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Short Term Efficacy of Adjunctive Intravitreal Triamcinolone Acetonide Injection During Vitrectomy for Epiretinal Membrane Peeling

Epiretinal Membran Soyulması İçin Yapılan Vitrektomide Yardımcı İntravitreal Triamsinolon Asetonid Enjeksiyonunun Kısa Dönem Etkinliği

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ABSTRACT Objective: To report whether adjunctive intravitreal (IV) triamcinolone acetonide (TA) (2 mg/0.05 mL) injection provided better anatomical and functional outcomes in patients having undergone pars plana vitrectomy (PPV) for idiopathic epiretinal membrane (ERM) peeling. **Material and Methods:** A total of 27 eyes of 27 patients with idiopathic ERM were enrolled in and were divided into 2 groups based on having injection of 2 mg/0.05 ml IV TA at the end of the surgery as TA (-) and TA (+) group. ERM was stained with brilliant blue. Mean change in best-corrected visual acuity (BCVA), central macular thickness (CMT) and intraocular pressure (IOP) from baseline was evaluated at postoperative visits over 6-month follow-up. **Results:** The mean BCVA improved from 0.35±0.16 logMAR (range: 0.15-0.7) and 0.48±0.30 logMAR (range: 0.15-1.30) at baseline to 0.20±0.16 (range: 0.05-0.5) and 0.34±0.23 logMAR (range: 0.1-1) at postop 6-month in TA (+) group (p=0.020) and TA (-) group (p=0.014), respectively. There was no significant difference in mean BCVA and CMT change at any follow-up visits between the 2 groups (p>0.05 for all visits). IOP remained stable in both groups during follow-up. **Conclusion:** IV injection of TA did not seem to provide additional benefit for post-operative anatomical and functional outcomes.

Keywords: Vitrectomy; epiretinal membrane; adjunctive triamcinolone injection; intravitreal; triamcinolone acetonide

ÖZET Amaç: İdiyopatik epiretinal membran (ERM) soyulması amacıyla pars plana vitrektomi (PPV) uygulanan hastalarda yardımcı intravitreal (IV) triamsinolon asetonid (TA) (2 mg/0.05 mL) enjeksiyonunun daha iyi anatomik ve fonksiyonel sonuçlar sağlayıp sağlamadığını belirlemek. **Gereç ve Yöntemler:** İdiyopatik ERM tanısı alan 27 hastanın toplam 27 gözü dâhil edildi. Hastalar, ameliyat sonunda IV TA (2 mg/0,05) uygulanıp uygulanmamasına göre TA(-) ve TA(+) olarak 2 gruba ayrıldı. ERM boyanması için brilliant mavisi kullanıldı. Olguların en iyi düzeltilmiş görme keskinliği (EİDGK), santral makula kalınlığı (SMK) ve göz içi basıncı (GİB)ndaki ortalama değişim, 6 aylık takipleri süresince değerlendirildi. **Bulgular:** TA (+) grubunda preoperatif olarak, LogMAR eşeline göre 0,35±0,16 (aralık: 0,15-0,7) olan EİDGK postoperatif 6. ayda 0,20±0,16 (aralık: 0,05-0,5) idi (p=0,020). TA (-) grubunda ortalama EDGK preoperatif 0,48±0,30 (aralık: 0,15-1,30) iken postoperatif 6. ayda 0,34±0,23 (aralık: 0,1-1) idi (p=0,014). İki grup arasında takip vizitlerinde ortalama EİDGK ve SMK değişimi açısından anlamlı fark yoktu (tüm vizitler için p>0,05). Takipler sırasında GİB değerleri her 2 grupta da değişim göstermedi. **Sonuç:** IV TA enjeksiyonu ameliyat sonrası anatomik ve fonksiyonel sonuçlar için ek bir fayda sağlamıyor gibi gözükmektedir.

