Vitrectomy with Internal Limiting Membrane Peeling for Diffuse Tractional Diabetic Macular Oedema

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Abstract: Aim: To determine the efficacy of internal limiting membrane (ILM) peeling during vitrectomy for diffuse tractional macularoedema regarding postvitrectomy epiretinal membrane (ERM) development and visual outcomes. **Patients and methods: This** study was a prospective, institutional, interventional, comparative case series of consecutive eyes with diffuse tractional diabetic macular oedema at the Nour –EL-Hayat eye center (Cairo). Series of 40 eyes of 31patientsunderwent pars planavitrectomy with peeling of internal limiting membrane for diffuse tractional diabetic macular oedema during the study period. Patients who underwent surgery between January 2014 to March 2015 with a follow -up period of at least 6 months after the initial vitrectomy, the availability of good –quality SD OCT images obtained at the follow –up visits to determine the presence of an ERM. **Results:** At 6 months there was a median 200µ decrease from baseline in the central subfield thickness (P<0.005). The mean change in the central subfield macular thickness was -150µ (SD± 130.56). There was one case developed iatrogenic break during removal of posterior vitreous and treated by endodiathermy, of greatest importance, 1 eye developed a vitreous hemorrhage treated by conservative treatment after B scan was done, and 1 eye developed a retinal detachment. All complications were successfully managed. 15 out 40 eyes (37.5%) underwent cataract surgery with IOL implantation within 6 months of pars plan a vitrectomy 9 out of 15 (60%) patients showed improvement. **Conclusion:** ILM peeling achieved higher anatomic success with a reduced need for additional surgical interventions and or event postoperative ERM formation that might result in subsequent visual loss.
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Introduction

The internal limiting membrane (ILM) is a very thin and transparent a cellular membrane on the surface of the retina. It is adjacent to Muller cell foot plates (lamina raraexterna (0.03-0.06 µ). The lamina densa is thinnest at the fovea and thicker in the posterior pole than at the equator or vitreous base, it plays an important role in the early stages of retinal development; however, its function in adults is not yet understood. [(1), (2)] Because the ILM rests on the retinal nerve fiber layer (RNF)-ganglion cell layer (GCL) complex, it can theoretically damage these layers during the process of peeling. Because RNF-GCL complex integrity has a significant bearing on postoperative visual acuity. [(3)] Diabetic macular edema (DME), caused by intraretinal fluid accumulation in the macula, is the most common cause of visual impairment in diabetic patients. The pathogenesis is multifactorial and includes breakdown of the blood-retinal barrier (BRB) secondary to weakened capillary intercellular tight junctions, loss of pericytes, and leukostasis in the retinal vessels and vasoactive factors such as vascular endothelial growth factor-A (VEGF-A), various growth factors, and matrix metalloproteinases. Abnormalities at the vitreoretinal interface (the posterior vitreous cortex and ILM) have also been found to promote DME. Specifically, the hyaloid becomes taut and thickened with induced cellular proliferation and production of cytokines. The fovea and the vitreous base, are the points at which the posterior vitreous cortex and the ILM have the strongest attachment. Advanced Glycation End-Products (AGEs), accumulated in the posterior vitreous cortex, increase cross-linking of collagen fibrils and induce structural changes in the posterior hyaloid that strengthen vitreomacular adhesions between the posterior hyaloid and ILM. This is further aggravated by AGE receptors (RAGEs), which are attached to the footplates of the Müller cells and extend to the external limiting membrane (ELM). RAGE activation by the binding of AGEs stimulates VEGF upregulation and retinal vessel permeability, further exacerbating DME. [(4)]

Patient and methods:

