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Assessment of Clinical Response to Aflibercept Treatment in Cases with Pigment Epithelial Detachment Associated with Neovascular Age-Related Macular Degeneration, Case Series

Neovasküler Yaşa Bağlı Makula Dejenerasyonu ile İlişkili Pigment Epitel Dekolmanı Olan Olgularda Aflibersept Tedavisine Klinik Yanıtın Değerlendirilmesi, Olgu Serileri

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ABSTRACT Objective: To evaluate the clinical results of intravitreal aflibercept in patients with pigment epithelial detachment (PED) associated with neovascular age-related macular degeneration (nvAMD). **Material and Methods:** The study included 50 patients who were newly diagnosed with nvAMD and had not received treatment. Patients with PED-related nvAMD received three loading doses of intravitreal aflibercept. The patients were followed up with a pro re nata protocol at 16, 24, and 32 weeks. Age, gender, best corrected visual acuity (BCVA), PED type, and PED localisation were recorded. PED width, PED height, central macular thickness (CMT), and the presence of intraretinal fluid, and subretinal fluid were recorded at the time of application and at subsequent follow-up examinations. **Results:** There were statistically significant decreases both in CMT and PED height compared to baseline in all follow-up measurements ($p<0.001$, $p<0.001$, respectively). There was a statistically significant increase in BCVA compared to baseline only at 32 weeks ($p=0.044$). The types of PED were compared according to height and width values and a statistically significant decrease was observed in hollow type PED values at 16 and 32 weeks compared to solid type ($p=0.011$, $p=0.029$) and mixed type PED values ($p=0.031$, $p=0.038$). **Conclusion:** Intravitreal aflibercept treatment is effective in decreasing the height and width of PED and CMT anatomically and increasing the BCVA functionally. Furthermore, there was seen to be less improvement in solid and mixed PED types than in the hollow type.

Keywords: Pigment epithelial detachment; aflibercept; neovascular age related macula degeneration

ÖZET Amaç: Bu çalışmanın amacı, neovasküler yaşa bağlı makula dejenerasyonu [neovascular age-related macular degeneration (nvAMD)] ile ilişkili pigment epitel dekolmanı (PED) olan hastalarda intravitreal aflibersептin klinik sonuçlarını değerlendirmektir. **Gereç ve Yöntemler:** Çalışmaya yeni nvAMD tanısı almış ve tedavi almamış 50 hasta dâhil edildi. PED ile ilişkili nvAMD'si olan hastalara 3 yükleme dozu intravitreal aflibersept uygulandı. Hastalar 16, 24 ve 32. haftalarda pro re nata protokolü ile takip edildi. Yaş, cinsiyet, en iyi düzeltilmiş görme keskinliği [best corrected visual acuity (BCVA)], PED tipi ve PED lokalizasyonu kaydedildi. PED genişliği, PED yüksekliği, santral makula kalınlığı [central macular thickness (CMT)], intraretinal sıvı ve subretinal sıvı varlığı uygulama anında ve takip eden muayenelerde kaydedildi. **Bulgular:** Tüm takip ölçümlerinde başlangıca kıyasla hem CMT hem de PED yüksekliğinde istatistiksel olarak anlamlı düşüşler vardı (sırasıyla $p<0,001$, $p<0,001$). Sadece 32. haftada başlangıca kıyasla BCVA'da istatistiksel olarak anlamlı bir artış oldu ($p=0,044$). PED tipleri boy ve genişlik değerlerine göre karşılaştırıldığında hollow tip PED değerlerinde 16 ve 32. haftalarda solid tip ($p=0,011$, $p=0,029$) ve mikst tip PED değerlerine ($p=0,031$, $p=0,038$) göre istatistiksel olarak anlamlı azalma gözlendi. **Sonuç:** İntravitreal aflibersept tedavisi anatomik olarak PED ve CMT'nin yükseklik ve genişliğini azaltmada ve fonksiyonel olarak BCVA'yı artırmada etkilidir. Ayrıca solid ve mikst PED tiplerinde hollow tipe göre daha az iyileşme olduğu görülmüştür.