Anahtar Kelimeler: Vitrektomi; epiretinal membrane; yardımcı triamsinolon enjeksiyonu; intravitreal; triamsinolon asetonid

Epiretinal membrane (ERM) is a vitreoretinal disorder causing structural retinal changes including retinal distortion and macular edema (ME).[1,2] Although ERM is considered to progress slowly, the condition can cause severe metamorphopsia and decreased visual acuity that requires surgical intervention.[3-6]

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Triamcinolone acetonide (TA) with varying concentrations (1 mg-4 mg) have traditionally been used as treatment for ME related to retinovascular disease.[7]

Intravitreal (IV) triamcinolone acetonide (TA) stimulates the adenosine signaling in Muller cells and down-regulates vascular endothelial growth factor production. In this way, IV TA facilitates the absorption of fluid in the retina and helps to regress retinal edema.[8,9]

Despite removing of ERM over the retinal surface can release traction, vision improvement and restoration of foveal contour may be somewhat limited in some cases due to persistence of intraretinal cysts and disruption of outer retinal layer integrity.[10]

Persistent macular edema is a common causative factor of poor visual activity after pars plana vitrectomy (PPV) for ERM peeling.[11] The development of inflammatory reaction in the retina after PPV is considered as one of the causes of persistent macular edema.[11] Administration of TA after ERM removing contributes the anatomical and functional recovery and also reduces the postoperative swelling of the retina.[12,13]

In the study, we aim to report if administration of IV TA injection could provide better anatomical and functional outcomes when given as adjunctive therapy for patients undergoing idiopathic ERM peeling.

MATERIAL AND METHODS

The present study was started after approved by local ethics committee of Kocaeli University, (GOKAEK: 2020/99), Turkey and conducted in agreement with international agreements and the Declaration of Helsinki. The study includes patients who underwent 23-gauge PPV for ERM peeling at a tertiary referral center, Kocaeli University Faculty of Medicine, Department of Ophthalmology by the same experienced retinal surgeon (L.K.).

STUDY POPULATION

The patients who were scheduled to PPV for ERM peeling were randomly assigned as TA (+) group (comprising patients who received IV injection of TA at the conclusion of the surgery) and TA (-) group (patients who did not receive any injection of TA) in the day of surgery. The indication for the surgery was the decrease in mean best-corrected visual acuity (BCVA) with/without significant metamorphopsia. The exclusion criteria included as follows: Macular hole, previous vitrectomy, any other retinal pathology that may interfere outcomes.

OPHTHALMOLOGICAL EXAMINATION

All patients underwent a through ophthalmological examination including measurement of BCVA, intraocular pressure measurement (IOP), slit-lamp biomicroscopy, dilated fundus examination, spectral-domain optical coherence tomography (SD-OCT) (Spectralis HRA+OCT, Heidelberg, Germany) and fundus photography at all visits. The central macular thickness (CMT) was measured within the central 1 mm of fovea automatically using the software of the OCT device, attention was paid for the proper alignment of the retinal layer boundaries. Foveal contour was classified three groups on SD-OCT image: normal, flat and evaginated.

SURGICAL TECHNIQUE

Standard transconjunctival three-port PPV with ERM peeling was performed using 23-gauge instruments (OS-4 Oertli, Berneck, Switzerland) under local anesthesia. Posterior vitreous detachment was generated without any triamcinolone staining. ERM was peeled tangentially and circularly with the assistance of brilliant blue G (view ILM, Alcimihia, Italy) using end-gripping intraocular forceps. A large sheet of membrane was gently removed form the macular area. ERM and internal limiting membrane was removed from the macular area and fovea in all cases. No tamponade was used. At the end of the surgery, IV TA (2mg/ 0.05ml) (Kenalog, Bristol-Myer squibb, NJ, USA) injection was given in some patients based on the study protocol. Phakic patients underwent combined phacoemulsification and intraocular lens implantation.

STATISTICAL ANALYSIS

All statistical analyses were calculated using SPSS 22 (Chicago, US) software. The primary outcomes were the mean change in BCVA (preop value-postop value), CMT, and IOP at follow-up visits. BCVAs were evaluated as logarithm of the minimum angle

of (logMAR). Due to non-parametric nature of data, Mann-Whitney U test was used for comparison of continuous variables between the two groups. Chi-square or Fisher's exact test was performed to compare categorical variables of the two groups.

RESULTS

The study included 27 eyes of 27 patients; 14 eyes of 14 patients in TA (-) group and 13 eyes of 13 patients in TA (+) group. The mean age of the patients was 68.59±8.94 years (range: 40-87 years). The demographics of the patients in the 2 groups are specified in Table 1. There was no significant difference in patient including mean age, gender, and preoperative lens status between the 2 groups (p>0.05).

