INTRODUCTION
A macular hole is a retinal break located in the macula. It usually exhibits early central visual loss, metamorphopsia and central scotomas. Women develop macular holes more commonly than men, typically in the 5th decade.1 Although mostly idiopathic, macular hole can develop secondary to uveitis, retinal detachment, cataract surgery, ocular trauma and photocoagulation. The diagnosis of a macular hole was traditionally made on clinical grounds. In 1988, Gass proposed a classification for idiopathic macular holes.2 Stage 1 is a pre-macular hole; stage 2 is a full thickness macular hole (FTMH) of < 400 microns diameter; stage 3 is a FTMH of > 400 microns diameter; and stage 4 denoted a stage 3 macular hole associated with posterior vitreous detachment (PVD). Some authors have designated as stage 0 the asymptomatic eye when the contralateral eye has been diagnosed with FTMH.

Optical coherence tomography (OCT) has gradually assumed an important role for diagnosing macular hole as well as for postoperative assessment of anatomical closure. Spectral domain OCT (SD-OCT) has become crucial in the preoperative diagnosis of macular hole, assessment of its dimensions, calculation of macular hole index (used in predicting the postoperative closure rates) and in postoperative follow-up to confirm the hole closure.

A strictly anatomic OCT-based classification for diseases of the vitreomacular interface (VMI),3 divided FTMH into small (< 250 microns), medium and large (> 400 microns), and included vitreomacular adhesion (VMA), vitreomacular traction (VMT) in the classification.3 VMA is an asymptomatic elevation of the cortical vitreous above the retinal surface, with the vitreous remaining attached within a 3 mm radius of the fovea, which is equivalent to stage 0. If there are associated detectable retinal anatomic changes detected on OCT, the eye is classified as having VMT, which is stage 1 in the Gass classification.

The basement membrane of Muller cells, the internal limiting membrane (ILM) has been suggested to be involved in pathogenesis of macular hole by disturbing the vitreomacular interface, causing vitreomacular traction; and subsequently, resulting in macular hole.4 This implied that once ILM is peeled off, it will remove the traction overlying the macular area and halt the process of hole formation. ILM is a thin and transparent acellular membrane, which is 138 ± 80 nm thick at the foveal center.5 Peeling of this almost indistinguishable

ABSTRACT

Objective: To evaluate the anatomical success of stage 3 and 4 macular hole surgery after removal of internal limiting membrane (ILM) with the help of Indocyanine green (ICG).

Study Design: An experimental study.

Place and Duration of Study: LRBT Tertiary Care Eye Hospital, Karachi, October 2015 to August 2016.

Methodology: Twenty patients with stage 3 and 4 macular hole (confirmed by spectral domain optical coherence tomography) underwent standard 3 ports pars plana vitrectomy. Staining of ILM was performed with the help of 0.5% ICG to aid in visualization. ILM was removed by using intraocular forceps in circular fashion. Finally, gas fluid exchange with internal tamponade of SF6 20% was performed. Postoperative face down posture was maintained for seven days. Patients were followed-up for 8 months and assessment of macular hole closure was done using SD-OCT.

Results: After a follow-up of 8 months, macular hole was closed in 17 eyes (85%) and vision had improved in 6 patients. Postoperative complications included cataract, hyphema and vitreous hemorrhage.

Conclusion: Surgery for stage 3 and 4 macular hole with ILM peeling has high anatomical success rate. Final visual acuity is dependent on preoperative macular hole stage and visual acuity at presentation.

internal limiting membrane (ILM) of the retina has been recommended to increase the postoperative anatomical and functional visual outcome of macular hole surgery. This is very challenging because the ILM is difficult to grip and the size of the peel is difficult to define. To make ILM visible a vital dye, such as indocyanine green (ICG), is used to stain the ILM, thereby aiding in its visualization and subsequently this reduces the time of ILM removal. ICG has also been shown to improve surgical outcomes by attaining a higher closure rate in macular hole surgery following a single surgical procedure. Different dyes are in use such as indocyanine green (ICG), Brilliant blue, Trypan blue, etc. Among these, ICG is seen to have the greatest propensity for staining ILM. Closure of idiopathic macular hole has reported in 58% of the cases using this technique. Over the years, however, the role of ILM removal in success of macular hole surgery has different experiences, as some consider this a critical and important step, while others have noticed no extra benefit in postoperative outcomes. This study was conducted to evaluate the anatomical success of stage 3 and 4 macular hole surgery, demonstrated by hole closure on SD-OCT, after removal of internal limiting membrane with the help of ICG staining.