Anahtar Kelimeler: Pigment epitel dekolmanı; aflibersept; neovasküler yaşa bağlı makula dejenarasyonu

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Age-related macular degeneration (AMD) can manifest clinically as subretinal fluid (SRF), intraretinal fluid (IRF), and retinal pigment epithelial detachment (PED). Retinal PED can be categorized clinically and angiographically as serous, drusenoid, haemorrhagic, and fibrovascular.[1] Drusenoid PED generally shows the typical characteristics of non-neovascular AMD. Serous PED is separated from the Bruch membrane associated with fluid accumulation and is elevated.[2] Vascularised PED is related to choroid neovascularisation and there is haemorrhage and fibrovascular material accumulation below the sub-retinal pigment epithelium (sub-RPE).

Various treatment methods have previously been attempted for the treatment of PED, such as laser, photodynamic therapy, intraocular gas, and intravitreal triamcinolone.[3-5] In recent years, anti vascular endothelial growth factor (VEGF) agents such as bevacizumab, ranibizumab, and aflibercept have been tested as the primary treatment option for PED. Aflibercept, which is a new VEGF-A blocker, has been shown to be effective in the treatment of neovascular AMD.[6] Aflibercept has a broad area of effect by inhibiting the placental growth factor (PGF) in addition to VEGF-A. It has also been shown that the effect of aflibercept in decreasing the dimensions of PED could be effective in improving visual prognosis.[7,8]

This theoretical advantage of aflibercept has led to several studies that have investigated changing ranibizumab and bevacizumab treatment to aflibercept for PED lesions which are resistant and contain recurrent fluid. However, there are very few studies that have investigated the efficacy of aflibercept in naive PED lesions associated with untreated neovascular AMD. The aim of the current study was to examine the long-term visual and anatomic outcomes of aflibercept treatment in cases with AMD-related PED, and to evaluate the effects of this treatment on vision level and PED.

MATERIAL AND METHODS

This retrospective, non-comparative study was conducted in Department of Ophthalmology, Faculty of Medicine, Selçuk University, Konya, Türkiye. Approval for the study was granted by the Non-Interventional Research Ethics Committee of Selçuk University Faculty of Medicine (date: March 22, 2017; no: 2017/06). The study procedures were applied in compliance with the principles of the Helsinki Declaration.

From a screening of patient records, cases were identified of patients diagnosed for the first time with PED that had developed secondary to AMD and had not received any treatment elsewhere, between September 2015 and September 2018. The fundus fluorescein angiography (FFA) findings of the patients at the time of presentation were examined and the development of PED secondary to AMD was confirmed on FFA. The presence of PED was also determined on the optical coherence tomography (OCT) images at the time of presentation.

Patients were excluded from the study if they had received any intravitreal anti-VEGF treatment other than aflibercept, if they had been treated at another centre, if they had previously received aflibercept treatment but had terminated treatment before completion of the loading dose and were presenting again for treatment, if aetiologies other than AMD causing PED were determined on FFA and OCT images, if PED height was <200 microns, or if they had not attended at least 3 follow-up examinations after completing or not completing the loading dose. Patients with OCT and FFA findings specific to polypoidal choroidal vasculopathy were excluded (thumb-like polyp, tomographic notch in PED, double-layer sign et.).

Age, gender and information about comorbidities were recorded from the patient files. The diagnosis of AMD was made from the swept-source OCT (SS-OCT, Atlantis DRI-OCT, Topson, Japan) and FFA findings. The type of PED was also recorded from these findings. Initial visual acuity was measured from the Snellen chart and the best corrected visual acuity (BCVA) values obtained from the first follow-up examination onwards after the loading dose were recorded from the patient files. For statistical reasons, these visual acuity values were converted to minimum resolution angle unit logarithms

(logMAR). At the follow-up examinations, the presence of IRF and SRF was also evaluated.

The central macula thickness (CMT) of each patient was recorded from the SS-OCT device at baseline and at each follow-up examination after the loading dose. PED height and width were measured manually from the highest and widest points of the PED on the SS-OCT image at the time of presentation. These measurements were repeated before the second and third injections, and at every follow-up examination after completion of the loading dose. PED height was measured as the maximum vertical distance from the RPE base to the Bruch membrane. PED width was measured as the horizontal PED diameter between the starting points of the elevations at the localisation of the greatest PED height. For consistency, both measurements were taken on a single SS-OCT slice passing within the fovea. The PED was classified as solid, hollow or mixed type based on the reflectivity of material below the RPE on OCT scan. PEDs with a mostly hyporeflective signal beneath the detached RPE layer were described as having a hollow appearance. Solid PEDs had a predominantly hyperreflective signal beneath the detached RPE layer on OCT and mixed PEDs were a combination of solid and hollow PEDs. They had a heterogeneous appearance of both hyperreflectivity and hyporeflectivity beneath the lesions. Fibrovascular PEDs were classified as mixed type. In addition, we observed drusenoid PEDs as solid excrescences under the RPE that were incidentally noted in eyes with exudative AMD. Hollow, mixed and solid type PEDs samples are presented in Figure 1a, Figure 1b, Figure 1c.