All patients provided written informed consent for each surgical procedure after explanation of the procedure. Ethical committee approval form the Faculty of Medicine, Al Azhar University, was obtained. A detailed clinical history that included the onset of visual disturbances and history of ocular diseases was obtained at the initial visit at which diabetic macular oedema was detected. Full history including medical history (duration of diabetes, controlled or not) other relative systemic diseases,

family history of diabetes, glycosylated hemoglobin and serum lipid profile were controlled. All patients underwent a full ophthalmic examination including measurement of decimal visual acuity and slit lamp examination and indirect ophthalmoscope. Pre –interventional fundus fluoresce in angiography using Topcon TRC 501X retinal camera, SD OCT to document macular thickness, configuration of macular oedema, vitreomacular traction and an taut posterior hyaloid. This study was a prospective, institutional, interventional, comparative case series of consecutive eyes with diffuse tractional diabetic macular oedema at the Nour –EL-Hayat eye center (Cairo). Patients who underwent surgery between January 2014 to March 2015 with a follow -up period of at least 6 months after the initial vitrectomy, the availability of good –quality SD OCT images obtained at the follow –up visits to determine the presence of an ERM. The exclusion criteria were lens opacity precluding OCT, massive hard exudates in the fovea, only focal macular oedema, history of previous vitreoretinal surgery, macular ischaemia and monocular patient. Subsequent intraoperative assessment included careful documentation of any surgical complications, instrumentation, and the gas used as the tamponading agent.

Surgical procedure

Standard surgical technique was followed for all patients, which involved a standard 3- port, 23 gauge pars planavitrectomy with triamcinolone –assisted posterior vitreous detachment induction. ILM blue (Brilliant blue G) dye (fig 1) was injected under air and left for 30 seconds to one minute, air fluid exchange were done and the excess dye was removed, a scratch was made in the stained ILM by 23 gauge needle and flap was initiated, ILM peeling was completed using 23 gauge ILM forceps.

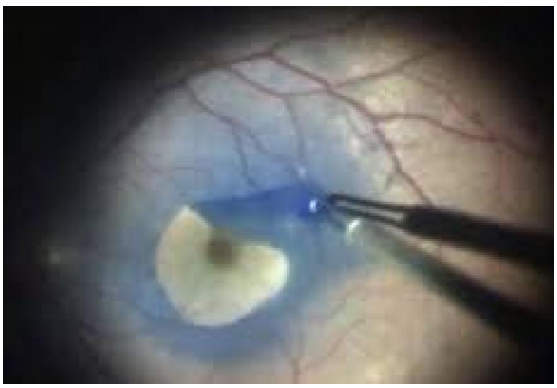


Fig (1): Staining ILM by brilliant blue G

After ILM peeling and examining the peripheral retina, a complete fluid- air exchange was carried out and trocars were removed and conjunctival diathermy to close the sclerotomy site. Uniform protocol was followed for postoperative review at one week, one month, 3 months, and 6 months follow – up. At each visit, best corrected visual acuity (BCVA), intraocular pressure, lens status, intraocular and post ocular complications and anatomical status of the retina.

Statistical Analysis

We calculate sample size according to Raosoft and All statistical calculations were done using SPSS (statistical package for the social science version 20.00) statistical program. at 0.05, 0.01 and 0.001 level of probability. Quantitative data with parametric distribution were done using Analysis of variance t test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered non significant (NS) at the level of > 0.05, significant at the level of < 0.05, 0.01 and highly significant at the level of < 0.001. Pearson linear correlation coefficient (r) was estimated to show the relationship between quantitative parameters.