The mean CMT showed a significant decrease at all visits compared to baseline in TA (+) group (p=0.007 at 1st month, p=0.004 at 2nd month, p=0.001 at 3rd month, and p=0.001 at 6th month) and in TA (-) group (Table 2). (p=0.002 at 1st month, p=0.003 at 2nd month, p=0.001 at 3rd month, and p=0.001 at 6th month) (Table 2). However, there was no significant difference in mean CMT change at any visit between the 2 groups during 6 months follow-up (p=0.981 at 1st month, p=0.550 at 2nd month, p=0.280 at 3rd month, and p=0.430 at 6th month). The mean change in CMT in the 2 groups is given in Figure 1A. The SD-OCT characteristics of the patients are given in Table 3.

The mean baseline BCVA was 0.48±0.30 logMAR (Snellen equivalent, »20/60) (range: 0.15-1.30) in TA (-) group and 0.35±0.16 logMAR (Snellen equivalent, »20/44) (range: 0.15-0.7) in TA (+) group. There was no significant difference in mean BCVA at any follow-up visits between the 2 groups (Table 2). The mean change in BCVA was 0.08±0.17 logMAR at 1st month, -0.04±0.21 logMAR at 2nd month, -0.06±0.2 logMAR at 3rd month, and -0.15±0.19 logMAR at 6th month in TA (+) group and 0.06±0.17 logMAR, -0.08±0.21 logMAR, -0.12±0.24 logMAR, and -0.13±0.17 logMAR in TA (-) group, respectively (Figure 1B). There was no significant difference in mean BCVA change between the 2 groups at any follow-up visits (p=0.458 at postop 1st month, p=0.720 at postop 2nd month, p=0.350 at postop 3rd month, and p=0.981 at postop 6th month). At postoperative 6th

TABLE 1: Demographics of the study population.

	Group TA (-)	Group TA (+)
Number	14	13
Mean age±SD (range), years	68.53±7.17 (54-87)	68.53±10.65 (40-85)
Gender, male, n	11	9
Lens status, phakia, n	8	9

TA: Triamcinolone acetonide; SD: Standard deviation; n: number.

TABLE 2: Anatomical and functional data of the study population.

	Group TA (-)	Group TA (+)
BCVA, mean, logMAR (range)	0.48±0.30 (0.15-1.30)	0.35±0.16 (0.15-0.7)
Baseline	0.54±0.30 (0.3-1.3)	0.43±0.25 (0.15-0.8)
Month-1	0.39±0.27 (0.1-1.30)	0.30±0.19 (0.1-0.7)
Month-2	0.35±0.23 (0.1-1)	0.28±0.18 (0.1-0.7)
Month-3	0.34±0.23 (0.1-1)	0.20±0.16 (0.05-0.5)
Month-6		
CMT, mean, microns (range)		
Baseline	518.85±63.08 (435-656)	481.46±72.24 (401-618)
Month-1	443.78±57.96 (362-541)	426.30±40.53 (481-337)
Month-2	430.50±61.0 (351-545)	421.46±35.70 (464-352)
Month-3	415.92±50.39 (352-521)	409.84±38.98 (464-338)
Month-6	406.28±51.40 (336-487)	399±35.09 (455-330)
IOP, mean, mmHg, range		
Baseline	14.28±3.0	15.07±2.10
Month-1	14.14±1.16	14.61±0.96
Month-2	14.21±1.18	14.84±1.28
Month-3	15.35±1.27	14.76±1.73
Month-6	15.42±2.56	13.84±2.33

TA: Triamcinolone acetonide; BCVA: Best-corrected visual acvity; CMT: Central macular thickness; IOP: Intraocular pressure.

TABLE 3: SD-OCT characteristics of the study population.

	Group TA (-) n=14	Group TA (+) n=13
Foveal contour, n (%)	4 (28.57)	5 (38.46)
minimally elevated/flat elevated	10 (71.42)	8 (61.53)
Intraretinal cyst, present, n (%)	8 (57.14)	5 (38.46%)
Ectopic inner retinal layers, n (%)		
Stage 1-2	1 (7)	6 (46.15)
Stage 3	8 (57.14)	4 (30.76)
Stage 4	5 (35.71)	3 (23.07)

SD-OCT: Spectral domain-optical coherence tomography; TA: Triamcinolone acetonide; n: number.