It was recorded from the patient files whether an intravitreal injection had been applied to the patient at each of three follow-up examinations following the loading dose. A reduction in the indications for PED treatment was seen with the presence of subretinal or intraretinal haemorrhage in examination and/or subretinal or IRF on OCT. Treatment was applied in the form of pro re nata with 2 months of follow up after the loading dose. The criteria for repeated treatment were defined as the loss of ≥1 row BCVA on the Snellen chart and the presence of recurrent or persistent IRF and/or SRF on OCT.

STATISTICAL ANALYSIS

Data obtained in the study were encoded and transferred to a computer program and statistical analyses were performed using SPSS vn. 23.0 software (SPSS, Inc., Chicago, IL, USA). Nominal data were weighted and then analysed with appropriate chi-square tests. Ordinal data were assessed in respect of conformity to normal distribution, and were then analysed with parametric and non-parametric tests according to the results. Data of the follow-up examinations were evaluated first with a repeated measures analysis of variance (ANOVA) or Friedman test according to the parametric status. When significant differences were found between the measurements in the ANOVA test, the post hoc test was applied. From the Bonferroni test, significant differences were determined between all the paired combinations. Data determined as significant in the Friedman test were analysed in paired groups with the Wilcoxon signed rank test. In the analysis of PED differences according to types, the one-way ANOVA test was used. In the correlation analyses, Pearson correlation analysis was applied to parametric data and Spearman correlation analysis to non-parametric data. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

Evaluation was made of a total of 50 patients with a mean age of 70.24 years, comprising 33 males with a mean age of 70.3 years and 17 females with a mean age of 70.12 years. PED was classified as mixed type in 44% of the patients, hollow in 32% and solid in 24%. The demographic data and statistics details are shown in Table 1.

BCVA, CMT and PED height and width measurements were measured four times in total: before the loading dose and at follow-up examinations after the loading dose at 16, 24, and 32 weeks. In the overall statistical examination, the changes of these values were shown in Figure 2 and Table 2.

Also a strong correlation was determined between PED height and PED width ($p<0.001$, $r=0.694$). No correlations were found between PED height and width and BCVA and mean CMT values at any of the measurement times. A decrease of

