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INDUCTION OF MACULAR DETACHMENT FOR THE TREATMENT OF PERSISTENT OR RECURRENT IDIOPATHIC MACULAR HOLES

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Purpose: To analyze the efficacy of induced macular detachment for the treatment of persistent or recurrent idiopathic macular holes after treatment with one or more standard pars plana vitrectomies (PPVs) with internal limiting membrane peeling.

Methods: This study is a retrospective consecutive case series of 10 patients who underwent a PPV with subretinal balanced salt solution injection from 2011 to 2014 to treat persistent or recurrent idiopathic macular holes. All patients had previously undergone PPV with internal limiting membrane peeling. Visual acuity, ocular examination findings, and optical coherence tomographic images were reviewed preoperatively and postoperatively to assess the anatomical and visual outcomes of this procedure.

Results: Nine of the 10 patients who underwent the procedure had closure of their macular holes postoperatively (90%) and remained closed 6 months postoperatively. Most patients reported a subjective visual improvement. A mean objective visual improvement of 16 letters (Early Treatment Diabetic Retinopathy Study, 0.324 logMAR) was seen between preoperative and 6-month postoperative assessments of all patients (pre = 1.490, post = 1.166; $P = 0.022$). Subgroup analysis of patients with successful closure revealed 20 letters of improvement (0.398 logMAR) in visual acuity (pre = 1.491, post = 1.093; $P = 0.004$). There were no intraoperative or postoperative complications.

Conclusion: In eyes with persistent or recurrent idiopathic macular holes after standard PPV with internal limiting membrane peeling, repeat PPV with subretinal balanced salt solution injection to create a macular detachment may be a viable surgical treatment option. Our results show improved anatomical and visual outcomes postoperatively that compare favorably to other case series describing various surgical treatments for these challenging cases.

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A macular hole is a break in the fovea that occurs most commonly in the elderly population, with a prevalence ranging from 0.2% to 0.8% in the general population.[1] This condition predominantly affects patients older than 65 years with a slight female preponderance and few known associated systemic risk factors.[2] Idiopathic macular holes are most commonly staged from I to IV according to the Gass[3] classification, established in 1988. Stage I holes have been shown to spontaneously close in 60% of cases[4]; however, Stage II to IV have much poorer outcome without intervention. Although newer treatment strategies exist for select cases, e.g., ocriplasmin,[5] the most common treatment of Stage II to IV macular holes is a pars plana vitrectomy (PPV) with or without internal limiting membrane (ILM) peel, gas endotamponade, and varying degrees of face-down positioning, which has a closure rate greater than 90%.[6] The reasons for failure are not completely understood but have been attributed to residual epiretinal membrane traction or poor patient compliance with face-down positioning.[7,8] For failed cases, including persistent or reopened holes, repeat vitrectomy has been performed with reportedly lower closure rates (46.7%) after initial ILM peel.[9]

A novel technique published in a single case report by Oliver and Wojcik[10] was shown to successfully treat a persistent macular hole using a subretinal

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infusion of balanced salt solution (BSS) during PPV, one that had failed to close with two previous PPVs and ILM peels. We present the anatomical and visual outcomes of a case series of 10 patients with persistent or recurrent macular holes that have undergone the same procedure, performed by 3 vitreoretinal surgeons from 2 centers. This is the largest series of cases using this technique reported to date.

Methods

The records of patients who received this surgery by one surgeon (R.H.M.) at St. Michael's Hospital in Toronto, ON, Canada, one surgeon (E.M.D.) at University Health Network, Toronto, ON, Canada, and one surgeon (M.K.W.) at Retina Associates Southwest in Tucson, AZ between March 1, 2011 and July 1, 2014 were retrospectively reviewed. Patients were included in the study if they had an idiopathic macular hole that failed to close or reopened after a PPV with ILM peel within the past year. Patients were also required to follow up for a minimum of 6 months postoperatively to adequately judge the surgical outcome. Of the 12 patients who underwent the procedure, 10 had follow-up for at least 6 months, with the other 2 patients lost to follow-up before we could assess outcome of surgery. Visual acuity, ocular history, and macular hole appearance visualized with spectral domain optical coherence tomography (SD-OCT; Zeiss Cirrus, Carl Zeiss Meditec, Dublin, CA) were obtained before and after the surgical intervention. Macular hole size was determined using a protocol previously described by Benson et al,[11] using digital calipers (Cirrus HD software) to measure the macular hole diameter on preoperative cross-sectional retinal OCT images.

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A.-A. Szigiato and F. Gilani performed a literature review, collected and analyzed data, and drafted the manuscript. R. H. Muni, E. D. Mandelcorn, and M. K. Walsh managed the cases, supervised the cases, and revised the manuscript critically for important intellectual content.

