

RESEARCH ARTICLE

Effects of Age, Peeled Membrane Type, Dye and Intraocular Tamponades on Final Visual Outcome in Cases with Idiopathic Epiretinal Membrane Surgery

İdiyopatik Epiretinal Membran Cerrahili Olgularda Yaşın, Soyulan Membran Tipinin, Boyanın ve Göz İçi Tamponadların Nihai Görsel Sonuca Etkileri

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ABSTRACT

Objective: To investigate the effects of age, peeled membrane type, dye type and intraocular tamponade type on the final best-corrected visual acuity (BCVA) in cases with idiopathic epiretinal membrane (ERM) surgery.

Material and Method: Twenty-two eyes of 22 idiopathic patients with ERM were included. Analyses were made according to age (≤ 65 years or >65 years), peeled membrane type (ERM or ERM+internal limiting membrane (ILM) peeling), membrane dye type (no dye or trypan blue) and tamponade type (sulphur hexafluoride (SF6), perfluoropropane (C3F8) or air).

Results: The number of patients aged ≤ 65 years was 7 (31.8%), while the number of patients aged >65 years was 15 (68.2%) ($p = 0.035$). Compared to preoperative period, there was a significant increase in BCVA in the postoperative period (0.24 ± 0.13 vs 0.37 ± 0.15 , $p < 0.001$). Trypan blue was used in 17 (77.3%) cases, whereas no dye was used in 5 (22.7%) cases ($p = 0.010$). Only ERM was peeled in 4 (18.2%) patients, while both ERM and ILM were peeled in 18 (81.8%) patients ($p < 0.001$). SF6 was used in 10 (45.4%) cases, C3F8 was applied in 6 (27.3%) cases, and air was used in 6 (27.3%) cases ($p = 0.594$). When comparisons of mean BCVA changes after surgery according to age ($p = 0.686$), peeled membrane type ($p = 0.131$), dye type ($p = 0.307$) and tamponade type ($p = 0.140$) were made, no significant difference was observed between the groups.

Conclusion: We found a significant visual improvement after surgery for idiopathic ERM. However, we detected no significant influence of the age, peeled membrane type, dye type and tamponade type on final visual outcome.

Keywords: Epiretinal Membrane, Internal Limiting Membrane, Intraocular Tamponade, Surgery, Trypan Blue.

ÖZET

Amaç: İdiyopatik epiretinal membran (ERM) cerrahili olgularda yaşın, soyulan membran tipinin, boya tipinin ve göz içi tamponad tipinin, nihai en iyi düzeltilmiş görme keskinliği (EİDGK) üzerine etkilerini araştırmak.

Gereç ve Yöntem: Çalışmaya 22 idiyopatik ERM hastasının 22 gözü dahil edildi. Yaşa (≤ 65 yaş veya >65 yaş), soyulan membran tipine (ERM veya ERM+iç limitan membran (İLM) soyulması], membran boya tipine (boyasız veya tripan mavisi) ve tamponad tipine [sülfür hekzaflorid (SF6), perfloropropan (C3F8) veya hava) göre analizler yapıldı.

Bulgular: Altmış beş yaş ve altı hasta sayısı 7 (%31,8) iken, 65 yaş üstü hasta sayısı 15 (%68,2) idi ($p = 0,035$). Ameliyat öncesi döneme kıyasla, ameliyat sonrası dönemde EİDGK de anlamlı bir artış vardı ($0,24 \pm 0,13$ vs

0,37±0,15, $p < 0,001$). On yedi (%77,3) olguda tripan mavisi kullanılırken, 5 (%22,7) olguda boya kullanılmadı ($p = 0,010$). Dört (%18,2) hastada sadece ERM soyulurken, 18 (%81,8) hastada hem ERM hem de İLM soyuldu ($p < 0,001$). On (%45,4) olguda SF6, 6 (%27,3) olguda C3F8 ve 6 (%27,3) olguda hava verildi ($p = 0,594$). Cerrahi sonrası ortalama EİDGK değişimlerinin karşılaştırması, yaşa ($p = 0,686$), soyulan membran tipine ($p = 0,131$), boya tipine ($p = 0,307$) ve tamponad tipine ($p = 0,140$) göre yapıldığında, gruplar arasında anlamlı bir fark gözlenmedi.