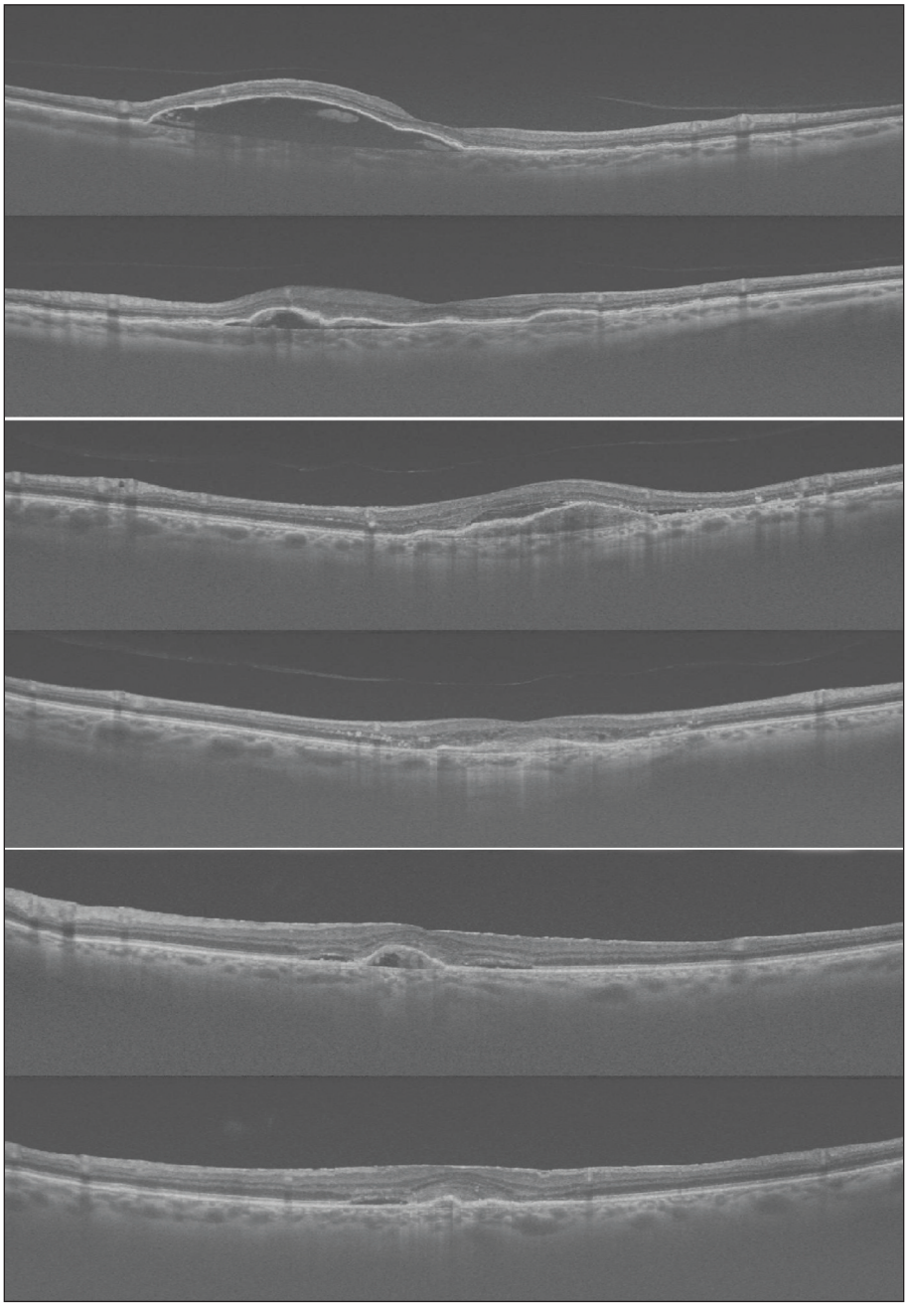

FIGURE 1: A: Pre- and post-treatment optical coherence tomography images of hollow pigment epithelial detachment. **B:** Pre- and post-treatment optical coherence tomography images of mixed pigment epithelial detachment. **C:** Pre- and post-treatment optical coherence tomography images solid pigment epithelial detachment.

141.54 µm in mean PED height was determined at 16 weeks and 149 µm at 32 weeks. In the PED width there was determined to be a decrease of mean 373 µm at 16 weeks and 344 µm at 32 weeks. In the CMT measurements, the decrease was determined to be mean 47 µm at 16 and 32 weeks. The mean BCVA value was seen to have increased from 0.53 logMAR to 0.42 logMAR in the 32nd week.

When the differences at 16 and 32 weeks according to PED types were calculated from microns, the most interesting change was that both the height and width values of the hollow type PED group showed a much greater decrease than in the other PED types. In the measurements taken at 16 weeks, there was a mean decrease of 273.2 µm in the hollow type PED group and the decreases in the mixed and

TABLE 1: Demographic datas.

		Gender			Age		
Variable	**Category**	**Female n (%)**	**Male n (%)**	**All n (%)**	**Minimum-maximum**	**$\bar{X}$**	**SD**
Type	Mixt	6 (35.3)	16 (48.5)	22 (44)	61-86	72.32	7.422
	Hollow	7 (41.2)	9 (27.3)	16 (32)	53-79	66.94	6.527
	Solid	4 (23.5)	8 (24.2)	12(24)	56-84	70.56	7.923
	All types	17 (100)	33 (100)	50 (100)	53-86	70.24	7.444
Eye	Right	6 (35.3)	13 (39.4)	19 (38)	53-86	69.74	9.188
	Left	11 (64.7)	20 (60.6)	31 (62)	56-84	70.55	6.292
	All eyes	17 (100)	33 (100)	50 (100)	53-86	70.24	7.444
Localisation	Foveal	10 (58.8)	23 (69.7)	33 (66)	53-86	71.45	7.583
	Juxtafoveal	5 (29.4)	6 (18.2)	11 (22)	62-74	68.18	4.285
	Extrafoveal	2 (11.8)	4 (12.1)	6 (12)	56-83	67.33	10.443
	All	17 (100)	33 (100)	50 (100)	53-86	70.24	7.444

SD: Standard deviation.

solid type PED groups were 81.14 µm and 56.78 µm, respectively. The decrease in the 16th week in the hollow PED group was determined to be statistically significantly greater than in the mixed and solid PED groups (p=0.031, p=0.011). In the measurements taken at 32 weeks, there was a mean decrease of 291.1 µm in the hollow type PED group and the decreases in the mixed and solid type PED groups were 68.9 µm and 59.8 µm, respectively. The decrease in the 32nd week in the hollow PED group was determined to be statistically significantly greater than in the mixed and solid PED groups (p=0.038, p=0.029).