3. Results

This study was a prospective series of 40 eyes of 31patients (table 1) underwent pars planavitrectomy with peeling of internal limiting membrane for diffuse tractional diabetic macular oedema during the study period. The mean age was 60.11± 5.67years with male to female ratio of 1.00:1.81 (11/40 men 35.5%, and 20/40 female 64.5%). The range of the duration of diabetes mellitus (years) in type I (14- 35) and mean ±SD 19.7±6.183 (P 0.374) and the range in Type II (10.000 -40.000) and mean ±SD 17.500 ± 7.811(P.374). Distribution of the study group according to the type of diabetes mellitus, where type I (6 right eye and 4 left eye 25.00%) and Type II (12 right eye and 18 left eye 75%). The percentage of eyes of patients who had associated systemic conditions among the study group, seven cases had hypertension 17.5%, one case with hypertension and ischemic heart disease 2.5%, one case with renal impairment and anemia2.5% (two eyes), one case with hepatitis C virus 2.5% and one heavy smoker case2.5%. Preoperative mean visual acuity in logarithm of minimal angle of resolution was (decimal notation) 0.1 (6/60) (SD±0.0871) ranged from 0.005 to 0.500 with mean of 0.083 in all patients. Mean BCVA (table2) was 0.01(6/60 Snellens equivalent) which improved after ILM peeling to 0.60 (6/24 Snellens equivalent) (P < 0.05) corresponding to 4 line improvement, vision improved to 0.1(SD± 0.098) to 0.3 (SD±0.10) at 4 weeks to 6 months post operatively. Mean postoperatively change in BCVA from base line was 0.0125(SD± 0.071) at 4 weeks and 0.043(SD±0.91) at 6 month (P0.003). There was a negative correlation number between of pre injection of anti VEGEF with the mean change of BCVA at 6 months follow up (p =0.42).

Careful measurements and documentation of pre- and postoperative intraocular pressure by applanation to nometry revealed an increase of 0.40 mmHg from mean preoperative intraocular pressure of 14.5 ± 1.45 mmHg 15.4 ± 3.5 mm Hgat6 months postoperatively (P 0.5). Mean pre-operative retinal central subfield macular thickness at baseline was 450.71 µ (SD±124.067). At 6 months there was a median 200µ decrease from baseline in the central subfield thickness (P<0.005). The mean change in the central subfield macular thickness was -150µ (SD± 130.56). There was one case developed iatrogenic break during removal of posterior vitreous and treated by endodiathermy, of greatest importance, 1 eye developed a vitreous hemorrhage treated by conservative treatment after B scan was done, and 1eye developed damage to external limiting membrane. All complications were successfully managed. 15 out 40 eyes (37.5%) underwent cataract surgery with IOL implantation within 6 months of pars plana vitrectomy9 out of 15(60%) patients showed improvement.

At 12 months, 5eyes (12.5%) received additional argon laser photocoagulation; 3eyes were injected with combined subtenon's corticosteroids with intravitreal bevacizumab. Median OCT central subfield thickness at 12 months was 240µ (SD±35) with the median change from the preoperative OCT measurement being a decrease in thickness of200µ.

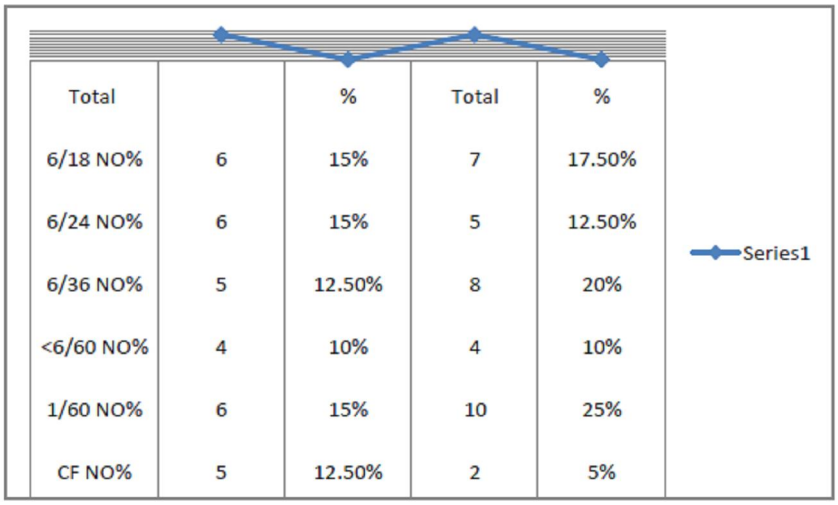
Table 1. Patients' Demographic Data

NO	Percentage	P	
Male	1133.5%	0.65†	
Female	2064.5%		
Age groups			
M±SD	60.11±5.67		
Laterality			
Right eye	18	(45%)	0.35 †
Left eye	22	(55%)	
Duration of symptoms (days)			
Mean	120.3	0.50≠	
Range	28-365		
Mean follow up			
Mean	160.2		
Range	35-290	0.66 ≠	
Duration of diabetes			
Type I	(14.35y) (mean ±SD19.7±6.18)		
Type II	(10.40) (mean ±SD17.5±7.81		
Systemic associated diseases	12 eyes (30%) (P 0.000)		HS