Sonuç: İdiyopatik ERM için yapılan ameliyat sonrası anlamlı bir görsel iyileşme olduğunu bulduk. Ancak yaşın, soyulan membran tipinin, boya tipinin ve tamponad tipinin nihai görsel sonuç üzerinde anlamlı bir etkisinin olmadığını belirledik.

Anahtar Sözcükler: Epiretinal Membran, İç Limitan Membran, Göz İçi Tamponad, Cerrahi, Tripan Mavisi.

Epiretinal membrane (ERM) is a translucent or semi-translucent fibrocellular proliferation that forms on the inner surface of the retina, mostly at the level of the macula (1). ERM is characterized by wrinkling or distortion of the macular surface caused by retinal cell migration and proliferation (2-4), and it has been associated with a variety of ocular diseases, such as diabetic retinopathy, retinal vein occlusion, retinal detachment and vitreoretinal inflammatory conditions (5, 6). Most cases, however, are termed idiopathic ERM, and they have no antecedent ocular pathology other than posterior vitreous detachment (PVD) or separation (4, 7). In these cases, the internal limiting membrane (ILM) disruption following PVD is thought to play an important role in ERM development (6). The evolution of ERM causes very few symptoms, but when it contracts, it can cause varying degrees of distortion, intraretinal edema and degeneration of the underlying retina, causing visual loss and metamorphopsia (4, 8).

Pars plana vitrectomy (PPV) and membrane peeling are usually indicated for symptomatic ERM (4). Complication rates have been decreased following the developments in vitreoretinal surgery methods, as well as better results (6, 9). In previous studies, visual acuity was used as an indicator for timing of surgical intervention and its outcomes (10-12). In this study, the main outcome measure was the mean best-corrected visual acuity (BCVA) change between baseline and postoperative fourth month. We aimed to evaluate the functional changes as well as surgical outcome in cases with idiopathic ERM by analysing the influence of the age, type of the peeled membrane, type of the membrane dye and type of the intraocular tamponade on the final visual outcome.

MATERIAL AND METHOD

This study was approved by the Izmir Katip Celebi Medical Research Ethical Committee (approval number: 254/27-12-2013), and it was conducted according to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients and/or their families. The charts of patients who were diagnosed with idiopathic ERM and who underwent ERM surgery at the Tepecik Training and

Research Hospital Ophthalmology Clinic and who were followed up regularly for at least four months after the surgery, were analysed retrospectively. Subjects who had previously undergone PPV surgery, the cases with a previous history of ocular trauma, the individuals with corneal pathology, glaucoma, uveitis or any retinal disease other than idiopathic ERM were not included in the study. Twenty-two eyes of 22 patients with idiopathic ERM were evaluated. Demographic data such as age and gender, medical history, preoperative and postoperative BCVA and intraocular pressure (IOP) levels, anterior segment and fundus findings, surgical techniques including the type of the peeled membrane, type of the membrane dye and type of the intraocular tamponade were recorded. BCVA was measured by using Snellen chart, while IOP was measured with a Goldmann applanation tonometry. Anterior segment structures were examined with a slit-lamp biomicroscope, and fundus structures were assessed by 78 and 90 D lens after pupil dilation. The existence of ERM and its relationship with the retinal surface and posterior hyaloid were evaluated by an optical coherence tomography (OCT) device (Heidelberg Spectralis; Heidelberg Engineering, Germany). Preoperative BCVA and IOP levels were compared with those at the fourth postoperative month. The increase in BCVA after the surgery was accepted as functional success. Evaluations were made according to the age groups (≤ 65 years or > 65 years), type of the peeled membrane (ERM peeling or ERM+ILM peeling), type of the membrane dye (no dye or trypan blue) and type of the intraocular tamponade [sulphur hexafluoride (SF6) gas or perfluoropropane (C3F8) gas or air]. In addition, the influences of the age, type of the peeled membrane, type of the membrane dye and type of the intraocular tamponade on the final visual outcome were analyzed.