After 32 weeks of follow-up, all patients received on average of 4.58 injections. The mean number of injections by PED types were 4.35, 5.08 and 3.67 in hollow, mixed and solid type PED, respectively (p=0.028). In the present study, no complications developed, including RPE tear.

DISCUSSION

The goal of this study was to evaluate the real-life anatomic and functional results of the response to intravitreal aflibercept treatment given to treatment-naive patients who developed PED secondary to AMD. The reason for not including treatment-naive AMD patients with chronic changes other than in the retinal layers was to be able to obtain better anatomic and functional responses than previous studies that changed the anti-VEGF drugs used. The present study results showed significant anatomic and functional recovery at the end of a 32-week follow-up period. To determine the specific aflibercept response, PEDs subdivided into 3 groups as hollow, solid and mixed types. Therefore, of the PED types determined according to the reflective properties on OCT, in the hollow type PEDs, which showed less reflectivity, a better response resulted from the application of aflibercept.

As a functional result of the current study, a statistically significant increase was obtained in BCVA from 0.53 logMAR at baseline to 0.42 logMAR in the 32nd week. This indicated an increase of ≥1 row on the Snellen chart. Some previous studies have reported no statistically significant gains in BCVA following the loading dose and at the end of the study period, while others have recorded not only no gain, but losses in BCVA.[7,9-13] However, similarly to the current study, there have been previous studies that obtained gains in BCVA.[14-17] Of these studies, Zinkernagel et al. reported a gain of 11 letters on the ETDRS chart at the end of one year of treatment of naive patients and Rouvas et al. obtained a significant increase at 3 months and 12 months compared to baseline in an aflibercept group.[17,18] In addition, Tyagi et al. reported that the greatest increase in BCVA was determined in hollow type PED.[12] Therefore, in the hollow PED group, a statistically significant increase was determined in all of the measurements compared