≠ Mann-Whitney U test †Chisquartest HS highly significant

Table2: Pre and Post -Operative Visual Acuity

Total		%	Total	%
6/18 NO%	6	15%	7	17.50%
6/24 NO%	6	15%	5	12.50%
6/36 NO%	5	12.50%	8	20%
<6/60 NO%	4	10%	4	10%
1/60 NO%	6	15%	10	25%
CF NO%	5	12.50%	2	5%



Discussion:

Tangential and anteroposterior traction on the layers of the macula are considered the primary pathologies behind occurrence of refractory macular oedema. Study considered it in patients who has been treated with focal / grid photocoagulation and persists. [(5)]

In this study35 eyes (87.5%) showed marked decrease in mean central macular thickness with marked improvement in macular volume compared to pre – operative values. This anatomical improvement is attributed to surgical removal of the posterior hyaloid which causes a hydrostatic pressure gradient and relieves extravascular leakage and oedma. [(6)] This study is in accordance to Shah et al., [(7)]. Moreover, vitrectomy enhances the intraocular oxygen pressure as it passes from arterial blood into the fluid in the vitreous cavity. Vitrectomy also removes substances that enhance vascular permeability and removal of the posterior hyaloid after injection of the TA which ensure complete removal of cortical vitreous. The antioedema effect of TA was minor at total drug aspiration during repeated fluid air gas exchange, besides, the half –life of TA is shorter in vitrectomized

eye (1.57days) compared to non vitrectomizedeye (2.89 days). [8, 9] ILM peeling was found to enhance the functional and anatomical outcome by a significant magnitude, even preventing recurrences; thus, clearly establishing the fact that peeling the ILM has a definite advantages. [10] Onecase (2.5%) developed ERM during the period of follow up. This result is correlated with the result of Yamamoto et al in 2001, they reported 3% occurrence of ERM after PPV. [11] The preventive effects of ILM peeling are attributed both to complete removal of cellular components on the ILM surface that might develop into an ERM and to removal of the scaffold that promotes cellular proliferation. TA staining also was related to prevention of postoperative ERM. [12] Onecase (2.5%) developed damage to external limiting membrane. (fig2-7)

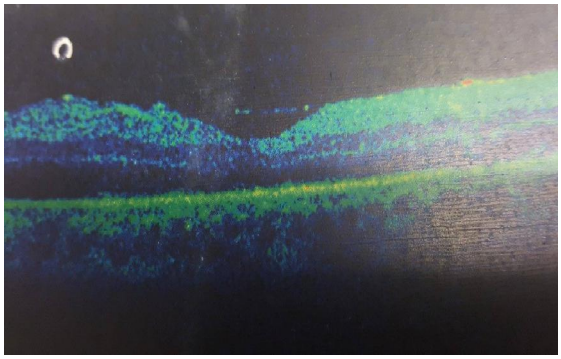


Fig (2) PRE retinalfibrosis with focal thickening sparing fovea.