**METHODOLOGY**

This was a prospective experimental study which included 20 eyes of 20 patients, who presented with stage 3 and 4 macular hole. Patients were enrolled using non-probability convenience sampling technique. Subject recruitment started from 1st October 2015 and patient recruitment was done till 31st December 2015. Follow-up time was 8 months ending on 31st August 2016. The Hospital Ethics Committee approval was taken prior to the commencement of this study. Complete ocular history was taken to rule out any past ocular surgery, ocular trauma, past history of uveitis or any other ocular disease which can lead to secondary macular hole. Preoperative examination included best corrected visual acuity, slit lamp examination with Watzke-Allen test, intraocular pressure (applanation tonometer). Fundoscopy for posterior pole and peripheral retina was performed with Goldmann 3 mirror lens. Spectral domain optical coherence tomography (Spectralis, Heidelberg Engineering) was used to confirm the diagnosis and stage of macular hole. Written informed consent was taken from patients who fulfilled the criteria for the study, after explanation of its benefits and risks.

Pars plana vitrectomy 25-gauge was performed by a single vitreoretinal surgeon. After completion of core vitrectomy, posterior vitreous detachment was induced (if not already done) by suction of vitrectomy cutter placed closed to optic disc. ICG powder 25 mg was dissolved in 0.5 ml of sterile saline which is diluted in 4.5 ml of balanced salt solution to make up a 0.5% solution; 0.2 - 0.4 ml of this solution was used to stain the ILM. This was left there for approximately 2 minutes and then washed away. Peeling of ILM around the macular hole was done in circumferential manner, size of which was approximately 2 disc diameters. ILM was removed by using flat tipped vitreo-retinal forceps which is used to grasp ILM, lifting it to make a break in it. Once an edge is formed, it is then removed in a circular pattern. Vitreous was cleaned from the periphery and an iso-volumic concentration of SF6 (20%) was injected at the end of the surgery after air-fluid exchange. Post-operative face down posture was maintained for 7 days. All patients were examined on first postoperative day, first week, first month, third month, fifth month and eighth month. On every visit, complete ocular exam was performed, which included visual acuity using the Snellen chart, anterior segment examination, IOP assessment, posterior pole evaluation, and assessment of macular hole closure using SD-OCT. Complications were recorded and managed accordingly.

IBM SPSS Statistics 21 was used to analyze the data. Frequencies with percentages were used to present qualitative variables and mean ±SD were calculated for the quantitative variables. Macular hole closure rate was stratified with respect to macular hole stage and gender, while visual improvement was stratified with respect to macular hole stage. Fisher's Exact tests were used to calculate the p-value, and a value of ≤0.05 was considered statistically significant.

**RESULTS**

The study was started with 26 patients enrolled, but 6 of them were lost to follow-up and did not complete their 8 months of postoperative assessment. They were excluded from the final analysis.

In total, 20 patients were included in this study, comprising of 16 females (80%) and 4 males (20%). Mean age was 62.45 ±1.46 years (range 54 - 70 years). Out of 20 patients, 17 patients (85%) had stage 3 macular hole, while 5 patients (25%) had stage 4 macular hole. Preoperative VA was 0.136 ± 0.079 (in Snellen decimal notation) which improved to 0.203 ±0.154 postoperatively. All patients were presented with complains of decreased central vision or a central scotoma, and the diagnosis of macular hole was confirmed by SD-OCT.

During the follow-up time, the macular hole was closed at the end of 8 months follow-up in 17 patients (85%), while three patients (15%) did not show closure of the macular hole. Stratification was done to assess the macular hole closure rate with regard to macular hole stage and gender, presented in Tables I and II. The
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Table I: Macular hole closure rate with regard to macular hole stage.

<table>
<thead>
<tr>
<th>Macular hole closure</th>
<th>Macular hole stage</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage 3</td>
<td>Stage 4</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Yes</td>
<td>15 (75%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (75%)</td>
<td>5 (25%)</td>
</tr>
</tbody>
</table>

p-value = 0.009 (statistically significant).

Table II: Macular hole closure rate with regard to gender.