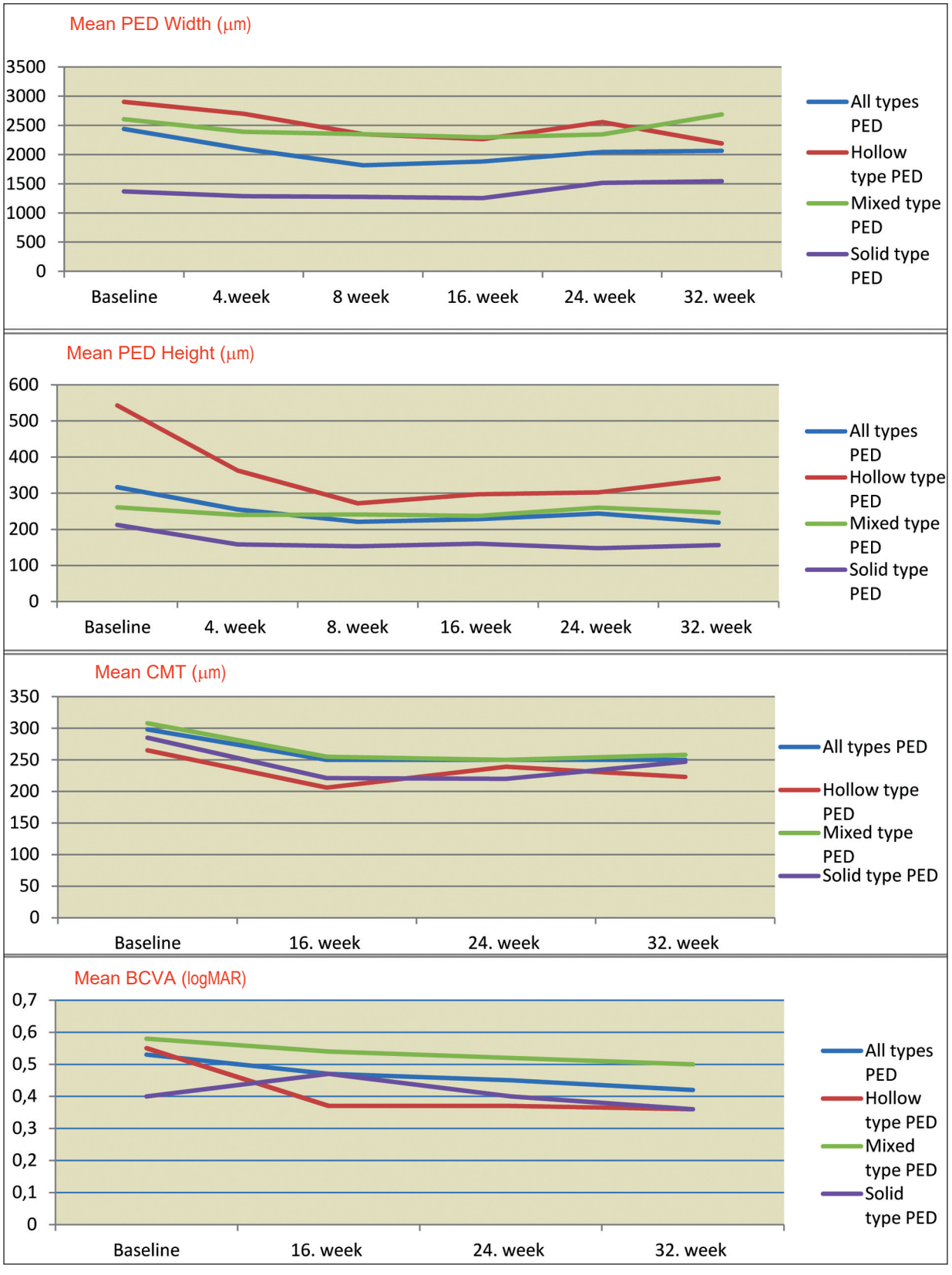

FIGURE 2: The vertical column in the graph shows the mean PED width, height, central macular thickness, and best corrected visual acuity. The horizontal column shows the weeks. PED types are also shown in color and show the change according to weeks.

CMT: Central macula thickness; BCVA: Best corrected visual acuity; PED: Pigment epithelial detachment; logMAR: Logarithms.

TABLE 2: CMT, BCVA, PED width ve height statistical values.

		Baseline	16. week	24. week	32. week		Baseline-16. week	Baseline-24. week	Baseline-32. week
CMT (µM)	All type PED	298 (±82)	250.88 (±61)	250.30 (±53)	250.96 (±57)	p value	0.000	0.000	0.000
	Mixt PED	308.7 (±67)	255.7 (±53)	250.6 (±55.0)	258.7 (±49)		0.013	0.000	0.001
	Hollow PED	299.9 (±107.78)	237.5 (±56.33)	246.8 (±53.76)	244.6 (±63.43)		0.030	0.058	0.049
	Solid PED	285.5 (±61)	221.0 (65)	235.9 (±56.42)	247.0 (±71)		0.110	0.086	0.953
BCVA (logMAR)	All type PED	0.53 (±0.26)	0.47 (±0.26)	0.45 (±0.30)	0.42 (±0.32)		0.210	0.110	0.044
	Mixt PED	0.58 (±0.25)	0.54 (±0.27)	0.52 (±0.31)	0.50 (±0.34)		0.570	0.522	0.270
	Hollow PED	0.55 (±0.27)	0.37 (±0.30)	0.37 (±0.33)	0.36 (±0.33)		0.034	0.040	0.040
	Solid PED	0.40 (±0.24)	0.47 (±0.027)	0.40 (±0.24)	0.36 (±0.025)		0.350	1.000	0.950
PED height (µm)	All type PED	317.5 (±209)	228.5 (±137)	244 (±165)	219.5 (±49)		0.000	0.000	0.000
	Mixt PED	321.6 (±112.3)	240.9 (±110.4)	258.6 (±91.4)	268.1 (±80.4)		0.003	0.003	0.001
	Hollow PED	543 (±215)	297.5 (±172)	336.8 (±214.76)	341.5 (±222)		0.001	0.003	0.003
	Solid PED	212.0 (±12)	160.0 (±46)	157.1 (±47.63)	156.0 (±46)		0.008	0.011	0.011
PED width (µm)	All type PED	2437.5 (±1087)	1882.5 (±1185)	2043.5 (±1175)	2064.5 (±140)		0.000	0.035	0.043
	Mixt PED	2604.1 (±775.9)	2297.3 (±859.7)	2343.5 (±883.2)	2685.3 (±854.9)		0.013	0.171	1.000
	Hollow PED	2903.3 (±1186.41)	2265.1 (±1409.05)	2557.7 (±1505.27	2190.0 (±1442.68)		0.048	1.000	0.195
	Solid PED	1369.0 (±661.07)	1256.0 (±723.54)	1515.0 (±665.34)	1544.0 (±648.68)		0.441	0.859	0.953