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The procedure is described as follows. A standard three port 25-gauge or 23-gauge PPV approach was used. All patients had a detailed intraoperative examination of the macular area with a flat contact lens and/or the use of an indocyanine green stain to elucidate the extent of the original ILM peel, with exploration using 23-gauge or 25-gauge forceps. In all cases, the surgeon determined that there was no residual perifoveal ILM and no additional membrane that required peeling, with each initial peel wide from arcade to arcade. Puncture retinotomies were made in multiple quadrants within the major retinal vascular arcades, as needed, with a 41/23-gauge rigid retinal hydrodissection cannula (Dutch Ophthalmic, MedOne, Zuidland, Netherlands), with up to 5 punctures overall. Balanced salt solution was infused through the retinotomy into the subretinal space until each bleb connected with the macular hole. This infusion was manually controlled with a syringe and cannula, connected by extension tubing or connected to the viscous fluid infusion apparatus of the Constellation vitrectomy machine (Alcon Laboratories, Inc., Fort Worth, TX) at a setting of ~18 to 20 mmHg, enough to obtain a steady stream of BSS when tested outside the eye. After total macular detachment was achieved with variable degrees of detachment extending beyond the major posterior vascular arcade but never out to the equator, there was no further manipulation of the macular area in 8 cases (R.H.M. and E.M.). M. K. Walsh would additionally massage the macular retina gently with a diamond dusted scraper (Tano brush, Synergetics, O'Fallon, MO) with gentle teasing of the edges of the macular hole also with 25-gauge Eckardt forceps in 2 cases (Dutch Ophthalmics). An air–fluid exchange was performed without draining the subretinal fluid, after which 12 to 15% C3F8 gas was injected into the vitreous chamber (see **Video, Supplemental Digital Content 1**, demonstrating induced macular detachment technique; http://links.lww.com/IAE/A428). Patients were instructed to maintain face-down positioning for 1 week. Patients were followed up 1 day, 1 week, and up to 12 months, as needed after surgery. Continued closure of the hole was confirmed by OCT performed at approximately 6 months postoperatively (Table 1) and with clinical observation. The macular detachment was resolved on the postoperative Day 1 visit in all patients. The best-corrected visual acuity was assessed at 6 months.

Results

A total of 4 male and 6 female patients had at least 6-month postsurgical follow-up, with an average age

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Table 1. Visual Acuity and Surgical Outcomes Before and After PPV With Internal Limiting Membrane Peel and Subretinal Infusion of BSS

Patient	Sex/Age (years)/ Lesion, Eye	Previous Surgery/ Time to PPV-IMD (months)	Lens Preoperative	Preoperative VA/LogMAR	Postoperative VA/LogMAR	Change in VA (Early Treatment Diabetic Retinopathy Study Letters/LogMAR)	Hole Diameter (μm)	Hole Closed	OCT Confirming Closure (months)
1 (VF)	F/70/OD	PPV w. MP/11	Pseudophakic	CF 4–5 ft/1.648	CF 3–4 ft/1.756	–5.5/0.109	775	Y	6
2 (GF)	M/86/OD	PPV w. MP/12	Phakic	CF 4–5 ft/1.648	20/200/1.000	32.4/–0.648	441	Y	11
3 (AY)	F/60/OD	PPV w. epiretinal membrane and ILM peel/11	Pseudophakic	CF 3 ft/1.824	20/400/1.301	26.1/–0.523	—	Y	2
4 (ZJ)	F/72/OD	PPV w. MP/3	Pseudophakic	20/150/0.875	20/100/0.699	8.8/–0.176	775	Y	5
5 (AJ)	M/73/OS	PPV w. MP/5	Phakic	20/800/1.602	20/600/1.477	6.2/–0.125	334	Y	5–6
6 (MU)	M/73/OS	PPV w. MP/4	Pseudophakic	20/600/1.477	CF 3 ft/1.824	–17.3/0.347	584	N	—
7 (MB)	F/75/OS	PPV w. epiretinal membrane, cataract surgery/2	Pseudophakic	20/400/1.301	20/200/1.000	15.1/–0.301	401	Y	7
8 (MR)	M/78/OD	PPV w. MP/1	Pseudophakic	CF 3 ft/1.824	20/200/1.000	41.2/–0.824	658	Y	6
9 (DJ)	F/71/OD	PPV w. MP/33	Pseudophakic	20/200/1.000	20/80/0.602	19.9/–0.398	1,097	Y	7
10 (LS)	F/69/OS	PPV w. MP/1	Phakic	CF 4 ft/1.699	20/200/1	35.0/–0.699	815	Y	11
Average (closed)	Age: 72.7			1.491 (logMAR)	1.093 (logMAR)	16.2/–0.398 (P = 0.004)	662.0		6.7
Average (all)	Age: 72.7			1.490 (logMAR)	1.166 (logMAR)	19.9/–0.324 (P = 0.022)	653.3		

PPV-IMD, pars plana vitrectomy with induced macular detachment; PPV w. MP, pars plana vitrectomy with membrane peel; CF, counting fingers; Y, yes; N, no.

