3F8. Successful hole closure was subsequently observed with vision improved by four Snellen lines. Subthreshold laser has several advantages over conventional laser techniques, including reduced collateral thermal damage to the adjacent cells. This case has demonstrated a new use for subthreshold laser, which combined with push-pull technique may be an effective treatment option for persistent MH.

Introduction
Macular hole (MH) is a foveal defect in all layers of the retina and results in a significant decline in central visual acuity. This occurs as a result of persistent vitreomacular adhesion that exerts traction on the fovea. This traction may eventually lead to a MH [1, 2]. Since the 1990s, surgery has been the mainstay of treatment for MHs [3]. Surgical management consists of induction of posterior vitreous detachment, vitrectomy, internal limiting membrane (ILM) peeling, and intravitreal injection of long-acting gas. This surgery neutralizes the tractional
forces of the vitreous, promoting hole closure. Anatomical success rate of this procedure is typically 90–95% [4].

Laser application for treatment of MH has been assessed by various studies. Laser therapy was initially introduced as an experimental technique to prevent retinal detachment [5]. Since 1990, laser application has been used as a combined therapy with vitrectomy surgery. In 1999, Min et al. [6] demonstrated MH closure in eight eyes with vitrectomy combined with a single application of laser to the retinal pigment epithelium (RPE). Patients in this study also exhibited improvement in 3 or more ETDRS lines [6].

Subthreshold laser has been examined in recent years as a therapeutic alternative to conventional laser for the treatment of retinal diseases. “Subthreshold” refers to photocoagulation that does not produce clinical or histologic evidence of retinal damage. “Micropulse” mode is when laser impact is divided into many repetitive micro-second impulses, between which are intervals that enable retinal tissue to cool down. In subthreshold micropulse laser, diffusion of heat to surrounding tissues is minimized and therefore scarring is prevented [7]. This technique is used mostly for macular diseases, such as macular edema secondary to diabetes, retinal vein occlusion, and central serous chorioretinopathy. The advantage of subthreshold laser is that it yields similar therapeutic effects to conventional laser while minimizing thermal damage to adjacent cells [7].

The push-pull technique is often used as a component of retinal hole management and involves replacing intravitreal fluid content with gas in order to increase intraocular volume. In this technique, a 10 mL syringe containing 5 mL of nonexpanding gas attached to a 30-gauge needle is used. The patient’s head is tilted to the side of the eye being treated such that fluid is shifted, and the needle is inserted in an inferotemporal fashion through the pars plana. Initially, slow injection of gas into the vitreous cavity followed by aspiration of the fluid is performed. This procedure is repeated several times until a complete gas bubble fills the vitreous cavity. In this case, we present a novel indication for subthreshold laser, demonstrating success in its use in combination with push-pull fluid exchange for persistent MH closure.

**Case Report**

A 55-year-old male with bilateral myopia (−6 D) presented with an acute decrease in vision in his right eye. His past ocular history included vitrectomy with cataract extraction due to chronic retinal detachment and proliferative vitreous retinopathy. He also had poor vision in his left eye (20/200). At admission, vision was counting finger in his right eye, in which a superior retinal detachment with macula off and a 12 o’clock horseshoe retinal tear was visualized. With this presentation, he underwent same-day pneumatic retinopexy. Two weeks later, the retina was flat, and his vision improved to 20/100. However, OCT imaging revealed a full thickness MH of 400 μm (Fig. 1a). The patient then underwent cataract extraction with vitrectomy and ILM peeling. In 3 weeks follow-up, his vision had not improved further and OCT images confirmed persistence of the MH (Fig. 1b). The patient refused further surgery and was not compliant with face-down positioning. As such, we decided to perform subthreshold laser combined with push-pull technique. Subthreshold laser was applied in circular patterns directly to the RPE within the base of the MH. Three circular burns, each 100 μm, were applied with 5% duty cycle and titration of 50% power (Fig. 2). Laser application was followed by fluid-gas exchange using the push-pull technique with euvoletic C3F8 (Fig. 3). Due to lack of compliance with face-down positioning, no face-down positioning was maintained post-treatment. One (1) month after this procedure, his vision had improved to 20/40 and complete closure of the MH was confirmed (Fig. 1c).
Fig. 1. OCT panel showing the 400 μm MH with an elevation cuff and intraretinal fluid (a), 3 weeks post-vitrectomy demonstrating persistence of the MH with worsening cystoid changes and the intraretinal fluid (b) and 1 month after subthreshold laser and push-pull technique, demonstrating hole closure with foveal contour restored (c).
Discussion

Despite improvements in surgical technique over recent years, about 10% of surgeries to close MHs fail [8]. Risk factors for surgical failure include the size of the hole, absence of an elevated cuff and/or subretinal fluid, delayed treatment, and poor compliance with face-down positioning [4, 8]. Although the literature suggests that face-down positioning increases the likelihood of success, the technique described in this case achieved MH closure with no face-down positioning post-procedure.