In surgical treatment, standard three-port transconjunctival 23 gauge (G) PPV was made by the help of a vitrectomy device (DORC, Dutch Ophthalmic Research Center, Zuidland, Netherlands). Hand-held light source, pneumatic vitreus cutter (2500-6000 cuts per minute) and noncontact wide-angle imaging system (Eibos; Moeller-Wedel GmbH, Wedel, Germany) were used. After ERM peeling, ILM peeling was also performed in cases where a secondary membrane structure and ILM wrinkles

were observed on the retinal surface. In cases requiring staining for visualization of the boundaries and structure of membranes, trypan blue (Meran Medical Products, İstanbul, Türkiye) was used as a surgical dye. Peroperatively, air or one of these gases (SF6 or C3F8) in nonexpansive concentration (10%) was preferred as a tamponade. Topical antibiotic, steroid and cycloplegic agents were given after surgery.

The statistical analysis of the data was made with a 95% confidence interval in Statistical Package for the Social Sciences (SPSS 15.0; IBM, USA) software. Descriptive characteristics were given as mean±standard deviation (minimum-maximum) values. Categorical variables were shown as percentage. The assumption of the normality was evaluated by Kolmogorov-Smirnov test. Pearson's chi-square and Fisher's exact tests were employed for the comparison of categorical data between the groups. Mann Whitney U test was performed to compare two independent groups, while Kruskal Wallis test was used for the comparison of more than two independent groups. Wilcoxon signed rank test was employed to compare two dependent groups. $p < 0.05$ was accepted as statistically significant.

RESULTS

The mean age of the cases was 67.68 ± 8.45 (46-89) years. The number of patients aged ≤ 65 years was 7 (31.8%), while the number of patients aged > 65 years was 15 (68.2%) ($p = 0.035$). Fourteen (63.6%) of the individuals were male and 8 (36.4%) of them were female ($p = 0.046$). Compared with the preoperative period, there was a significant increase in BCVA in the postoperative period (0.24 ± 0.13 vs 0.37 ± 0.15 , $p < 0.001$). IOP in the postoperative period was similar to that in the preoperative period (12.32 ± 1.46 vs 12.27 ± 2.49 mmHg, $p = 0.848$). Comparisons of BCVA and IOP values before and after surgery were shown in table 1.

Table 1. Comparisons of BCVA and IOP values before and after surgery.

	Mean±standard deviation value	Min	Max	p*
Preoperative BCVA	0.24 ± 0.13	0.04	0.50	< 0.001
Postoperative BCVA	0.37 ± 0.15	0.10	0.60	
Preoperative IOP	12.27 ± 2.49	10	18	
Postoperative IOP	12.32 ± 1.46	10	15	

BCVA: Best-corrected visual acuity, IOP: Intraocular pressure, *Wilcoxon signed rank test, $p < 0.05$ statistically significant.

In surgery, trypan blue was used in 17 (77.3%) cases, whereas no dye was used in 5 (22.7%) cases ($p = 0.010$). Only ERM was peeled in 4 (18.2%) patients, while both ERM and ILM were peeled in 18 (81.8%) patients ($p < 0.001$). For intraocular tamponade, SF6 gas was given used in 10 (45.4%) cases, C3F8 gas was applied in 6 (27.3%) cases, and air was used in 6 (27.3%) cases ($p = 0.594$). Compared to the preoperative value, in postoperative period, an increase of ≤ 2 lines in BCVA was detected in 14 (63.6%) patients, while an increase of > 2 lines in BCVA was determined in 8 (36.4%) patients ($p = 0.046$). When the comparisons of the increases in BCVA (≤ 2 lines or > 2 lines) after surgery according to age groups ($p = 0.784$), type of the peeled membrane ($p = 0.117$), type of the membrane dye ($p = 0.613$) and type of the intraocular tamponade ($p = 0.109$) were made, no statistically significant difference was found between the groups (Table 2).

Table 2. Comparisons of the increases in BCVA (≤ 2 lines or > 2 lines) after surgery according to age groups, type of the peeled membrane, type of the membrane dye and type of the intraocular tamponade.