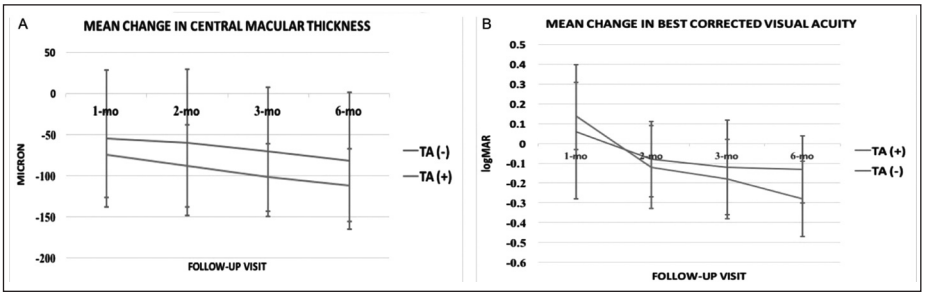

FIGURE 1A-1B: The mean change in CMT (A) and BCVA (B) over follow-up.

month, the mean BCVA showed an increase of 0.13 Snellen lines (6.5 letters) in TA (-) group and increase of 0.15 Snellen lines (7.5 letters) in TA (-) group.

Preoperative foveal contour irregularity and BCVA were observed to improve in postoperative visits in both groups (Figure 2A-2B-2C-2D, Figure 3A-3B-C-3D).

With regard to safety, there was no significant change in mean IOP change between the 2 groups at follow-up (p=0.488 at 1st month, p=720 at postop 2nd month, p=302 at postop 3rd month, and p=0.076 at postop 6th month). No complication occurred during perioperative and postoperative period.

DISCUSSION

In the study, we showed that 23-Gauge PPV with ERM peeling was an effective and safe method in eyes with symptomatic ERM. However, in idiopathic ERM eyes, injection of 2 mg/mL IV TA at the conclusion of the surgery did not yield superior functional and anatomical outcomes compared to those without peroperative injection of TA. Though eyes having had IV TA injection tended to have more decrease in macular thickness, the mean change in CMT between the 2 groups was not significant over 6 months follow-up.

Visual acuity may improve for longer than 1-year following ERM peeling, whereas major improvement in visual acuity usually occurs between 2-3 months after the surgery.[14] In the study, we observed statistically significant visual acuity improvement at 6-month follow-up in both groups

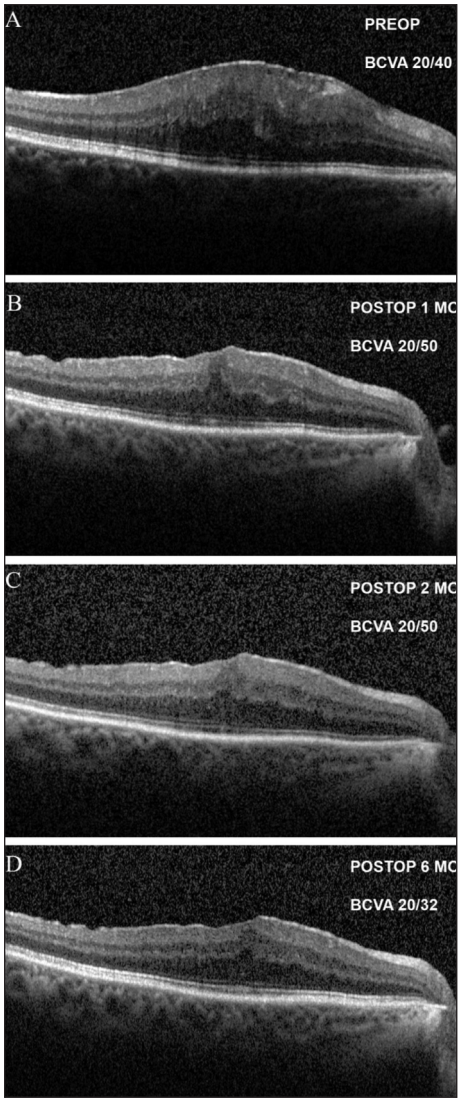

FIGURE 2: The panel shows the follow-up SD-OCT scans of a 62-year-old female patient who underwent PPV+ERM peeling combined with adjuvant IV injection of TA. Evaginated foveal contour with disorganization of inner retinal layer is appreciated at preoperative visit (Figure A). Foveal contour improved and BCVA increased from 20/40 to 20/32 following the surgery (B, C, D).