<table>
<thead>
<tr>
<th>Macular hole closure</th>
<th>Gender</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (20%)</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>Total</td>
<td>4 (20%)</td>
<td>16 (80%)</td>
</tr>
</tbody>
</table>

p-value = 0.491

Table III: Improvement in visual acuity with regard to macular hole stage.

<table>
<thead>
<tr>
<th>Visual acuity improvement</th>
<th>Macular hole stage</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage 3</td>
<td>Stage 4</td>
</tr>
<tr>
<td>No</td>
<td>8 (40%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Yes</td>
<td>7 (35%)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>15 (75%)</td>
<td>5 (25%)</td>
</tr>
</tbody>
</table>

p-value = 0.083

results showed a statistically significant association of macular hole closure with a lower macular hole stage.

Improvement in visual acuity was noted in 6 patients (30%), unchanged in 10 patients (50%), while 4 patients (20%) had worsening of vision, which included 3 patients (15%) of unsuccessful hole closure. All patients who had preoperative visual acuity of 6/60; experienced some improvement in their vision postoperatively. The effect of macular hole stage on the improvement in visual acuity was also assessed for better interpretation of results (Table III). However, unlike the association seen between the macular hole stage and macular hole closure rate (p = 0.009), the p-value obtained for this association was not statistically significant (p<0.083). Three patients (15%) developed cataract later on, two patients (10%) had hyphema which resolved within seven days postoperatively and only one patient (5%) developed vitreous hemorrhage which needed vitrectomy.

**DISCUSSION**

Collagen and cellular elements are responsible for creating tangential traction on either side of ILM, which in turn creates macular hole. Myofibroblastic contracture of ILM is an important factor for the enlargement of macular hole. Gass proposed that the initiating factor is the degeneration of Muller cone - vitreous cortex interface which then leads to glial migration, proliferation and contraction.

In the last 20 years, success rate of macular hole surgery has improved greatly, which in turn reflects upon the enhancements of the surgical instrumentation and technique. In 2000, Mester and Kuhn revealed that ILM peeling improved the anatomical outcomes of macular hole surgery to 96% and functional success up to 81%, which in contrast to 77% and 55% respectively in surgeries where ILM peeling was not performed. Yet, there were other reports where the authors found no improvement with ILM peeling. But largely, the researchers supported the idea that ILM peeling was important in the success of macular hole surgery. In 2014, Cornish et al. carried out a meta-analysis of randomized control trials comparing vitrectomy for macular hole with and without ILM peel showed a statistically superior closure rate in cases where ILM peeling was done.

Use of ICG in staining the ILM, which facilitates its better visualization, is also recommended by authors. While it affords excellent visualization of the ILM on one hand, on the other hand it has been shown to have its toxic effects on the retina as well, if the concentration, osmolarity or exposure time exceeds a certain safe limit. Retinal toxicity of ICG can be avoided by using the recommendations proposed in the American Academy of Ophthalmology Meeting in 2001 (ICG solution concentration of 0.5%, osmolarity of 270 mOsm, retinal contact time of 1-3 minutes).

The purpose of this study was to assess the closure of stage 3 and 4 macular hole after ILM peeling and our result showed 85% anatomical success rate which is comparable with other studies. A few recent studies have reported anatomical success rate of 100%, but these could not be directly compared with this study since the parameters do not match with our study; primarily because the study participants are stage 2 and 3 macular hole patients. The authors suggest that this may circuitously reflect the improved healthcare system and/or improved patient awareness in developed countries where a macular hole patient is able to get surgical treatment in earlier stages of the disease, however this is subject for a different study.

Improvement in visual acuity was achieved in about 30%, which are very close to a study done in 2005 by Posselt et al. Postoperatively, the patients developed cataract, hyphema and vitreous hemorrhage, which are consistent with the complications observed by other authors conducting similar studies. Final visual acuity in these cases was considerably dependent on factors such as preoperative macular hole stage and pre-operative visual acuity; an association that was also seen in the current study.

**CONCLUSION**

Good rate of anatomical success of macular hole surgery, confirmed on SD-OCT, was observed after ILM peeling. ICG is an important tool for staining the ILM, which helps in its visualization and thus reduces the operative time. Final visual acuity is dependent on pre-operative macular hole stage and visual acuity at presentation.
REFERENCES