Given the small number of patients who present with a persistent MH, the literature surrounding treatment options and outcomes is somewhat limited. Several different surgical options have been proposed for the management of persistent MH, including expansion of ILM peeling, the ILM flap technique, autologous retinal graft, use of an amniotic membrane, autologous blood clot, and use of a lens capsule flap [9]. However, there are very few nonsurgical management options for persistent MH.
In modern practice, the theoretical basis of adding laser is to enhance the stimulation of the RPE to produce cytokines. These cytokines will stimulate glial cells, which will form a template for migration to close the MH [10]. In 2006, Cho et al. [11] showed a significantly better outcome for large MH (>400 μm) closure in patients who underwent combined ILM peeling and laser treatment versus ILM peeling alone. Outcome visual acuity improvement was also greater in the combined treatment group [11]. The use of subthreshold micropulse laser in our case is thought to have achieved the therapeutic effect of conventional laser while minimizing any lethal consequence on the RPE and surrounding cells, thus avoiding scarring [7]. To the author’s knowledge, this is the first report outlining treatment of persistent MH with combined push-pull technique and subthreshold laser.

In vitrectomized eyes, the push-pull technique is appealing as it may be used as an in-office procedure. The exchange of intravitreal fluid content with gas in order to increase the intraocular volume has been shown to be an efficient treatment for vitreous hemorrhage and recurrent rhegmatogenous retinal detachment [12]. Several studies have demonstrated persistent MH closure after combined push-pull technique with conventional laser treatment to the center of the MH [13, 14]. However, these studies required the patient to maintain prolonged face-down positioning. In our case, we describe successful closure without face-down positioning in accordance with patient preferences.

This report describes a technique which may assist the vitreoretinal surgeon in treating patients with persistent refractory MH. The technique described in this report requires a prospective randomize study to further the benefits from this procedure.

Conclusions

From this case, it has been demonstrated that combined push-pull technique with subthreshold laser may be an effective treatment option for persistent MH. The addition of laser may shorten or even eliminate the need for head down posture post-intervention.

Statement of Ethics

This study protocol was reviewed and the need for approval was waived by the Advarra Center for IRB Intelligence (CIRBI). Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

No conflicting relationship exists for any author.

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Author Contributions

Dr. Efraim Berco and Sunil Ruparelia have contributed to this manuscript by means of data collection, manuscript preparation, and manuscript approval. Dr. Nir Shoham-Hazon has contributed to this manuscript by means of conception of the work, manuscript revising, and manuscript approval.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1. Steel DH, Lotery AJ. Idiopathic vitreomacular traction and macular hole: a comprehensive review of pathophysiology, diagnosis, and treatment. Eye. 2013 Oct;27 Suppl 1(Suppl 1):S1–21.
2. Gaudric A, Haouchine B, Massin P, Paques M, Blain P, Erginay A. Macular hole formation: new data provided by optical coherence tomography. Arch Ophthalmol. 1999 Jun;117(6):744–51.
3. Tornambe PE. The evolution of macular hole surgery twenty years after its original description. Am J Ophthalmol. 2009 Jun;147(6):954–6.
4. Ittarat M, Somkijrungroj T, Chan sangpetch S, Pongsachareonnont P. Literature review of surgical treatment in idiopathic full-thickness macular hole. Clin Ophthalmol. 2020 Jul 30;14:2171–83.
5. Schocket SS, Lakhanpal V, Miao XP. Treatment of macular holes with the argon laser. Trans Am Ophthalmol Soc. 1987;85:159–75.
6. Min WK, Lee JH, Ham DI. Macular hole surgery in conjunction with endolaser photocoagulation. Am J Ophthalmol. 1999 Mar;127(3):306–11.
7. Scholz P, Altay L, Fauser S. A review of subthreshold micropulse laser for treatment of macular disorders. Adv Ther. 2017 Jul;34(7):1528–55.
8. Zhao PP, Wang S, Liu N, Shu ZM, Zhao JS. A review of surgical outcomes and advances for macular holes. J Ophthalmol. 2018 Apr 18;2018:7389412.
9. Wu AL, Chuang LH, Wang NK, Chen KJ, Liu L, Yeung L, et al. Refractory macular hole repaired by autologous retinal graft and blood clot. BMC Ophthalmol. 2018 Aug 29;18(1):213.
10. Errera MH, Wickham L, Keane PA, Bird AC, Ezra E. Spontaneous macular hole closure without posterior vitreous detachment in a patient previously treated for diabetic maculopathy. Acta Ophthalmol. 2013 Mar;91(2):e156–7.
11. Cho HY, Kim YT, Kang SW. Laser photocoagulation as adjuvant therapy to surgery for large macular holes. Korean J Ophthalmol. 2006 Jun;20(2):93–8.
12. Lambrou FH, Devenyi RG, Han DP. Fluid-gas exchange after vitrectomy using long-acting gases in an outpatient setting. Arch Ophthalmol. 1988 Oct;106(10):1344.
13. Ohana E, Blumenkranz MS. Treatment of reopened macular hole after vitrectomy by laser and outpatient fluid-gas exchange. Ophthalmology. 1998 Aug;105(8):1398–403.
14. Imano Y, Kamei M, Saito Y, Ohji M, Tano Y. Photocoagulation and fluid-gas exchange to treat persistent macular holes after prior vitrectomy. Ophthalmology. 1998 Aug;105(8):1411–8.