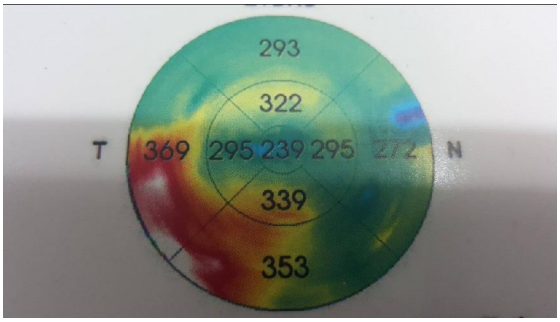


Fig (3): retinal thickening 239 µ

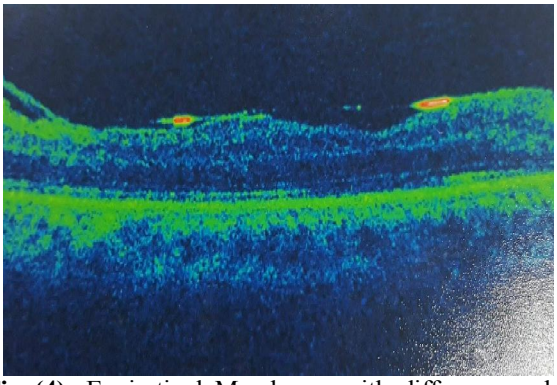


Fig (4): Eepiretinal Membrane with diffuse macular edema

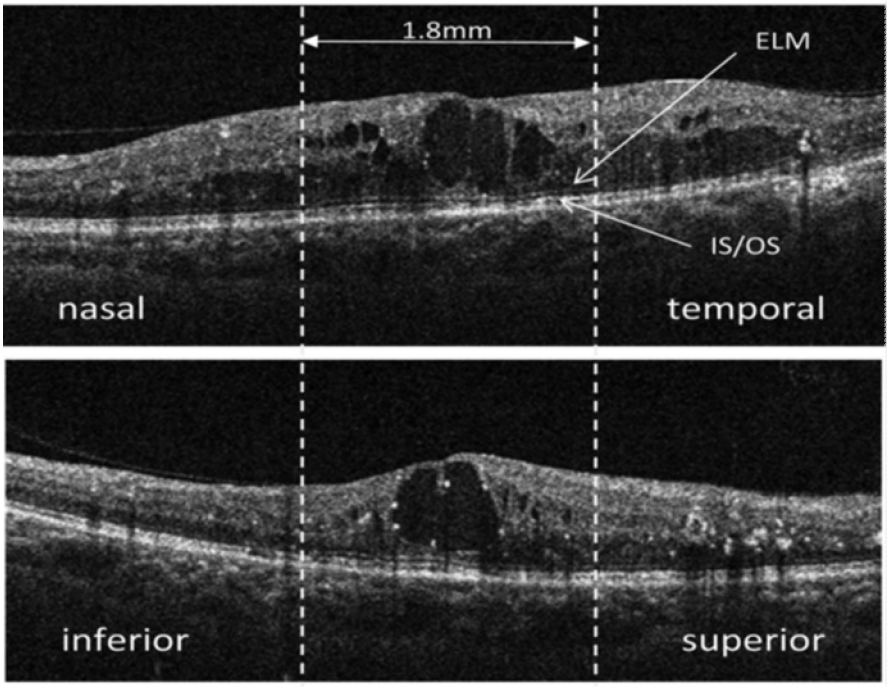


Fig (5): Diffuse macular oedema

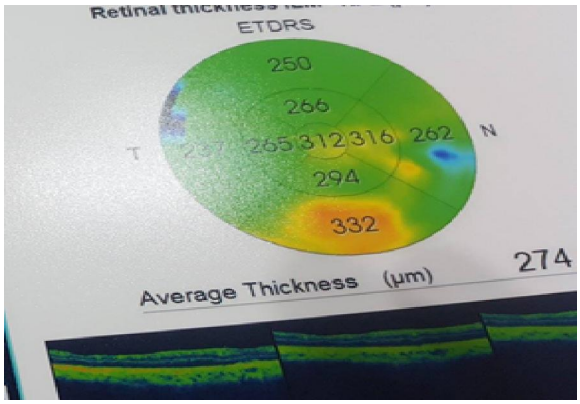


Fig (6): thickening more worse 312µ

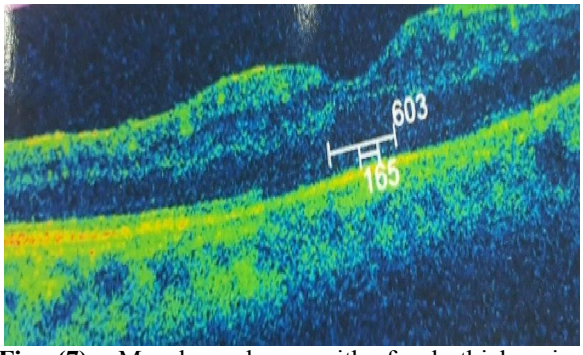


Fig (7): Macular edema with focal thicknening involving fovea ELM & IS/OS length is 603 micron & 165 respectively.

Otanietal., performed spectral-domain optical coherence tomography in all eyes. The authors defined central subfield thickness as the average retinal thickness of the 1-mm central scanned area. The length of disruption of the external limiting membrane and the inner and outer segments of the photoreceptors in the fovea (1.8 mm in diameter) were measured and graded according to their length as follows: 1) >1.4 mm; 2) >0.4 mm but <1.4 mm; or 3) <0.4 mm. Spectral-domain optical coherence tomography showed that the integrity of the external limiting membrane and inner and outer segments of the photoreceptors was more strongly correlated with best-corrected visual acuity when compared with central subfield thickness in diabetic macular edema. [13]

Preoperative visual acuity in logarithm of minimal angle of resolution was (decimal notation) 0.1 (6/60) (SD±0.0871) ranged from 0.005 to 0.500 with mean of 0.083 in all patients. Mean BCVA was 1.01(6/60 Snellen's equivalent) which improved after ILM peeling to 0.60 (6/24 Snellen's equivalent) ($P < 0.05$) corresponding to 4 line improvement, vision improved to 0.1 (SD± 0.098) to 0.3 (SD±0.10) at 4 weeks to 6 months post operatively. Mean postoperatively change in BCVA from base line was 0.0125(SD± 0.071) at 4 weeks and 0.043(SD±0.91) at 6 month (P0.003). It was also found that visual improvement at 3 months post-operatively was positive 0.6 ($P < 0.05$). Thomson et al 1986 defined six preoperative and three intra operative factors were found to be associated with an improved likely hood of attaining a final visual acuity of 5/200 or better. The preoperative factors