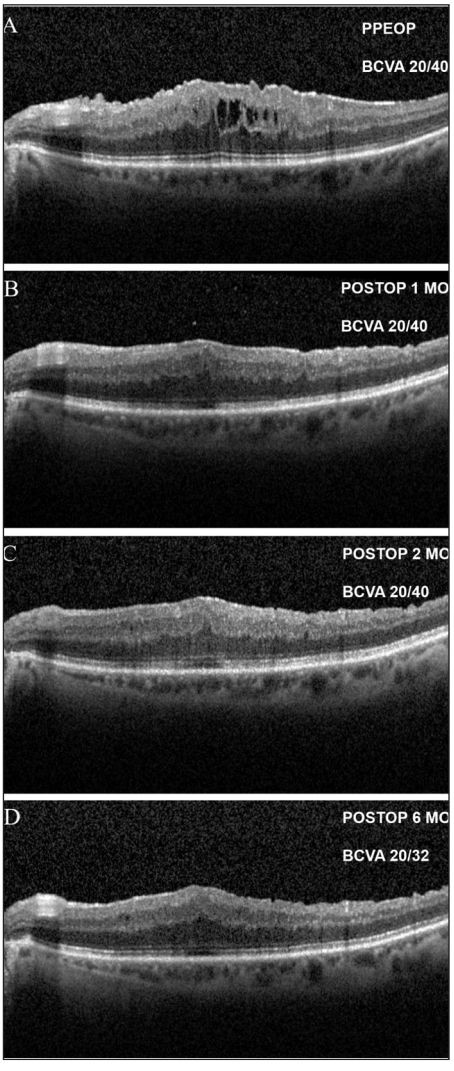

FIGURE 3: Figure shows the longitudinal SD-OCT images of a 65-year-old male patient having undergone PPV+ERM peeling without adjuvant IV injection of TA. Preoperative OCT scan reveals multiple intraretinal cysts, corrugated foveal contour with thickening of inner retinal layers. Improved foveal contour with resolution of intraretinal cyts are seen at postoperative visits (B, C, D). BCVA increased from 20/40 to 20/32 following the surgery.

(approximately a mean of 7 ETDRS letters) with prompt significant decrease in macular thickness. This finding supports that functional improvement was slower than anatomical restoration in ERM eyes.

Previous studies showed that preoperative visual acuity, the duration of the symptoms and macular thickness are the strongest predictors of vision improvement in eyes undergoing ERM peeling.[15,16] It has been stated that the stability of the outer retinal layers is associated with visual improvement though we did not evaluate SD-OCT parameters other than macular thickness, that was not case in our study.[17]

The safety profile of IV TA was being assessed by measuring the IOP at follow-up visits and we found that IOP remained stable during 6-months follow-up in the 2 groups. Formation of cataract could not be evaluated due to surgeon's preference of performing combined surgery in phakic eyes.

Our study has some strengths including standardized surgery technique performed by a single experienced retina surgeon and availability of high resolution SD-OCT scans for all follow-up visits. However, small number of patients, relatively short follow-up duration, lack of photoreceptor integrity evaluation are the limitations of the study. On the other hand, since there has been evidence that the half life and the duration of action of TA decreased in vitrectomized eyes, the dose of injected TA, 2 mg/0.05 mL, may be insufficient to provide anatomical and functional superiority. Though some studies suggested that even dose of 4 mg/mL IV TA injection failed to show superiority in visual and anatomical rehabilitation, vitrectomized eyes may even require higher dose of IV TA injection for better outcomes.[18,19]

CONCLUSION

In conclusion, PPV and ERM peeling introduced in significant development in visual acuity and restoration of foveal contour. However, additional use of 2 mg IV TA did not seem to affect postoperative outcomes.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Levent Karabaş;* ***Design:*** *Levent Karabaş;* ***Control/Supervision:*** *Levent Karabaş, Ecem Önder Tokuç;* ***Data Collection and/or Processing:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu, Levent Karabaş;* ***Analysis and/or Interpretation:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu, Levent Karabaş;* ***Literature Review:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu;* ***Writing the Article:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu, Levent Karabaş;* ***Critical Review:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu, Levent Karabaş;* ***References and Fundings:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu, Levent Karabaş;* ***Materials:*** *Ecem Önder Tokuç, İlkay Kılıç Müftüoğlu, Levent Karabaş.*

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