		Increases in BCVA (Scale)				p*
		≤ 2 lines		> 2 lines		
		n	%	n	%	
Age groups	≤65 years	5	35.7	2	25.0	0.784
	>65 years	9	64.3	6	75.0	
Peeled membrane	ERM	1	7.1	3	37.5	0.117
	ERM+ILM	13	92.9	5	62.5	
Membrane dye	No dye	4	28.6	1	12.5	0.613
	Trypan blue	10	71.4	7	87.5	
Intraocular tamponade	SF6	4	28.6	6	75.0	0.109
	C3F8	5	35.7	1	12.5	
	Air	5	35.7	1	12.5	

BCVA: Best-corrected visual acuity, n: Case number, ERM: Epiretinal membrane, ILM: Internal limiting membrane, SF6: Sulphur hexafluoride, C3F8: Perfluoropropane, *Fisher's exact test, $p < 0.05$ statistically significant.

Additionally, when the comparisons of mean BCVA changes after surgery according to age groups ($p = 0.686$), type of the peeled membrane ($p = 0.131$), type of the membrane dye ($p = 0.307$) and type of the intraocular tamponade ($p = 0.140$) were done, no statistically significant difference was observed between the groups (Table 3).

Table 3. Comparisons of mean BCVA changes after surgery according to age groups, type of the peeled membrane, type of the membrane dye and type of the intraocular tamponade.

		BCVA change		p	
		Mean±standard deviation	Min.	Max.	
Age groups	≤65 years	0.12±0.10	0	0.30	0.686*
	>65 years	0.14±0.14	-0.10	0.42	
Peeled membrane	ERM	0.24±0.15	0.06	0.40	0.131*
	ERM+ILM	0.11±0.11	-0.10	0.42	
Membrane dye	No dye	0.10±0.19	-0.10	0.40	0.307*
	Trypan blue	0.15±0.11	0	0.42	
	SF6	0.18±0.12	0	0.42	
Intraocular tamponade	C3F8	0.10±0.06	0	0.20	0.140**
	Air	0.09±0.17	-0.10	0.40	

BCVA: Best-corrected visual acuity, Min: Minimum value, Max: Maximum value, ERM: Epiretinal membrane, ILM: Internal limiting membrane, SF6: Sulphur hexafluoride, C3F8: Perfluoropropane, *Mann Whitney U test, **Kruskal Wallis test, p <0.05 statistically significant.

While a decrease in BCVA was noted in one (4.5%) case after surgery due to macular edema, no serious perioperative and postoperative complications were observed in other cases.

DISCUSSION

Idiopathic ERM may cause visual impairment and metamorphopsia over time (12). Decreased visual acuity is one of the main presenting symptoms of idiopathic ERM, and the reduction in visual acuity cannot be correlated with the degree of metamorphopsia (13). The reason for the reduction in BCVA due to ERM may be related to the scattering, light-filtering and distortion effects of the membrane, axoplasmic flow inhibition, intraretinal edema and/or the membrane's traction effect causing the separation between RPE and photoreceptor outer segments (12). Traditionally, when deciding on surgery, the severity of symptoms and their impact on visual function are assessed (12, 13). In many ERM studies, visual acuity was used as the sole measure of visual outcome (10-12). In a previous study, the improvement in BCVA after idiopathic ERM surgery was evaluated as functional success (11). In a study including 1131 patients, it was reported that preoperative median visual acuity was 0.25 and that there was a statistically significant increase in visual acuity level after primary ERM surgery (14). It was also stated that visual increase of approximately two Snellen lines was observed in 41.7% of the cases at postoperative period (14). Bouwens et al. (15) detected the visual improvement in 66% of the patients at the third month after idiopathic ERM surgery, while Dawson et al. (11) reported this rate as 69.6%. Our preoperative BCVA value was 0.24, and we determined statistically significant increase in visual acuity in the postoperative period. In our study, BCVA improved in 18 (81.8%) cases, decreased in 1 (4.5%) case and

remained same in 3 (13.7%) cases after surgery. We also found an increase of more than two Snellen lines in BCVA in 8 (36.4%) patients at postoperative period. Our visual results appear to be consistent with the literature.