CMT: Central macula thickness; BCVA: Best corrected visual acuity; PED: Pigment epithelial detachment; logMAR: Logarithms.

to the baseline BCVA values and when the BCVA was compared between the PED types, no statistically significant difference was determined in the current study. In the current study, the most improvement in BCVA was in the hollow group, while the least improvement was in the solid group. That no statistically significant increase was obtained after the loading dose in the current study can be attributed to the majority of PED types with moderate and high reflectivity.

In the present study, at all three follow-up measurements CMT values statistically significantly decreased compared to the baseline. In the 16th week there was a decrease of 47.98 µm from baseline and in the 32nd week a decrease of 47.12 µm for all patients. In studies with various changes in drugs, decreases were determined in CMT ranging from 9 µm to 148 µm after changing to aflibercept and in studies where aflibercept was administered to treatment-naive patients, decreases of 43 µm to 148 µm were determined.[7,9,10,13,17,19] However, in some studies, no significant decrease has been obtained in CMT.[15] In the current study, while a statistically significant decrease was obtained in the hollow and mixed type PED groups compared to the baseline values, no statistically significant decrease was obtained in the solid PED group. In the current study, at the end of the 32nd week, the highest decrease in CMT was in the mixed type PED group and this decrease was 50 µm. Also, a previous study showed a more significant decrease in CMT in patients with serous PED than in those with fibrovascular PED.[17] As CMT values were compared between the PED types, no statistically significant difference was determined in the present study.

When the present studies were assessed in terms of PED height, it showed a statistically significant decrease in all of the measurements taken in the 32-week follow-up period compared to baseline. In the studies with various switch of anti-VEGF agents, statistically significant decreases have been reported of 37 µm to 122 µm.[7,10-14,16,18,20,21] Tran et al. reported a decrease of 28 µm in the 6th month of their study but no significant decrease was shown in the second year.[15] In the current study, 98 µm reduction was detected in all PED types at the end of the 32nd week. Broadhead et al. also reported a significant decrease compared to baseline in all PED types, and while Vaze et al. found a significant decrease in hollow and solid type, the decrease in mixed type PED was not found to be statistically significant.[16,20] In a study con-

ducted by Kocak, there was reported to be a 68% decrease in PED height in hollow type PED and a 38% decrease in solid and mixed type PED (p=0.0133).[14] Tyagi et al. reported that the greatest decrease in PED height in mixed type PED.[12] In the current study, at the end of the 32nd week, the highest decrease in PED height was hollow PED with 198 µm, while the least decrease was mixed type PED with 15 µm.

In the current study, there was a statistically significant decrease in all of the PED width measurement values compared to baseline and a statistically significant decrease compared to baseline was only obtained at 16 weeks in the hollow and mixed type PED groups, while no statistically significant decrease was obtained in any of the measurements of the solid PED group. In previous studies with various switches of anti-VEGF agents, statistically significant decreases have been reported of 88 µm to 512 µm.[7,13,14,20] Kocak reported a decrease of 25% in PED width in hollow type, and 18% in mixed and solid type (p=0.288).[14] Vaze et al. found a significant decrease in the serous and solid PED groups and not in the mixed type.[16] In the study by Broadhead et al., decreases in PED width and height were found to be statistically significant in hollow and mixed type PED as compared to solid type (p<0.05), but no significant difference was determined between the mixed type and hollow type PED groups.[20] de Massougnes et al. separated PEDs into 2 groups as serous and vascularized, and reported no statistically significant difference between the groups, while Dirani et al. reported that serous PEDs responded better to any intravitreal injection than vascularised PEDs.[10,21] Zinkernagel et al. reported to be a significant decrease in PED width in both fibrovascular and serous types after the loading dose (p=0.04, p=0.015, respectively).[17] Consistent with the results of the current study, Balaskas et al. reported that PEDs with less reflectivity had better responses to anti-VEGF treatment.[22] All these relationships can be said to be related to the mechanical potential of hollow PED, and the underlying neovascular complex in PEDs with high reflectivity can be said to present a barrier to reducing PED height. In addition to the neovascular membrane, PEDs with high reflectivity sometimes contain significant lipid and fibrous components. This explains the lesser response given to anti-VEGF treatment by solid or fibrous PEDs. As there is exudation in the composition of mixed type PEDs, they can be said to give a better response than solid types. In patients with larger vascularised PED, RPE tears occur more often because of high intraluminal pressure.[23] In the present study, no complications developed, including RPE tear.