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of 73 years. There were two patients with recurrent macular holes and eight with persistent holes. Cataract extraction with IOL implantation was previously performed on seven eyes. All patients had one previous PPV with ILM peel, with an average duration of 8 months from primary surgery to PPV with induced macular detachment. Visual acuity in the affected eye before intervention was poor, with patients having approximately 20/200 to counting fingers vision (1.490 logMAR). Average macular hole diameter was measured to be 653.3 μm. Nine of 10 patients had stable closure of the macular hole after an average of 6 months after surgery, which was confirmed with OCT and clinical observation (see **Figure 1, Supplemental Digital Content 3**, http://links.lww.com/IAE/A430). Most patients reported a subjective improvement in vision. A mean objective visual improvement of 16 Early Treatment Diabetic Retinopathy Study letters (0.324 logMAR) was seen between preoperative and 6-month postoperative assessments of all patients, as measured by Snellen chart (pre = 1.490, post = 1.166; P = 0.022). Subgroup analysis of patients with successful closure revealed a 20 Early Treatment Diabetic Retinopathy Study letter improvement (0.398 logMAR) in visual acuity (pre = 1.491, post = 1.093; P = 0.004). Among the patients with successful closure, all but 2 had postoperative vision better than 20/400. Visual acuity worsened in one patient whose macular hole failed to close, from 20/600 to counting fingers at 3 ft (17 letters, 0.347 change in logMAR). There were no intraoperative or postoperative complications, such as retinal detachment or endophthalmitis.

Discussion

The mechanism explaining hole closure after vitrectomy with ILM peel may be multifactorial. It is believed that removal of the vitreous and ILM may reduce tangential traction on the hole and allow the edges to be brought together,[12,13] and that the peeling of the ILM also softens the retina, making it more compliant thus allowing the edges of the hole to come together. Histologically, closure of full-thickness macular holes is associated with a healing response mediated by the proliferation of glial cells, notably fibrous astrocytes and Müller cells.[14] Macular holes that fail to close using PPV are hypothesized to have an additional factor that prevents the approximation of hole edges, such as a rigid underlying retina. Intraoperatively, we have noted that the macular tissue in eyes that have previously had ILM peeling is stiffer and more rigid than during the initial vitrectomy during which time the ILM was peeled. We hypothesize that subretinal BSS reduces tension and stiffness intrinsic to the retina thus making it more compliant and allowing the edges of the hole to reapproximate. Moreover, subretinal injection of BSS separates the tight adhesions of the retina and the retinal pigment epithelium as can be seen at the edge of a chronic macular hole on the OCT. It is important, when injecting the BSS during the procedure, to ensure that the retinal–retinal pigment epithelium adhesions are completely lysed 360° around the macular hole so that the edges will reapproximate and allow the hole to close. This may require up to five puncture sites as outlined in the Methods section.

With this macular detachment technique for recurrent or persistent idiopathic macular holes, most patients with successful hole closure experienced a substantial subjective and objective improvement in their vision. This could be attributed to a reduction in the size or disappearance of their scotomas with improved fixation stability.[14,15] Partial restoration of central vision was observed with this technique as patients demonstrated an improvement in objective visual acuity, a finding not observed in the first case report by Oliver and Wojcik.[10]

Other novel techniques for chronic macular hole closure have been published including radial retinal incisions to the margin of the macular hole[16] and the use of heavy silicone oil with or without autologous platelet concentrate.[17] It is difficult to determine which method is ideal as most techniques have been described in studies using small numbers of patients. A study by Da Mata et al resulted in two of three holes closed with silicone oil[18] and another by Rizzo et al[19] closed two of two with heavy silicone oil. A larger study by Hillenkamp et al[17] of 28 eyes noted no difference in closure rate between gas and silicone oil tamponade, with or without platelet concentrate, but found lower rates of closure with flat holes, identified by a lack of a cuff of subretinal fluid at the margin of the hole on preoperative OCT. One of eight such holes was closed with standard reoperation in the previously mentioned study. Of the estimated 8 "flat" macular holes in our series based on the definition of Hillenkamp et al, 7 were successfully closed after induced macular detachment (87.5%). For all macular holes, the closure rate of 90% shown in this case series is also substantially higher than the reported 46.7% closure rate of PPV with additional ILM peeling for recurrent or persistent idiopathic macular holes after previous vitrectomy with ILM peeling.[9] The reasons for initial failure of PPV with ILM peel in this case series may have been attributed to poor compliance with face-down positioning or the

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flat configuration of the majority of the macular holes.[7,17]

In conclusion, induced macular detachment during vitrectomy with subretinal injection of BSS may be a viable alternative surgical technique for these challenging cases and may be particularly effective for closing flat macular holes. This technique should also be considered in any case where a 360° ILM peel with a 2-disc diameter radius was previously performed, as the retina may become intrinsically stiff after ILM peeling.

Key words: macular hole, subretinal BSS infusion, persistent/recurrent macular hole, vitrectomy.

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