The prevalence of idiopathic ERM can alter from 2% to 34% depending on some factors such as ethnicity and age (12). It was reported that the incidence and prevalence of idiopathic ERM increased with age (2, 16). In our study, the number of ERM patients aged >65 years was significantly higher than the number of ERM patients aged ≤65 years. However, we detected that mean BCVA changes after surgery in cases aged >65 years were similar to those in cases aged ≤65 years. The main purpose of the ERM surgery is to remove the membrane and release the retinal traction (4, 17, 18). ERM surgery was stated to reduce or eliminate the epiretinal, inner and outer retinal distortions, reconstruct the foveal region, and improve the macular architecture (19). Since it was thought that ILM could serve as a scaffold for the cellular proliferation, ERM/ILM double peel was recommended by some authors (4, 20, 21). In literature, it was reported that in many cases, peeling of the ILM occurred simultaneously with peeling of the ERM either en bloc peeling or spontaneously (12). In our study, the number of patients who underwent both ERM and ILM peeling was significantly higher than the number of patients applied only ERM peeling. Park et al. (22) and Bovey et al. (23) determined that combined peeling of ILM with ERM provided better visual results and lower recurrence rates than ERM removal alone. In contrast to these studies, Ahn et al. (24) showed that ERM peeling alone had better visual results at 1st month than the combined removal of ERM and ILM, but they found similar visual results at subsequent visits. The other studies reported that ILM peeling did not appear to improve the visual outcomes (12, 17, 20, 21, 25). Similarly, we detected that

mean BCVA changes after surgery in cases applied both ERM and ILM peeling were similar to those in cases applied only ERM peeling. Chromovitrectomy was defined as the usage of vital dyes for staining the transparent membranes, making them easier to visualize and remove during the vitreoretinal surgery (26). Thus, it can be easier to distinguish the ERM from retinal layers with the help of dyes (18). In our study, the number of patients in whom trypan blue was significantly higher than the number of patients with no dye. Dawson et al. (11) reported that the use of dye during idiopathic ERM surgery did not affect the visual improvement. Ozdek et al. (27) determined that the use of different stains in ERM surgery had no effect on visual outcome. Similarly, we found that visual acuity increases of the cases being used trypan blue were not difference from those of the cases with no dye. Based on the surgeon's decision, intraocular gas tamponade such as air, SF6 or C3F8 was used to fill vitreous cavity at the end of the vitreoretinal surgery (28-30). In literature, the use of different gases was recommended to prevent early postoperative ocular hypotony by providing the maximum leakproofing in self-sealing sclerotomies and to reduce the retinal folds (28, 29). In our study, in order to ensure rapid rehabilitation of the macular anatomy and to prevent ocular hypotony, intraocular gas tamponade (SF6, C3F8 or air) was used peroperatively in all cases. In our study, the numbers of patients given SF6, C3F8 or air were similar to each other. Leitritz et al. (28) and Leisser et al. (30) found that air tamponade usage in idiopathic ERM surgery did not make a significant difference in postoperative visual outcomes. Chabot et al. (29) detected that ERM peeling with air tamponade or SF6 tamponade had similar visual improvement after surgery. Ozdek et al. (27) showed that air or gas tamponade usage in ERM surgery did not affect the visual outcome. Similarly, we found that visual acuity increases in patients given SF6, C3F8 or air were not different from each other after surgery.

There were some limitations in our study. Data were collected retrospectively. It had relatively small case number and short follow-up period. Another limitation was the use of visual acuity as the sole measure of surgical success. Due to technical reasons and retrospective design, OCT data could not be accessed. Planning the future prospective studies with larger populations and longer follow-up periods, in which other parameters are used in addition to visual acuity, may provide more extensive data about the effects of the surgery for idiopathic ERM. In conclusion, we found that there was a significant visual improvement after surgery for idiopathic ERM. However, we detected no significant influence of the age, type of the peeled membrane, type of the membrane dye and type of the intraocular tamponade on final visual outcome.

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was conducted with approval of Izmir Katip Celebi Medical Research Ethical Committee (approval number: 254/27-12-2013), adhering to the ethical principles of the Declaration of Helsinki.

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