were as follows: preoperative visual acuity of 6/60 or better, the absence of iris neovascularization, a clear crystalline lens or only a minimal cataract, minimal or no preoperative vitreous hemorrhage, PRP of at least one fourth of the retina, and the absence of severe retinal neovascularization. The intraoperative factors were as follows: the avoidance of performing a lensectomy, the absence of an iatrogenic retinal break, and the avoidance of using intraocular gas bubbles. [14] In current study; improvement in mean BCVA agreement with Stolba et al., [15]. Pendergast and associates series, 2000 the most common postoperative complication after vitrectomy was cataract formation, which occurred in 24 (63.2%) of the 38 phakic eyes. In our study, cataract occurred 15 out 40 eyes (37.5%) underwent cataract surgery with IOL implantation within 6 months of pars plana vitrectomy9 out of 15(60%) patients showed improvement. Phakic eyes with silicone oil internal tamponade (16 cases, 40%) [16]. The incidence of postoperative cataract formation in our study is comparable to the previous results of other researchers. Cataract extraction with IOL implantation was done during silicone oil removal at least four months after surgery. Glaucoma was described by many authors in varying percentages (from 1.7% to 8%) after vitrectomy. [17]

Transient increase in IOP was realized in 3 eyes (7.5%). Medical treatment in the form of IOP lowering drops was successful in managing those cases without need for glaucoma filtering surgery. In our study glaucoma did not affect the final visual outcome of our patients. The intraoperative and postoperative complications of the surgery in this study were few and did not affect the final visual outcome.

In conclusion, ILM peeling achieved higher anatomic success with a reduced need for additional surgical interventions and orevent postoperative ERM formation that might result in subsequent visual loss.

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Nil

Conflicts on interest

There are no conflicts of interest

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