In the light of all of this information, the significant anatomic and functional results of this study can be explained by several mechanisms. Aflibercept binds to the VEGF-A ligand with high affinity, resulting in a longer duration of effect. In addition, the binding of aflibercept to VEGF-B and PGF may also cause it to be more effective. PGF is produced during ischaemia, inflammation, and wound healing, and thereby stimulates VEGF production. PGF has also been determined in the process of choroidal neovascularisation. It is thought that if the roles of all the components of the VEGF family were sufficiently understood, it would show that different components have a role in different age related macular degeneration types. VEGF receptor 1 and 2 expression has been shown to be expressed differently in different pathological states.[24] Therefore, VEGF secretion has been found to be polarised towards the choriocapillaris. This polarised secretion has also been shown to be more evident under ischaemic conditions.[25] In a recent study of the retina of healthy monkeys, aflibercept and ranibizumab were shown to display different behaviours in the retinal tissue. The effects of ranibizumab were only determined in the intercellular area in ganglion cells, RPE cells, and internal and external retina cells.[26] Aflibercept causes hypertrophy and death of the pigment epithelial cells which more usually make stasis and haemolysis in the choriocapillaris.[26] Thus, death of the pigment epithelial cells that cause neovascular AMD and PED accelerates decompensation, impairs the pump function and flattens the PED by decreasing its dimensions.[10] It is known that the fluid under the RPE in hollow PED is caused by the ions and materials expressed by the RPE cells that are impaired by the thickened Bruch membrane. Furthermore, neovascular complexes are known to be formed below the RPE in vascularised PEDs. Therefore, because of the toxic effect to the

pump function in pigment epithelial cells, hollow PED will show a better response to aflibercept than vascularised PED. In addition, hollow PEDs have a higher mechanical potential for a response to aflibercept than PEDs with an underlying neovascular complex.[27]

Limitations of this study could be said to be the retrospective design, the lack of a control group, the low number of patients, and the short follow-up period. As in other previous studies, the PED height and width measurements were used in this study when evaluating PED. It is not possible to determine the actual volume of PED with the existing OCT software. In some studies, mathematical formulas have been used to calculate PED volume. However, these formulas have been applied to a certain morphology of the PED, but there are various PED morphologies, and the morphology of the PED changes with treatment. Therefore, such studies made on a single PED morphology can result in mathematical errors. Another disadvantage is that while some studies have made quantitative classifications using the pixel properties of the OCT software, a qualitative classification was made in the current study when determining the PED types. As indocyanine green angiography and optic coherence tomography-angiography were not available, whether or not the PED was related to polypoidal choroidal vasculopathy could not be absolutely discounted, which could be said to be another limitation of the study.

CONCLUSION

In conclusion, the results of this study of a 32-week follow-up period of intravitreal aflibercept treatment of PEDs which had developed secondary to AMD showed significant anatomic and functional outcomes. A strong aspect of the study was that the patients included were newly diagnosed and had not previously received any treatment. Aflibercept seems more effective in hollow PED than in solid PED and mixed PED. When selecting a drug in clinical applications, it can be kept in mind that PED types with less reflectivity respond better to treatment. The results of this study may serve to guide future prospective, more extensive studies.

Source of Finance

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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: *Raşit Dilek, Berker Bakbak;* ***Design:*** *Raşit Dilek, Berker Bakbak;* ***Control/Supervision:*** *Raşit Dilek, Berker Bakbak;* ***Data Collection and/or Processing:*** *Raşit Dilek, Berker Bakbak;* ***Analysis and/or Interpretation:*** *Raşit Dilek, Berker Bakbak;* ***Literature Review:*** *Raşit Dilek, Yalçın Karaküçük;* ***Writing the Article:*** *Raşit Dilek, Yalçın Karaküçük;* ***Critical Review:*** *Banu Turgut Öztürk, Şaban Gönül, Şansal Gedik, Süleyman Okudan.*

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